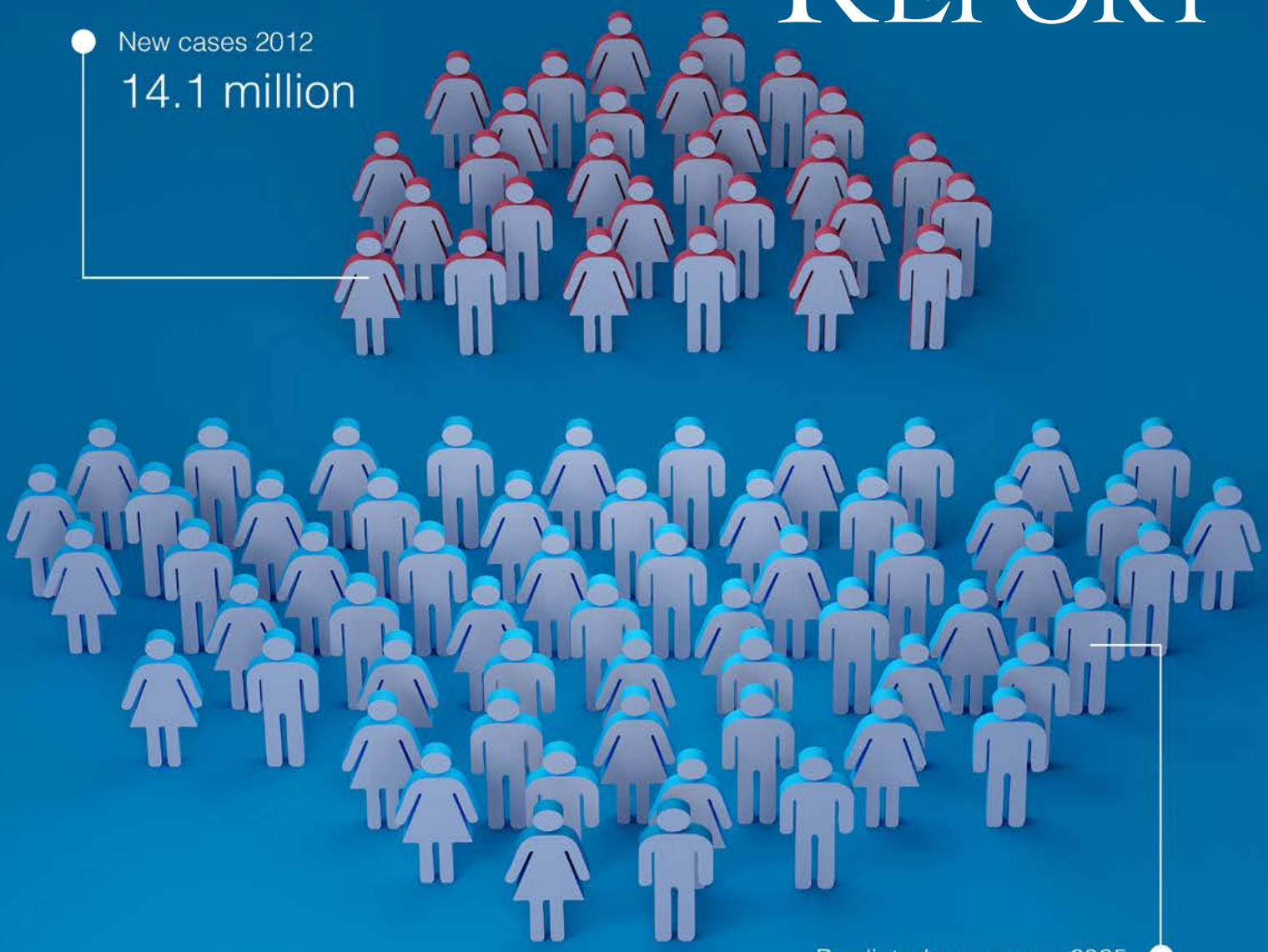
International Agency for Research on Cancer
World Health Organization

Biennial Report



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International Agency for Research on Cancer

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SC/54/2
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Biennial Report

2016–2017

International Agency for Research on Cancer

Lyon, France

2017

The cover depicts the growing global cancer burden. Each human figure represents 0.5 million persons. The estimated number of new cancer cases worldwide in 2012 (14.1 million) is based on data from GLOBOCAN 2012. The predicted number of new cases in 2035 (29.4 million) takes into account both population projections and changes in the incidence rates of the major cancers worldwide. © IARC/Morena Sarzo

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World Health Organization
PRESIDENCIA
CONFERENCIA MUNDIAL DE LA OMS SOBRE LAS ENT
Montevideo, Uruguay 18-20 de octubre de 2017

Introduction

By necessity, this Biennial Report presents just a selection of the research conducted by the International Agency for Research on Cancer (IARC) during the period 2016–2017. One of the most common questions about the Agency, when the number of its scientists or the size of its budget become known, is how it manages to achieve all it does with such limited resources. The answer is straightforward: the Agency does not work alone. True to its statute, it serves to promote international collaboration in cancer research. Consequently, what you read about here is a product of cooperation. Perhaps surprisingly in a field not unfamiliar with the drive for individual recognition, promoting cooperation rather than competition is like pushing at an open door.

Why do researchers around the globe agree to work with IARC? High scientific quality is certainly one element, as is relevance, with the research frequently responding to important questions faced at the local level. The neutrality that comes with being part of the World Health Organization (WHO) also undoubtedly helps, particularly when coordinating international networks or working on politically or socially sensitive topics. However, I am also convinced that the demonstration over the past 50 years of the values that the Agency adheres to has resulted in a foundation of trust, respect, and goodwill that enables cooperation. The values of IARC include courtesy, honesty, generosity, integrity, and independence – all easy to write down but demanding to display. What is remarkable to witness is how a commitment to these values is returned manifold by our colleagues around the world.

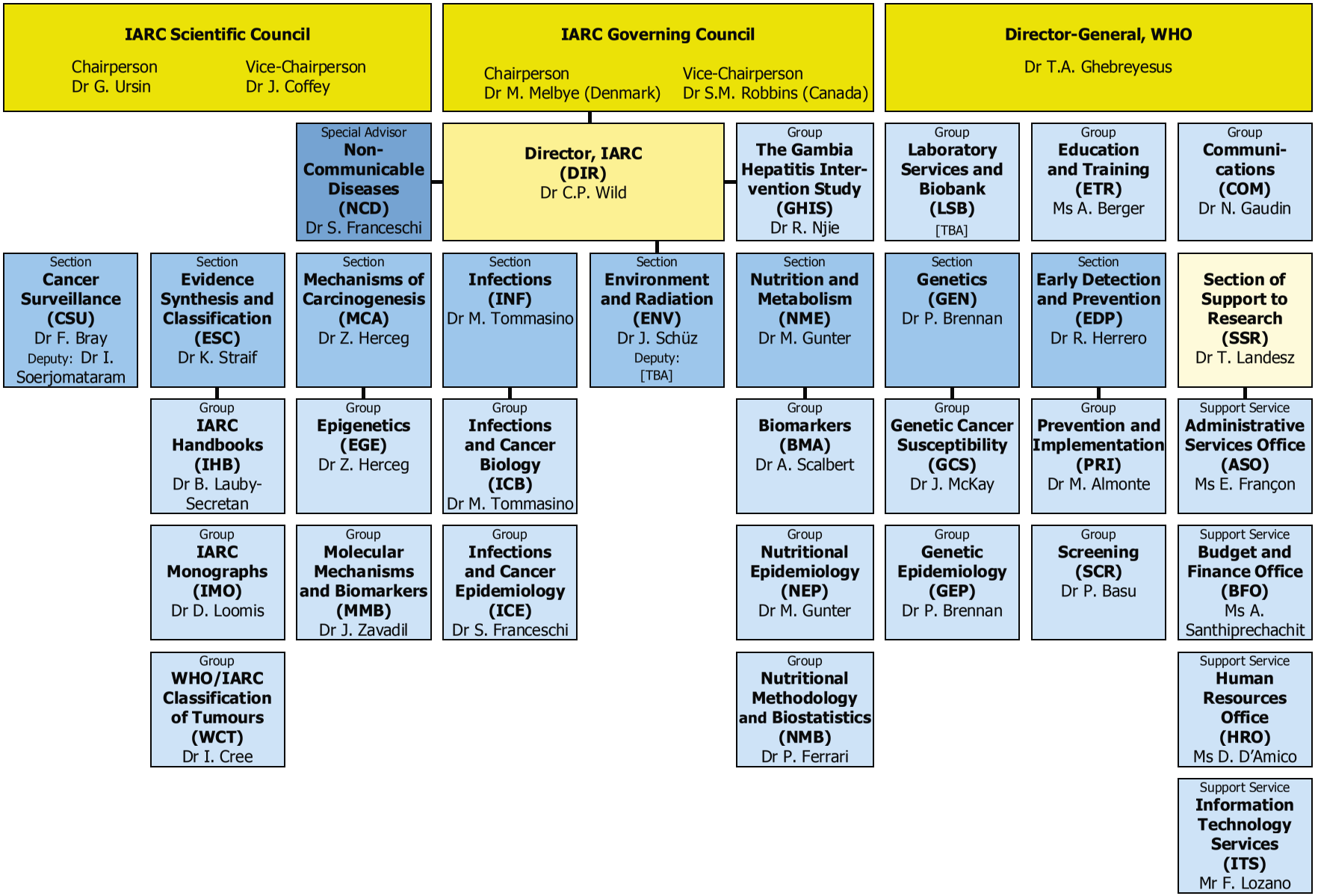
The cancer burden continues to rise globally. The increasing calls to move from *words* to *action* are well justified, but cancer control *actions* must be informed by scientific evidence, provided through research. Research is needed about the scale and patterns of cancer, and about its causes, prevention, early detection, and treatment. This research must be multidisciplinary; it should stretch from the submolecular to the suprapolitical, embracing everything from molecular pathways through to multisectoral policy interventions, in order to address the questions that are critical to saving lives. And research must not stop with the implementation of cancer control *actions*; research must accompany implementation, track it, evaluate it, and drive refinements where needed. Research is not an optional extra. Neither is it an esoteric exercise. Research must be an urgent, smart, and cool-headed yet passionate search for knowledge that enables informed policies to preserve and enhance human life.

When attending the WHO Global Conference on Noncommunicable Diseases (NCDs), hosted by the President of Uruguay in Montevideo in October 2017, I was struck by the political will that offers remarkable opportunities for tackling the growing burden of cancer and other NCDs on a global scale. In thinking about what IARC's response to this challenge should be, I was drawn to the words of former United Nations Secretary-General Dag Hammarskjöld, who wisely noted, "The 'great' commitment is so much easier than the ordinary everyday one." This Biennial Report relates the everyday efforts of IARC, accompanied by its many friends around the world, to provide cancer research for cancer prevention. In this light, it is a pleasure to commend the report to the reader in recognition of exceptional people, who achieve extraordinary things with remarkably little.

Dr Christopher Wild. © IARC/Roland Dray.

International Agency for Research on Cancer
World Health Organization

1 November 2017



IARC Medals of Honour

The IARC Medals of Honour are awarded to acknowledge and reward the work of scientists whose research has made an outstanding contribution to advancing our understanding of the biology or of the epidemiology of cancer.

On the occasion of the scientific conference "Global Cancer: Occurrence, Causes, and Avenues to Prevention", held in Lyon in June 2016 to celebrate the 50th anniversary of the establishment of IARC, the IARC Medals of Honour were awarded to Elizabeth Blackburn and Lynette Denny. Dr Blackburn presented a lecture on "Telomeres, biology, and cancer", and Dr Denny presented a lecture on "Screening and early detection of cervical cancer in Africa".

The Agency also invites outstanding speakers to present the IARC Cancer and Society Lecture to address the ways in which cancer research has a broad relevance for society, in a style that is accessible to all IARC personnel, both scientists and non-scientists. Ms Karin Holm (Patient Advocates for Cancer Research & Treatment) presented the fourth IARC Cancer and Society Lecture, on "Patient power for better research: I can, we can", on 3 February 2017, timed to mark World Cancer Day (4 February).

IARC Medals of Honour

Roger Sohier Lecture

1993 Gérard Orth (Institut Pasteur, Paris) – Papilloma virus and human cancer
1994 Guy Blaudin de Thé (Institut Pasteur, Paris) – Epidémiologie moléculaire des retrovirus oncogènes
1995 Richard Peto (Oxford University, United Kingdom) – Avoidance of premature death
1996 Dirk Bootsma (Erasmus University, Rotterdam, The Netherlands) – DNA repair: maintaining nature's perfection
1997 Luca Cavalli-Sforza (Stanford University, USA) – Gènes, peuples, langues, cultures
1998 Charles Weissmann (University of Zurich, Switzerland) – Biology and transmission of prion diseases
1999 Jan Pontén (Uppsala University, Sweden) – Sunlight and skin cancer: new insights
2000 Richard Klausner (National Cancer Institute, Bethesda, USA) – The war on cancer: where we are and where research is taking us
2001 Oliver Brüstle (Institut für Neuropathologie, University of Bonn, Germany) – Embryonic stem cells: basic concepts and therapeutic applications
2002 Jeffrey Koplan (Centers for Disease Control, Atlanta, USA) – Bioterrorism and public health preparedness
2003 Paul Kleihues (Director, IARC) – Poverty, affluence and the global burden of cancer
2004 Umberto Veronesi (European Institute of Oncology, Milan, Italy) – Breast cancer management and care: current results and future perspectives
2005 David Lane (University of Dundee, United Kingdom) – p53 and human cancer: the next 25 years
2006 Georg Klein (Karolinska Institutet, Sweden) – Viral contributions to tumorigenesis
2007 Mariano Barbacid (Centro Nacional de Investigaciones Oncológicas, Spain) – Ras genes, Ras oncogenes and cancer
2008 Jan Hoeijmakers (Rotterdam, The Netherlands) – Genome maintenance and the link with cancer and ageing

2009 Harald zur Hausen (German Cancer Research Center, Heidelberg) – The search for infectious agents in human cancers
2010 Gerald N. Wogan (Massachusetts Institute of Technology, Cambridge, USA) – Aflatoxins and human liver cancer
2011 Robert A. Smith (American Cancer Society, USA) – The challenge and potential of early detection to reduce the global burden of cancer
2012 John D. Potter (University of Washington, Seattle, USA and Massey University, Wellington, New Zealand) – Nutrition, environment, development, and cancer: casting a wider net
2013 Harold Varmus (National Cancer Institute, Maryland, USA) – Promoting the discovery and application of knowledge about cancer

Richard Doll Lecture

2004 Richard Doll (London, United Kingdom) – Fifty years follow-up of British doctors
2005 Brian MacMahon (Needham, Massachusetts, USA) – Epidemiology and the causes of breast cancer
2006 Joseph Fraumeni Jr (National Institutes of Health, USA) – Genes and the environment in cancer causation: an epidemiologic perspective
2007 Dimitrios Trichopoulos (Harvard School of Public Health, USA) – Breast cancer: epidemiology and etiology
2008 Sir Richard Peto (Oxford, United Kingdom) – Halving premature death
2009 Nubia Muñoz (National Cancer Institute of Colombia) – From etiology to prevention: the case of cervical cancer
2010 Julian Peto (London School of Hygiene & Tropical Medicine and the Institute of Cancer Research, United Kingdom) – Future cancer mortality due to past and continuing worldwide asbestos use
2011 You-Lin Qiao (Chinese Academy of Medical Sciences & Peking Union Medical College, China) – Implementation of cancer screening and prevention in China – evidence and reality
2012 Walter C. Willett (Harvard School of Public Health, USA) – Diet and cancer: a three-decade follow-up
2013 Pelayo Correa (Vanderbilt University Medical Center, Nashville, USA) – The gastric precancerous cascade

IARC Lecture

2005 Tadao Kakizoe (National Cancer Center, Tokyo, Japan) – Bladder cancer: a model of human cancer determined by environmental factors and genetics
2006 Ketayun Dinshaw (Tata Memorial Hospital, India) – Cancer treatment and control
2007 LaSalle D. Leffall on behalf of Ambassador Nancy G. Brinker (Komen Foundation, USA)
2008 Maurice Tubiana (Paris, France) – La prévention des cancers, de l'analyse scientifique des données à la prise en compte des facteurs psychosociologiques

IARC Cancer and Society Lecture

2012 David Michaels (Department of Labor and Occupational Safety and Health Administration, USA) – Research is necessary but not sufficient: challenges in preventing occupational and environmental cancer
2014 Michael G. Marmot (University College London, United Kingdom) – Fair society, healthy lives
2015 W. Philip T. James (London School of Hygiene & Tropical Medicine, United Kingdom) – Cancer prevention: the challenge of dietary change and obesity
2017 Karin Holm (Patient Advocates for Cancer Research & Treatment) – Patient power for better research: I can, we can

IARC 50th Anniversary Celebrations, 15 May 2015

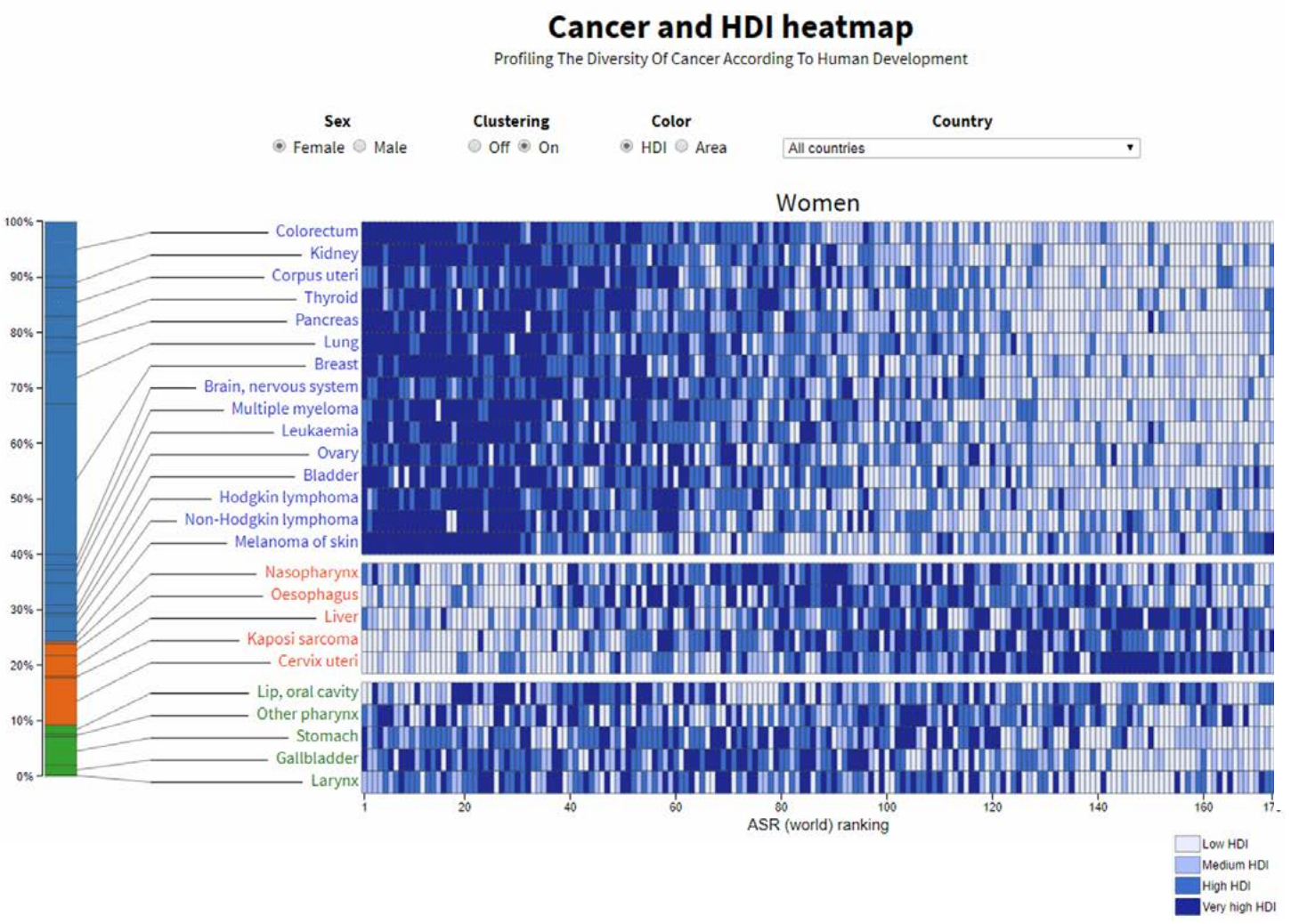
Her Royal Highness Princess Dina Mired of Jordan (King Hussein Cancer Center, Jordan) – Caring for cancer patients in developing countries

Her Royal Highness Princess Lalla Salma of Morocco (Fondation Lalla Salma, Morocco) – La lutte contre le cancer en Afrique du Nord

IARC 50th Anniversary Scientific Conference, 7–10 June 2016

Elizabeth Blackburn (Salk Institute for Biological Studies, USA) – Telomeres, biology, and cancer

Lynette Denny (Groote Schuur Hospital and the University of Cape Town, South Africa) – Screening and early detection of cervical cancer in Africa


Cancer and HDI heatmap
Profiling The Diversity Of Cancer According To Human Development
Sex
Female
Male
Clustering
Off
On
Color
HDI
Area
Country
All countries
Women
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Colorectum
Kidney
Corpus uteri
Thyroid
Pancreas
Lung
Breast
Brain, nervous system
Multiple myeloma
Leukaemia
Ovary
Bladder
Hodgkin lymphoma
Non-Hodgkin lymphoma
Melanoma of skin
Nasopharynx
Oesophagus
Liver
Kaposi sarcoma
Cervix uteri
Lip, oral cavity
Other pharynx
Stomach
Gallbladder
Larynx
1
20
40
60
80
100
120
140
160
ASR (world) ranking
Low HDI
Medium HDI
High HDI
Very high HDI

Section of Cancer Surveillance (CSU)

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Deputy section head
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Dr Claire Marant Micallef
Dr Adalberto Miranda-Filho
Dr Robin Ohannessian
(until May 2016)
Dr Sophie Pilleron
Dr Kevin Shield
(until June 2017)

The global number of new cancer cases per year is predicted to double during the next two decades, to 29.4 million by 2035. During the course of this century, cancer will become the leading cause of death worldwide and the single most important barrier to further gains in life expectancy. There is a growing disparity in the cancer burden, with the greatest increases in incidence projected to occur in many lower-resource countries that are undergoing major social and economic transitions. This is matched by an equivalent inequity in the availability of reliable surveillance data to inform cancer control programmes. From a global perspective, currently only one in three countries have high-quality population-based cancer registries (PBCRs) to disseminate cancer incidence and survival statistics, and only one in five countries can report medium- or high-quality national mortality data to the World Health Organization (WHO).

It is in this rapidly evolving landscape that the Section of Cancer Surveillance (CSU) operates. CSU is responsible for the systematic and ongoing collection, analysis, interpretation, and dissemination of global cancer data and statistics for cancer control action. The 2016–2017 biennium has provided unprecedented opportunities to further develop a comprehensive and truly global programme via collaborations with multidisciplinary partners. Highlights from three highly complementary core areas of activity are described here.

Cancer registry support and collaboration

CSU's long-standing collaborative relationships with PBCRs worldwide — members of the International Association of Cancer Registries (IACR; http://www.iacr.com.fr) — remain vital to improving the quality and use of registry data. CSU provides the secretariat and, among its functions, co-develops the annual international meeting of the IACR; the 38th annual meeting was held in Marrakesh in 2016, and the 39th was

held in Utrecht in 2017. There have been efforts to fully align the activities of the IACR, as the professional society of registries worldwide, with those of the IARC-led Global Initiative for Cancer Registry Development (GICR; http://gicr.iarc.fr).

The GICR is a partnership of international and national agencies committed to working collaboratively to increase the quality and availability of cancer incidence data in low- and middle-income countries (LMICs). Local reference centres – IARC Regional Hubs – assist in the planning and development of PBCRs through targeted support, training, advocacy, and networking. The Hubs are now operational across defined regions of Africa, the Americas, and Asia that comprise 85% of the world's population and more than 150 countries. The sixth Hub is being established in the Pacific Islands, after a financial contribution from the Australian Government.

The GICR is expanding its strategic goals of global coordination, regional support, and country leadership to increase Hub capacity and accelerate delivery of targeted actions. The knowledge has enabled the selection of GICR Partner Countries – a designation of sufficient evidence of commitment to a joint action plan to increase the availability, quality, and use of cancer data. Signed agreements with IARC are used to formalize the collaboration and to monitor progress. To strengthen support to countries, Hubs have been identifying organizations that can provide assistance. This has resulted in three new IARC–GICR Collaborating Centres for the Mumbai Hub region, each focused on a set of complementary activities: the National Cancer Institute of Thailand, the National Cancer Center Japan, and the National Cancer Center in China. In 2016–2017, site visits to 19 countries were conducted by experts to assess opportunities to improve the level of cancer registration; 19 GICR-led or GICR-affiliated courses were delivered, and 23 new agreements were signed, and others are in development (Table 1; Figure 1).

Figure 1. Participants in the International Atomic Energy Agency (IAEA)–WHO–African Cancer Registry Network (AFCRN)–IARC course held in Accra, Ghana, in December 2016, as part of the work of the Global Initiative for Cancer Registry Development (GICR). © IARC/ Freddie Bray.

Table 1. Global Initiative for Cancer Registry Development (GICR)-affiliated activities in 2016–2017, by region: site visits conducted, courses delivered, and formal agreements signed

Region[a]	Site visits[b] [total: 19]	Courses [total: 19]	Agreements [total: 23]
Africa	Burundi; Sierra Leone; Swaziland [3]	Libreville, Gabon (March 2017); Accra, Ghana (December 2016); Eldoret, Kenya (February 2017 and March 2017); Marrakesh, Morocco (October 2016) [5]	Benin; Côte d'Ivoire; Ethiopia; Kenya; Malawi; Mali; Mozambique; Seychelles; Uganda; United Republic of Tanzania; Zimbabwe [11]
Asia	Afghanistan; Azerbaijan; China; Iraq; Japan; Kazakhstan; Republic of Korea; Libya; Sri Lanka; Turkmenistan; Viet Nam [11]	Mumbai, India (November 2016); Yogyakarta, Indonesia (May 2016); Erbil, Iraq (April 2016); Almaty, Kazakhstan (April 2016); Bishkek, Kyrgyzstan (November, 2016); Kuala Lumpur, Malaysia (March 2016); Yangon, Myanmar (June 2017); Moscow, Russian Federation (September 2017); Obninsk, Russian Federation (September 2016); Colombo, Sri Lanka (March 2017); Izmir, Turkey (September 2016) [11]	Bhutan; China; Cyprus; Japan; Jordan; Malaysia; Myanmar; Thailand; Turkey [9]
Caribbean	Bahamas; Barbados [2]	Providenciales, Turks and Caicos (June 2016); Washington DC, USA (November 2016) [2]	Trinidad and Tobago [1]
Latin America	Belize; Brazil [2]	Quito, Ecuador [1]	Panama; Paraguay [2]
Pacific Islands	Fiji [1]	—	—

[a] Classified into continents according to IARC Hub involvement.

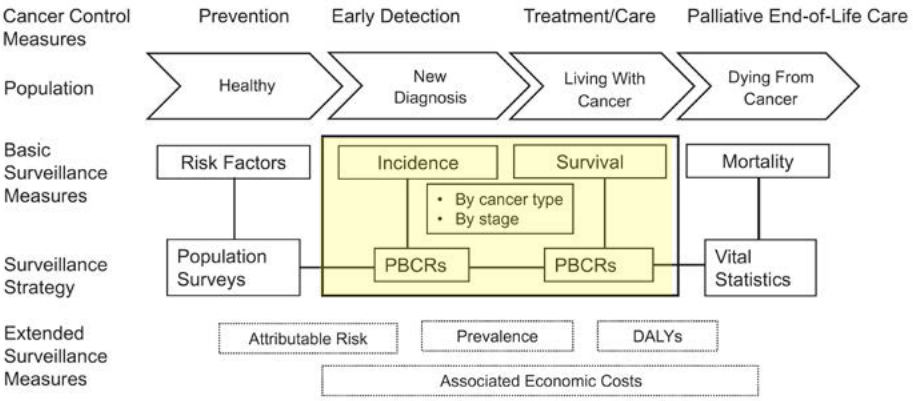
[b] Designates initial country visits only, as of 1 January 2012.

To meet the growing demand for technical training, the GICR has widened the use of local experts and technology through its Knowledge Transfer and Training programme. The GICR*Net* uses a "train the trainer" model to form a network of experts to serve as a resource to registry staff in each Hub region. Masterclasses on CanReg5 and coding and staging practices were held at IARC in 2016 and 2017, respectively, and 30 GICR*Net* experts were trained.

Many of the activities are jointly developed with the IACR. They include: enhancement and training in the use of CanReg5, IARC's open-source tool to support collection of cancer registry data; the production of "Essential TNM", a simplified version of the tumour–node–metastasis (TNM) staging system, to help registrars to code stage using available clinical information; and the development of a much-expanded and updated third edition of the definitive textbook for registries, *Cancer Registration: Principles and Methods*, which is scheduled for publication in 2018.

To advocate the centrality of PBCRs in cancer control and support their integration into surveillance systems for noncommunicable diseases (NCDs), a position paper clarified similarities and differences between surveillance systems for communicable diseases and NCDs, and proposed an expanded framework for cancer surveillance (Figure 2) (Piñeros et al., 2017b).

Figure 2. Measures and strategies for cancer surveillance at the population level. DALYs, disability-adjusted life-years; PBCRs, population-based cancer registries. Figure reprinted from Piñeros et al. (2017b).

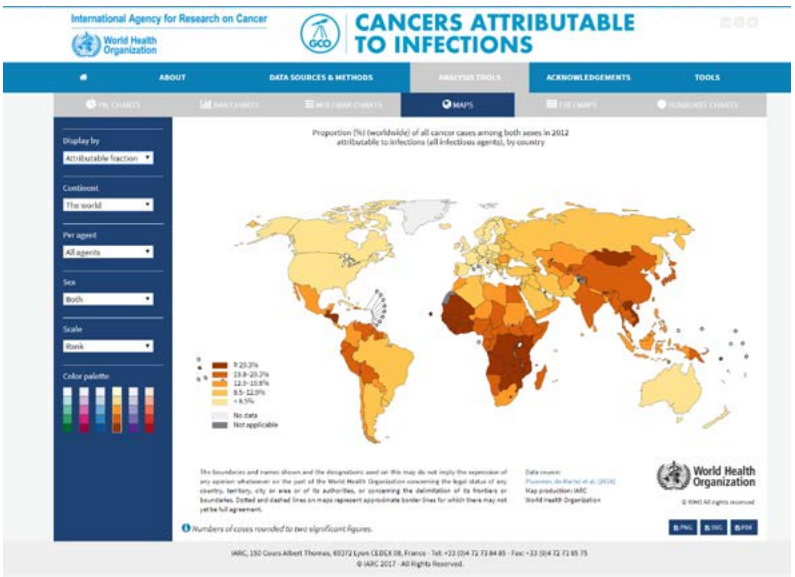


Global cancer indicators

The guiding principle in developing global estimates in CSU remains to validate estimates against local recorded data of high quality where they are available, and where such data are not available, to pursue in-country investments in cancer registration through the GICR, where feasible. The Global Cancer Observatory (GCO) was launched in 2016 to showcase an expanding range of indicators developed through CSU flagship projects, and increasingly via specific research studies. The GCO, which makes use of data-driven technology, has four subsites (Figure 3).

The GLOBOCAN database, built on the data from cancer registries worldwide, permits cancer statistics to be available at the national level through the GCO's Cancer Today subsite. A validation study comparing GLOBOCAN estimates with high-quality recorded national incidence data in Norway emphasized the utility of trends-based estimation approaches and population-based data to accurately estimate incidence (Antoni et al., 2016).

Figure 3. Screenshots of (left) the four subsites of the Global Cancer Observatory (GCO; http://gco.iarc.fr); (right) a global map from the GCO's Cancer Causes subsite showing the proportion of cancers attributable to infections in 2012. © IARC.

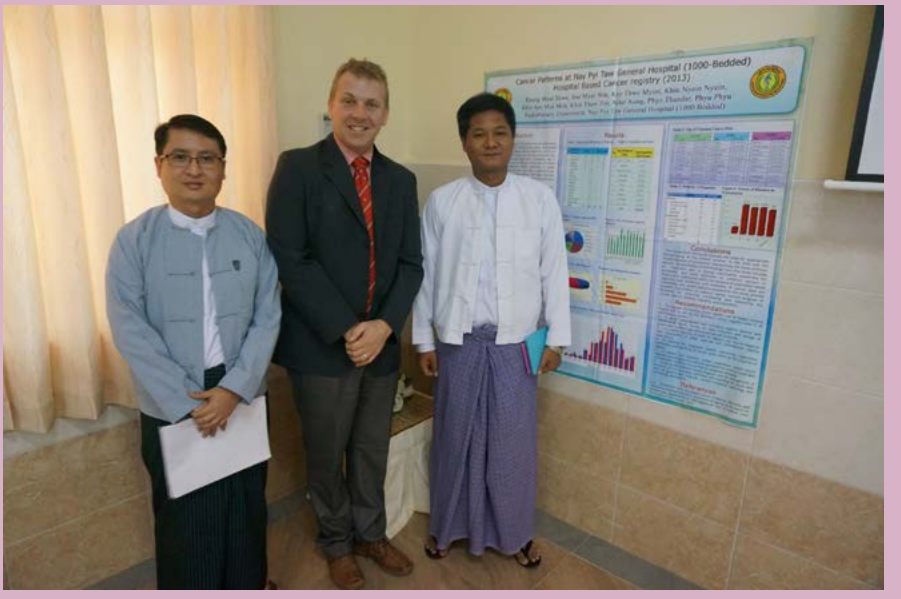


Developing registry capacity in Myanmar

Case study of capacity-building through the Global Initiative for Cancer Registry Development (GICR): Myanmar

GICR phases	Key activities by year	IARC partners[a]
1 COUNTRY ASSESSMENT ■ Review cancer and vital registries to determine opportunities ■ Identify local leaders	**2014** ■ Discussions with local contacts on needs – leading to a course on basic cancer registration in Yangon ■ Installation and customization of IARC CanReg5 software ■ Agreement with the Ministry of Health and Sports (MoH) to launch pilot cancer registry, Nay Pyi Taw General Hospital	■ Myanmar MoH ■ IARC Mumbai Hub ■ National Cancer Institute, Thailand ■ International Association of Cancer Registries
2 SITE VISIT ■ Establish the basis for an implementation plan ■ Meet with stakeholders to provide recommendations	**2015** ■ ImPACT Mission to review cancer control services in Mandalay, Nay Pyi Taw, and Yangon ■ Debriefing with senior MoH staff to refine recommendations	■ International Atomic Energy Agency ■ World Health Organization ■ United Nations Interagency Task Force
3 DIRECTED SUPPORT ■ Establish the IARC Hub as the first point of contact ■ Coordinate opportunities with other partners for efficiency ■ Promote accountability via a signed agreement and the use of a monitoring framework	**2016** ■ Engagement with surveillance leaders to establish a plan for PBCR, Myanmar Cancer Control Leadership Forum ■ Elaboration of cancer registry plan, including costing and milestones at the National Cancer Control Programme Meeting ■ Nay Pyi Taw PBCR staff selected as IARC “50 for 50” Programme **2017** ■ IARC–MoH Collaborative Research Agreement finalized ■ Delivery of a national training course ■ Revisions to CanReg5 to include new fields and local language ■ Nay Pyi Taw PBCR staff training at IARC Summer School	■ National Cancer Institute, USA ■ National Cancer Center Japan
4 GENERATE EVIDENCE ■ Implement quality improvement methods ■ Publish data from the cancer registry ■ Communicate results for cancer control action	**2018 (PLANNED)** ■ Mentorship exchange with GICR–IARC Collaborating Centres ■ Initial data quality review of Nay Pyi Taw PBCR ■ Networked version of CanReg5 system to other centres – Mandalay, Yangon, and Taunggyi ■ Assessment of feasibility for the implementation of PBCRs in other regions of the country	■ Union for International Cancer Control

PBCR, population-based cancer registry.
[a] Listed in chronological order by involvement.



Mr Les Mery with Dr Kaung Myat Shwe and Dr Soe Myat, supporting the development of a cancer registry in Nay Pyi Taw, Myanmar. Courtesy of Kaung Myat Shwe.

New estimates are being developed for release in early 2018 based on *Cancer Incidence in Five Continents*, Volume XI (CI5-XI) alongside survival data from SURVCAN-3 (see below). GLOBOCAN 2018 will have an increased granularity of data available, with estimates for 35 cancer entities, and will include uncertainty intervals that take into account the quality of the source information.

Publication of the electronic version of CI5-XI was timed to coincide with the 39th IACR annual meeting, in October 2017. Key challenges in the compilation of CI5-XI were the ever-expanding number of data sets received, as well as legal issues of confidentiality affecting registries' ability to submit their data. An abridged CI5-XI will be disseminated in early 2018, and further development of the GCO's Cancer Over Time subsite will refocus attention on the enormous value of the underlying data in descriptive epidemiological research.

There has been an expansion of the range of indicators available. The estimation of population attributable fractions (PAF) has become a key tool in assessing the potential for prevention. Interactive tools for visualizing the global cancer incidence attributable to obesity and infections in 2012 were launched on the GCO's Cancer Causes subsite.

The third iteration of *International Incidence of Childhood Cancer* (IICC-3; http://iicc.iarc.fr/results) was launched on International Childhood Cancer Day 2017. As with CI5, the series provides high-quality recorded data built on long-standing registry collaborations worldwide. IICC-3 comprises data on cancer incidence in children and adolescents (ages 0–19 years) from 309 cancer registries. An accompanying article showed that leukaemia was the most common cancer in children younger than 15 years, making up almost a third of childhood cancers diagnosed in 2001–2010; tumours of the central nervous system ranked second, and lymphomas ranked third (Steliarova-Foucher et al., 2017).

Descriptive epidemiology of cancer

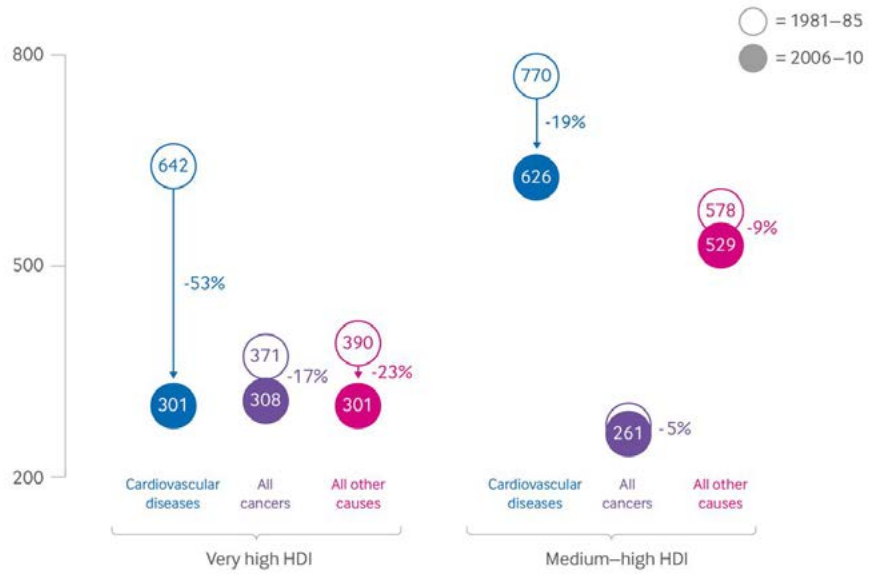
CSU seeks to document global variations in incidence, mortality, and survival as well as the changing magnitude and transitional nature of cancer profiles worldwide. Recently, emphasis has been placed on assessing cancer trends relative to other major NCDs (Figure 4) (Cao et al., 2017) and on the economic impact of cancer as a leading cause of premature death. More broadly, there are efforts to disseminate additional surveillance indicators of relevance to cancer control policy both in high-impact peer-reviewed journals and on the GCO website.

Descriptive studies provide critical insights into the changing cancer patterns, the underlying determinants, and priorities for cancer control. Invited chapters on the global cancer burden were provided for *Holland-Frei Cancer Medicine, 9th Edition* (Ferlay et al., 2017) and the *International Encyclopaedia of Public Health, 2nd Edition* (Bray and Shield, 2017). A diverse set of peer-reviewed articles included an assessment of women's cancers (Ginsburg et al., 2017), a surveillance profile of Peru (Piñeros et al., 2017a), and registry status requirements in the Eastern Mediterranean region (Kulhánová et al., 2017) and in Latin America and the Caribbean (Bray and Piñeros, 2016). A commentary assessed the evolving landscape of cancer (Bray, 2016).

The relationship between the incidence of 27 cancer types and the Human Development Index (HDI) level (Fidler et al., 2016) and the association between HDI and colorectal cancer incidence rates (Fidler et al., 2017) have been reported. There are ongoing efforts to better understand the impact of cancer in specific age ranges, with a recent global assessment of cancer among young adults published in *The Lancet Oncology*; a similar exercise looking at cancer profiles among the elderly is in preparation.

Cancer-specific reports provide insight into the differing distribution of known risk factors and can generate novel hypotheses regarding putative factors. Highlights included the global estimation and epidemiological assessment of the subsites of oral cavity and pharyngeal cancers (Shield et al., 2017) and global projections of oesophageal cancer incidence by histological subtype in 12 countries (Arnold et al., 2017a), liver cancer incidence in 30 countries, and pancreatic mortality in the 28 Members States of the European Union (Ferlay et al., 2016). Efforts to quantify the long-term impact of cervical screening in six

Figure 4. Changes in age-standardized (world) mortality rates per 100 000 people in adults aged 40–84 years between 1981–1985 and 2006–2010 due to cardiovascular diseases, all cancers, and all other causes of death in men and women combined, by Human Development Index (HDI) level. Figure reproduced from Cao et al. (2017). © Cao et al., 2017.



Baltic, central, and eastern European countries, where there is rising incidence and almost no screening, showed that an effective launch of screening from 2017 could prevent almost 180 000 new cervical cancer diagnoses by 2040 (Vaccarella et al., 2016). An age–period–cohort analysis of kidney cancer in 16 populations worldwide reported attenuations in period-specific increases in incidence rates, hinting at changing imaging practice and a possible mitigation of overdiagnosis (Znaor et al., 2017). An assessment of incidence of cancers of the brain and the central nervous system revealed a 5-fold difference between the highest rates (mainly in Europe) and the lowest rates (mainly in Asia) (Miranda-Filho et al., 2017).

The GCO's Cancer Causes subsite incorporates recently published results for the global PAF for infections (Plummer et al., 2016) and for solar radiation, and will soon include those for the global PAF for alcohol consumption. More detailed overviews of important cancer risk factors include an ongoing analysis of 10 major risk factors in the Eastern Mediterranean region. An assessment of 24 risk factors and their impact on cancer in France in 2015 is being performed with 70 local experts. The first paper on the impact of alcohol consumption reveals that 8% of all cancers in France are attributable to excess consumption.

Benchmarking cancer survival estimates provides a relative measure of health system effectiveness, in part reflecting the extent of early diagnosis and adequate treatment of patients. In 2016, SURVMARK-2 and SURVCAN-3 were launched to provide up-to-date cancer survival statistics worldwide (http://survival.iarc.fr/Survcan/en/). SURVMARK-2 focuses on 21 jurisdictions in six high-income countries to assess underlying reasons for survival differences in countries with similar health systems via in-depth stage-specific assessments of coding and registry practices. Supporting the sustained development of cancer registries, the SURVCAN-3 project expands the global coverage of high-quality survival statistics to more than 70 cancer registries in LMICs, which have submitted their data for initial quality review; formal agreements have been established with registries to support the collection of complete follow-up and develop local expertise in survival methods. The second IARC Summer School module on this topic was held in Lyon in June 2017 (Figure 5).

Figure 5. During the IARC Summer School module on Cancer Survival Methods for Cancer Registries held in Lyon in June 2017, Dr Rajaraman Swaminathan lectured to participants on methods for active follow-up of patients with cancer. © IARC/Roland Dray.

To document the complexity of health transitions requires a *populations within populations* approach, whereby more granular data can be informative, as evidenced by the recent assessment of survival patterns among Indigenous populations (Moore et al., 2016a). The first World Indigenous Cancer Conference was held in 2016 as a partnership with the Menzies School of Health Research, Australia (http://www.wiccnetwork.org), and a network bringing together Indigenous groups, researchers, and governments under the umbrella of the World Indigenous Cancer Consortium (WICC) is being developed. Recent work has focused on cancer surveillance (Tervonen et al., 2017a) and cancer epidemiology (Tervonen et al., 2017b) in the Pacific Islands, with a view to linking this to the Hub developments.


IARC HANDBOOKS
BREAST CANCER SCREENING
VOLUME 15
IARC HANDBOOKS OF CANCER PREVENTION
IARC MONOGRAPHS
SOME ORGANOPHOSPHATE INSECTICIDES AND HERBICIDES
VOLUME 112
IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS
WHO Classification of Head and Neck Tumours
Edited by
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The Section of Evidence Synthesis and Classification (ESC) was created by merging the teams of the *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* and the *IARC Handbooks of Cancer Prevention* (formerly the Section of IARC Monographs [IMO]) with the team of the *WHO Classification of Tumours* (formerly within the Section of Molecular Pathology [MPA]) to fully benefit from synergies of similar procedures in producing the three flagship publication series, each forming a Group within the new Section. The enhanced structure came into effect on 1 August 2017.

For each volume of the *WHO Classification of Tumours*, the *IARC Monographs*, and the *IARC Handbooks*, IARC convenes international, interdisciplinary Working Groups of expert scientists to systematically review the pertinent scientific literature and to develop consensus evaluations and classifications. IARC selects these experts based on their knowledge and experience and the absence of real or apparent conflicting interests.

The *WHO Classification of Tumours* series provides an evidence-based classification of all cancer types to enable

diagnosis and research worldwide. The definitions are incorporated into the International Classification of Diseases (ICD) codes. They are fundamental to treatment of individual patients, monitoring of global cancer occurrence, and research into all aspects of cancer causation, prevention, and therapy.

The *IARC Monographs* are a series of scientific reviews that identify environmental factors that can increase the risk of cancer. Sometimes called WHO's "Encyclopaedia of Carcinogens", the *IARC Monographs* have reviewed more than 1000 agents and have identified almost 500 known, probable, and possible carcinogens.

The *IARC Handbooks* complement the *IARC Monographs*' evaluations of carcinogenic hazards, providing evidence synthesis and evaluations of the cancer-preventive effects of chemopreventive agents and of primary interventions and cancer screening, using the same rigorous evaluation process as the *IARC Monographs*.

National and international health agencies can then take action to prevent avoidable exposures to known, probable, and possible carcinogens and to implement cancer-preventive strategies. Individuals, too, can use this information to make better choices that will reduce their risk of cancer.

IARC Monographs Group (IMO)

The IARC Monographs Group (IMO) is responsible for producing the *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. The *IARC Monographs* are fundamental to the Agency's mission of identifying the causes of cancer. Since their inception in 1971, more than 1000 agents have been evaluated for carcinogenicity. This international, interdisciplinary endeavour provides an authoritative reference for researchers, health authorities, and the public. Health agencies worldwide rely on the *Monographs* for scientific support of actions to control exposures and prevent cancer. In addition to producing this important resource, IMO's scientific personnel contribute to the scientific literature on topics related to the *Monographs*' methodology and contents.

Major accomplishments

The Group and its predecessor, the Section of IARC Monographs, organized six Working Group meetings during the 2016–2017 biennium (Figure 1). The agents evaluated at these meetings included 10 that were recommended as high priorities for evaluation and 8 others judged to be medium or medium-to-high priorities by an Advisory Group that met in 2014. The six meetings were the following:

- Volume 115: Some industrial chemicals (2–9 February 2016)
- Volume 116: Coffee, mate, and very hot beverages (24–31 May 2016)
- Volume 117: Pentachlorophenol and some related compounds (4–11 October 2016)
- Volume 118: Welding, welding fumes,

Figure 1. An *IARC Monographs* Working Group in action. © IARC/Roland Dray.

Table 1. Summary of evaluations from the six *Monographs* meetings held in 2016–2017

Agent (Volume)	Evaluation[a]	Tumour site or type in humans with *sufficient evidence* (**bold**) or *limited evidence*	Level of evidence for carcinogenicity in experimental animals	Key characteristics of carcinogens with strong evidence[b]
Some industrial chemicals (Volume 115)				
N,*N*-Dimethylformamide	Group 2A	Testes	*Sufficient*	Multiple (1, 3, 10)
Hydrazine	Group 2A	Lung	*Sufficient*	Multiple (1, 2, 5, 10)
2-Mercaptobenzothiazole	Group 2A	Urinary bladder	*Sufficient*	None
3-Chloro-2-methylpropene	Group 2B		*Sufficient*	2
1-Bromopropane	Group 2B		*Sufficient*	Multiple (1, 5, 6, 7, 10)
N,*N*-Dimethyl-*p*-toluidine	Group 2B		*Sufficient*	None
Tetrabromobisphenol A	Group 2A[c]		*Sufficient*	Multiple (5, 7, 8)
Coffee, mate, and very hot beverages (Volume 116)				
Coffee drinking	Group 3		*Inadequate*	None[d]
Consumption of very hot beverages (> 65 °C)	Group 2A	Oesophagus	*Limited*	None
Pentachlorophenol and some related compounds (Volume 117)				
Pentachlorophenol	Group 1	**Non-Hodgkin lymphoma**	*Sufficient*	Multiple (1, 2, 5, 8, 10)
2,4,6-Trichlorophenol	Group 2B		*Sufficient*	None
Dieldrin, and aldrin metabolized to dieldrin	Group 2A	Breast	*Sufficient*	None
3,3′,4,4′-Tetrachloroazobenzene	Group 2A[c]		*Sufficient*	Multiple (6, 8, 10)
Welding, welding fumes, and some related chemicals (Volume 118)				
Welding fumes	Group 1	**Lung**, kidney	*Limited* (gas metal arc-stainless steel welding fumes)	Multiple (6, 7)
Ultraviolet radiation from welding	Group 1	**Eye (melanoma)**	N/A	None
Indium tin oxide	Group 2B		*Sufficient*	6
Molybdenum trioxide	Group 2B		*Sufficient*	None
Some chemicals that cause tumours of the urinary tract in rodents (Volume 119)				
1-*tert*-Butoxypropan-2-ol	Group 2B		*Sufficient*	None
β-Myrcene	Group 2B		*Sufficient*	None
Furfuryl alcohol	Group 2B		*Sufficient*	1
Melamine	Group 2B		*Sufficient*	6
Pyridine	Group 2B		*Sufficient*	None
Tetrahydrofuran	Group 2B		*Sufficient*	None
Vinylidine chloride	Group 2B		*Sufficient*	None
Benzene (Volume 120)				
Benzene	Group 1	Acute non-lymphocytic leukaemia	*Sufficient*	Multiple (1, 2, 3, 5, 7, 8, 10)

N/A, not applicable.

[a] Group 1, carcinogenic to humans; Group 2A, probably carcinogenic to humans; Group 2B, possibly carcinogenic to humans; Group 3, not classifiable as to its carcinogenicity to humans; Group 4, probably not carcinogenic to humans.

[b] Numbers correspond to one or more of the 10 key characteristics of carcinogens, as identified by Smith et al. (2016) and indicated in the *IARC Monographs* Instructions to Authors.

[c] The Group 2A classifications of tetrabromobisphenol A and 3,3′,4,4′-tetrachloroazobenzene are based on *sufficient evidence of carcinogenicity* in experimental animals and strong mechanistic evidence.

[d] Strong evidence for antioxidant effects.

and some related chemicals (21–29 March 2017)
• Volume 119: Some chemicals that cause tumours of the urinary tract in rodents (6–13 June 2017)
• Volume 120: Benzene (10–17 October 2017).

The focus and results of these meetings (Table 1) illustrate the unique ability of the *Monographs* to evaluate the carcinogenicity of diverse agents, ranging from chemicals tested only in animal bioassays to widely consumed beverages with data from hundreds of epidemiological studies.

The 23 evaluations achieved in these meetings included 13 new classifications of agents never before evaluated by IARC and re-evaluations of 10 agents considered previously. All of the re-evaluations except for those of coffee drinking and benzene resulted in a higher classification as a result of evidence accumulated since the agent was last considered. For benzene, three new cancer sites with *limited evidence* of carcinogenicity were identified, and analyses suggesting a linear exposure–response relationship were completed.

A concise summary of each evaluation with the classification, accompanying rationale, and key references is published in *The Lancet Oncology*. Full details and supporting data are provided in the complete *Monograph*, which is expected to be published about a year after the meeting. Both are available for free download on the *Monographs* website (http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php).

Publications

During the 2016–2017 biennium, the following *IARC Monographs* were published:

- Volume 113: 2,4-Dichlorophenoxyacetic acid (2,4-D) and Some Organochlorine Insecticides (Monograph on 2,4-D) (2016)
- Volume 112: Some Organophosphate Insecticides and Herbicides (2017)
- Volume 111: Some Nanomaterials and Some Fibres (2017)
- Volume 110: Some Chemicals Used as Solvents and in Polymer Manufacture (2016)
- Volume 109: Outdoor Air Pollution (2016)
- Volume 108: Some Drugs and Herbal Products (2016)
- Volume 107: Polychlorinated Biphenyls and Polybrominated Biphenyls (2016).

Lessons learned from the glyphosate evaluation

The March 2015 classification of glyphosate as *probably carcinogenic to humans* (Group 2A) has had worldwide impact. IARC has since served as a scientific resource, providing invited presentations to the European Parliament and to national and international health agencies, disseminating scientific references, and accelerating the publication of the *Monograph*. IARC's reach is exemplified by subsequent health agency actions, including California's listing of glyphosate as a carcinogen (https://oehha.ca.gov/proposition-65/crnr/notice-intent-list-tetrachlorvinphos-parathion-malathion-glyphosate; https://oehha.ca.gov/proposition-65/chemicals/glyphosate). IARC's evaluation revealed important data gaps (e.g. on exposure during manufacturing, community spraying operations, and in the general population) and stimulated scientific research publications (https://www.ncbi.nlm.nih.gov/pubmed/?term=glyphosate).

The glyphosate evaluation also triggered orchestrated and unprecedented threats to IARC's scientific independence. The Agency has had positive impacts through its response to these serious challenges. On its website, IARC documented attempts by interested parties to intimidate and harass the glyphosate Working Group, IARC scientists, and the Agency itself. This proved an important resource for IARC's governing and scientific bodies, who were also lobbied by vested interests and worked closely with the Agency in responding. At the same time, IARC has reinforced its strong procedures on conflict of interest disclosure and transparency. IARC collaborated closely with the WHO legal team to protect independent scientists serving future *Monograph* evaluations from harassment. In conducting evaluations, IARC continues to rely on studies in the public domain and available for independent scientific review, a transparent practice being discussed and adopted internationally (http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000526.jsp&mid=WC0b01ac0580789730). Further to its interests in transparency, IARC has pursued full disclosure of conflicts in stakeholder-sponsored publications aimed at discrediting independent science.

IARC Handbooks Group (IHB)

The IARC Handbooks Group (IHB) is responsible for producing the *IARC Handbooks of Cancer Prevention*. The *IARC Handbooks* programme was initiated in 1995 to complement the *IARC Monographs* by providing evaluations of interventions and strategies to cancer prevention. The same rigorous procedures of critical review and evaluation as for the *IARC Monographs* are used. *Handbook* evaluations have included chemopreventive agents, preventive actions, effectiveness of screening, and effectiveness of tobacco control.

Volume 16: Body fatness (5–12 April 2016)

The topic of this *Handbook* was selected in relation to the United Nations/WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases to reduce obesity worldwide.

Evidence has accumulated to show that obesity is a risk factor for several cancers in addition to those identified in a previous *Handbook* (Volume 6). A Working Group of 20 international experts met in Lyon and reviewed data from more than 1000 studies to evaluate (i) the association between various anthropometric

measures of body fatness and some 25 cancer sites or types, (ii) the impact of overweight/obesity at different ages on cancer risk, including the impact on cancer risk of weight change during early life or young adulthood, and (iii) the effect in cancer patients of overweight/obesity and of weight loss on cancer recurrence or cancer-related survival.

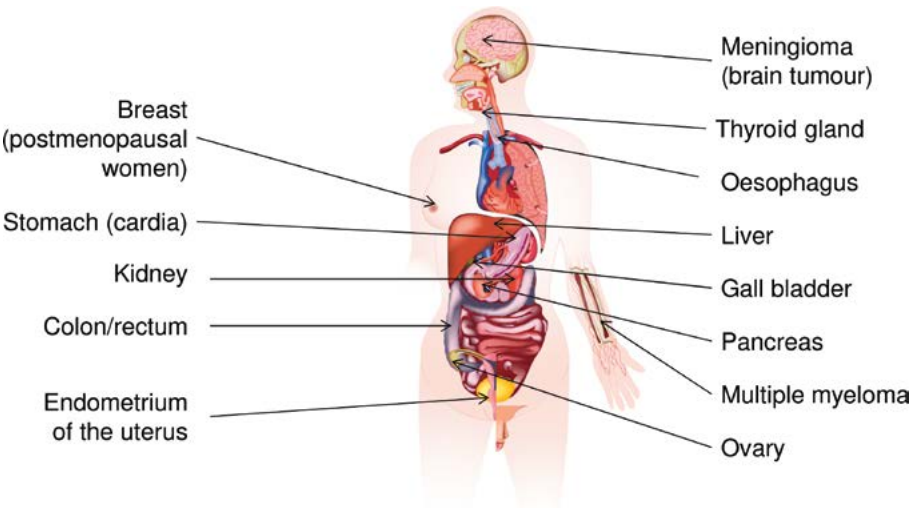
The Working Group concluded that there is *sufficient evidence* in humans for the cancer-preventive effect of absence of excess body fatness. Absence of excess body fatness reduces the risk of cancers of the colon and rectum, pancreas, gall bladder, oesophagus (adenocarcinoma), gastric cardia, liver (hepatocellular carcinoma), kidney (renal cell carcinoma), ovary, endometrium of the uterus, breast in postmenopausal women, and thyroid, and of meningioma and multiple myeloma. In addition, it may reduce the risk of fatal prostate cancer, diffuse large B-cell lymphoma, and breast cancer in men. Results of studies in experimental animals concur with those in humans. There is *sufficient evidence* in experimental animals for a cancer-preventive effect of limitation of body weight gain by dietary restriction, for cancers of the mammary gland, colon, liver, pancreas, skin, and pituitary gland. In addition, an association between limitation of body weight gain by dietary restriction and reduced cancer occurrence was observed for cancer of the prostate and for lymphoma and leukaemia. Several mechanisms linking excess body fatness with carcinogenesis were identified, including chronic inflammation and dysregulation of the metabolism of sex hormones. These results provide further scientific evidence that absence of excess body fatness can reduce the risk of many cancers, and highlight eight additional cancer sites that have now also been linked with overweight/obesity (Figure 2).

Volume 17: Colorectal cancer screening (14–21 November 2017)

In November 2017, the *IARC Handbooks* evaluated the published scientific evidence on the benefits and harms of colorectal cancer screening. This evaluation was timely because of the increasing incidence of colorectal cancer worldwide, including in low- and middle-income countries, and because several countries have set up screening programmes with different procedures and strategies. A Working Group of 23 international experts met at IARC. The Working Group reviewed the available data for endoscopic methods (colonoscopy and flexible sigmoidoscopy), stool-based tests for blood (guaiac-based and immunochemical tests), computed tomography colonography, and other emerging tests. The beneficial effects of colorectal cancer screening were evaluated in terms of reduction in incidence, reduction in mortality, and benefit-to-harm ratio.

The systematic review of the scientific literature and the Working Group's conclusions can support the development of guidelines by WHO and the implementation of organized screening programmes by health care systems. The outcome of the meeting will be published in the *New England Journal of Medicine* in early 2018.

Figure 2. Absence of excess body fatness reduces the risk of these types of cancer (*IARC Handbooks* Volume 16). © IARC.



WHO/IARC Classification of Tumours Group (WCT)

The WHO/IARC Classification of Tumours Group (WCT) is a new Group within the new Section of Evidence Synthesis and Classification (ESC), established on 1 August 2017. WCT has taken over responsibility for production of the *WHO Classification of Tumours* series (WHO Blue Books) from the former Section of Molecular Pathology (MPA). Dr Hiroko Ohgaki, who retired in July 2017, provided the leadership to the Blue Books volumes during the majority of the biennium covered in this report.

The information and cases illustrated within the WHO Blue Books provide the standards against which cancers are classified and diagnosed worldwide. The diagnosis and classification of individual cancers underpins research into cancer causation, prevention, diagnosis, and treatment. Now in its fourth edition, the WHO Blue Books series has become an essential resource for diagnosis by histopathologists and an important reference for all involved in cancer research.

During the 2016–2017 biennium, the following volumes were published:

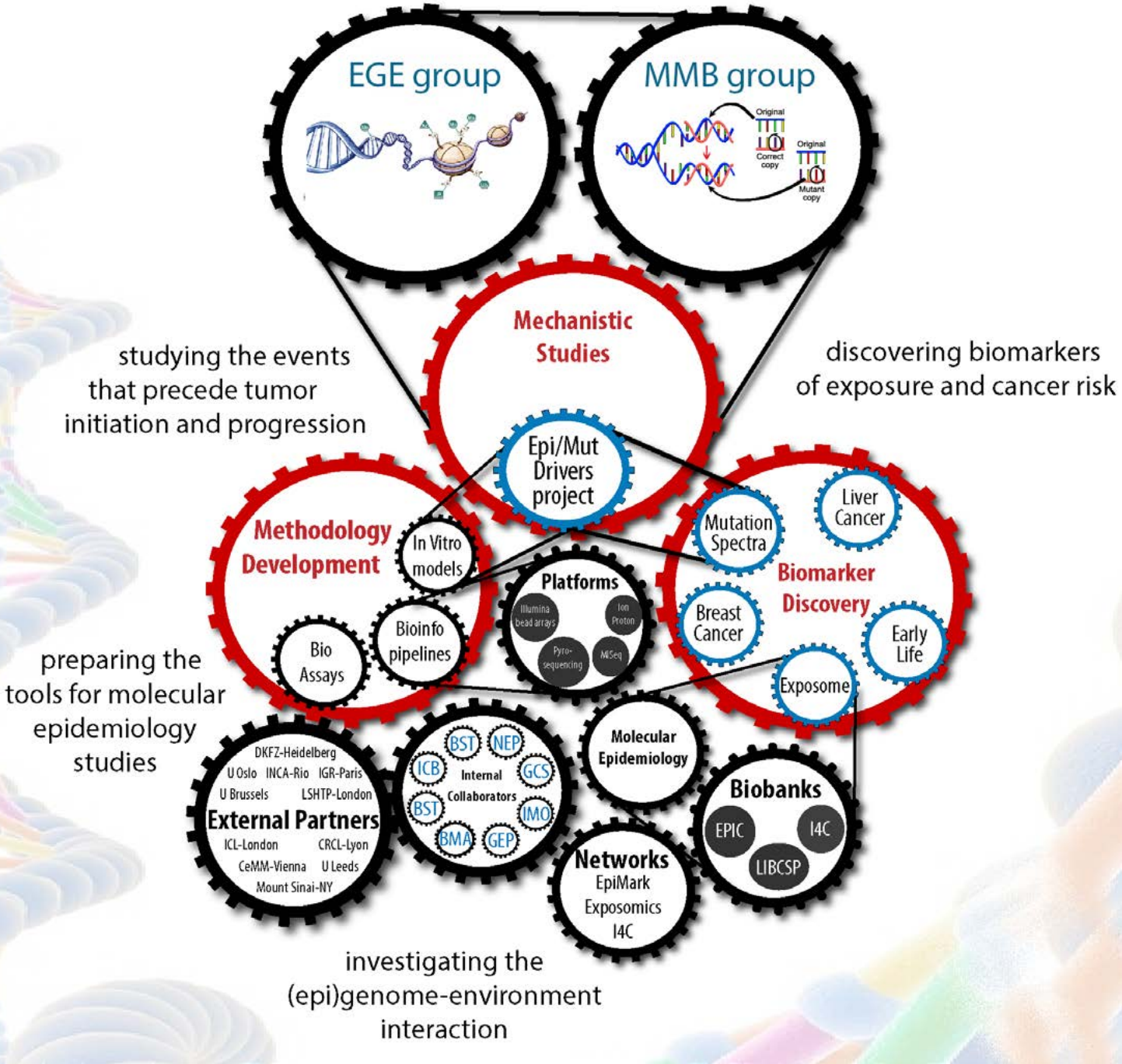
- *WHO Classification of Tumours of the Urinary System and Male Genital Organs*, 4th edition (2016)
- *WHO Classification of Tumours of the Central Nervous System*, revised 4th edition (2016)
- *WHO Classification of Head and Neck Tumours*, 4th edition (2017)
- *WHO Classification of Tumours of Endocrine Organs*, 4th edition (2017)
- *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*, revised 4th edition (2017).

Pathology is currently undergoing a more rapid transformation than at any time during the past 30 years, as a result of the introduction of new technologies. Whereas cancer classification has previously been based on consensus of histopathological opinion, the understanding of cancer at a molecular level is now at a point where it needs to be integrated into diagnosis. In addition, digital pathology and image analysis are producing new insights, and providing quantitative justification of many existing diagnostic criteria, while challenging others. Finally, the pace of improvement in computer technology, including artificial intelligence, is already producing clinically applicable aids to diagnosis, and this trend is likely to accelerate. There is an urgent need to integrate these facets of diagnosis into cancer classification.

WCT is taking a leading role in cancer classification and pathology internationally, and in the next year will be responsible for the publication of the two remaining volumes of the fourth edition. *WHO Classification of Skin Tumours* is being prepared by four volume editors (Dr David E. Elder, Dr Daniela Massi, Dr Richard Scolyer, and Dr Rein Willemze) and 178 contributors from 25 countries. The consensus and editorial meeting was held at IARC on 24–26 September 2017, and the volume is scheduled to be published in spring 2018. *WHO Classification of Tumours of the Eye*, the last volume of the fourth edition, is being prepared by three volume editors (Dr Hans Grossniklaus, Dr Charles Eberhart, and Dr Tero Kivelä) and 61 contributors from 21 countries. The consensus and editorial meeting will be held at IARC on 11–13 January 2018. The volume is scheduled to be published in autumn 2018.

Planning for the fifth edition is at an advanced stage. This will incorporate new information and electronic content, based on expert consensus review of reproducible peer-reviewed published evidence. It will define the requirements for diagnosis, applicable to patients living in high-, middle-, or low-income countries. The major pathology organizations worldwide are nominating members of a new Editorial Board, which will be tasked with improving the timeliness and quality of the WHO Blue Books.

Understanding molecular mechanisms for cancer prevention



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Improving the knowledge of mechanisms of carcinogenesis related to environmental exposures provides a foundation for studies of cancer etiology, cancer prevention, and carcinogen evaluation, the core activities of IARC. The overarching objective of the Section of Mechanisms of Carcinogenesis (MCA) is to provide the evidence base for the study of cancer causation and prevention by elucidating the molecular mechanisms by which genetic and epigenetic alterations alter critical molecular pathways and promote cancer development. Major emphasis is placed on discerning events that precede or drive tumour initiation and progression related to environmental exposures.

The research of MCA focuses on two priority areas. First, MCA studies are aimed at providing critical insights into mechanisms of carcinogenesis through the identification of molecular alterations and molecular pathways deregulated by specific cancer risk factors. This is achieved through mechanistic studies of functionally important (epi)genetic "driver" events and molecular pathways altered by specific cancer risk agents (with a focus on a set of genotoxic and non-genotoxic agents prioritized according to their relevance to cancer etiology and prevention), using in vitro models and state-of-the-art approaches including (epi)genome-wide screens and functional genomics. Second, MCA is involved in identifying molecular biomarkers of exposure and cancer risk. To this end, MCA uses cutting-edge (epi)genomics, population-based cohorts, and innovative bioinformatics tools to investigate (epi)genomic profiles of specific cancers and surrogate tissues and to identify signatures of cancer risk and exposures. The primary focus is on cancers of the breast, urinary tract, and liver and childhood malignancies. MCA also participates in an interdisciplinary approach aimed at characterizing exposures throughout the life-course (with a particular focus on the fetal exposome and childhood cancer) by building on unique samples from international birth cohorts and other population-based studies.

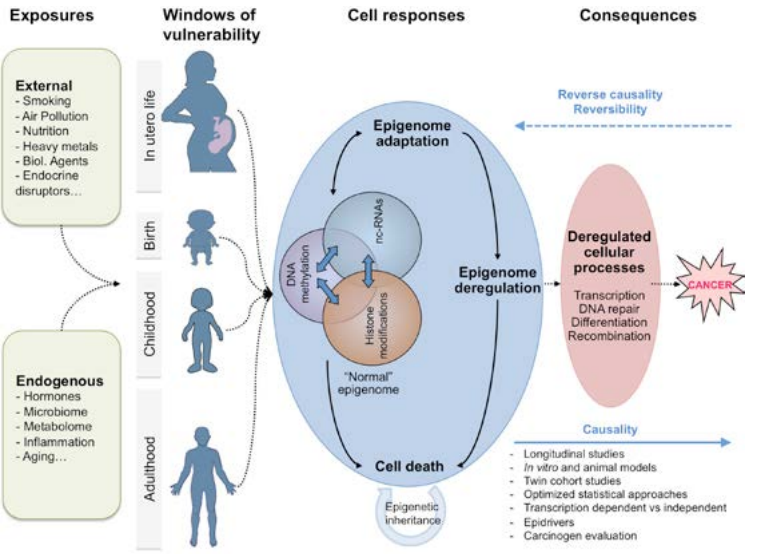
The expected outcome of these studies is the opening up of an opportunity to identify and characterize the key molecular events and pathways that underpin carcinogenesis, thereby elucidating important aspects of cancer etiology and opportunities for prevention.

The Section consists of two Groups: the Epigenetics Group (EGE) and the Molecular Mechanisms and Biomarkers Group (MMB).

Epigenetics Group (EGE)

The Epigenetics Group (EGE) conducts mechanistic studies and epigenetic profiling aimed at enhancing the understanding of epigenetic mechanisms underlying tumour development and progression as well as discovering new cancer biomarkers (Figure 1). EGE exploits new concepts in cancer epigenetics, the availability of unique population-based cohorts, and recent technological advances in epigenomics. EGE also develops epigenomic methodologies, profiling strategies, and bioinformatics tools, applicable to population-based cohorts and molecular epidemiology studies coordinated by IARC researchers and external collaborators. Outcomes of the recent studies are an improved knowledge of mechanisms of carcinogenesis associated with environmental factors and the provision of an evidence base for studies of cancer causation and prevention.

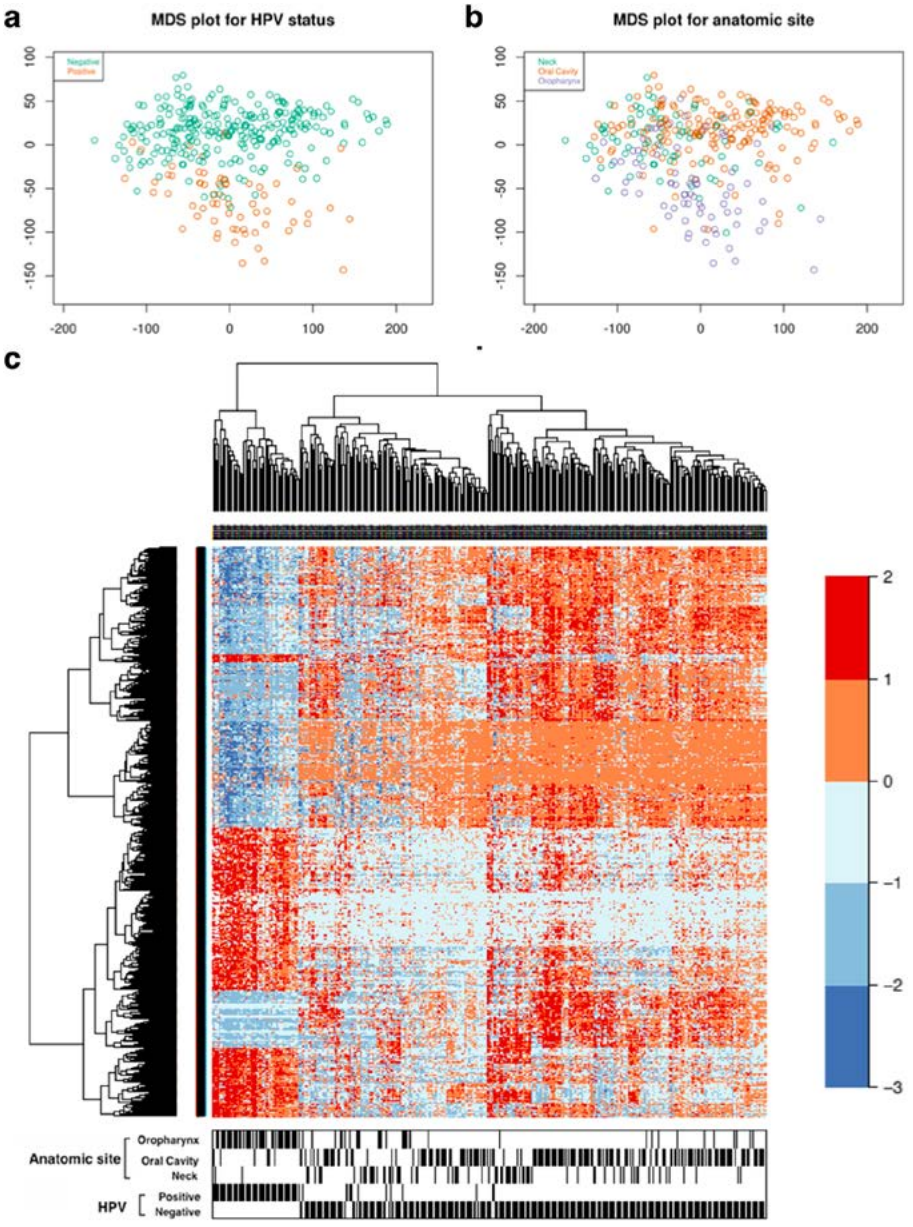
Figure 1. Studying epigenetic mechanisms and environmental origins of cancer. Exposures arising from external sources (e.g. environmental chemicals, air pollution, infectious agents, diet, tobacco use, alcohol consumption, and endocrine disruptors) and internal processes (e.g. metabolism, hormones, inflammation, gut microflora, and ageing) may induce stable and potentially reversible changes in the epigenome. The patterns ("signatures") and persistence of these alterations depend on multiple factors, including the types of epigenetic changes, the dosage and duration of the exposure, the tissue type, and the developmental stage. Thus, epigenetic mechanisms may represent "sensors" of exposure and "mediators" of the outcomes, including cancer development. Figure reprinted from Herceg et al. (2017). Roadmap for investigating epigenome deregulation and environmental origins of cancer. Int J Cancer. http://dx.doi.org/10.1002/ijc.31014 PMID:28836271. © 2017 IARC/WHO; licensed by UICC.



Identifying epigenomic signatures associated with exposures to risk factors

EGE plays a key role in several multidisciplinary studies aimed at testing the hypothesis that epigenetic changes may be risk factor-specific ("signatures") and that this may prove instrumental in the discovery of new biomarkers in cancer. By applying powerful epigenomic methodologies to unique case–control and population-based studies, EGE has led studies that resulted in important discoveries, including: (i) identification of an epigenetic signature of human papillomavirus (HPV) infection in head and neck cancer that is independent of the anatomical site (Figure 2), is functionally correlated with gene expression, and may be leveraged for improved stratification of prognosis (Degli Esposti et al., 2017b); (ii) comprehensive identification and cataloguing of the DNA methylation alterations associated with tobacco smoking (Ambatipudi et al., 2016, Joehanes et al., 2016); (iii) demonstrating that normal gastric mucosa from gastric cancer cases and healthy controls exhibits methylome-wide changes associated with current and past infection with *Helicobacter pylori*; (iv) demonstrating that specific DNA methylation changes in lung tumours are associated with asbestos exposure and identifying potential causal pathways induced by asbestos exposure (Kettunen et al., 2017); and (v) demonstrating that despite a marked reversibility of methylation changes after exposure removal (such as smoking cessation and *H. pylori* eradication), a significant number of genomic regions remained differentially methylated years later, suggesting the existence of a long-term "epigenetic memory" (Ambatipudi et al., 2016).

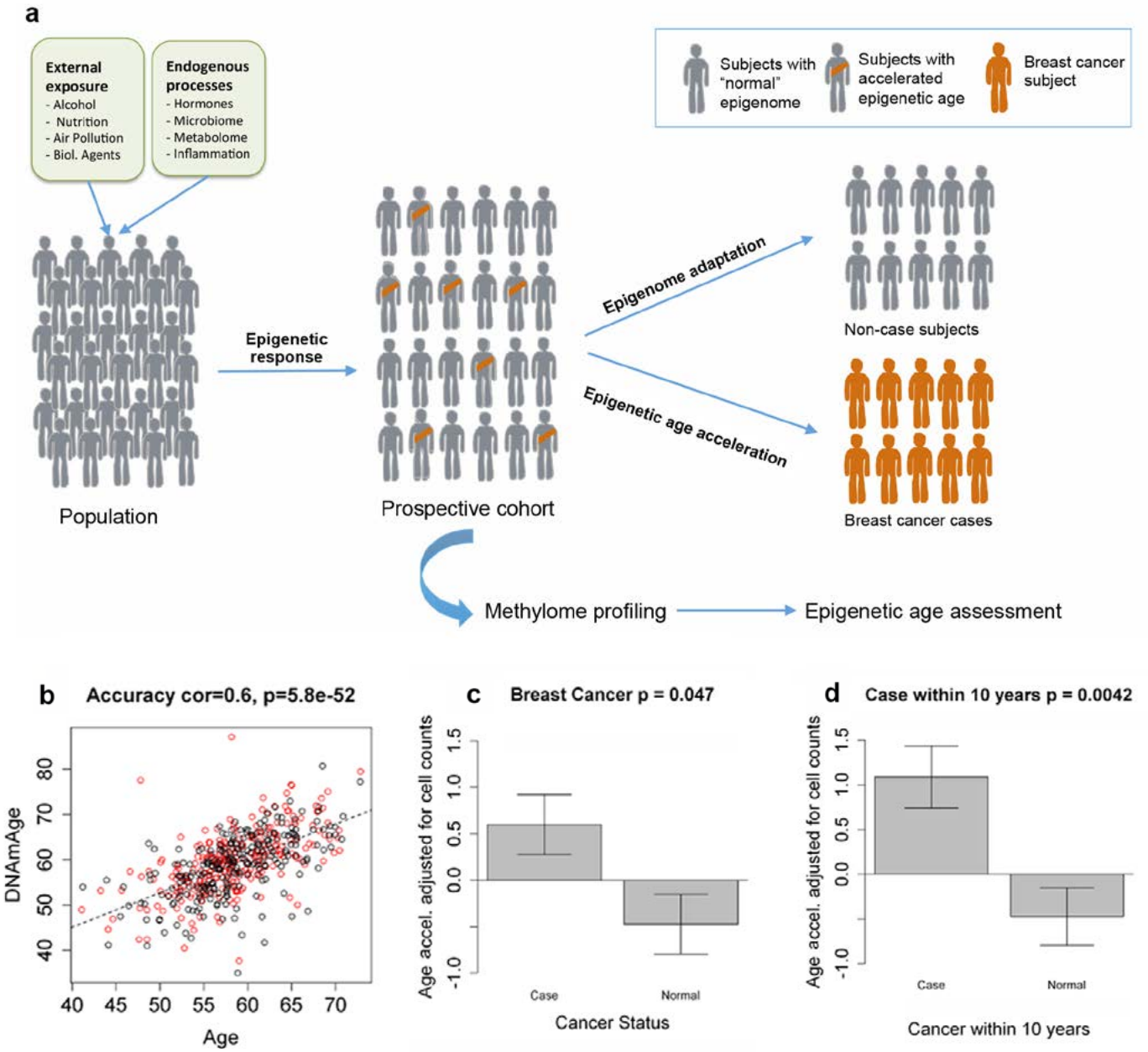
Figure 2. Human papillomavirus (HPV) infection leaves a clear DNA methylation signature in head and neck cancer. (a, b) Multidimensional scaling (MDS) plots showing sample clustering grouped by different variables: (a) HPV status; (b) organ site. (c) Heat map showing the 2410 differentially methylated positions associated with HPV status (false discovery rate < 0.05, differential methylation Δβ > 20%). Figure adapted from Degli Esposti et al. (2017b). © Degli Esposti et al., 2017.



DNA methylome-wide analysis of a prospective cohort identifies accelerated epigenetic ageing associated with cancer susceptibility

EGE coordinated a large study aimed at identifying the potential of epigenetic changes in peripheral blood as a marker of risk factor exposure and cancer risk. This approach combined the advantages of methylome-wide profiling and a large prospective cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC) study with adequate statistical power. The study revealed that higher epigenome-wide methylation at CpG islands was associated with breast cancer risk and that DNA methylation-based markers of ageing (known as the "epigenetic clock") are associated with susceptibility to postmenopausal breast cancer (Figure 3) (Ambatipudi et al., 2017). This study demonstrates that prospectively collected blood samples harbour epigenetic changes that may serve as potential markers of risk factor exposure and breast cancer risk.

Figure 3. DNA methylome-wide analysis of a prospective cohort identifies epigenetic ageing associated with cancer susceptibility. (a) The general study design. (b) DNA methylation age (vertical axis) versus chronological age (horizontal axis). Points correspond to female subjects. Red indicates a breast cancer case, and black indicates a control. The dashed line indicates a regression line. (c) Epigenetic age acceleration versus breast cancer status. Each bar plot depicts the mean value and standard deviation and reports a non-parametric group comparison test *P* value (Wilcoxon test). (d) Epigenetic age acceleration versus breast cancer status (developed within 10 years after the blood draw). Each bar plot depicts the mean value and standard deviation and reports a non-parametric group comparison test *P* value (Wilcoxon test). Figure compiled from Ambatipudi et al. (2017). © IARC.



Identifying epigenetic changes induced by in utero and early-life exposures and their causal relationship with childhood cancer

One of the major focuses of EGE in recent years has been the development of a multidisciplinary study aimed at investigating the causal relationship between in utero and early-life exposures and increased risk of cancer in childhood and adulthood. EGE played a central role in developing an epigenetic epidemiology framework at IARC and several major international consortia focusing on the early-life period. In particular, EGE manages the International Biospecimen Coordinating Center of the International Childhood Cancer Cohort Consortium (I4C), the largest prospective investigation into childhood cancer, comprising about 500 000 mother–child pairs. This has led to exciting synergies and cross-interactions among I4C, the EXPOsOMICS Consortium (Vineis et al., 2017), and the Pregnancy and Childhood Epigenetics (PACE) Consortium, all of which comprise the early-life period. Building on these large and rich data resources, EGE has started cataloguing epigenetic signatures of early-life exposures (Joubert et al., 2016) and deciphering their effects on phenotypic

outcomes during this period (Table 1), with a primary focus on childhood cancer as an end-point. The prioritized exposures include tobacco smoking and air pollution, for which the effects on childhood cancer risk remain elusive. As for the phenotypes, EGE has focused on birth weight and associated covariates (pre-pregnancy body mass index, sex, and gestational age), because high birth weight (apart from ionizing radiation) is currently the only prospectively based risk factor for all childhood cancer. The current studies focus on epigenetic precursors of childhood cancer (Table 1) that may help to decipher complex exposure-to-phenotype patterns.

Table 1. Summary of epigenetic signatures of early-life exposures, phenotypes, and cancer identified to date

Exposure/phenotype/disease	Number of newborns	Number of CpGs identified agnostically after FDR [or Bonferroni] adjustment*	Major finding	Reference
Exposures during pregnancy				
Maternal smoking	6685 (13 cohorts)	6073 [568]	Many of these CpGs span genes associated with cancer, and all persist years later, throughout childhood.	Joubert et al. (2016)
Air pollution, NO_2	1508 (4 cohorts)	3 [0]	Although only a few CpGs were identified, all represented mitochondria-related genes.	Gruzieva et al. (2017)
Air pollution, $PM_{2.5}$ Air pollution, PM_{10}	1551 (8 cohorts) 1949 (7 cohorts)	5 [0] 8 [1]	$PM_{2.5}$ and PM_{10} have different impacts on the epigenome of the newborn.	In preparation
Phenotypes perinatally				
Birth weight	8365 (28 cohorts)	8620 [1071]	Birth weight is largely associated with epigenomic variations, ~5% of which remain significant until adulthood.	In preparation
Maternal pre-pregnancy BMI	9340 (19 cohorts)	Several thousand [9044]	Only 8 CpGs are due to a direct intrauterine effect of maternal BMI; the remaining CpGs are associated with blood cell proportions, genetics, and lifestyle factors.	Sharp et al. (2017)
Gestational age	6937 (19 cohorts)	12 799 [9515]	Gestational age has a major impact on the epigenome of the newborn, but only ~1.5% of the CpGs persist until age 7–9 years. The epigenome also accurately predicts gestational age.	In preparation
Sex	Ongoing	Ongoing	Ongoing	Ongoing
Type of cancer				
Childhood leukaemia	857 (3 cohorts)	3 regional clusters, each encompassing ~15 CpGs	Large, sex-specific effects were observed, replicable in three different continents; all regions encompassed imprinted and metastable epialleles.	In preparation
Childhood central nervous system tumours	1205 (4 cohorts)	Ongoing	Common signatures exist with childhood leukaemia.	Ongoing

BMI, body mass index; FDR, false discovery rate; NO_2, nitrogen dioxide; PM_{10}, particulate matter with particles of aerodynamic diameter < 10 μm; $PM_{2.5}$, particulate matter with particles of aerodynamic diameter < 2.5 μm.

EEOC conference

In 2016, EGE organized the Epigenetics and Environmental Origins of Cancer (EEOC) conference, which brought together more than 20 leading scientists in the field and about 150 researchers from different disciplines and many countries around the globe. The leading scientists in the field reviewed the state of the science of epigenetics associated with environmental stimuli and cancer risk, highlighting key developments in the field. Critical knowledge gaps and research needs were discussed, as well as advances in epigenomics that may help in understanding the functional relevance of epigenetic alterations. The scientific exchanges during and after the meeting resulted in an opinion paper jointly written by the invited speakers, and the scientific exchanges promoted international collaboration in the field and contributed to the visibility of the Section and IARC.

Participants in the Epigenetics and Environmental Origins of Cancer (EEOC) conference, held at IARC in June 2016. © IARC/Roland Dray.

Molecular Mechanisms and Biomarkers Group (MMB)

The Molecular Mechanisms and Biomarkers Group (MMB) aims to identify critical molecular processes and markers of carcinogenesis associated with specific environmental and lifestyle risk factors, to facilitate evidence-based cancer prevention strategies. MMB focuses in particular on screening genomic alterations such as mutational signatures in experimental systems and in human and animal tissues, to reveal the impact of environmental factors on the genome and on tumour development. MMB also develops experimental methods and bioinformatics tools in this area that are applicable to molecular cancer epidemiological studies.

Multisystem approach for the identification of mutation spectra of human carcinogens

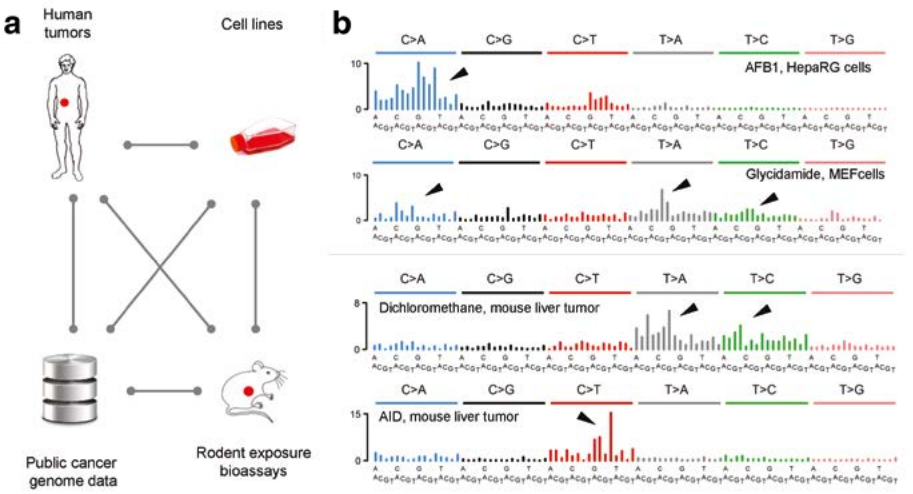
Many carcinogens are mutagenic and can induce specific alterations in the genome, in characteristic imprints that can be used to identify tumours that arise as a result of exposure to these carcinogens. MMB has devised a multisystem approach that includes genome-wide mutation screening in in vitro cell models of exposure, tissues from in vivo animal studies (such as from the United States National Toxicology Program), and tumour samples from exposed humans to characterize the genome-wide impact of several new

candidate human mutagenic factors (Figure 4).

In a recent example, MMB collaborated with the Duke-NUS Medical School, Singapore, to characterize the genome-wide mutational signatures of aflatoxin B_1 from in vivo and in vitro exposure assays. This innovative study showed that evidence of exposure to aflatoxin B_1 is present in 16% of liver cancer cases from Hong Kong Special Administrative Region, compared with 0.7% of cases from North America and 1% of cases from Japan. These results show that aflatoxin exposure apparently remains a substantial public health issue in some areas (Huang et al., 2017a). This integrative approach is thus a powerful strategy for the identification of human tumours linked to various environmental carcinogens, supporting the development of evidence-based cancer prevention measures.

Moreover, to streamline this type of analysis and make it available to the wider cancer research community, MMB has developed a user-friendly bioinformatics package for the analysis and interpretation of mutational signatures in various systems (Ardin et al., 2016).

Figure 4. Identification of mutational signatures of human carcinogens in mutually cross-validating comparison of primary tumours and experimental systems. (a) Genome-wide sequencing data are generated from human tumours, experimentally established cell culture clones, and tumour tissues from rodents experimentally exposed to carcinogens. This framework can be used to study the mechanistic effects of numerous candidate carcinogens. (b) Examples of mutational signatures newly identified by MMB. The bar graphs depict frequencies of single base substitutions for each mutation type, shown as six condensed types (C>A = C:G → A:T, C>G = C:G → G:C, etc.), in a particular trinucleotide context (top row under each graph shows preceding base, lower row shows following base). From top to bottom: whole-genome signature of the carcinogenic mycotoxin aflatoxin B_1 (AFB1), observed in the human liver cancer cell line HepaRG; exome-scale signature of glycidamide, the genotoxic metabolic product of acrylamide, established in mouse embryonic fibroblasts (MEF); exome-scale signature of dichloromethane, an industrial solvent, identified in the liver tumours of exposed mice; and whole-genome signature of activation-induced cytidine deaminase (AID), identified as a result of transgenic activity driving the development of mouse liver tumours. © IARC.



Laboratory studies to elucidate the mechanisms of carcinogen-induced cell transformation

Because of the accumulation of genetic and epigenetic alterations, oncogenic stress can result in the evasion of critical biological barriers that protect normal cells from uncontrolled division. MMB is exploiting the resulting clonal expansion of immortalized cells by applying massively parallel sequencing strategies to study the relationship between genetic alterations and epigenetic changes in the context of specific carcinogen exposures. Therefore, integrated genome-wide analyses of mutations and epigenetic features are being used to identify characteristic profiles of carcinogen exposure and cell transformation in human and murine cell models. Cell-type-of-origin chromatin structure strongly influences mutation landscapes in corresponding tumours. In a second line of experiments, in vitro cell immortalization strategies are being applied to model this interplay in controlled exposure settings (Huskova et al., 2017). Findings from these mechanistic studies may be used to better understand carcinogen-driven tumour development and provide clues on cancer etiology.

Genomic features of premenopausal breast cancer in Latin American women: the PRECAMA study

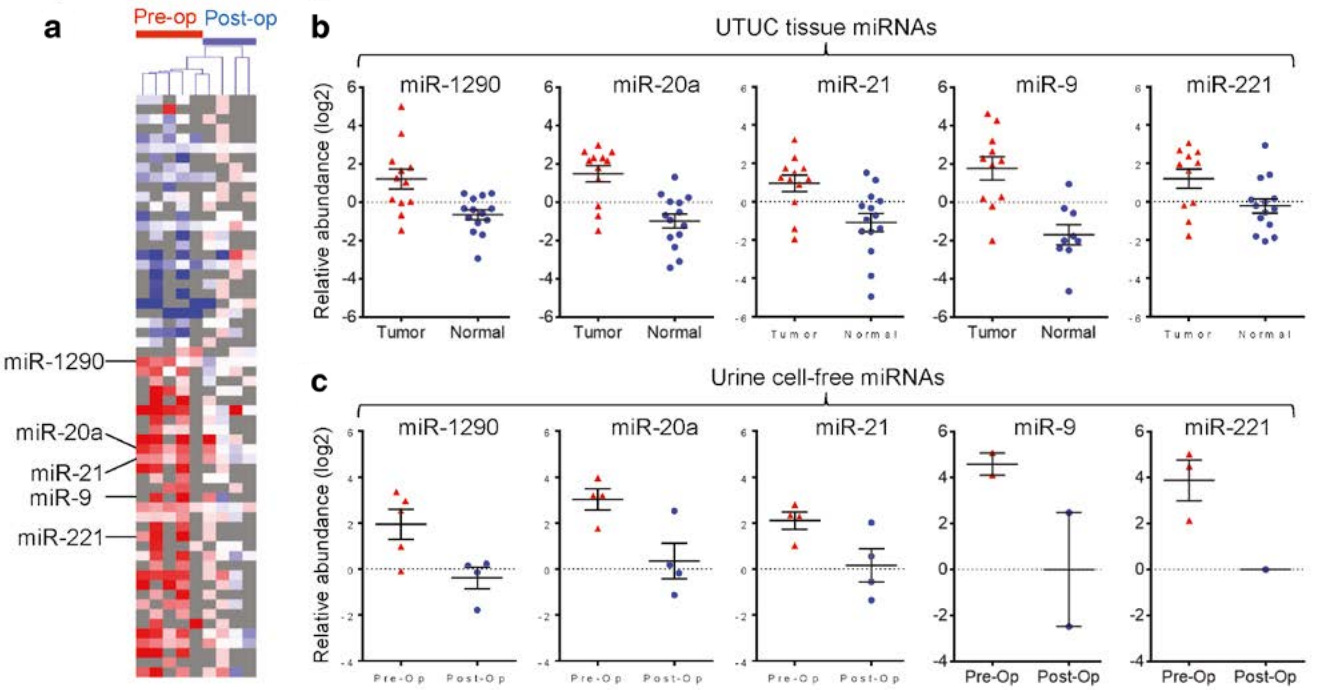
MMB is actively collaborating with the Section of Nutrition and Metabolism (NME) on the Molecular Subtypes of Premenopausal Breast Cancer in Latin American Women (PRECAMA) study (precama.iarc.fr), a multicentre population-based case–control study on breast cancer in young Hispanic women, an understudied group. MMB is screening genomic alterations in tumour samples recruited in PRECAMA to better characterize the molecular features of breast cancer in this population. Preliminary results showed that a majority of tumours were hormone receptor-positive and that *TP53* and *PIK3CA* were the most frequently mutated genes. Interestingly, some unexpected mutational signatures were observed in the *TP53* gene and exome-wide. Further omics analyses of a larger number of cases in the near future will enable the investigation of relationships between genomic characteristics and risk factors.

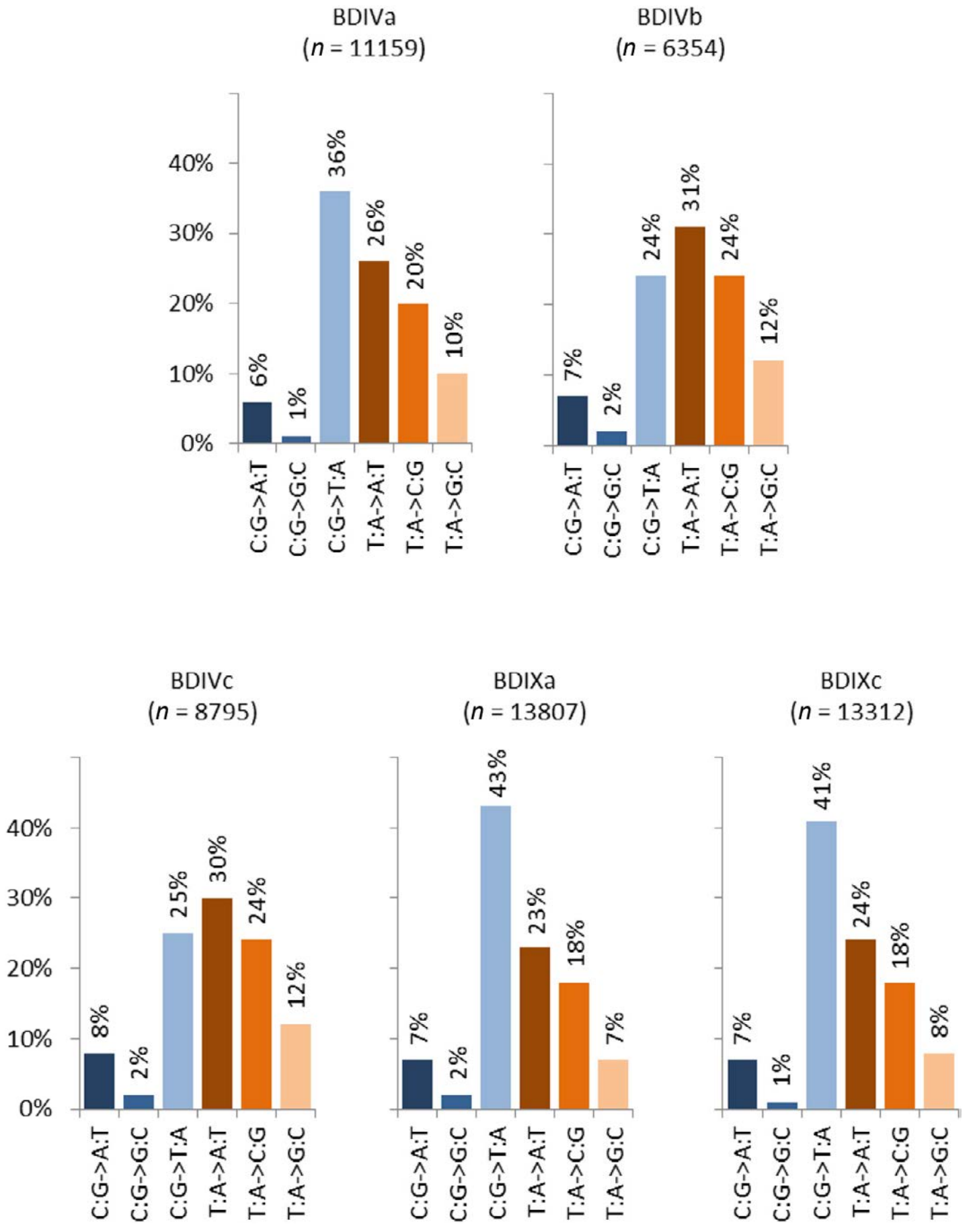
Multiomics analysis of urothelial tumours of patients exposed to aristolochic acid

Ingestion of *Aristolochia* herbs containing aristolochic acid leads to aristolochic acid nephropathy, which is marked by severe renal damage and formation of cancer in the upper urinary tract urothelium, in the renal cortex, and at other anatomical sites. Focusing on

the upper tract urothelial tumours, MMB applied a highly integrative multiomics approach to profile the transcriptomes, the protein levels, and the mutations at both the DNA and RNA levels in these tumours, and to investigate urinary microRNAs as markers of tumour presence. This study generated insights into complex candidate mechanisms of carcinogenesis associated with aristolochic acid, and demonstrated the suitability of urine microRNAs as non-invasive biomarkers of early recurrence of urothelial cancer in patients with aristolochic acid nephropathy (Figure 5), which is potentially applicable to non-invasive surveillance of urothelial cancer development.

Figure 5. Tumour-specific microRNAs (miRNAs) can be detected in the urine of patients with upper tract urothelial carcinoma (UTUC). (a) The heat map shows relative abundance levels of urinary miRNA in urine samples collected before (Pre-op) and after (Post-op) tumour removal surgery. (b) Scatter plots show relative abundance levels of miRNA in the tumour and normal adjacent tissues for five distinct UTUC-specific miRNAs. Error bars present the mean and the standard error of the mean. (c) Scatter plots show relative abundance levels of miRNA in the urine collected before (Pre-op) and after (Post-op) the tumour removal surgery, for five UTUC-specific miRNAs. Error bars present the standard error of measurement around the mean. © IARC.




BDIVa
(n = 11159)
BDIVb
(n = 6354)
BDIVc
(n = 8795)
BDIXa
(n = 13807)
BDIXc
(n = 13312)
40%
30%
20%
10%
0%
6%
1%
36%
26%
20%
10%
7%
2%
24%
31%
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12%
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41%
24%
18%
8%
C:G->A:T
C:G->G:C
C:G->T:A
T:A->A:T
T:A->C:G
T:A->G:C

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until July 2017

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The Section of Molecular Pathology (MPA) conducts original research to elucidate the molecular basis and genetic pathways of human neoplasms. The specific aims of MPA are to provide genetic information that will be used as the basis for future molecular diagnosis and classification of brain tumours, to identify genetic markers for prognosis and novel treatment strategies, and to use genetic data to identify new clues to understand the etiology of human tumours. Genetic studies are carried out, using tumour samples from patients with excellent clinical data which have been collected at a population level or internationally, to provide unique data combining the pathology, genetics, clinical features, and epidemiology of tumours. The research programme of MPA is part of IARC's goals of elucidating the mechanisms of carcinogenesis and understanding the etiology of cancer.

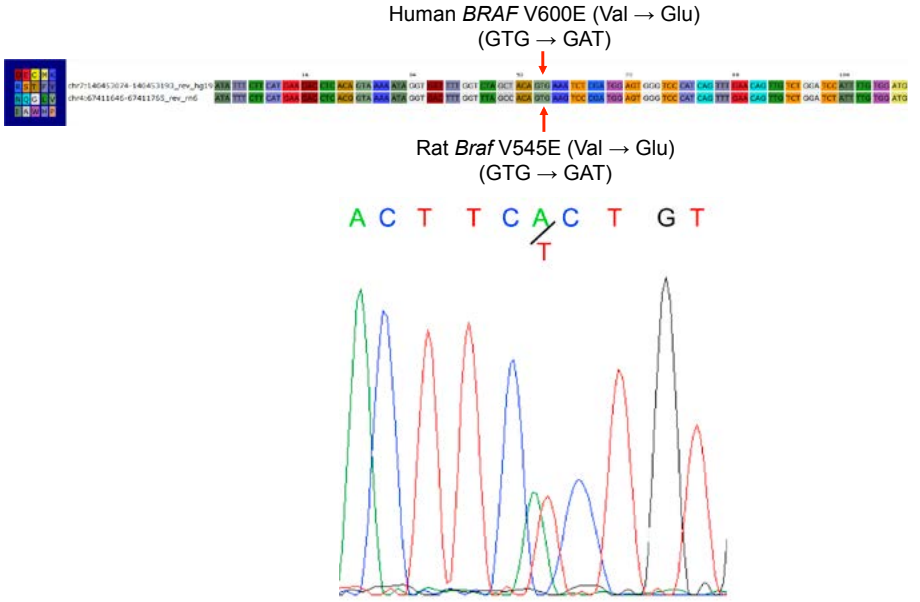
In addition, MPA is responsible for the publication of the World Health Organization (WHO) Classification of Tumours series (WHO Blue Books). MPA works with internationally recognized pathologists from around the world to reach consensus regarding tumour classification. Most human tumours have been diagnosed and classified based on histological features; more recently, molecular markers are increasingly being used to define disease entities, taking advantage of rapid progress in understanding of the genetics of human neoplasms.

Several of the main projects of MPA over the 2016–2017 biennium are detailed here.

Braf mutations initiate the development of rat gliomas induced by postnatal exposure to *N*-ethyl-*N*-nitrosourea

A single dose of *N*-ethyl-*N*-nitrosourea (ENU) during late prenatal or early postnatal development induces a high incidence of malignant schwannomas and gliomas in rats. Although T → A mutations in the transmembrane domain of the *Neu* (*c-ErbB-2*) gene are the driver mutations in ENU-induced malignant schwannomas, the molecular basis of ENU-induced gliomas remained enigmatic. Whole-genome sequencing was performed of gliomas that developed in three BDIV and two BDIX rats exposed to a single dose of 80 mg ENU per kilogram of body weight on postnatal day one. T:A → A:T and T:A → C:G mutations, which are typical for ENU-induced mutagenesis, were predominant (41–55% of all somatic single nucleotide mutations). T → A mutations were identified in all five rat gliomas at *Braf* codon 545 (V545E), which corresponds to the human *BRAF* V600E (Figure 1). Additional screening revealed that 33 gliomas in BDIV rats and 12 gliomas in BDIX rats all carried a *Braf* V545E mutation, whereas peritumoural brain tissue of either strain had the wild-type sequence. The gliomas were immunoreactive to BRAF V600E antibody. These results indicate that *Braf* mutation is a frequent early event in the development of rat gliomas caused by a single dose of ENU (Wang et al., 2016a).

Figure 1. *Braf* mutations initiate the development of rat gliomas induced by postnatal exposure to *N*-ethyl-*N*-nitrosourea (ENU). Whole-genome sequencing revealed that all rat gliomas induced by ENU contain *Braf* V545E mutation, which corresponds to human *BRAF* V600E mutation. Reprinted from Wang et al. (2016a), copyright 2016, with permission from Elsevier.



Population-based study on glioblastoma in the Canton of Zurich, 2005–2009

MPA researchers previously carried out a population-based analysis of patients with glioma diagnosed in 1980–1994 in the Canton of Zurich, Switzerland. To explore changes in outcome, registry data were re-evaluated for patients diagnosed in 2005–2009. Patients with glioblastoma who were diagnosed in 2005–2009 were identified by the Zurich and Zug Cancer Registry. A total of 264 patients with glioblastoma were identified, for an annual incidence of 3.9 per 100 000 people per year, compared with the incidence of 3.7 per 100 000 people per year in the previous study (1980–1994). The mean age of the patients at the time of diagnosis was 59.5 years in the current cohort, compared with 61.3 years previously. The overall survival rate was 46.4% at 1 year, 22.5% at 2 years, and 14.4% at 3 years in the current study, compared with 17.7% at 1 year, 3.3% at 2 years, and 1.2% at 3 years as reported previously. The median overall survival for all patients with glioblastoma was 11.5 months, compared with 4.9 months in the former patient population. The median overall survival was 1.9 months for best supportive care, 6.2 months for treatment with radiotherapy alone, 6.7 months for treatment with temozolomide alone, and 17.0 months for treatment with radiotherapy plus temozolomide. Multivariate analysis revealed that age, Karnofsky performance score, extent of tumour resection, first-line treatment, year of diagnosis, and *MGMT* promoter methylation status were associated with survival in patients with *IDH1* wild-type glioblastoma. The overall survival of patients newly diagnosed with glioblastoma in the Canton of Zurich in Switzerland markedly improved from 1980–1994 to 2005–2009 (Gramatzki et al., 2016).

Genetic alterations in gliosarcoma and giant cell glioblastoma

The majority of glioblastomas develop rapidly with a short clinical history (primary glioblastoma *IDH* wild-type), whereas secondary glioblastomas (*IDH* mutant) progress from diffuse astrocytoma or anaplastic astrocytoma. Gliosarcomas and giant cell glioblastomas are rare histological glioblastoma variants, which usually develop rapidly. The genetic patterns of 36 gliosarcomas and 19 giant cell glioblastomas were determined. *IDH1* and *IDH2* mutations were absent in all 36 gliosarcomas and in 18 of 19 giant cell glioblastomas analysed, indicating that they are histological variants of primary glioblastoma. Furthermore, loss of heterozygosity (LOH) on chromosome 10q (88%) and *TERT* promoter mutations (83%) were frequent in gliosarcomas. Giant cell glioblastomas had LOH 10q in 50% and LOH 19q in 42% of cases. Loss of ATRX expression was detected immunohistochemically in 19% of giant cell glioblastomas, but was absent in gliosarcomas. These and previous results suggest that gliosarcomas are a variant of, and genetically similar to, primary glioblastomas, except for a lack of *EGFR* amplification, and that giant cell glioblastoma occupies a hybrid position between primary and secondary glioblastomas (Oh et al., 2016).

CASP9 germline mutation in a family with multiple brain tumours

A novel *CASP9* germline mutation was identified in a family in which three brain tumours had developed within three generations, including two anaplastic astrocytomas occurring in cousins. The cousins were diagnosed at similar ages (29 and 31 years), and their tumours showed similar histological features. Genetic analysis revealed somatic *IDH1* and *TP53* mutations in both tumours. However, no germline *TP53* mutations were detected, despite the fact that this family fulfils the criteria of Li–Fraumeni-like syndrome. Whole-exome sequencing revealed a germline stop-gain mutation (R65X) in the *CASP9* gene, which encodes caspase-9, a key molecule for the p53-dependent mitochondrial death pathway. This mutation was also detected in DNA extracted from blood samples from the two siblings who were each a parent of one of the affected cousins. Caspase-9 immunohistochemistry showed the absence of caspase-9 immunoreactivity in the anaplastic astrocytomas and normal brain tissues of the cousins. These observations suggest that *CASP9* germline mutations may have played a role, at least in part, in the susceptibility to development of gliomas in this Li–Fraumeni-like family lacking a *TP53* germline mutation.

Figure 2. Working Group members at consensus and editorial meetings for two volumes of the *WHO Classification of Tumours* series: (top) *WHO Classification of Head and Neck Tumours*; meeting held at IARC on 14–16 January 2016; (bottom) *WHO Classification of Tumours of Endocrine Organs*; meeting held at IARC on 26–28 April 2016. © IARC/Roland Dray.

WHO Classification of Tumours series (WHO Blue Books)

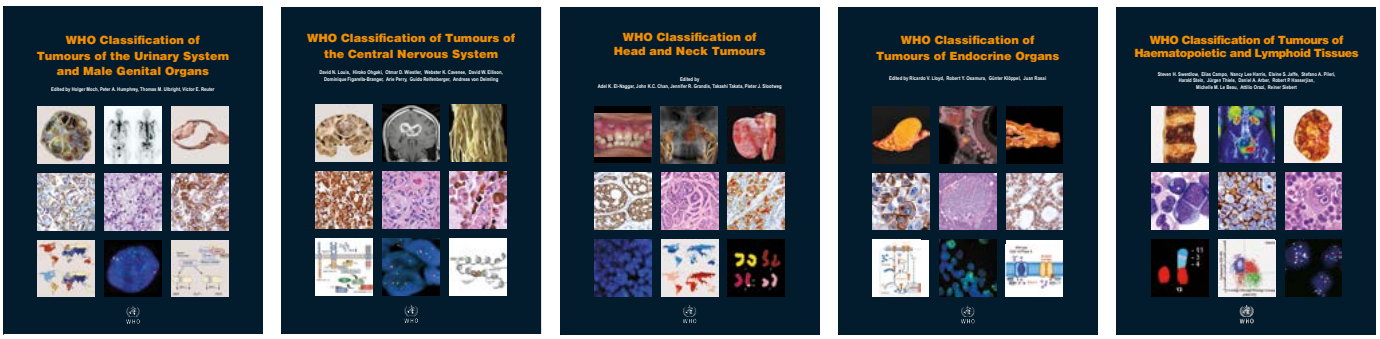
The objective of this project is to establish a histopathological and molecular classification and grading of human tumours that is accepted and used worldwide. Without clearly defined clinical and histopathological diagnostic criteria and, more recently, genetic and expression profiles, epidemiological studies and clinical trials are difficult to conduct. Therefore, this project is of great importance not only for pathology communities but also for cancer registration, epidemiological studies, clinical trials, and cancer research in general.

IARC has been responsible for this project since the third edition (2000–2005; 10 volumes). The current (fourth) edition of the *WHO Classification of Tumours* series was initiated in 2006 with four series editors (Dr Fred Bosman, Dr Elaine Jaffe, Dr Sunil Lakhani, and Dr Hiroko Ohgaki). So far, 10 volumes and 2 revisions have been published, and for each volume, 15 000–50 000 copies were printed and distributed worldwide. In 2016–2017, the following five volumes were published (Figures 2 and 3).

WHO Classification of Tumours of the Urinary System and Male Genital Organs. This volume was prepared by four volume editors (Dr Holger Moch, Dr Peter A. Humphrey, Dr Thomas M. Ulbright, and Dr Victor E. Reuter) and 110 contributors from 21 countries. The consensus and editorial meeting was held on 11–13 March 2015 in Zurich, Switzerland, in collaboration with the University of Zurich. The volume was published in January 2016.

WHO Classification of Tumours of the Central Nervous System. This volume was the revision of the fourth edition (published in 2007) and was prepared by four volume editors (Dr David N. Louis, Dr Hiroko Ohgaki, Dr Otmar D. Wiestler, and Dr Webster K. Cavenee), five senior advisors (Dr David W. Ellison, Dr Dominique Figarella-Branger, Dr Arie Perry, Dr Guido Reifenberger, and Dr Andreas von Deimling), and 122 contributors from 19 countries. The consensus and editorial meeting was held on 21–24 June 2015 in Heidelberg, Germany, in collaboration with the

Figure 3. Covers of the five volumes of the *WHO Classification of Tumours* series published in 2016–2017: *WHO Classification of Tumours of the Urinary System and Male Genital Organs*, fourth edition (January 2016); *WHO Classification of Tumours of the Central Nervous System*, revised fourth edition (May 2016); *WHO Classification of Head and Neck Tumours*, fourth edition (January 2017); *WHO Classification of Tumours of Endocrine Organs*, fourth edition (June 2017); and *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*, revised fourth edition (September 2017).

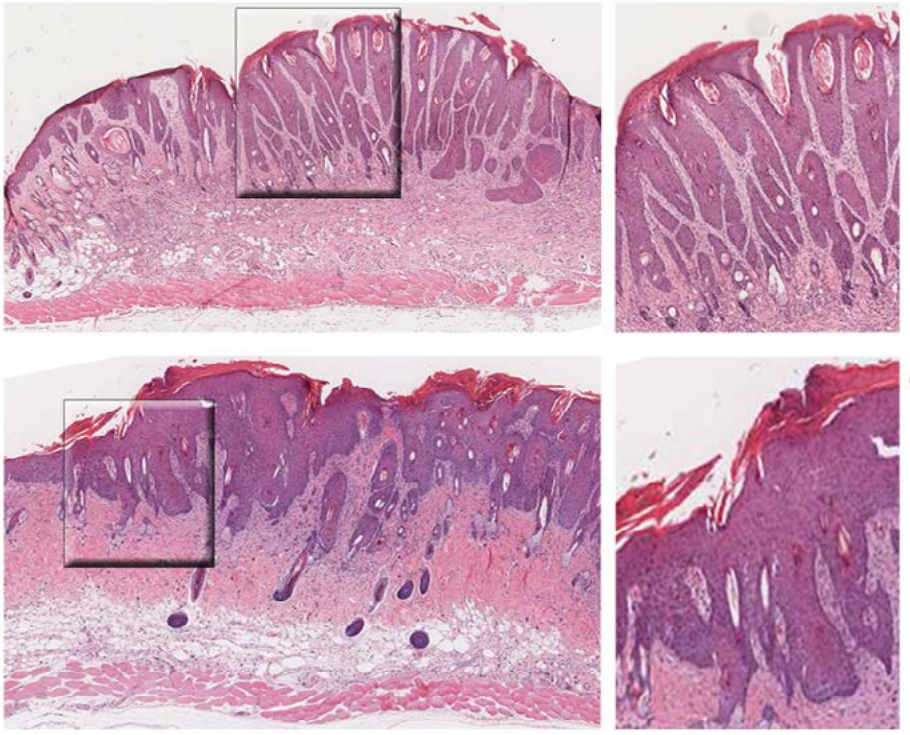


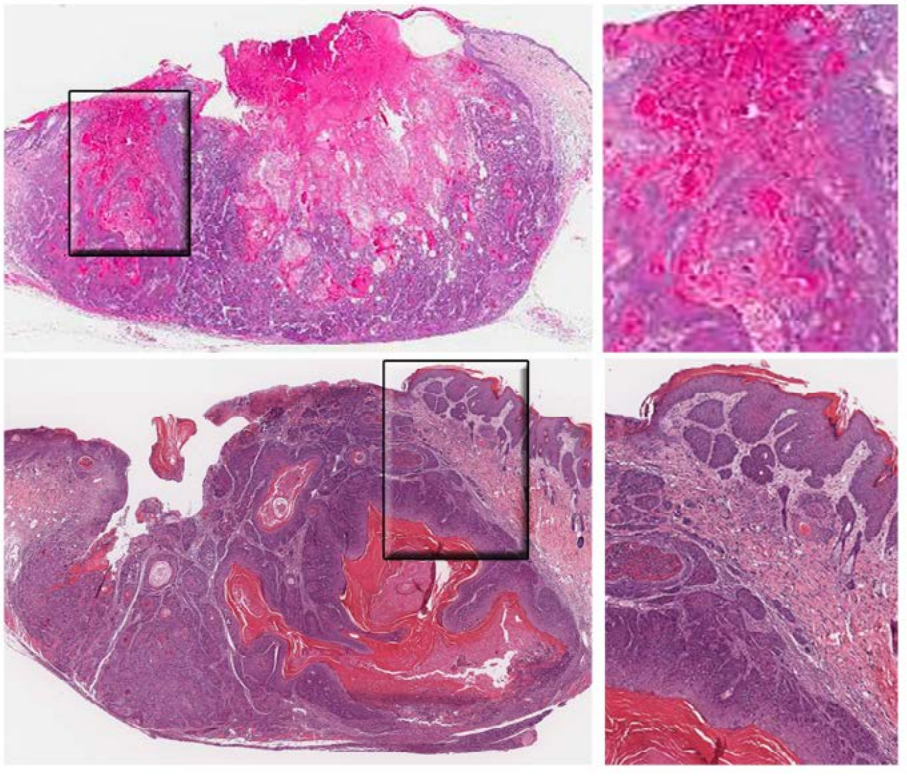
German Cancer Research Center (DKFZ). The volume was published in May 2016.

WHO Classification of Head and Neck Tumours. This volume was prepared by five volume editors (Dr Adel K. El-Naggar, Dr John K.C. Chan, Dr Jennifer R. Grandis, Dr Takashi Takata, and Dr Pieter J. Slootweg) and 135 contributors from 35 countries. The consensus and editorial meeting was held at IARC on 14–16 January 2016, and the volume was published in January 2017.

WHO Classification of Tumours of Endocrine Organs. This volume was prepared by four volume editors (Dr Ricardo V. Lloyd, Dr Robert Y. Osamura, Dr Günther Klöppel, and Dr Juan Rosai) and 166 contributors from 25 countries. The consensus and editorial meeting was held at IARC on 26–28 April 2016, and the volume was published in June 2017.

WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. This volume was the revision of the fourth edition (published in 2008) and was prepared by seven volume editors (Dr Steven H. Swerdlow, Dr Elias Campo, Dr Nancy Lee Harris, Dr Elaine S. Jaffe, Dr Stefano A. Pileri, Dr Harald Stein, and Dr Jürgen Thiele), five senior advisors (Dr Daniel A. Arber, Dr Robert P. Hasserjian, Dr Michelle M. Le Beau, Dr Attilio Orazi, and Dr Reiner Siebert), and 132 contributors from 23 countries. The volume was published in September 2017.





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Ms Eliane Rohner

The Section of Infections (INF) consists of two groups: the Infections and Cancer Biology Group (ICB) and the Infections and Cancer Epidemiology Group (ICE). The research activities of both Groups aim to evaluate the role of infectious agents in human cancers through biological and epidemiological studies.

ICB uses in vitro and in vivo experimental models and focuses on (i) the characterization of the transforming properties of well-established and novel potential oncogenic viruses, and (ii) the evaluation of possible cooperation between viruses and other environmental risk factors,such as ultraviolet (UV) radiation, in promoting cancer development (Hernandez-Vargas et al., 2017; Mattoscio et al., 2017; Pacini et al., 2017). In addition, ICB collaborates intensively with epidemiologists at IARC and worldwide, offering many diagnostic laboratory assays for the detection of more than 200 infectious agents in human specimens (Donà et al., 2016; Anantharaman et al., 2017; Gheit et al., 2017a; Hampras et al., 2017; Moscicki et al., 2017).

ICE focuses on (i) the prevention of cervical cancer through human papillomavirus (HPV) vaccination and HPV-based screening, with a focus on low- and middle-income countries (LMICs) (Schiffman et al., 2016; Vaccarella et al., 2016a); (ii) the natural history of infection-associated cancers, with a particular focus on HIV-positive populations, among whom immunodeficiency tends to worsen the outcome of oncogenic viral infections (Clifford et al., 2017b; Combes et al., 2017b; Franceschi and Clifford, 2017); and (iii) quantitative methods to estimate cancer burden and model the impact of interventions, particularly for infection-associated malignancies (Plummer et al., 2016) and thyroid carcinoma.

In addition, ICB and ICE have several collaborative studies to further characterize the natural history of mucosal high-risk (HR) HPV infection and other oncogenic viruses in the oral cavity, with the final aim of better defining the role of viral infections in the etiology of head and neck cancers.

Infections and Cancer Biology Group (ICB)

Beta HPV types and non-melanoma skin cancer

To date approximately 50 different beta HPV types have been fully characterized, which have been isolated mainly from the skin of healthy individuals. The first beta HPV types were identified in the skin of individuals with a genetic disorder, epidermodysplasia verruciformis (EV), which confers high susceptibility to beta HPV infection and UV-induced non-melanoma skin cancer (NMSC). Many epidemiological and biological findings now support the role of beta HPV in skin carcinogenesis, also in non-EV individuals (Tommasino, 2017; Viarisio et al., 2017a). ICB's previous studies in a transgenic (Tg) mouse model demonstrated that the expression of beta HPV38 early oncogenes, E6 and E7, in the basal layer of the epidermis strongly increases the susceptibility to UV-induced skin carcinogenesis (Viarisio et al., 2017a). Recent findings provide additional support for the role of beta HPV38 in skin cancer development (Viarisio et al., 2017b). Patients with metastatic melanoma harbouring a specific *BRAF* mutation are effectively treated with a BRAF inhibitor (vemurafenib or dabrafenib). However, as a side-effect, a proportion of these patients develop NMSC, which is in part attributed to beta HPV infections in the skin (Tommasino, 2017). Consistently with the scenario in humans, we observed in HPV38 E6/E7 Tg mice that vemurafenib treatment strongly enhanced the development of skin malignant lesions induced by UV (Viarisio et al., 2017b).

In other mechanistic studies, ICB has provided a possible explanation for the cooperation of HPV38 E6 and E7 oncoproteins and UV irradiation in promoting NMSC (Viarisio et al., 2016; Pacini et al., 2017). Indeed, the two viral oncoproteins deregulate cellular pathways known to be activated by stress induced by UV. In normal skin, UV irradiation leads to activation of the inflammasome, with consequent secretion of interleukin 18 (IL-18). In Tg animals, HPV38 E6 and E7 oncoproteins decrease the expression of IL-18 induced by UV irradiation (Viarisio et al., 2016).

UV irradiation also activates, via p53, the expression of Toll-like receptor 9 (TLR9), which in turn senses endogenous ligands generated during the stress, such as damage-associated molecular patterns (Pacini et al., 2017). HPV38 E6 and E7 severely affect the TLR9 expression induced by UV irradiation, altering the functions of p53 (Pacini et al., 2017).

A possible model is that beta HPV types play a role at an early stage of carcinogenesis, facilitating the accumulation of UV-induced mutations in the host genome, which in turn can lead to cellular transformation.

Biology and epidemiology of β-3 HPV types

Recent studies have shown that, in addition to the skin, beta HPV types can be detected in the oral cavity, anal canal, and external genital sites (Donà et al., 2016; Hampras et al., 2017; Smelov et al., 2017a). Beta HPV types are subdivided into five different species: β-1, β-2, β-3, β-4, and β-5. The β-1 and β-2 species comprise the majority of the beta HPV types that are abundantly present in the skin of normal individuals and have been linked to NMSC. In contrast, the β-3

species includes only four HPV types, HPV49, 75, 76, and 115, which appear to infect cutaneous and mucosal epithelia (Hampras et al., 2017). Interestingly, HPV49 E6 and E7 display some functional similarities to mucosal high-risk HPV16 oncoproteins (Viarisio et al., 2016, 2017a). HPV49 or HPV16 E6/E7 Tg mice are highly susceptible to upper digestive tract carcinogenesis upon initiation with 4-nitroquinoline 1-oxide (4NQO), a molecule that mimics exposure to tobacco products. In contrast, wild-type animals as well as β-2 HPV38 E6/E7 Tg mice are not significantly affected by 4NQO treatment. Together, these data highlight biological differences in the beta HPV group. Future molecular and epidemiological studies are warranted to further confirm the mucosal tropism of β-3 HPV types and their possible link to human diseases.

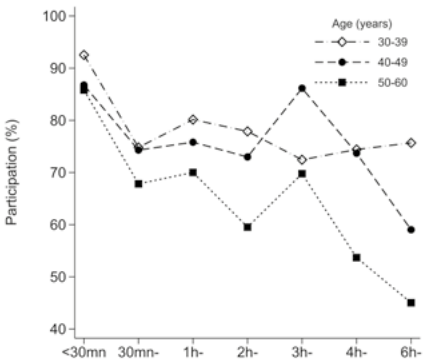
Infections and Cancer Epidemiology Group (ICE)

HPV-based screening and HPV vaccination in LMICs

In Bhutan, HPV testing improved the performance of cervical screening over cytology (Tshomo et al., 2017a), and HPV-based screening of 2500 women using self-collected samples achieved high coverage in rural areas (Baussano et al., 2017c), although the participation rate was inversely related to age and travel time to the screening centre; travelling to the centre was often challenging (Figure 1). In Rwanda, a pre-vaccination cervical cell survey of women older than 20 years revealed a high prevalence of HPV and cervical disease, worsened by HIV (Ngabo et al., 2016). In both countries, a urine survey to monitor vaccine effectiveness already showed decreases in the prevalence of HPV among young women 3 years after the introduction of HPV vaccination (Franceschi et al., 2016).

Using our dynamic HPV transmission model, we predicted that the indirect protection provided by vaccinated individuals to unvaccinated individuals (herd immunity) differs by HPV type and population. Indeed, HPV16 is more difficult to eliminate from the population than the other high-risk types, because of its greater ability to persist and induce

Figure 1. Effect of travel time (on foot) on participation rate in cervical cancer screening in Bhutan in 2016, by age group. Figure reprinted from Baussano et al. (2017a). © Baussano et al., 2017.



Cervical cancer prevention in Bhutan and Rwanda

For a long time, ICE has been engaged in cervical cancer prevention in many low- and middle-income countries. Since 2010, ICE has worked especially with the ministries of health and public hospitals in Bhutan and Rwanda to strengthen screening activities and monitor human papillomavirus (HPV) vaccination.

Several capacity-building initiatives in 2016–2017 have focused on the training of local staff and the transfer of medical technologies. For instance, ICE supported the introduction of HPV DNA-based cervical cancer screening in Bhutan and performed validation studies on HPV test accuracy in Bhutan and Rwanda. Capacity-building initiatives were especially crucial to make the new diagnostic technologies available in typically underserved rural populations. In both countries, training courses were organized and medical equipment provided to improve the diagnosis and treatment of cervical lesions identified during screening.

Finally, ICE helped create computerized medical databases and biobanks of urine samples, cervical cells, and cancer tissue samples and facilitated exchanges between local and international experts at IARC and at international scientific meetings. A few master's students and doctoral students from Bhutan and Rwanda are being supervised by ICE staff, and many more have had the chance to spend short periods at IARC or attend the IARC Summer School.

A Bhutanese nurse on her way to a rural health centre to perform cervical cancer screening. © Chhimi Wangmo.

malignant transformation (Baussano et al., 2017b). Furthermore, HPV control is harder when pre-vaccination HPV prevalence is high (Baussano et al., 2017a). In LMICs where sexual behaviour is based on traditional norms, it is advantageous to introduce vaccination while HPV prevalence in young women is low, anticipating any increase that may occur with liberalization of social attitudes (Baussano et al., 2016).

Variations in HPV prevalence by HIV status and body site

ICE performed large international systematic reviews that showed the predominance of HPV16 in cervical cancer and precancer in HIV-positive women (Clifford et al., 2016a, 2017a). Furthermore, the ICE cervical cancer biobank contributed to a whole viral genome sequencing effort of 5570 HPV16-infected samples, showing that strict conservation of the 98 bp of the HPV16 *E7* gene is critical for cervical carcinogenesis (Mirabello et al., 2017). ICE also showed that HPV infection is infrequent in tonsil brushings of cancer-free children and adults, whereas HPV infection in gargles in adults is rather common (Combes et al., 2017b). Low agreement in paired tonsil brushings and gargles suggests that gargle is not representative of HPV prevalence in the tonsils, where the majority of HPV-related oropharyngeal cancer is located (Lacau St Guily et al., 2017).

Global burden of cancer due to infections

Of 14 million new cancer cases in 2012, approximately 2.2 million (15%) were attributable to carcinogenic infections (Plummer et al., 2016), mainly *Helicobacter pylori*, HPV, and hepatitis B and C viruses. The attributable fractions for infection varied from less than 5% in the USA, Canada, Australia, New Zealand, and some countries in western and northern Europe to more than 50% in some countries in sub-Saharan Africa. HPV alone accounts for 630 000 cancer cases per year (Table 1), 9% of all cancers in women and less than 1% of all cancers in men (de Martel et al., 2017). Cervical cancer accounts for 83% of HPV-attributable cancer cases, two thirds of which occur in less developed countries. Other HPV-attributable ano-genital cancers include cancer of the vulva (8500 cases), vagina (12 000), anus (35 000, of which half occur in men), and penis (13 000) (Table 1). HPV-attributable head and neck cancers represent 38 000 cases, of which 21 000 are oropharyngeal cancers occurring in more developed countries.

Overdiagnosis of thyroid cancer

The experience in cervical cancer led ICE to assess other cancers for which the incidence is rapidly changing, such

Table 1. Number of all cancer cases attributable to human papillomavirus (HPV) and corresponding attributable fraction (%) for all cancers, by cancer site(s), sex, and age group; world, 2012. Table reproduced from de Martel et al. (2017). © 2017 IARC/WHO; licensed by UICC.

HPV-related cancer site (ICD-10 code)	Number of incident cases[a,b]	Number attributable to HPV	Attributable fraction (%)	Number attributable to HPV by sex		Number attributable to HPV by age group		
				Males	Females	< 50 years	50–69 years	≥ 70 years
Cervix uteri (C53)	530 000	530 000	100.0	0	530 000	250 000	220 000	58 000
Anus[c] (C21)	40 000	35 000	88.0	17 000	18 000	6 600	17 000	12 000
Vulva[c] (C51)	34 000	8 500	24.9	0	8 500	2 600	3 400	2 500
Vagina[c] (C52)	15 000	12 000	78.0	0	12 000	2 500	5 200	3 900
Penis[c] (C60)	26 000	13 000	50.0	13 000	0	2 700	5 800	4 400
Oropharynx[c] (C01, C09–10)	96 000	29 000	30.8	24 000	5 500	5 400	18 000	6 000
Oral cavity[c] (C02–06)	200 000	4 400	2.2	2 900	1 500	890	2 300	1 200
Larynx (C32)	160 000	3 800	2.4	3 300	460	420	2 200	1 200
Other pharynx[c] (C12–C14)	78 000	0	0	—	—	—	—	—
Total HPV-related sites	1 200 000	630 000	54.0	60 000	570 000	270 000	270 000	88 000

ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision.

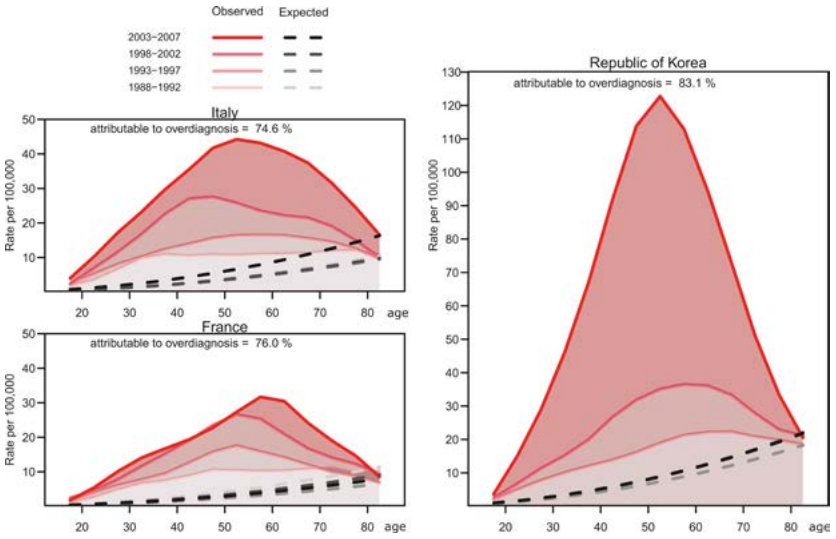
[a] Source of data: Ferlay et al. (2013). GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: IARC. Available from: http://globocan.iarc.fr.

[b] Numbers are rounded to two significant digits.

[c] These cancer sites were not directly available in GLOBOCAN 2012; therefore, data from the Cancer Incidence in Five Continents, Volume X (CI5-X) database were used to estimate the corresponding number of cases. Source of data: Forman D et al., editors (2013). Cancer Incidence in Five Continents, Vol. X (electronic version). Lyon: IARC. Available from: http://ci5.iarc.fr.

as thyroid carcinomas. ICE provided indirect evidence that the vast increases in the numbers of differentiated thyroid carcinoma in the past two decades are due largely to overdiagnosis of tumours that would not cause symptoms or death during a person's lifetime (Vaccarella et al., 2016b). Increasing use of ultrasonography and other imaging techniques may have been responsible for approximately 470 000 extra cases of thyroid carcinoma in women and 90 000 in men in 12 well-studied high-income countries. Figure 2 shows the progressive rise in the incidence of thyroid carcinoma in young and middle-aged adults in three countries that have been especially affected by the thyroid carcinoma epidemic. Of note, most patients with thyroid carcinoma undergo total thyroidectomy and other harmful treatments.

Figure 2. Rises in age-specific incidence of thyroid cancer per 100 000 women, 1988–2007. The pink area of the curves above the bold dashed line represents the part of disease attributable to overdiagnosis in different periods. Figure adapted from Vaccarella et al. (2016b). Copyright © 2016, Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.



Chrysotile processing facility. © IARC/Joachim Schüz

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The overall objectives of the Section of Environment and Radiation (ENV) are to investigate environmental, lifestyle, occupational, and radiation-related causes of cancer and death from cancer in human populations. With this wide remit, ENV focuses its endeavours in three main areas: (i) research in settings where levels of exposure to putative or established carcinogens are high, and research is thus warranted; (ii) studies of common cancers and of specific exposures occurring in under-researched settings, particularly but not exclusively in low- and middle-income countries (LMICs); (iii) studies evaluating the role of broader social as well as biological factors throughout the course of the disease. The objectives of ENV are achieved through the conduct of collaborative international epidemiological studies, including coordination of international consortia or through the initiation of targeted individual analytical epidemiological studies. In selecting projects, an effort is made to ensure that the involvement of the Agency makes a specific and substantial difference, by facilitating international collaboration, by overcoming political barriers, by assisting local collaborators in targeted studies with expertise and with increased local visibility and trust in their work, and by using the general expertise, international network, and special function of the Agency as part of WHO.

With a strong focus on environmental (including occupational and radiation-related) and lifestyle risk factors, ENV fills a major research gap to further understand the cancer burden attributed to these factors. Although estimates vary, in developed countries up to 50% of cancers are potentially preventable. The remaining half, with an unknown etiology to date, may have a larger contribution

from environmental factors than current research has established. ENV has steered its research focus to LMICs in particular, a direction that is warranted because in these settings, levels of environmental pollution are often higher and occupational protection regulations are often lacking or not adhered to. Capacity-building as well as establishing research platforms is another vision of IARC to which ENV contributes through its conduct of research in under-researched settings.

Key questions currently studied in ENV involve asbestos and other lung carcinogens, pesticides, uranium, ionizing radiation (environmental, occupational, and medical), and non-ionizing radiation (electromagnetic fields) as main exposures, as well as cancer types with unusual geographical occurrence in relation to the environmental or lifestyle-related contribution to causes or prognosis, such as breast cancer, oesophageal cancer, childhood cancer, testicular cancer, and thyroid cancer. Selected examples are described here.

In utero irradiation and subsequent risk of cancer

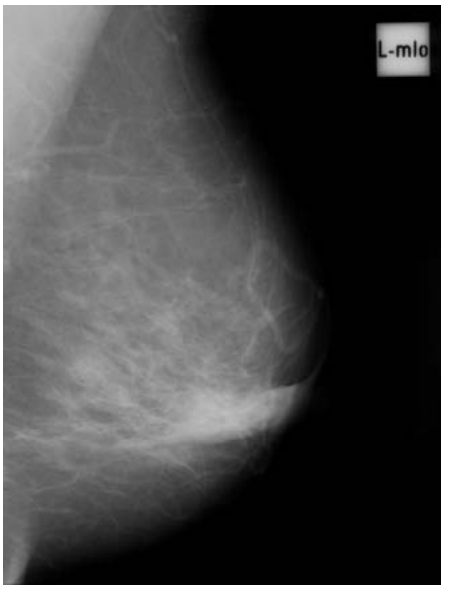
Two cohorts from the Southern Urals – offspring of female workers of one of the country's largest nuclear facilities (Mayak Production Association, Ozyorsk) and of women living in areas along the Techa River (Figure 1) contaminated by nuclear accidents and nuclear waste dumping – were analysed to estimate the lifetime risk of cancer related to in utero exposure to irradiation (Deltour et al., 2016; Krestinina et al., 2017). The combined cohort had a total of about 20 000 subjects, and follow-up lasted to the maximum age of 61 years. The highest in utero exposures were more than 1 Gy. A weak positive association was observed with incidence of haematological malignancies (Schüz et al., 2017), whereas for solid cancers no association was seen (Akleyev et al., 2016). Postnatal exposure to ionizing radiation showed an association with solid cancer but not with haematological malignancies. Because the cancer peak in the cohort is expected to occur in the next 10 years, a new project with further follow-up of this unique cohort is recommended.

Figure 1. The Techa River as seen from the highway between Yekaterinburg and Chelyabinsk in the Southern Urals, Russian Federation. In the 1950s, nuclear waste from the nearby Mayak Production Association – one of the country's biggest nuclear facilities – was dumped into the river, leading to major radioactive contamination of residents of the riverside villages, including irradiation of the fetus in women who were pregnant during that time. ENV, together with colleagues from the Urals Research Center of Radiation Medicine (URCRM), Chelyabinsk, and the Southern Urals Biophysics Institute (SUBI), Ozyorsk, has analysed the cancer risk of offspring exposed in utero. © IARC/Joachim Schüz.

Changes in breast density with age seen internationally

Breast density, a measure of the amount of dense tissue compared with fatty tissue in the breast, is a strong marker of breast cancer risk. Determinants of breast density have been studied in high-income countries but not in women worldwide. ENV initiated the International Consortium of Mammographic Density (ICMD), with the collection of images to centrally assess mammographic density based on almost 12 000 mammograms from 27 studies in 22 countries (Burton et al., 2016) (Figure 2). One aim was to study how breast density differed by age and menopausal status. Regardless of the country and ethnic group, breast density was much lower in postmenopausal women than in premenopausal women of the same age (Burton et al., 2017). In addition, as a relative proportion of breast area, breast density was lower in older women among both premenopausal and postmenopausal women. Among premenopausal women, breast density changed with age without an increase in breast area, but among

Figure 2. Mammograms used in the International Consortium of Mammographic Density (ICMD) project, coordinated by ENV. For the joint analyses, three readers evaluated almost 12 000 mammograms, i.e. indicating on the image the dense area of the breast and breast edges, for the calculation of dense area, non-dense area, breast area, and percentage density. © IARC/Valerie McCormack.



postmenopausal women, there was also an increase in breast area. The consistency of these changes in breast density with age internationally suggests that the change is due to a universal biological mechanism inherent to all women. If cumulative breast density is a key determinant of breast cancer risk, younger ages may be the more critical exposure periods for primary prevention research efforts to identify lifestyle modifications aimed at reducing breast density and later breast cancer risk.

High occurrence of oesophageal squamous cell carcinoma in East Africa

Oesophageal squamous cell carcinoma (ESCC) is among the three most common cancers in most of East Africa. However, the etiology in this African ESCC corridor is little understood and has hardly been studied. ENV has initiated a spectrum of ESCC research in Africa, including Kenya, the United Republic of Tanzania, Malawi, and Ethiopia, with the perspective of investigating a broad range of factors, prioritizing factors that have been identified as established or probable ESCC carcinogens, and interpreting findings from both a local and an Africa-wide perspective (McCormack et al., 2016). Candidate risk factors include consumption of hot beverages (Figure 3), nutrient deficiencies, and alcohol consumption and tobacco use, the roles of which may have been underestimated in some of the settings. The ENV-led African consortium initiated for these epidemiological studies (ESCCAPE) is a prominent example of research coupled with capacity-building, training, knowledge transfer in both directions, and fostering collaboration (see text box).

Figure 3. Consumption of hot tea, especially milky tea, may be an important and modifiable risk factor for oesophageal squamous cell carcinoma (ESCC) in the United Republic of Tanzania. The contribution of this habit to the risk of ESCC needs to be evaluated in this setting, jointly with that of the many risk factors that act synergistically in this multifactorial disease. A cross-sectional study initiated by ENV showed that participants started drinking at a mean temperature of 70.6 °C, which exceeds that in all previous studies. © IARC/Valerie McCormack.

The ESCCAPE project

Oesophageal squamous cell carcinoma (ESCC) in East Africa is a neglected research area, despite the fact that it is the most common cancer in some of Africa's oesophageal cancer hot spots. Extremely poor prognosis makes primary prevention through modification of risk factors essential, in addition to screening for early disease. However, in Africa, there are no robust data to inform either of these efforts.

ENV initiated the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESCCAPE) consortium of unified case–control studies on risk factors in Eldoret (Kenya), Moshi (United Republic of Tanzania), Blantyre (Malawi), and Ethiopia (pilot stage), which is in the process of merging and expanding with other activities on ESCC in sub-Saharan Africa. In addition to the core work, effects on capacity-building, training, and international collaboration were of equal importance and beneficial to all partners. Short-term fellowships at ENV enabled training of African partners in methodology, joint analytical work, and building up of international research partnerships. Regular visits of ENV personnel to Africa enabled the training of local staff in methodology and fieldwork in these settings. Pathology training by an IARC senior pathologist was held for local pathologists. Creating the network, including clinicians, fostered exchange in matters of diagnostics, dealing with patients, and palliative care, creating a platform to learn from each other.

Participants in the kick-off meeting of the oesophageal squamous cell carcinoma study as part of the ESCCAPE project, held in October 2015 at the Kilimanjaro Clinical Research Institute (KCRI), Moshi, United Republic of Tanzania. © Mr Kennedy Ngowi, KCRI.

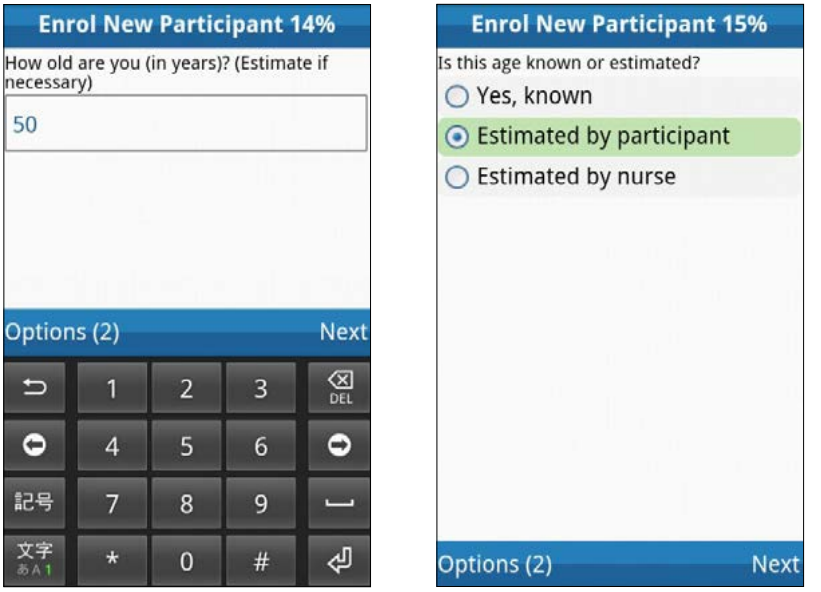
Enabling follow-up studies in Africa with the implementation of mHealth technologies

Breast cancer is the most common cancer in women in sub-Saharan Africa, with the burden projected to double between 2012 and 2030 as a result of population ageing and expansion. Prognosis is poor, and an understanding is needed of the determinants of breast cancer outcomes. ENV aims to fill this knowledge gap by conducting, across multiple African settings, a comprehensive study of a woman's entire journey with and after breast cancer: the African Breast Cancer–Disparities in Outcomes (ABC-DO) study (McKenzie et al., 2016a). The study aims to provide information about when and how to implement strategies to improve breast cancer survival, through an understanding of context-specific societal, health systems, and individual-level barriers to early detection, diagnosis, and appropriate treatment.

ENV has embraced the use of modern technologies for the implementation of epidemiological studies, especially those involving fieldwork, by using mobile health (mHealth) technologies throughout (Figure 4). The first of these was ABC-DO, which is an almost paperless mHealth implemented study. Mobile phones are used for face-to-face immediate data input and also to conduct follow-up and batch-send text messages to participants. This has several significant advantages, which all lead to improved efficiency, speed, and quality. Notably, ENV and local investigators have real-time access to live data, and thus quality control can be conducted immediately and any issues resolved in a very short time frame. The app also improves data completeness. Because researchers can monitor recruitment in real time, they are up to date with study progress and can contact local collaborators with any queries. Finally, the app also acts as a pre-programmed study protocol to implement study management uniformly across sites. For example, for the regular follow-up calls that need to be made to all women in the ABC-DO study, the app automatically sends an alert to the site's phone with a reminder of who to call.

Another major advantage is the close interaction between the teams, which is highly motivating for those doing the fieldwork, especially in settings where experience in larger-scale fieldwork is lacking (Figure 5). Finally, mHealth is a breakthrough for the first population-based study in Africa of this kind, because no other means of communication exist, and for women who do not return to the hospital, the course of disease would otherwise not be known.

Figure 4. Screenshot of the app developed for the African Breast Cancer–Disparities in Outcomes (ABC-DO) study, coordinated by ENV in five countries in sub-Saharan Africa: Namibia, Nigeria, South Africa, Uganda, and Zambia. © IARC/Valerie McCormack.



Low impact of parental exposures to chemicals on risk of testicular cancer in the offspring

The incidence of testicular cancer has increased rapidly and has shown temporal and geographical variations, suggesting an etiological role of environmental factors. Parental occupational exposure before the child's birth or maternal

Figure 5. Research nurses in Uganda enjoying the interviewer training using the app developed for the African Breast Cancer–Disparities in Outcomes (ABC-DO) study. The real-time data assessment enables a closer link between the local collaborators and their ENV partners thousands of miles away. © IARC/Fiona McKenzie.

exposure during pregnancy may play a role, in particular exposures to agents with potential endocrine-disrupting capabilities. In a registry-based linkage study in the Nordic countries with almost 10 000 cases of testicular cancer, no overall association was observed between paternal or maternal exposure to pesticides and the risk of testicular cancer in their offspring. For solvents, no association was seen with paternal exposure, but maternal exposure to aromatic hydrocarbon solvents was associated with a modest increase in risk (Le Cornet et al., 2017). Furthermore, the study provided little evidence of associations between parental exposures to heavy metals or welding fumes and testicular cancer risk, with the potential exception of high paternal exposure to chromium (Togawa et al., 2016). Overall, this study cannot exclude weak associations between parental occupational exposures and testicular cancer risk in the offspring, but if those associations were causal, they would explain only a small proportion of cases.

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Ms Coralie Morel (until June 2016)
Ma Agata Muzsik (until April 2017)
Ms Flavie Perrier (until June 2016)
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The Section of Nutrition and Metabolism (NME) comprises the Biomarkers Group (BMA), the Nutritional Epidemiology Group (NEP), and the Nutritional Methodology and Biostatistics Group (NMB). The Section combines large-scale population-based studies with laboratory and biostatistical expertise to identify causal links between nutrition, metabolic factors, and cancer. The goal of NME is to provide robust evidence on the role of nutrition in cancer development that can translate to clinical interventions and public health policy.

After the retirement of Dr Isabelle Romieu and the arrival of Dr Marc Gunter in February 2016, the Section was reorganized to align with its new research priorities. Greater emphasis has been placed on conducting molecular research that integrates omics data, including metabolomics, hormone measurements, genomics, and epigenomics within population-based cohorts in Europe as well as in low- and middle-income countries. NME also benefits from extensive international collaborations and leads projects in international consortia comprising millions of study participants. Major research themes within the Section include understanding the biological basis for the link between obesity, metabolic dysfunction, and cancer; identifying nutritional biomarkers and metabolic fingerprints of diet through interventions and observational studies and studying their relationship with cancer; and studies on multimorbidity that identify common pathways underlying the development of cancer, diabetes, and cardiovascular disease.

Biomarkers Group (BMA)

Biomarkers of meat consumption

A human intervention study was conducted in collaboration with Imperial College London and University College Dublin to identify biomarkers of meat and fish intake using a metabolomic approach based on high-resolution mass spectrometry (Cheung et al., 2017). Several compounds detected in urine or blood were found to be highly specific for intake of chicken (3-methylhistidine and anserine), fish (trimethylamine-*N*-oxide), and red meat (acylcarnitines and carnosine). These markers were also found to accurately predict intake of the same foods in 475 subjects from the European Prospective Investigation

into Cancer and Nutrition (EPIC) cross-sectional study (Figure 1).

Exposome-Explorer

Exposome-Explorer, a new database on biomarkers of exposure to environmental risk factors, was developed and is available in the public domain (Figure 2) (Neveu et al., 2017). This database contains detailed information collected from peer-reviewed publications on the nature of 692 dietary and pollutant biomarkers, more than 10 000 concentration values in various populations, and data on correlations with food intake and on biological reproducibility over time. This database also enables the comparison of the performance of biomarkers of exposure for various dietary factors – information that can be used to define panels of biomarkers for dietary-wide association studies on cancer.

Biomarkers of mammographic density

Associations between circulating leptin and adiponectin and mammographic density were evaluated in Mexican premenopausal women from the large Mexican Teachers' Cohort. Leptin and

Figure 1. Correlation heat map of the 18 biomarkers associated with meat and fish intake in the European Prospective Investigation into Cancer and Nutrition (EPIC) cross-sectional study. The size and colour of the circles indicate the magnitude of correlation between biomarkers. Reproduced with permission from Cheung et al. (2017).

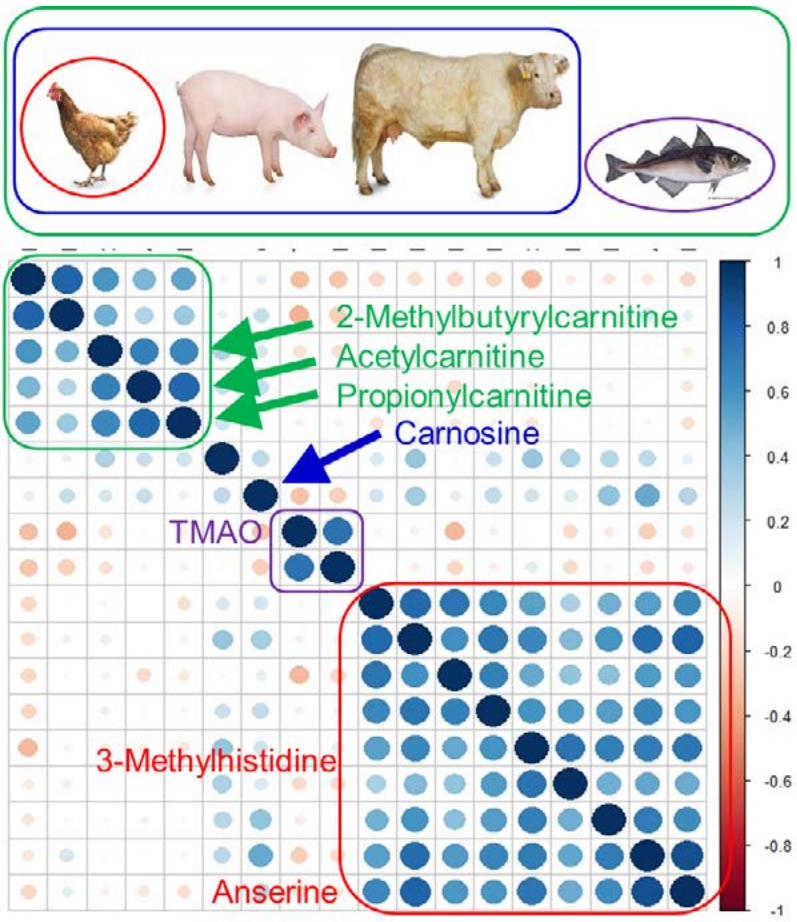
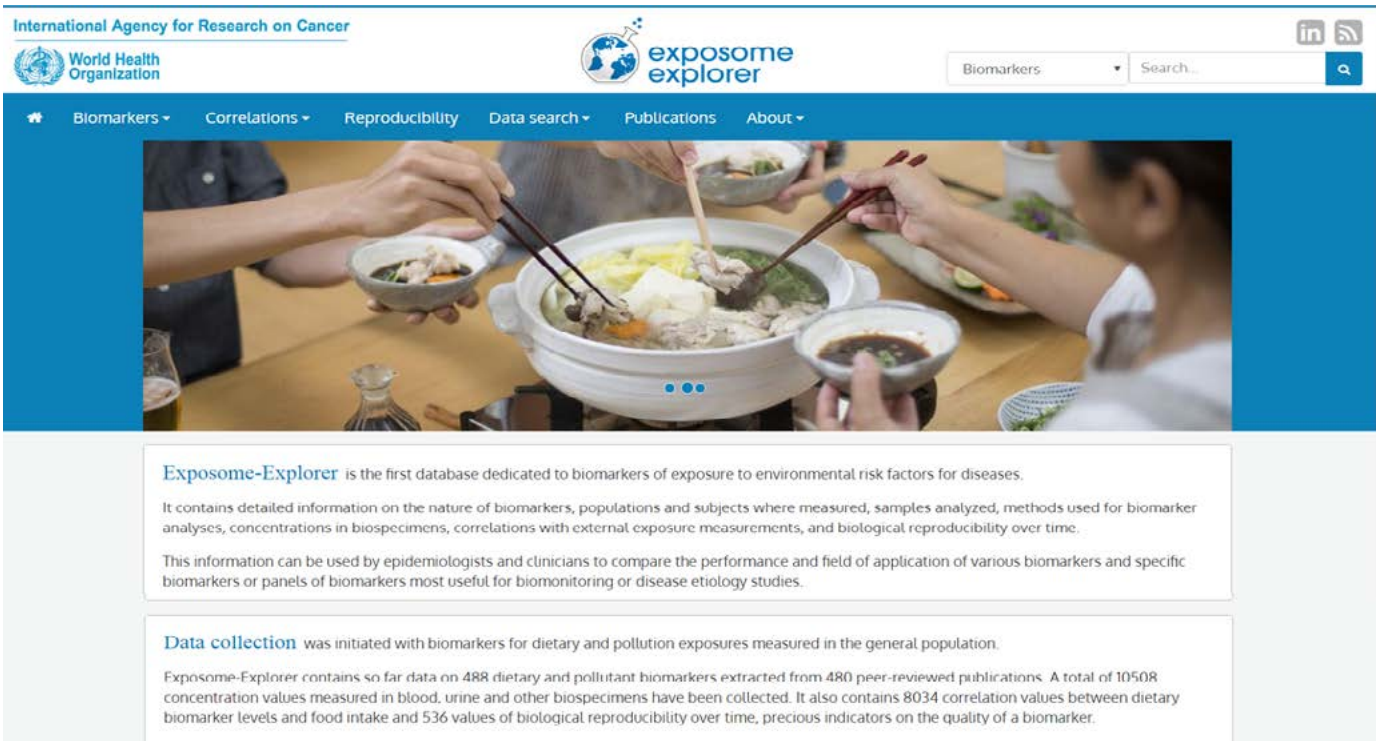


Figure 2. Screenshot of the homepage of the Exposome-Explorer website (http://exposome-explorer.iarc.fr/).



adiponectin are adipose tissue-derived cytokines that regulate cell proliferation and apoptosis. Variation in circulating levels of these cytokines has been linked to breast cancer development, but few studies have assessed their association with mammographic density – a marker for breast cancer risk. In this study, high leptin levels and the leptin/adiponectin ratio were found to be significantly associated with lower mammographic density in premenopausal women. These findings may shed light on potential mechanisms linking adiposity to lower risk of breast cancer in premenopausal women.

Thyroid cancer studies

One focus of BMA is exploring the etiology of thyroid cancer, which is the most common endocrine malignancy worldwide. Following on from a series of studies that examined hormonal factors in relation to thyroid cancer risk in EPIC, BMA explored the association between various dietary factors and thyroid cancer development. No significant associations were observed for fish consumption overall or for any specific type of fish, or for fruits and vegetables; however, a positive borderline trend with intake of fruit juice was observed, possibly related to its high sugar content (Zamora-Ros et al., 2017a).

Dietary Exposure Assessment Group (DEX)

until June 2016

Global Nutrition Surveillance initiative

The Dietary Exposure Assessment Group (DEX) launched the Global Nutrition Surveillance initiative (GloboDiet) to support the collection of standardized dietary data worldwide for surveillance and research for prevention of cancer and other noncommunicable diseases. Seven European countries have already implemented GloboDiet in their national surveys, and the concept was subsequently expanded to other regions worldwide. Brazilian and Mexican versions of GloboDiet have been advanced or completed (Bel-Serrat et al., 2017) for local implementation, for example in the Brazilian Longitudinal Study of Adult Health (ELSA) cohort. For Africa, preparatory work has enabled the evaluation of the specific needs and constraints in applying GloboDiet in this region (Aglago et al., 2017a) and the proposal of new approaches for optimizing its implementation across Africa. IARC continues to support where possible the transfer of the GloboDiet methodology to interested users at the national level.

In addition, DEX pursued a series of activities on the compilation of new international nutrient databases (Nicolas et al., 2016), meal pattern analyses, and new approaches for analysing nutrient patterns and their association with cancer and its risk factors (Freisling et al., 2016; Moskal et al., 2016), in close collaboration with the other Groups in NME.

Nutritional Epidemiology Group (NEP)

Fatty acid metabolism and breast cancer

In a case–control study nested within EPIC, 60 plasma phospholipid fatty acids were measured by gas chromatography in 2982 incident breast cancer case–control pairs. Levels of palmitoleic acid were positively associated with risk of breast cancer, and higher levels of industrial trans-fatty acids were specifically associated with estrogen receptor (ER)-negative breast tumours. These findings suggest that increased de novo lipogenesis, acting through increased synthesis of palmitoleic acid, could be a relevant metabolic pathway for breast tumorigenesis (Chajès et al., 2017).

Metabolically defined body size phenotypes and colorectal cancer

Obesity is a metabolically heterogeneous condition, and although metabolic abnormalities such as hyperinsulinaemia are common in obesity, not all obese individuals exhibit elevated insulin levels. Furthermore, a subset of individuals of normal weight are hyperinsulinaemic. In a nested case–control study within EPIC comprising 750 case–control pairs, we found that lean individuals with elevated insulin levels were at equivalent elevated risk of colorectal cancer as their obese hyperinsulinaemic counterparts. Conversely, metabolically healthy obese

individuals did not have excess risk of colorectal cancer (Figure 3). These findings suggest that metabolic health defined by insulin sensitivity may be an important and etiologically relevant phenotype for colorectal cancer, rather than obesity per se (Murphy et al., 2016a).

Coffee drinking and mortality

The association of coffee drinking with cause-specific mortality was investigated in EPIC, where 41 693 deaths have occurred following a mean follow-up of 16 years. Compared with non-consumers, consumers in the highest quartile of coffee consumption experienced lower all-cause mortality: 12% lower for men, and 8% lower for women. Inverse associations were particularly pronounced for digestive disease and cardiovascular mortality. Coffee consumption was also associated with a healthier liver enzyme profile, defined by lower serum alkaline phosphatase, alanine transaminase, and aspartate transaminase, lower C-reactive protein, and better glucose control (Gunter et al., 2017).

Metabolomics and liver cancer

Our previous research has shown that unhealthy lifestyle exposures have a diverse range of metabolic consequences. To explore these in more detail, in collaboration with BMA, we applied mass spectrometry-based metabolomics to pre-diagnostic blood samples taken from hepatocellular cancer cases and matched controls. Our findings show that development of hepatocellular cancer is associated with liver dysfunction, marked alterations in amino acid levels, and alterations in bile acid and bilirubin metabolism (Figure 4) (Stepien et al., 2016a, 2016b).

Microbial exposures and colorectal cancer

Within a prospective analysis in EPIC, we showed that unhealthy lifestyle exposures can alter gut barrier function, allowing leakage of toxic bacterial metabolites into the systemic circulation, and possibly even bacterial translocation (Kong et al., 2016). In a follow-up study in the same population, we observed statistically significant higher levels of circulating antibodies to *Streptococcus gallolyticus* subspecies *gallolyticus* (SGG), a commensal bacterium that can induce infective endocarditis and can directly colonize colorectal tissue.

Figure 3. Association of metabolically defined body size subtypes with risk of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC). Figure compiled from Murphy et al. (2016a).

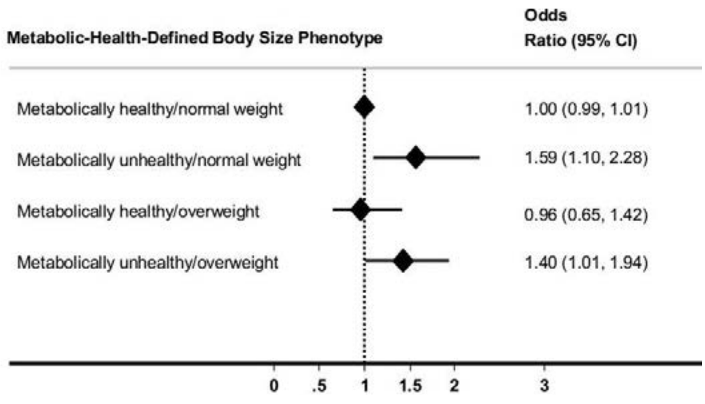
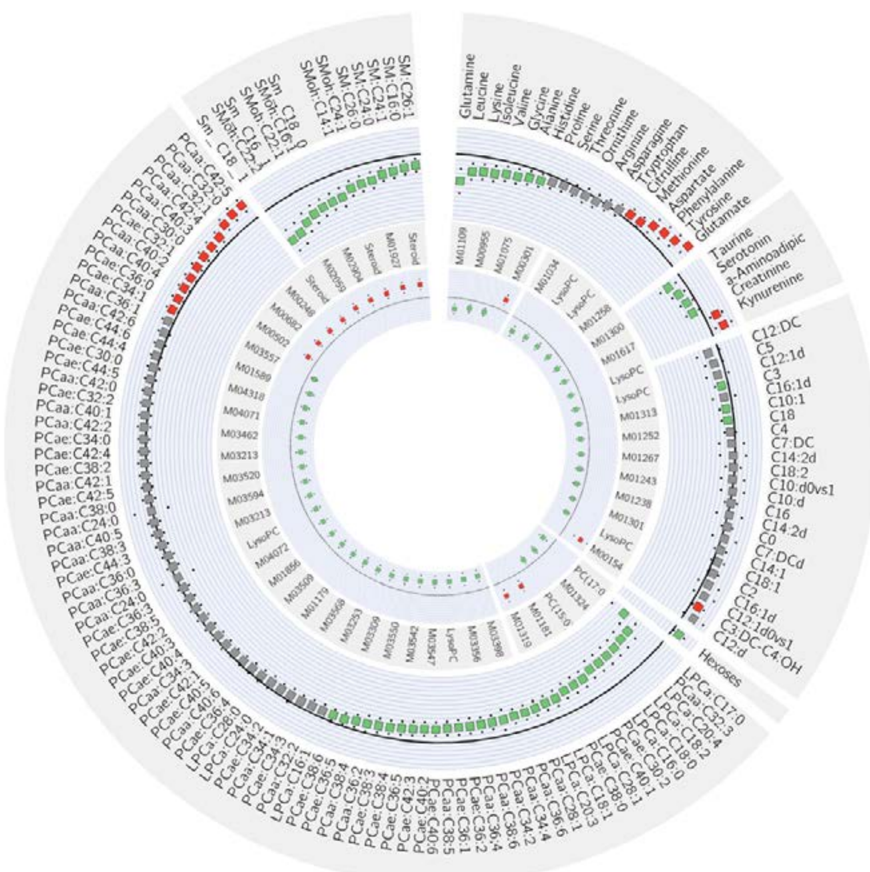


Figure 4. Metabolites linked to higher (red) or lower (green) risk of hepatocellular carcinoma. Figure compiled from Stepien et al. (2016a).



Studies of breast cancer in low- and middle-income countries

Together with BMA, NEP coordinates three new studies on breast cancer in low- and middle-income countries, specifically in Morocco (Determinants of Breast Cancer in Morocco; EDSMAR), South Africa (South Africa Breast Cancer; SABC), and Latin America (Molecular Subtypes of Premenopausal Breast Cancer in Latin American Women; PRECAMA).

Within these studies, the recruitment of cases and matched controls is complete or ongoing. Questionnaire data are being collected, as well as blood and tumour tissue and, for EDSMAR, urine, stool samples, and adipose tissue.

Preliminary analyses in PRECAMA have revealed associations of breast cancer with reproductive factors concordant with data from other regions and an inverse association between adiposity measures and breast cancer. Tumour mutation analyses are currently under way, in collaboration with MMB.

Nutritional Methodology and Biostatistics Group (NMB)

from July 2016

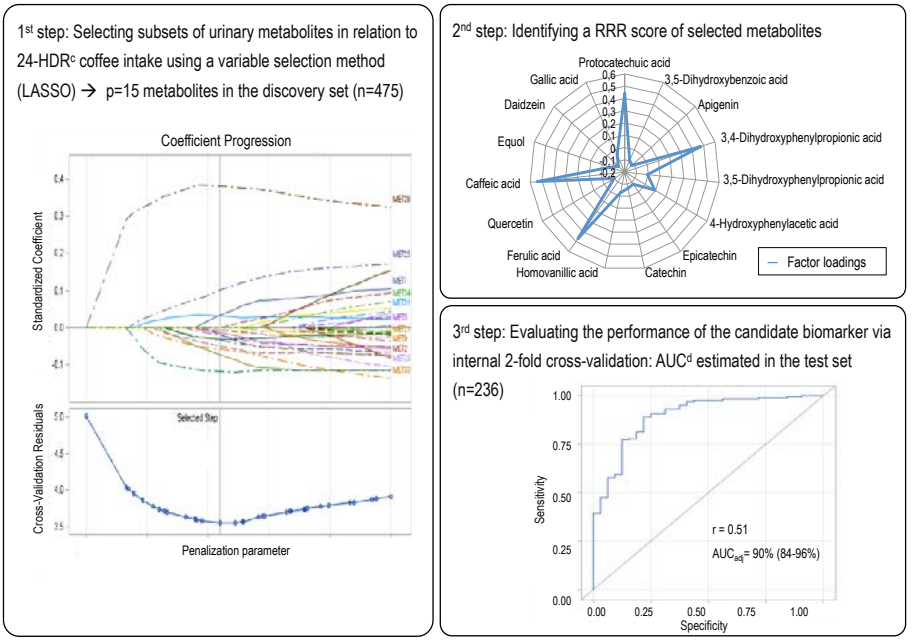
Alcohol and cancer

The Nutritional Methodology and Biostatistics Group (NMB) coordinates a large pooled analysis within the National Cancer Institute (NCI) Cohort Consortium, including data from 36 cohort studies and more than 2.7 million participants to comprehensively investigate the role of alcohol consumption and drinking patterns on risk of cancer. A systematic review of current epidemiological evidence on the relationship between alcohol intake and risk of oesophageal cancer was conducted, evaluating putative mechanisms and genetic susceptibility markers (Matejcic et al., 2017a). Furthermore, a study in EPIC including 1802 cases of urothelial cell carcinoma showed that baseline and lifetime intakes of alcohol were not associated with risk of urothelial cell carcinoma (Botteri et al., 2017). An analysis investigating the interaction between dietary fibre and alcohol intake in EPIC showed that high fibre intake can potentially mitigate the positive association of alcohol intake with risk of breast cancer (Romieu et al., 2017a).

Statistical methodology

A novel algorithm combining dimension reduction and variable selection methods was developed to identify urinary polyphenol metabolite patterns through the application of the least absolute shrinkage and selection operator (LASSO) and reduced rank regression (RRR) (Figure 5) (Noh et al., 2017). An analytical framework to model the "meeting-in-the-middle" principle demonstrated the utility of modelling metabolite profiles compared with questionnaire-based data in relating a healthy lifestyle index score to risk of hepatocellular carcinoma. Study design and statistical considerations to evaluate the validity of dietary biomarkers were extensively described and discussed (Ferrari, 2017). The estimation of specific quantiles of the distribution of laboratory data is greatly hindered by

Figure 5. A novel algorithm combining variable selection (least absolute shrinkage and selection operator [LASSO]) with dimension reduction (reduced rank regression [RRR]) to identify urinary polyphenol metabolite patterns. 24-HDR, 24-hour dietary recall; AUC, area under the curve. Figure compiled from Noh et al. (2017).



the presence of observations below the limit of detection, leading to left-censored data. Two different model-averaged quantile estimators derived from semi-nonparametric extensions of the log-normal distribution were defined and compared through simulations and then illustrated using data on cadmium concentration in food products (Nysen et al., 2016).

Obesity, dietary patterns, and cancer

In a treelet transform analysis, which combines features for dimension reduction with a clustering technique for individual nutrients, a treelet transform component reflecting plant-based nutrients was inversely associated with breast cancer risk (Assi et al., 2016). The healthy lifestyle index score – reflecting smoking, alcohol consumption, physical activity, body mass index, and healthy diet – was related to the risk of cancer, overall and by major subgroups (McKenzie et al., 2016b). A comparison of different measurements of adiposity was shown to predict risk of obesity-related cancer in older adults in a similar manner (Freisling et al., 2017).

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The Section of Genetics (GEN) includes the Genetic Epidemiology Group (GEP) and the Genetic Cancer Susceptibility Group (GCS). The work of the Section combines large population-based studies with laboratory and bioinformatics expertise to identify specific genes and genetic profiles that contribute to the development of cancer and elucidate how they exert their effect along with environmental factors. GEN also tries to identify individuals who are at high enough risk that they are likely to benefit from potential screening strategies.

The Section's projects usually involve extensive fieldwork in collaboration with external investigators in order to develop large-scale epidemiological studies with appropriate clinical and exposure data, as well as biosample collection. This typically occurs within GEP. Genetic analysis comprises either candidate gene or genome-wide genotyping studies, as well as extensive sequencing work. GEP studies also assess non-genetic exposures, partly in recognition of the importance of non-genetic factors in driving cancer incidence, and also to facilitate accurate assessment of gene–environment interactions. In contrast, GCS places more focus on identification of uncommon or rare genetic variants that may have a larger effect than common single nucleotide polymorphisms but that are not sufficiently frequent to be captured by current genome-wide association genotyping arrays. The approach of GCS has been to use genomic and bioinformatic techniques to complement more traditional approaches for the study of rare genetic variants. GCS also uses genomics to explore how the variants may be conferring genetic susceptibility to cancer. Thus, the research programme of GCS complements that of GEP, and also provides a facility for high-throughput genomic techniques and the related bioinformatics to support GEN's large-scale molecular epidemiology projects and other IARC genomics projects.

Genetic Epidemiology Group (GEP)

The overall goal for the Genetic Epidemiology Group (GEP) is to contribute to understanding the causes of cancer through the study of genetic susceptibility variants of various cancer sites, and also patterns of genetic mutations that are observed in tumours. An additional goal is to develop accurate risk prediction models that take into account both demographic information (e.g. age and sex) and biomarkers (genetic and non-genetic). The work of GEP includes studies of cancers related to tobacco use and alcohol consumption (lung and aerodigestive tract cancers) and cancers related to obesity (such as kidney, pancreatic, and colorectal cancers). GEP devotes substantial resources to extensive fieldwork, with the goal of recruiting large series of cases and controls, comprising extensive questionnaire information and biological samples. Genetic analyses of inherited susceptibility usually comprise a genome-wide approach initially, with subsequent large-scale coordinated replication studies in diverse populations. This latter aspect is aided by the development of international consortia in which GEP takes a leading role. Confirmed susceptibility loci are investigated in more detail with a variety of techniques, including in silico, expression, and sequencing studies, which are often conducted in collaboration with other IARC Groups. Analysis of these large genome-wide studies also includes a Mendelian randomization approach that aims to understand how lifestyle factors influence cancer onset.

GEP is also undertaking a large international study of the causes of cancer by analysis of mutation patterns (or mutation signatures) in cancer genomes. Most of the Group's efforts in this domain are included in the Mutographs project, which aims to understand the causes of five different cancers across five continents (see text box).

In addition to studies of genetic factors, GEP is conducting a wide range of studies involving non-genetic factors, including evaluations of circulating biomarkers such as human papillomavirus (HPV) antibodies for head and neck cancers, and a wide range of protein and other biomarkers for lung cancer. The overall goal of these studies is to identify individuals at sufficiently high risk to justify screening and early detection.

Some prominent examples of the Group's work over the 2016–2017 biennium are described here.

Elucidating the etiological role of obesity and related risk factors in multiple cancers – a Mendelian randomization approach

Elevated body mass index (BMI) and obesity-related risk factors have been associated with multiple cancers studied by GEP. Because these risk factors are inherently interrelated, traditional epidemiological studies have not been able to untangle which specific factors exert a causal influence and which are merely correlated with the underlying causal factor.

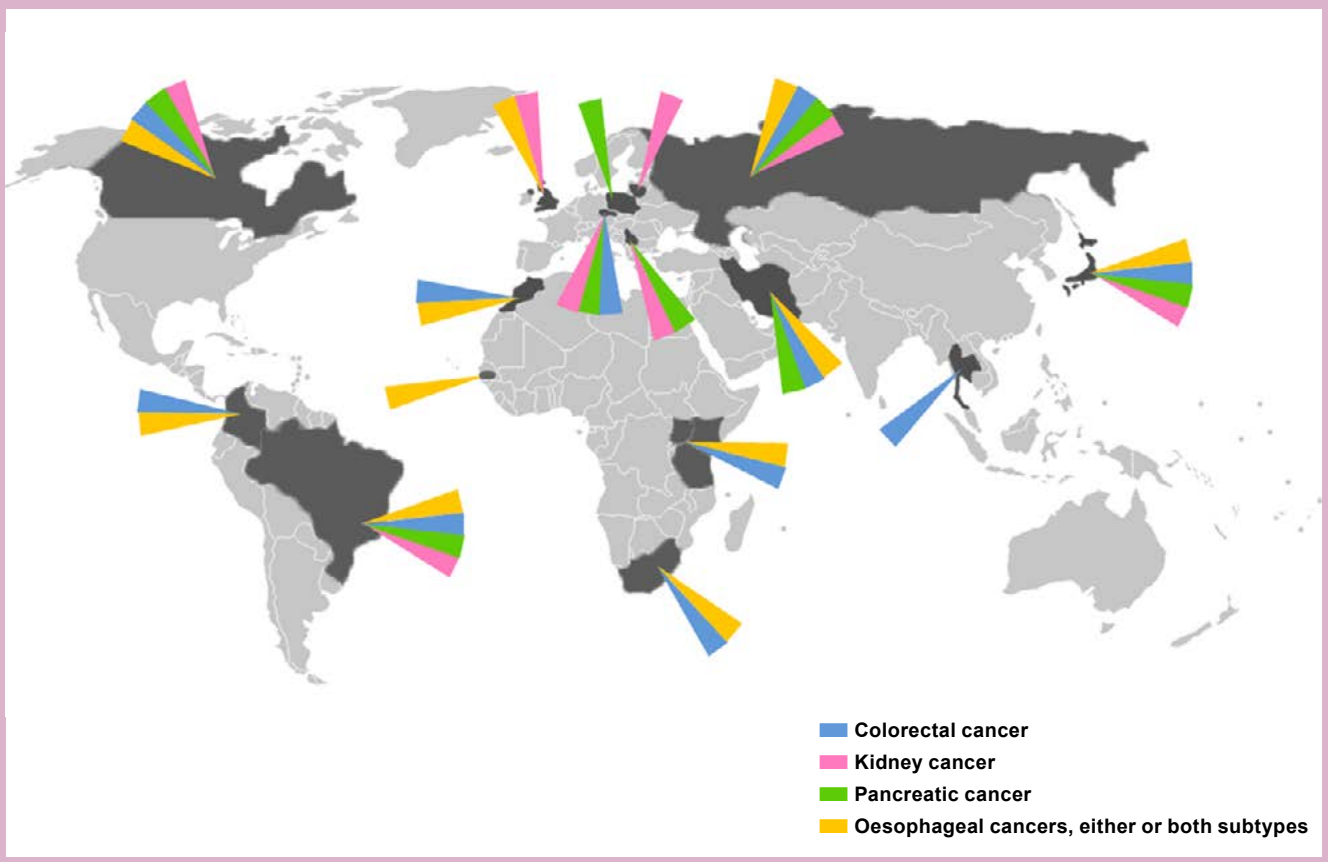
By leveraging data from genome-wide association studies of tens of thousands of cancer cases and controls that GEP has led or contributed to, we have conducted a series of studies where we have interrogated the causal relevance for several obesity-related risk factors for various cancers. Because these analyses were based on genetic instruments, they are not influenced by reverse causation and are less sensitive

Mutographs of cancer

A new and major initiative of the Section is an effort to understand the causes of cancer by generating mutation signature profiles based on whole-genome sequence data. The study results from a major Cancer Research UK (CRUK) Grand Challenge grant – one of the world's most ambitious cancer research awards – and is co-led by Dr Paul Brennan together with overall principal investigator (PI) Professor Sir Mike Stratton from the Sanger Institute (Cambridge, United Kingdom) and four other co-PIs. The overall name of the project is Understanding of the Causes of Cancer through Studies of Mutational Signatures – Mutographs.

Different patterns of somatic mutation are generated by the different environmental, lifestyle, and genetic factors that cause cancer; many of them are still unknown. Within the Mutographs project, GEP is coordinating the recruitment of 5000 individuals with cancer (colorectal cancer, kidney cancer, pancreatic cancer, oesophageal adenocarcinoma, or oesophageal squamous cancer) across five continents to explore whether different mutational signatures explain the marked variation in incidence. Through an international network of collaborators, biological materials are collected, along with demographic, histological, clinical, and questionnaire data. Whole-genome sequences of tumour–germline DNA pairs are generated at the Sanger Institute. Extracted somatic mutational signatures are then correlated with data on risk factors.

Through an enhanced understanding of cancer etiology, the unprecedented effort within the Mutographs project is anticipated to outline modifiable risk factors, lead to new approaches to prevent cancer, and provide opportunities to empower early detection, refine high-risk groups, and contribute to therapeutic development.



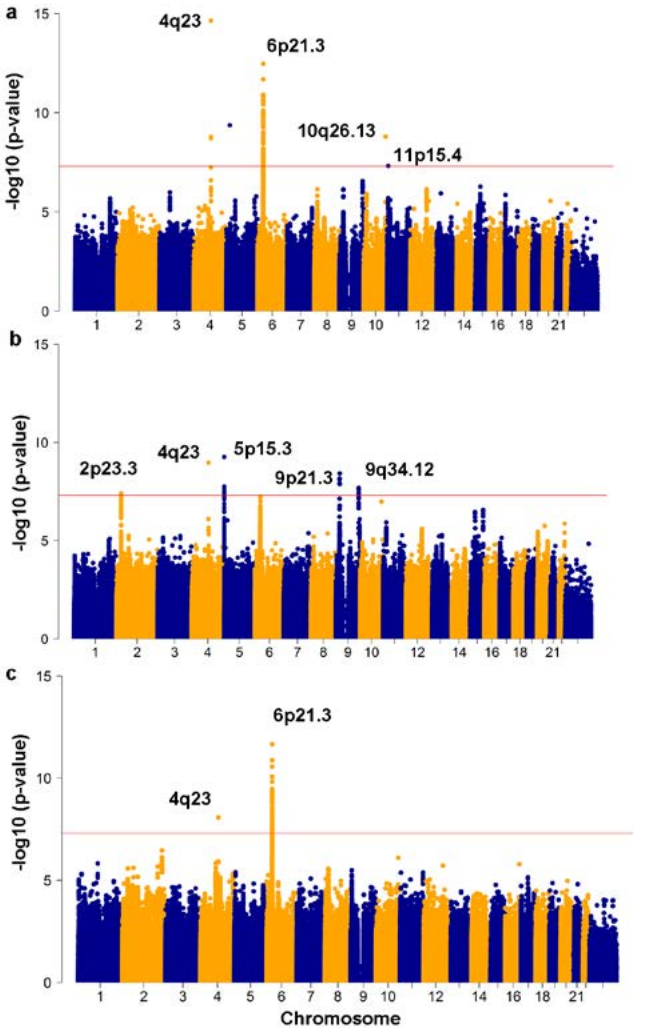
Countries contributing to Mutographs recruitment.

to confounding than those using direct exposure measures. The results were illuminating for both kidney cancer and pancreatic cancer, not only because they confirmed elevated BMI as an important cause of these cancers, but in particular because they highlighted insulin as an important mediator of the risk increase caused by higher BMI. These findings significantly improved the understanding of the importance of obesity in the etiology of kidney cancer and pancreatic cancer. They have also highlighted a potentially important role for obesity and insulin resistance in lung cancer (Carreras-Torres et al., 2017a, 2017b).

Genome-wide analysis of tobacco-related cancers

GEP has coordinated a large OncoArray analysis of more than 7000 cancers of the oral cavity or oropharynx, along with a similar number of controls. A prominent finding from this study is the important role of the HLA region for oropharyngeal cancer. Further analysis of this locus identified a HLA haplotype that was also associated with cervical cancer, suggesting an important interaction with this specific haplotype and papillomavirus (Lesseur et al., 2016) (Figure 1). GEP also led a large genome-wide association analysis of more than 10 000 renal cancer cases and 20 000 controls, in partnership with the United States National Cancer Institute, and identified an additional seven susceptibility loci for renal cancer in addition to six that had been previously discovered (Scelo et al., 2017).

Figure 1. Genome-wide association meta-analysis results. Red lines correspond to $P = 5 \times 10^{-8}$. The vertical axes show $-\log_{10}(P\text{-values})$. (a) Overall oral cavity and pharyngeal cancer analysis with 6034 cases and 6585 controls. (b) Oral cavity cancer analysis with 2990 cases and 6585 controls. (c) Oropharyngeal cancer analysis with 2641 cases and 6585 controls. Loci with technically validated genome-wide significant single nucleotide polymorphisms are tagged by genomic location. Reprinted from Lesseur et al. (2016) by permission from Macmillan Publishers Ltd, copyright 2016.



Genetic Cancer Susceptibility Group (GCS)

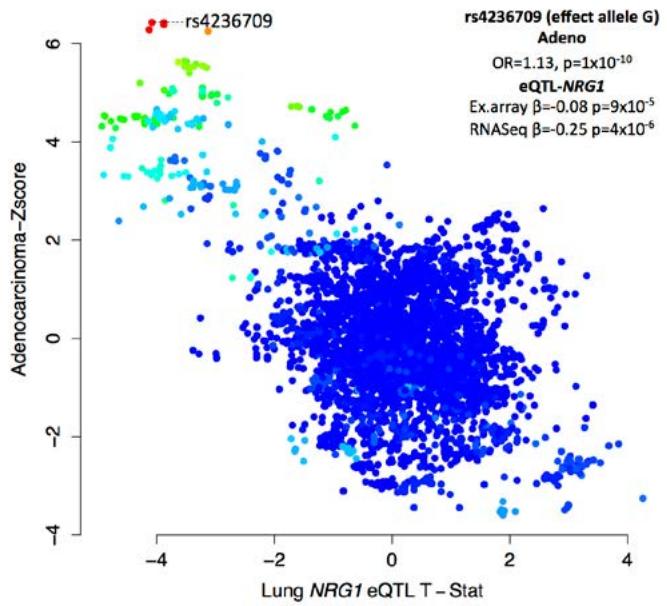
The Genetic Cancer Susceptibility Group (GCS) contains a multidisciplinary scientific team, covering genetics, genomics, bioinformatics, and pathology. These combined skills are used to undertake genetic and genomic research to identify cancer-related genes and explore their mechanisms of action. Through this knowledge, the aim is to gain insights into cancer etiology and apply that to early cancer detection and prevention.

In the context of germline genetics, working within the International Lung Cancer Case–Control Consortium (ILCCO) and the United States National Cancer Institute Genetic Associations and Mechanisms in Oncology (GAME-ON) OncoArray consortium, GCS undertook a genome-wide association study (GWAS) of lung cancer that included nearly 30 000 lung cancer patients and 57 000 controls. This GWAS identified 18 susceptibility loci, including 10 novel loci. These susceptibility alleles have been explored by integrating additional genetic data from more than 250 000 people, including from studies of gene expression in the lung and other tissues,

measures of smoking propensity, lung spirometry (forced vital capacity [FVC]/ forced expiration volume [FEV]), and leukocyte telomere length (McKay et al., 2017a). The analysis of lung epithelial tissue gene expression implicated genes not previously implicated in lung cancer etiology, such as *RNASET2* or *SECISBP2L*, and genes like *NRG1*, a gene infrequently somatically translocated in lung adenocarcinomas (Figure 2). In addition, we identified lung cancer susceptibility variants at 8p12 that influence expression levels of *CHRNA2*, a cholinergic nicotinic receptor. In contrast with our previous observation with genetic variants in cholinergic nicotinic receptor genes and lung cancer, these 8p12 variants were not associated with the amount smoked but with factors such as age at smoking initiation. These variants appeared to be linked with *CHRNA2* expression levels, particularly in the cerebellum, adding to the emerging evidence that this region of the brain may indeed play a role in aspects of addictive behaviour. In addition, GCS has been awarded funding to continue to explore the mechanisms of action of these genetic susceptibility variants (from France Genomique and the Institut national du Cancer, France) and has initiated projects to investigate genomic events in rare thoracic tumours, such as lung carcinoid tumours (supported by La Ligue nationale contre le Cancer Rhône-Alpes, France; the Dutch Cancer Society, The Netherlands; and the National Cancer Institute, USA) and mesothelioma (supported by the Institut national du Cancer, France).

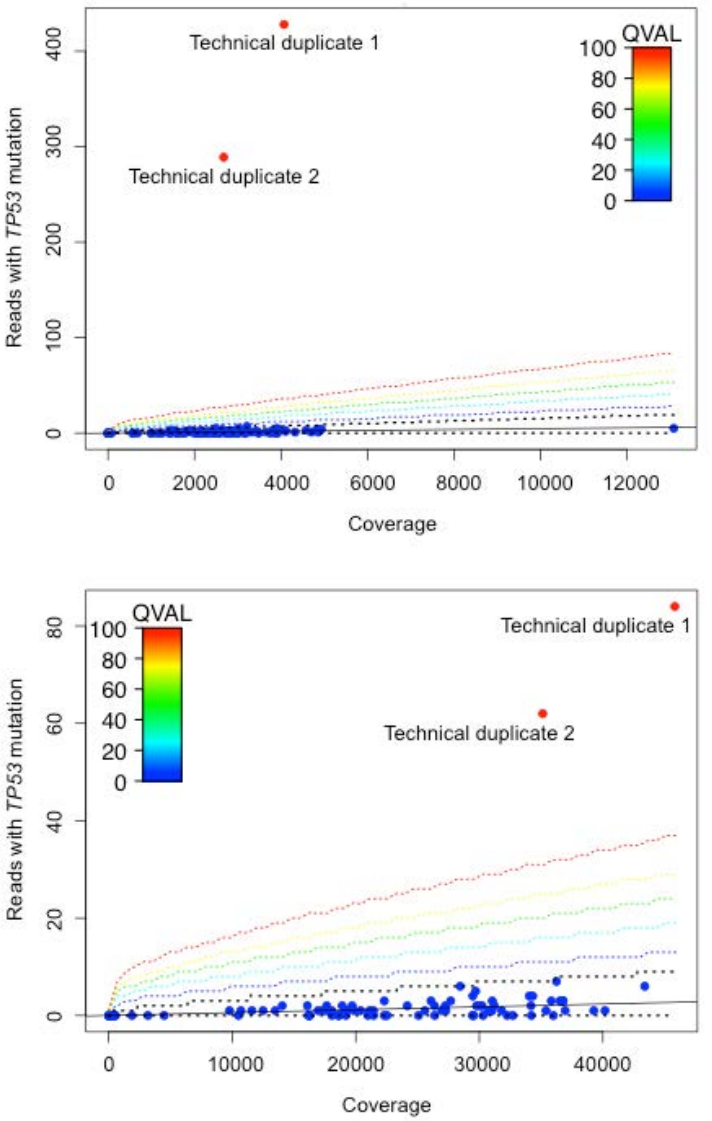
GCS has also explored the potential of circulating tumour DNA (ctDNA) as a biomarker for cancer detection. The study of ctDNA presents important technical challenges; both the DNA quality and the allele fractions of tumour-derived genetic alterations in the total cell-free DNA (cfDNA) in plasma are lower than that usually acceptable for next-generation sequencing analysis. Furthermore, to be applicable in early detection, mutations must also be identified without the prior knowledge of the tumour genotype and across any region of the gene. We have combined our laboratory and bioinformatic skills to develop an analysis pipeline specifically tailored to ctDNA, called Needlestack (https://github.com/IARCbioinfo/needlestack; Figure 3). We applied this approach to retrospective case–control studies of lung and pancreatic cancer, demonstrating that ctDNA is found in cases and, importantly, in patients with early-stage disease (Fernandez-Cuesta et al., 2016; Le Calvez-Kelm et al., 2016). Whereas ctDNA is strongly over-represented in patients, tumour-related mutations were also consistently noted in an unexpected proportion of controls (~3–10%). This somewhat surprising observation in controls, with the limitations that it implies, highlights the insights that can be gained when these techniques are applied to molecular epidemiology-based studies at IARC. We are now exploring the application of these methods for ctDNA in additional settings, particularly bladder cancer (supported by the Association pour la Recherche en biologie moléculaire, France, and La Ligue nationale contre le Cancer Rhône-Alpes, France) and oesophageal cancer (supported by the National Institute for Medical Research Development, Islamic Republic of Iran).

Figure 2. Scatter plots comparing variants across the 5417 variants at the 8p12 susceptibility loci and their associated with lung adenocarcinoma (vertical axis) and the lung *cis* expression quantitative trait loci (eQTL) Genotype-Tissue Expression (GTEx) (horizontal axis). Each variant is coloured relative to the degree of linkage disequilibrium (R^2) with a sentinel lung cancer variant (rs4236709 marked) at that locus (red for high, blue for low). Inset table (top right): association between sentinel variant and lung adenocarcinoma as well as the eQTL evidence in lung epithelium in five cohorts, first RNA expression based on microarray and RNASeq technologies. The variants associated with lung adenocarcinoma tend to be those that are lung *cis*-eQTL for *NRG1*. Curiously, while somatic translocations are generally linked with ectopic NRG1 activation and never-smokers, the germline genetic risk correlated with decreased *NRG1* expression and was present in lung adenocarcinomas from ever- and never-smokers. © IARC.



GCS plays an active role in the development of genomics capabilities at IARC. GCS, with important contributions from other Groups, has continued to build links within the genomics community at IARC, through a role in the Bioinformatics Steering Committee and the related Bioinformatics Working Group, and through the Laboratory Steering Committee, as well as providing access to the laboratory techniques, pathology expertise, and computational resources for genomics-related activities at IARC. These developments are also made available to the scientific community via a GitHub site: https://github.com/IARCbioinfo/.

Figure 3. Two examples of variants called using Needlestack's regression model to detect rare allele fraction in outlying individuals (variant carriers). Each dot represents a sequenced individual (two dots per sample) coloured according to its phred-scaled *q*-value. The black regression line shows the estimated sequencing-error rate along with the 99% confidence interval (black dotted lines) containing samples. Coloured-dotted lines correspond to the limits of regions defined for different significance *q*-value thresholds. Both technical duplicates appear as outliers from the regression (in red), and are therefore classified as carrying the given mutation. Reprinted from Fernandez-Cuesta et al. (2016). Copyright 2016, with permission from Elsevier.



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Prevention and Implementation Group (PRI)

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Prevention and early detection, including interventions to reduce exposure, screening, and early diagnosis, can decrease cancer incidence and mortality and improve quality of life. The Section of Early Detection and Prevention (EDP) is composed of two groups: the Prevention and Implementation Group (PRI) and the Screening Group (SCR).

EDP carries out research on resource-appropriate public health policies and feasible, quality-assured, and cost-effective prevention and early detection strategies for the control of common cancer types such as breast, cervical, colorectal, oesophageal, oral, and gastric cancer globally, with an emphasis

on low- and middle-income countries (LMICs). Prevention offers the most cost-effective long-term strategy for cancer control. The Section's main focus areas in primary prevention are the development and implementation of safe, effective, and affordable vaccination schemes for human papillomavirus (HPV)-related cancers and the evaluation of the impact of *Helicobacter pylori* eradication on gastric cancer. The major focuses of EDP's early detection research are assessing new technologies and alternative screening approaches, as well as the impact of improved awareness and access to health services for the early detection of major cancer types such as breast, cervical, colorectal, and oral cancer.

The Section designs and conducts research studies in collaboration with investigators in national cancer organizations, health services, universities, and other key groups within and outside the Agency. EDP works closely with other international organizations to develop, implement, and promote effective strategies for preventing and controlling cancer in the context of national cancer control programmes. In the Section's studies, there is a continuing emphasis on developing training resources, augmenting capacity for cancer prevention and early detection initiatives, and scaling up of prevention and early detection services within local health systems. The establishment of cancer research networks in LMICs to exchange experiences and enhance the local capacity is among EDP's priorities.

More recently, the Section has expanded its focus on implementation research, to support the efforts of national health systems to translate scientific findings into the well-being of the population.

Prevention and Implementation Group (PRI)

The Prevention and Implementation Group (PRI) investigates cancer epidemiology and prevention, with a focus on HPV vaccines, *H. pylori* eradication for gastric cancer prevention, triage methods for HPV-positive women, and the promotion and evaluation of cervical cancer control programmes. Recently, PRI has included implementation research objectives in ongoing projects and national implementation activities, including consideration of the cost–effectiveness of preventive interventions.

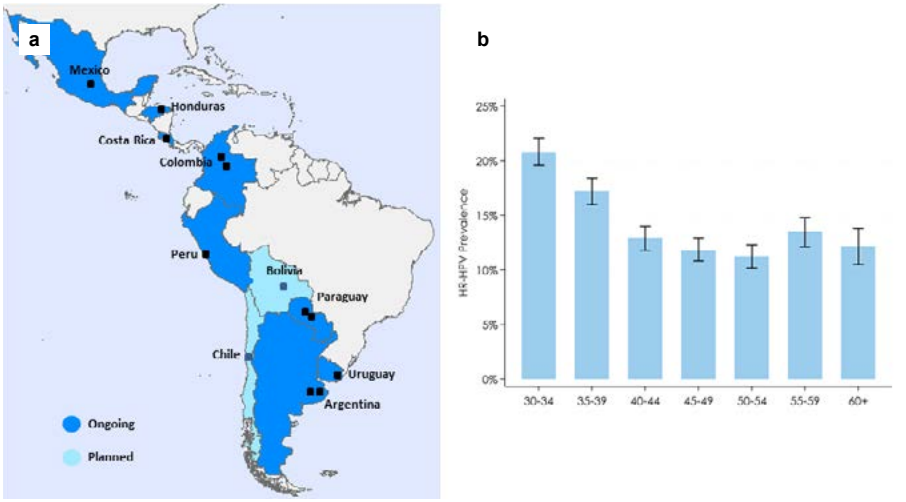
Cervical cancer studies in Guanacaste, Costa Rica

Given the demonstrated efficacy of the HPV vaccines against persistent infection with vaccine types regardless of the number of doses (one, two, or three) and stable antibody levels extending to 7 years, and considering the public health potential of one-dose vaccination, PRI is initiating a large randomized trial of the non-inferiority of one versus two doses of the bivalent and nonavalent vaccines. The ESCUDDO study will recruit 20 000 adolescent girls (ages 12–16 years) in Costa Rica, who will be randomized to receive the bivalent or nonavalent vaccine. At the 6-month visit, they will be randomized to a second dose of the same vaccine or a control vaccine (diphtheria–pertussis–tetanus). The study will evaluate the non-inferiority of one or two doses for each of the two vaccines. In addition, approximately 4000 women aged 17–20 years will be recruited as a control group to estimate the efficacy of the vaccination schedules.

Multicentre study of HPV screening and triage (ESTAMPA)

The ESTAMPA study investigates emerging cervical cancer screening and triage techniques in Latin America. About 50 000 women aged 30–64 years are being invited for HPV screening. All HPV-positive women receive colposcopy, biopsy, and treatment as needed, and are recalled for a second screening after 18 months. The main outcome is precursors of advanced cancer. The performance of visual, cytological, and molecular triage methods will be evaluated. The study is under way in 11 centres (Figure 1a) (recruitment, ~23 500). Based on 22 390 study records, the global prevalence of high-risk HPV infection is 14.6% (95% confidence interval [CI], 14.2–15.1%), decreasing from 20.8% in those aged 30–34 years to 12.1% in those older than 60 years, and showing a second peak, of 13.5%, in women aged 55–59 years (Figure 1b).

Figure 1. The ESTAMPA study of HPV screening and triage: (a) map of study centres; (b) overall high-risk HPV prevalence by age group. © IARC.



Epidemiology and prevention of *H. pylori* infection and gastric cancer

The ENIGMA study investigates the prevalence of *H. pylori* infection, precancer, and cofactors in population samples from areas with high and low risks of gastric cancer. The study plans to assess age-specific infection prevalence as well as bacterial (including microbiome), host, and environmental factors that explain geographical patterns. ENIGMA has been completed in Chile and is under way in the Islamic Republic of Iran (Figure 2). Additional study sites include China, Colombia, Costa Rica, the Republic of Korea, and Uganda.

In collaboration with the National Cancer Center of the Republic of Korea, PRI is conducting a randomized controlled trial of *H. pylori* eradication for gastric cancer prevention (the HELPER study), which aims to recruit 11 000 subjects aged 40–65 years who are attending endoscopy within the National Cancer Screening Program (Park et al., 2017). *H. pylori*-positive subjects are randomized to quadruple eradication therapy or placebo. All participants (current recruitment, ~5000) will be routinely screened within the National Cancer Screening Program every 2 years for 10 years (Figure 3).

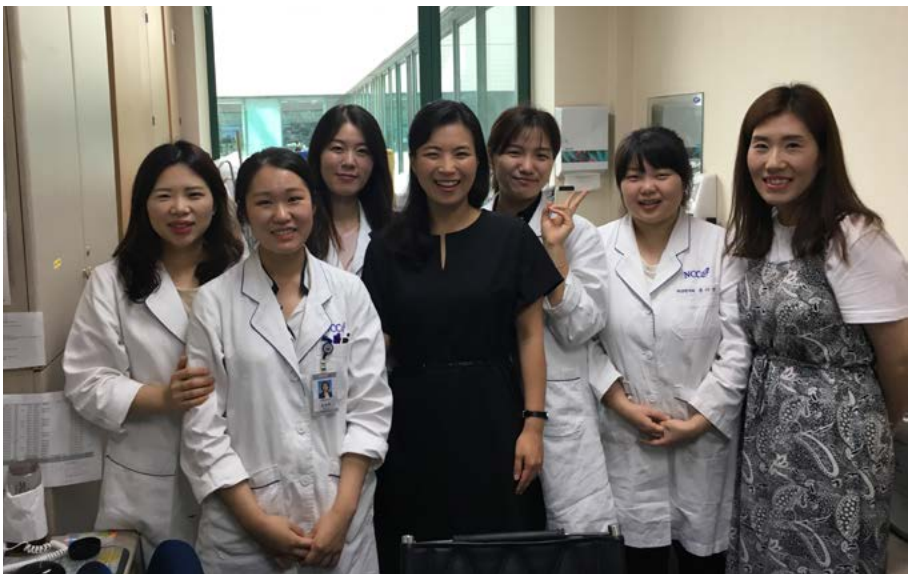
A randomized trial with the University of Latvia (GISTAR) aims to determine whether combined *H. pylori* and pepsinogen screening followed by eradication therapy in *H. pylori*-positive subjects and endoscopic follow-up of those with serological atrophic gastritis reduces gastric cancer mortality compared with standard care (Leja et al., 2017). The study aims to recruit 30 000 subjects aged 40–64 years in Latvia and neighbouring countries (current recruitment, ~5000).

Cervical cancer prevention in Africa

PRI is collaborating with the World Health Organization (WHO) Department of Reproductive Health and Research (RHR) and the United Republic of Tanzania in a study with 1500 women

Figure 2. ENIGMA study coordination meeting in Ardabil, Islamic Republic of Iran, in August 2017. © IARC/Rolando Herrero.

Figure 3. The HELPER study team at the National Cancer Center, Republic of Korea, in July 2017. © IARC/Rolando Herrero.



to build HPV testing capacity and to assess the reproducibility, feasibility, and acceptability of rapid HPV testing at different levels of the health care system (the AISHA study). Also with RHR, PRI is planning a large trial of two screen-and-treat algorithms using HPV testing currently recommended by WHO (the CESTA study). The first CESTA pilot studies will be in Senegal and South Africa.

Support of HPV vaccination and screening programmes

PRI continues to provide support to cervical cancer screening programmes in Mongolia, Myanmar, Romania, and several countries in Latin America. PRI is collaborating with RHR to develop new guidelines on thermal ablation and other novel ablative treatments for cervical intraepithelial neoplasia (CIN)

beyond cryotherapy. Within the BELMED project, in collaboration with the WHO Regional Office for Europe and national offices, PRI is facilitating the preparation and implementation of pilot screening programmes for breast cancer to implement population-based screening in Belarus (Figure 4).

Implementation research to increase HPV vaccination coverage in France

The PAPRICA project aims to evaluate whether an innovative educational intervention about HPV vaccination directed at doctors in Lyon can be effective in increasing vaccination coverage. With the collaboration of academic groups in France, PRI has developed and piloted at Saint-Étienne an HPV educational intervention based on behaviour change theories, and will test this intervention through a randomized clinical trial in Lyon.

Figure 4. Training course on breast cancer epidemiology and screening in Belarus, in December 2016. Courtesy of the Belarus Project Management Team.

Screening Group (SCR)

The main focus of the Screening Group (SCR) is research on primary prevention and early detection of common cancers through interventions that are particularly relevant in LMICs. SCR contributes evidence to support resource-appropriate cancer control policy-making, and engages in producing training resources and organizing educational programmes.

HPV vaccination

The effectiveness of fewer than three doses of quadrivalent HPV vaccine in preventing cervical neoplasia is being evaluated among 17 729 participants in India (Figure 5). Two doses were reported to be as immunogenic as three doses against HPV 16 and 18; even recipients of a single dose demonstrated robust and sustained immune responses, albeit inferior to those of

Figure 5. HPV vaccination in girls 10–18 years old in India. © IARC/Partha Basu.

participants who received three or two doses (Sankaranarayanan et al., 2016a). Frequencies of cumulative incident and persistent HPV 16/18 infections over 7 years were low in all the vaccinated groups, including the recipients of a single dose, compared with the unvaccinated controls (Table 1).

Cervical cancer screening

SCR studies demonstrated the superior sensitivity of HPV testing over cytology in routine health-care settings in Thailand, and over visual inspection with acetic acid (VIA) in a demonstration project in India (Figure 6) (Mittal et al., 2017; Sangrajrang et al., 2017). The study in Thailand also demonstrated the high efficacy of liquid-based cytology in triaging the HPV-positive women (Sangrajrang et al., 2017). A point-of-care HPV 16/18 E6 test to triage the HPV-positive women was evaluated in China (Zhang et al., 2017a). Although the E6 test had a much lower test positivity (9.9%) compared with liquid-based cytology (48.4%) and VIA (28.0%), E6-positive women had a much higher 10-year cumulative incidence rate (53.0%) of CIN of grade 3 or higher (CIN3+) compared with those who tested positive with cytology or VIA.

Figure 6. Cancer screening mobilization in a rural area in India. © IARC/Eric Lucas.

Table 1. Proportion (%) of one-time incident human papillomavirus (HPV) infections and persistent HPV infections in women in the IARC-India HPV vaccination study

HPV type	Dose received				Vaccinated group (total)	Unvaccinated group
	3 Doses (days 1, 60, and 180)	2 Doses (days 1 and 180)	2 Doses (days 1 and 60)	1 Dose		
	Incidence of HPV infection					
(Number of women assessed)	***(1180)***	***(1179)***	***(1473)***	***(1823)***	***(5655)***	***(1481)***
Vaccine-targeted types						
HPV 16/18	0.9	0.9	1.7	1.6	1.4	6.2
HPV 6/11	1.2	0.5	1.5	1.2	1.1	2.8
HPV 16/18/6/11	2.0	1.4	3.2	2.8	2.4	8.6
Non-vaccine-targeted types						
HPV 31/33/45	5.1	4.5	3.4	5.7	4.7	7.7
Other types excluding HPV 31/33/45[a]	14.4	13.2	10.8	13.8	13.0	18.0
Any HPV type[b]	18.9	16.7	15.3	19.0	17.5	26.8
	Persistence of HPV infection					
(Number of women assessed)	***(604)***	***(608)***	***(818)***	***(959)***	***(2989)***	***(1141)***
Vaccine-targeted types						
HPV 16/18	0.2	0.0	0.4	0.0	0.1	1.2
HPV 6/11	0.0	0.0	0.1	0.1	0.1	0.0
HPV 16/18/6/11	0.2	0.0	0.5	0.1	0.2	1.2
Non-vaccine-targeted types						
HPV 31/33/45	0.2	0.2	0.2	0.7	0.4	0.5
Other types excluding HPV 31/33/45[a]	2.2	0.8	1.1	1.6	1.4	2.3
Any HPV type[b]	2.8	1.2	1.8	2.3	2.0	3.8

[a] HPV types HPV 26/35/39/51/52/53/56/58/59/66/68/70/73/82.
[b] HPV types HPV 16/18/6/11/26/31/33/35/39/45/51/52/53/56/58/59/66/68/70/73/82.

The efficacy and safety of a new battery-powered portable thermocoagulator to treat cervical precancers is being evaluated in a randomized controlled trial (compared with cryotherapy and large loop excision of the transformation zone [LLETZ]) in Zambia, and in cross-sectional studies in Brazil, Bangladesh, China, India, Morocco, and Rwanda.

Breast cancer screening

In a randomized trial involving 130 000 women in India, the third round of screening to evaluate clinical breast examination (CBE) is in progress. SCR implemented a study evaluating the impact of increased awareness and better access to early breast cancer detection in a cohort of 22 500 women in India (Gadgil et al., 2017). With breast awareness, the proportion of women with early-stage tumours increased from 74% to 81% and the proportion with lymph node-negative cancers increased from 46% to 53%. A study on the pattern of breast cancer care in oncology centres in Morocco has been initiated to document time intervals in care pathways from onset of symptoms to detection of disease and initiation of treatment.

Oral cancer screening

The natural history of oral precancerous lesions is being addressed in the randomized trial of oral visual screening in Kerala, India. There was a 38% reduction in oral cancer incidence (95% CI, 8–59%) and a 81% reduction in oral cancer mortality (95% CI, 69–89%) in users of tobacco and/or alcohol who adhered to four screening rounds, at 15 years of follow-up. The study participants in both intervention and control arms have been linked to the Trivandrum Cancer Registry, and a 20-year follow-up analysis is planned in 2020.

Colorectal cancer screening

SCR initiated a pilot study in 2017 to assess the feasibility and efficacy of colorectal cancer screening with immunochemical faecal occult blood testing (iFOBT) followed by triage colonoscopy in Morocco, in collaboration with the National Institute of Oncology, Rabat. A pilot study in Thailand that involved 130 000 people demonstrated that iFOBT-based colorectal cancer screening could be implemented successfully in routine health services.

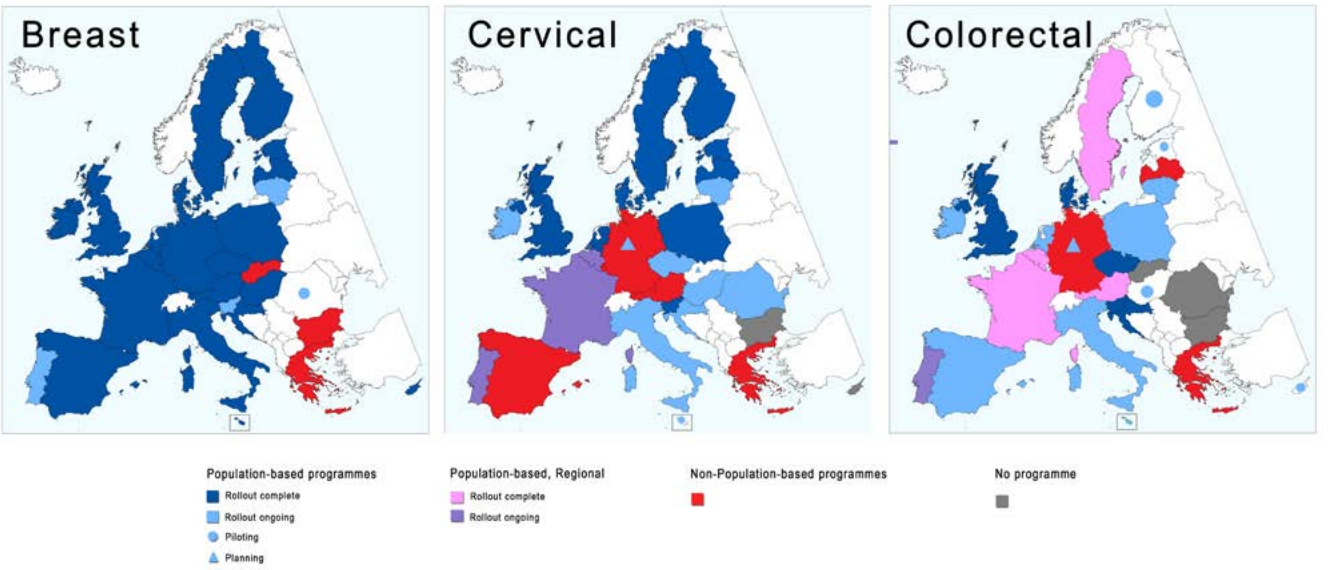
Comprehensive screening for noncommunicable diseases (NCDs)

SCR is evaluating the feasibility and efficacy of a comprehensive NCD control package administered by trained community health workers in rural India. The community health workers check people older than 30 years at their homes for body mass index, blood pressure, and blood sugar. Oral visual examination is performed on those who use tobacco and/or consume alcohol. Women are made aware of common symptoms of breast cancer, and they provide a self-collected vaginal sample for an HPV test for cervical cancer screening. The study is expected to recruit 13 000 individuals.

Evaluation of national cancer screening programmes

SCR prepared the second report on the implementation status of cancer screening in the European Union (Ponti et al., 2017). The report described implementation status, protocols, organization, screening coverage, and performance of breast, cervical, and colorectal cancer screening in the 28 European Union Member States (Figure 7). SCR evaluated the breast and cervical cancer screening programme of Morocco. In 2016, 1.6 million women were screened for breast cancer and 0.2 million women for cervical cancer. The programme was systematically evaluated and recommendations made to improve quality and performance. Evaluation of the breast and cervical cancer control programme in Japan demonstrated geographical disparities and the need to improve the participation rate (Sauvaget et al., 2016).

Figure 7. Status of implementation of the cancer screening programmes in the 28 European Union Member States. Figure reprinted from Basu P, Ponti A, Anttila A, Ronco G, Senore C, Vale DB, et al. (2018). Status of implementation and organization of cancer screening in the European Union Member States – Summary results from the second European screening report. Int J Cancer. 142(1):44–56. http://dx.doi.org/10.1002/ijc.31043 PMID:28940326



Technical support to national cancer control programmes

SCR provided scientific advice and support to national cancer control programmes in Bangladesh, Belize, Burundi, Congo, Kenya, Sierra Leone, Swaziland, Togo, Viet Nam, and other countries in collaboration with national governments, WHO, the International Atomic Energy Agency (IAEA), and the United Nations Population Fund (UNFPA). SCR is supporting the ministries of health in Burkina Faso, Chad, Côte d'Ivoire, and Senegal to implement and evaluate the first pilot projects on cervical cancer screening.

Training resources for cancer screening

The Screening Group has published a range of training resources for cancer screening, particularly relevant to trainees from low- and middle-income countries. All these resources are available on the newly designed website at http://screening.iarc.fr. The latest such publications are *Atlas of Colposcopy: Principles and Practice* and *Colposcopy and Treatment of Cervical Precancer*. Both of these publications, and many others, are freely accessible online.

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The Office of the Director comprises a small team that supports the Director in his oversight and coordination of the implementation of the Agency's scientific strategy and programme, as well as three Groups – the Communications Group (COM), the Education and Training Group (ETR), and the Laboratory Services and Biobank Group (LSB) – together with the Gambia Hepatitis Intervention Study (GHIS), a long-term scientific project of IARC, which is managed by the Director. The activities of these four Groups are described in the following sections.

In addition to providing administrative support to the Director's activities, the team in the Office of the Director assists in the coordination of a range of internal and external initiatives, including by supporting several internal advisory groups and committees, contributing to the preparation of Governing and Scientific Council meetings and related initiatives with current and prospective IARC Participating States, assisting the Director in the development of strategic partnerships with the Agency's network of institutional collaborators, in particular with WHO, and supporting the coordination of cross-cutting scientific initiatives and programmes with inputs from across the Agency. Some examples are given here of key activities in these areas during the 2016–2017 biennium.

The Director's office provides the secretariat to the regular meetings of the Senior Leadership Team, and in April 2017 organized a two-day off-site retreat, during which IARC senior personnel discussed topics related to engagement with non-state actors, management of reputational risks, and strategies for resource mobilization.

A new position of Bioethics and Compliance Officer was created in the Director's Office to address the increasing demands in support of two key areas: (i) providing a dedicated secretariat to the IARC Ethics Committee, which is responsible for the efficient and transparent ethical evaluation of all IARC projects, and (ii) ensuring the robust and consistent management across the Agency of potential conflicts of interests from external experts who participate in IARC activities.

Several high-level partnership agreements were signed or renewed during the biennium, in order to promote collaborations with other cancer research institutes around the world, including with the National Cancer Center of the Republic of Korea and the National Cancer Center Japan, with the Hospital Universitario San Ignacio in Colombia, and with the Centre Léon Bérard in Lyon, France. The Director attended the first International Conference on Cancer Prevention and Control in Beijing, China, in November 2017, and a partnership agreement was signed between IARC and the National Cancer Center of China to strengthen their collaboration in various areas.

The Director's Office assists in the coordination of collaborations with key partners in global policy development, technical cooperation, and advocacy for cancer prevention and control, including with WHO headquarters and regional offices and with other governmental and nongovernmental organizations. A major new initiative in this area supported by the Director's Office is the production of a global status report on cancer, jointly led by IARC and WHO (Management of Noncommunicable Diseases group). This report is being developed in response to a request from WHO Member States in the cancer resolution (WHA70.12) adopted at the Seventieth World Health Assembly in May 2017, which called for a public health and policy-oriented report providing evidence-based guidance on cancer prevention and control. The Director attended the WHO Global Conference on Noncommunicable Diseases (NCDs) held in Montevideo, Uruguay, on 18–20 October 2017. During the closing session, he delivered a speech about the role of research in addressing the NCD challenge within the context of the Sustainable Development Goals.

An example of a cross-cutting project supported by the Director's Office is the Cancer Prevention Europe initiative, which aims to develop a strong rationale for promoting cancer prevention research in Europe in the coming years. A consortium agreement was established with several major European research organizations with a strong focus on cancer prevention research, with the Director's Office coordinating and providing the secretariat to this initiative.

Finally, a major highlight in the biennium was the organization of the international scientific conference "Global Cancer: Occurrence, Causes, and Avenues to Prevention", to mark the 50th anniversary of the establishment of IARC. The resounding success of this initiative reflected an efficiently coordinated Agency-wide effort supported by the Director's Office.

The 50th anniversary celebrations vividly illustrated the impact of IARC's research worldwide but also brought into sharp relief the increasing demands on the Agency in the face of a growing global cancer burden. In times of economic restraint, to meet these challenges IARC must approach resource mobilization in innovative ways. In this context the Director's Office is leading an Agency-wide Resource Mobilization Task Force, supported by advice from external experts and Governing Council members, in order to identify and establish new partnerships and donor contributions in the coming biennium.

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Ms Solène Quennehen

The Communications Group (COM), as an integral part of the Director's Office, aims to present a clear and coherent image of IARC and its work to the scientific community, the media, and the general public. COM also provides information- and publication-related services to the research Sections.

Digital strategy

COM continued with its digital strategy of streamlining and standardizing publishing workflows, making careful technology choices, expanding its offerings of electronic formats, and engaging with readers.

The internal Manuscript Clearance System was launched in March 2016, with the aim of greater oversight and coordination of the Agency's scholarly outputs in mainstream journals.

The IARC Publications website (http://publications.iarc.fr), newly launched in December 2015, was further enhanced. The website has a modern and user-friendly design and offers seamless access to multiple formats to both individual and institutional users.

A subscription to Altmetric was integrated with the IARC Publications website in August 2017. Altmetric allows both the public and IARC personnel a view of the attention garnered by the Agency's publications in mainstream media, social media, policy documents, and other citing sources.

Dissemination of electronic books

COM has made it a priority to increase its channels of dissemination of electronic books. The IARC E-Bookshop was launched in June 2016. Because most of the Agency's titles are offered online in electronic format free of charge, the E-Bookshop offers a small range of for-sale titles. Investment in the E-Bookshop has continued in order to optimize efficient and cost-effective dissemination of the *WHO Classification of Tumours* ("Blue Books") series in electronic format.

Agreement with WHO Press

After an interim period in which COM conducted a review of print book

distribution options on the market, IARC and WHO Press renewed the publishing agreement in mid-2017. The agreement anticipates a sales model in which the Blue Books are released simultaneously in print and electronic formats, and thus clarifies the responsibilities of each party in coordinating bundle sales of the two formats.

Book promotion

COM prioritized user engagement as part of its digital dissemination strategy. September 2017 saw the release of a follow-up to the 2015 survey of the Blue Books readership.

In addition to its annual participation at the World Health Assembly and a booth at the 2016 World Cancer Congress, COM held booths at the United States and Canadian Academy of Pathology (USCAP) and the European Congress of Pathology (ECP) conferences in 2016, to engage directly with pathology audiences and promote the sale of Blue Books in electronic format.

Open Access

Following the creation in 2015 of an IARC Open Access (OA) fund in the amount of €50 000 per annum, the GCSF OA fund has supported 10 articles in 2016, along with project support for the 2016 publication of a series of OA articles on Cancer in Central and South America in a supplement issue of *Cancer Epidemiology*, and 21 articles in 2017 to date. The period available for analysis of the impact of the GCSF OA fund on OA publishing at IARC has been limited. However, comparison of 2015 and 2016 with 2014 as the baseline figure suggests that the GCSF OA fund has a positive impact on OA publishing at the Agency.

During the 2016–2017 biennium, IARC published several key reference publications:

WHO Classification of Tumours

WHO Classification of Tumours of the Urinary System and Male Genital Organs, 4th edition (print)
WHO Classification of Tumours of the Central Nervous System, revised 4th edition (print)
WHO Classification of Tumours of Female Reproductive Organs, 4th edition (PDF and EPUB)
WHO Classification of Tumours of the Breast, 4th edition (PDF and EPUB)
WHO Classification of Tumours of Soft Tissue and Bone, 4th edition (PDF and EPUB)
WHO Classification of Head and Neck Tumours, 4th edition (print)
WHO Classification of Tumours of Endocrine Organs, 4th edition (print)
WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, revised 4th edition (print)

IARC Monographs

Volume 107, Polychlorinated Biphenyls and Polybrominated Biphenyls (print)
Volume 108, Some Drugs and Herbal Products (print)
Volume 109, Outdoor Air Pollution (print)
Volume 110, Some Chemicals Used as Solvents and in Polymer Manufacture (print and PDF)
Volume 111, Some Nanomaterials and Some Fibres (print and PDF)
Volume 112, Some Organophosphate Insecticides and Herbicides (print and PDF)
Volume 113, 2,4-Dichlorophenoxyacetic acid (2,4-D) and Some Organochlorine Insecticides (Monograph on 2,4-Dichlorophenoxyacetic acid (2,4-D); PDF)

IARC Handbooks

Volume 15, Breast Cancer Screening (print, PDF, and EPUB)

IARC Working Group Reports

Energy Balance and Obesity, IARC Working Group Report No. 10 (print and PDF)

IARC Scientific Publications

Improving Public Health through Mycotoxin Control, IARC Scientific Publication No. 158 (PDF)
Molecular Epidemiology: Principles and Practices, IARC Scientific Publication No. 163 (PDF)

IARC Technical Publications

Planification et développement des registres du cancer basés sur la population dans les pays à revenu faible et intermédiaire, Publications techniques du CIRC N° 43 (print and PDF)
Planificación y desarrollo de registros de cáncer de base poblacional en los países de ingresos bajos y medios, IARC. Publicaciones técnicas N° 43 (print and PDF)
ПЛАНИРОВАНИЕ И РАЗВИТИЕ СИСТЕМЫ ПОПУЛЯЦИОННОЙ РЕГИСТРАЦИИ ЗЛОКАЧЕСТВЕННЫХ НОВООБРАЗОВАНИЙ В СТРАНАХ С НИЗКИМ И СРЕДНИМ УРОВНЕМ ДОХОДА. ТЕХНИЧЕСКАЯ ПУБЛИКАЦИЯ МАИР Номер 43 (print and PDF)
Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research, IARC Technical Publication No. 44 (print and PDF)
Colposcopy and Treatment of Cervical Precancer, IARC Technical Publication No. 45 (print and PDF)

Non-series publications

Centre international de Recherche sur le Cancer: Les 50 premières années, 1965–2015 (print, PDF, and EPUB)
World Cancer Report 2014 (PDF)

Electronic resources

Atlas of Colposcopy: Principles and Practice. IARC CancerBase No. 13: http://screening.iarc.fr/atlascolpo.php

Editing, layout, translation, and language services

As a result of the restructuring of IARC publishing in 2017, the COM Editing and Layout Team is now responsible for the post-production of the *IARC Monographs*, the *IARC Handbooks*, and the *WHO Classification of Tumours* (Blue Books) series, in addition to other established IARC Publications series. COM also provides English editing services to all IARC Groups, for articles for submission to peer-reviewed journals, book chapters, and other manuscripts.

COM provides translation services for short documents and administers external translation services for longer documents. COM also organizes successful language courses for the Agency's personnel in English, French, and Spanish.

Media services

IARC has expanded its media strategy, has increased its multimedia production, with the introduction of social media (Twitter, YouTube channel) to engage the wider public, and has an ever-wider base of media contacts. During the biennium, the Media team has increased the visibility of the Agency's research portfolio through more than 140 IARC news items and 12 press releases to date, along with Q&As, videos, interviews, and tutorials. Key dates such as World Cancer Day and Breast Cancer Awareness Month were marked with the production of a wide range of materials, including videos and interviews with IARC scientists, to raise awareness about the activities of the Agency in various fields of cancer research. The IARC Cancer and Society Lecture, timed to coincide with World Cancer Day, is aimed at all IARC personnel, providing an opportunity to consider where cancer research has an impact on society in a wider context.

The Media area and the broader Communications effort has strengthened and enhanced relationships with WHO, to better coordinate messaging between the two organizations. This area has expanded its personnel to include a professional visual designer, who translates scientific output in a visually enhanced fashion, to improve clarity and efficiency, particularly for prevention messaging. This has enabled the development of new tools, such as infographics and animations.

Web services

The Web services team has continued to ensure timely dissemination and promote IARC's core work through its website. The team has dedicated a substantial amount of work to improving the visibility of the increasing multimedia production through the new Media Centre page (http://www.iarc.fr/en/media-centre/index.php). In addition, during the biennium, the Web services team coordinated the process of developing and/or launching more than 10 research project and meeting websites.

The Web services team is currently continuing to improve the IARC Publications website by implementing the second phase of its development, which includes the consolidation of all IARC publications series, including the *IARC Monographs*, into the Publications website.

Public websites

Determinants of Breast Cancer in Morocco (EDSMAR) study: http://edsmar.iarc.fr

Thyroid Monitoring after Nuclear Accidents (TM-NUC) project: http://tmnuc.iarc.fr

Screening Group website: http://screening.iarc.fr

International Cancer Survival Benchmarking: http://survival.iarc.fr

International Incidence of Childhood Cancer (IICC) project (data update): http://iicc.iarc.fr/results

Exposome-Explorer: http://exposome-explorer.iarc.fr

South Africa Breast Cancer (SABC) study: http://sabc.iarc.fr

European Code Against Cancer in all EU languages: http://cancer-code-europe.iarc.fr/index.php/en/

Global Cancer Observatory (GCO): http://gco.iarc.fr

Cancer in Central and South America Project: http://gco.iarc.fr/resources/csa.php

Meeting website

Emerging Issues in Oncogenic Virus Research: http://www.iarc.fr/oncogenicviruses2018/en/

Education and Training Group (ETR)

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Assistant, fellowship programme
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Ms Eve El Akroud (until June 2016)

Assistant, courses programme
Ms Susan Anthony (until January 2016)
Ms Sandrine Montigny

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Ms Dominique Meunier

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Trainees
Ms Solène Coquery (until July 2016)
Mr Stanislas Jenatton (until September 2017)
Ms Manon Turlin (until July 2016)

Affiliated staff
Dr Maribel Almonte (Scientific director, Summer School module on Implementing Cancer Prevention and Early Detection)
Dr Partha Basu (Scientific director, Summer School module on Implementing Cancer Prevention and Early Detection)
Dr Freddie Bray (Scientific director, Summer School module on Cancer Survival Methods for Cancer Registries)
Dr Pietro Ferrari (Scientific director, Summer School module on Introduction to Cancer Epidemiology)
Dr Zdenko Herceg (Responsible officer, fellowship programme)
Dr Catherine Sauvaget (Scientific director, Summer School module on Implementing Cancer Prevention and Early Detection)
Dr Isabelle Soerjomataram (Scientific director, Summer School module on Cancer Survival Methods for Cancer Registries)
Dr Kurt Straif (Scientific director, Summer School module on Introduction to Cancer Epidemiology)

As a core statutory function of the Agency, IARC's education and training programme has made a substantial contribution to the development of human resources for cancer research in many countries and has also helped to shape the Agency's research strategy and widen its network of collaborators.

Key achievements of IARC's education and training programme during 2016–2017 are presented here. Whereas the Education and Training Group (ETR) coordinates the Agency's activities in these areas, many initiatives are led by the research Groups.

Postdoctoral Fellowships

During 2016–2017, new IARC Postdoctoral Fellowships were awarded to 14 postdoctoral fellows from 12 different countries. Research Return Grants were awarded to two fellows from low- and middle-income countries (LMICs), contributing to the establishment of their research activity in their own country.

Fellowships awarded in 2016 (7 new and 10 extensions) were co-funded by the European Union under the Marie Skłodowska-Curie Actions–People–COFUND Programme. Unfortunately, IARC was deemed ineligible to apply for European Commission MSCA–COFUND calls under the Horizon 2020 framework. Failure to complement funding from the IARC regular budget with additional sources of funds will lead to a significant reduction in the number of training opportunities for Fellows. In order to maintain an effective programme while pursuing alternative funding, the Agency will henceforth restrict the awarding of IARC Fellowships to candidates from LMICs. In view of additional constraints on the regular budget in 2018–2019, the call for applications was suspended in 2017.

In addition to agreements with Cancer Council Australia and the Irish Cancer Society, a new bilateral training agreement with the Research Council of Norway was negotiated, for the training of postdoctoral scientists from Norway at IARC. The 2016 call for proposals led to the award of the first fellowship in November 2016, and the Fellow joined IARC in early 2017.

Senior Visiting Scientist Award and Expertise Transfer Fellowship

Two Senior Visiting Scientist Awards were made in 2016–2017 (Table 1). Beyond the development of collaborative research projects, the Senior Visiting Scientist Award often leads to the expansion of important research initiatives or the joint production of key resources for capacity-building.

Short-term fellowships

In collaboration with the Union for International Cancer Control (UICC), the UICC-IARC Development Fellowship enables one participant of the IARC Summer School to return to IARC for a period of 3 months for further training and collaborative work. In 2017, this fellowship was awarded to a researcher from Kenya. Two other researchers, from Colombia and Libya, also benefited from a 1-month stay within the same call, funded by IARC. A fourth candidate, from Thailand, was supported by a UICC Technical Fellowship.

Hosting environment

The Agency also hosts a number of trainees, students, postdoctoral scientists, and visiting scientists supported by project funds from the research Groups. A total of 253 Early Career and Visiting Scientists from 59 different countries worked at IARC during the biennium.

All current rules and procedures pertaining to the IARC Research Training and Fellowship Programme were collected in one single handbook document. In parallel, a review of the programme was carried out, based on the feedback received from various sources, leading to the improvement of the terms and conditions under which Early Career and Visiting Scientists work while at the Agency.

Table 1. Senior Visiting Scientist Awards, 2016 and 2017

2016	
Professor Pär Stattin	Department of Urology, Uppsala University Hospital, Uppsala, and Register holder, National Prostate Cancer Register, Sweden
2017	
Dr John Brent Richards	Departments of Medicine, Human Genetics, Epidemiology and Biostatistics, McGill University, Montreal, Canada

The Agency continued to support the Early Career Scientists Association (ECSA), which was created in 2013. Among other activities, ECSA successfully held Scientific and Career Days in 2016 and 2017 (Figure 1). In 2017, the invitation was extended to scientists from the Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA) to present their work to peers in the field. Also, a Buddy Programme was launched in 2016, to provide complementary and informal support to newcomers.

Within the framework of the IARC Postdoctoral Fellowship Charter, ETR continued to develop the programme of internal generic skills courses. The close collaboration with the Human Resources Office, within the IARC Learning and Development Framework developed in 2015, led to an increase in the number of courses offered (Table 2). About 50 face-to-face courses were offered to Early Career Scientists in 2016–2017 and were attended by more than 110 different people. Online opportunities were also offered.

The relationship with the schools of the University of Lyon has been strengthened, in particular through the opening of some of the above-mentioned courses to local students.

IARC Summer School in Cancer Epidemiology

In view of budget constraints, the IARC Summer School in Cancer Epidemiology was not held in 2016. The event was held in Lyon in June–July 2017, with the goal of improving the methodological and practical skills of cancer researchers and health professionals. A new one-week module on Implementing Cancer Prevention and Early Detection (Figure 2) was organized and ran in parallel with the module on Cancer Survival Methods for Cancer Registries, followed by the two-week module on Introduction to Cancer Epidemiology. Additional financial support for the

Figure 1. ECSA Scientific and Career Day 2016. © IARC/Anouk Berger.

Table 2. Generic courses for Early Career Scientists, 2016 and 2017

Research skill development
Basic UNIX for handling large datasets
Cancer pathology: basic principles (twice)
Causality in cancer epidemiology
Data analysis for life sciences 1: statistics and R (massive open online course [MOOC])
Data preparation and formatting
Data science: exploratory data analysis (MOOC)
Epidemiology for non-epidemiologists (twice)
Galaxy: introduction to Galaxy
Galaxy: administration and development of tools
Galaxy: DNA methylome analyses
Galaxy: mutational signatures analyses with MutSpec
Generalized linear models using Stata
Introduction to biostatistics
Laboratory safety: biological risks (twice)
Linux cluster
Research ethics
Biomedical research ethics: an introductory course (twice)
IT skills
Adobe Acrobat Pro: PDF mastery (online)
Excel intermediate course
Writing skills
Effective scientific posters
EndNote basic (twice a year)
EndNote advanced (three times)
Grant writing (twice)
Open Access workshop (three times)
Publishing in scientific journals (twice)
PubMed workshop
Systematic reviews search methodology (twice a year)
Web of Science (twice a year)
Zotero
Communication skills
Effective interpersonal communication
Effective presentation skills
IARC Learning Week: harassment session
Instructor development course
Leadership and management
Financial management (twice)
Project management (twice)
Task management (twice)

Summer School came from the United States National Cancer Institute (NCI) as well as from the Nordic Cancer Union (NCU).

The Summer School was very well received by the 77 participants from 47 countries, of whom about 90% were from LMICs.

IARC "50 for 50" initiative

The IARC "50 for 50" initiative, organized in conjunction with the scientific conference held in Lyon on 7–10 June 2016 to celebrate the 50th anniversary of the establishment of IARC, was a fellowship programme that brought together, in Lyon, 50 future leaders in cancer research from LMICs, one for each year of IARC's existence. The selected participants came from 36 countries across the globe. The one-week programme included participation in the three-day scientific conference, a two-day pre-conference workshop, and a series of networking events to foster collaborations. A dedicated online space was set up for preparatory work, providing access to a variety of resources and networking. The vast majority of the participants rated the initiative very positively, stressing the quality of the interactions and the opportunity to learn about a wide variety of research topics and meet world experts in those fields.

Figure 2. IARC Summer School 2017, module on Implementing Cancer Prevention and Early Detection. © IARC/Sandrine Montigny.

eLearning

IARC has brought learning and training resources closer to their target audiences by developing eLearning material and initiatives.

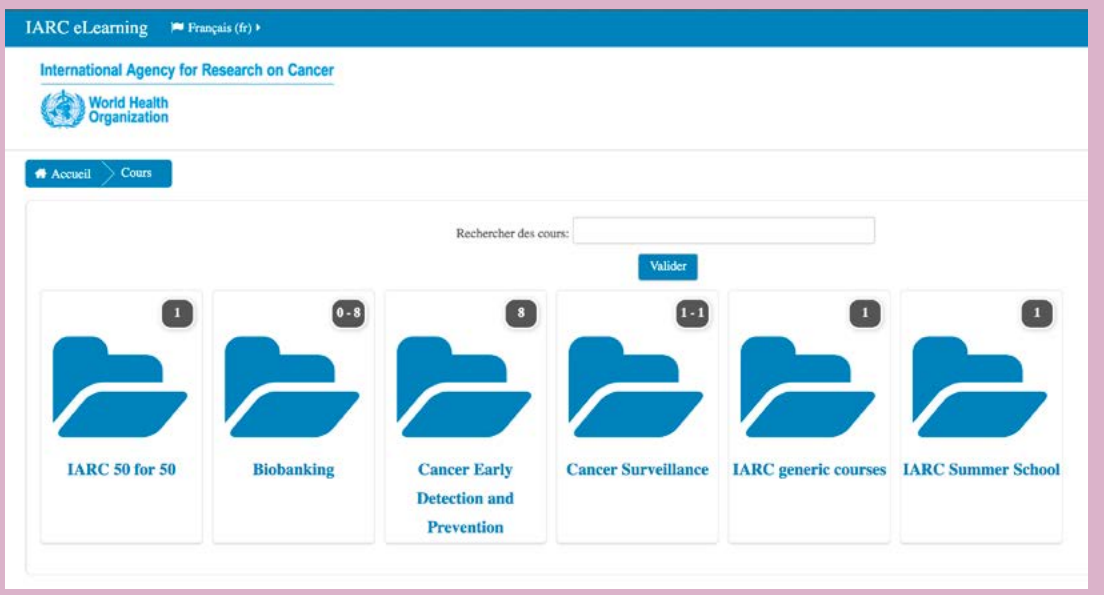
A learning management system was set up in 2016, enabling the design and deployment of online spaces for course participants to access practical information and learning resources before, during, and after the event (learning.iarc.fr).

Video-based learning resources were produced using the recording infrastructure set up at the Agency during the previous biennium, and made available from IARC WebTV (video.iarc.fr), from the learning management system, or from other IARC webpages.

eLearning modules were developed that combine videos and quizzes and are used as online material for participants to prepare before a face-to-face course (blended approach).

Webinar series were organized, reaching out to an increasing number of professionals worldwide (in biobanking and cancer registration).

Finally, partnership initiatives have been pursued to develop eLearning materials and courses. The collaboration established with the Institut Català d'Oncologia (ICO), Spain, led to the launch of the second joint online course in cancer epidemiology aimed at Latin American countries (http://www.e-oncologia.org/cursos/postgrado-fundamentos-metodologicos-investigacion/#.Wdhz82iCzD4).



IARC eLearning website. © IARC.

Specialized and advanced courses

Specialized or advanced courses are organized by IARC's scientific Groups, with increasing support from ETR. Most of these courses are associated with collaborative research projects, where IARC is transferring skills needed to conduct the projects and to enable the subsequent implementation of the research findings in the countries concerned. In some instances, specialized courses are co-organized with external partners and held at diverse locations throughout the world (Table 3). During the biennium, more than 60 courses were organized, enabling the training of a total of about 2500 scientists and health professionals.

Table 3. Specialized and advanced courses, 2016 and 2017

Course title	Location	Number of participants	External collaborations
2016			
CanReg5: train the trainers workshop	IARC	14	UICC; Regional Hubs for Cancer Registration in Sub-Saharan Africa, Asia, and Latin America
Basic cancer registration course	Malaysia	80	Regional Hub for Cancer Registration in Southern, South-East, and Eastern Asia; National Cancer Institute Thailand; Ministry of Health, Malaysia
Cancer registration workshop	Kazakhstan	27	Regional Hub for Cancer Registration in Northern Africa, Central and Western Asia; Kazakh Institute of Oncology and Radiology
Cancer registration assessment and workshop	Iraq	18	Regional Hub for Cancer Registration in Northern Africa, Central and Western Asia; WHO Regional Office for the Eastern Mediterranean
Basic cancer registration course	Indonesia	60	Regional Hub for Cancer Registration in Southern, South-East, and Eastern Asia; National Cancer Institute Thailand; Ministry of Health, Indonesia
Cancer registration workshop	Australia	45	Cancer Council Australia and other regional partners
Caribbean cancer registry workshop	Turks and Caicos Islands	22	Caribbean Public Health Agency (CARPHA); North American Association of Central Cancer Registries (NAACCR); United States National Cancer Institute (NCI), National Institutes of Health (NIH)
Cancer registration course	Russian Federation	44	WHO Regional Office for Europe
IARC–GICR course: Descriptive epidemiology research and analytical approach using population-based cancer registry data	Turkey	35	Regional Hub for Cancer Registration in Northern Africa, Central and Western Asia; Ministry of Health, Turkey
Workshop on cancer survival methods for population-based registries in low-and middle-income countries	Morocco	50	African Cancer Registry Network/Regional Hub for Cancer Registration in Sub-Saharan Africa; International Association of Cancer Registries
Online course on reports for cancer registries	Argentina	33	Regional Hub for Cancer Registration in Latin America; INC Argentina for Argentinian registries (hospital- and population-based)
Basic cancer registration course	India	35	Regional Hub for Cancer Registration in Southern, South-East, and Eastern Asia; WHO Regional Office for South-East Asia
CanReg regional training course	USA	10	Caribbean Public Health Agency (CARPHA); North American Association of Central Cancer Registries (NAACCR); United States National Cancer Institute (NCI), National Institutes of Health (NIH); Regional Hub for Cancer Registration in Latin America
Coding course (ICD-O-3) for hospital-based cancer registries and population-based cancer registries (online outreach for the Hub)	Chile	59	Ministry of Chile for Chilean registries; Regional Hub for Cancer Registration in Latin America
Cancer registration course	Kyrgyzstan	26	WHO Regional Office for Europe
Cancer registration course	Ghana	25	African Cancer Registry Network/Regional Hub for Cancer Registration in Sub-Saharan Africa; IAEA
CME on breast cancer management	India	100	Christian Hospital Ambilikkai and Cancer Control Foundation of India, Pollachi
Interactive workshop: strengthening the cancer control programme in Ukraine	IARC	5	
Orientation course on cervical and breast cancer early detection and control	Bangladesh	200	Directorate General of Health Services, Ministry of Health and Family Welfare, Government of Bangladesh; Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka; WHO country office for Bangladesh
Leadership training in colposcopy and advocacy for cervical cancer control	India	22	American Cancer Society
Training on thermocoagulation treatment of cervical precancerous lesions	Zambia	30	National Coordinator Cancer Prevention, Ministry of Health, Zambia
Training course on colposcopy and LEEP procedures in the management of abnormal cervical cancer screening results	Indonesia	23	Thai Society for Colposcopy and Cervical Pathology (TSCCP), Thailand; Department of Obstetrics and Gynaecology, Faculty of Medicine, Gadjah Mada University, Indonesia

Table 3. Specialized and advanced courses, 2016 and 2017 (continued)

Course title	Location	Number of participants	External collaborations
Project staff training for the follow-up phase of the 2- versus 3-dose HPV vaccine clinical trial in India	India	39	
Oncological screening: cervical cancer	Russian Federation	50	Petrov Research Institute of Oncology, Saint Petersburg, Russian Federation
Training course on the role of colposcopy in the early detection and prevention of cervical cancer for medical officers and nursing officers at colposcopy units	Sri Lanka	50	National Cancer Control Programme, Ministry of Health, Nutrition and Indigenous Medicine, Colombo, Sri Lanka; WHO country office for Sri Lanka
Training course for master trainers in cervical cancer prevention, early detection, and management (participants from Morocco and Gabon), blended training (online/face-to-face course in India), in French	India	16	Lalla Salma Foundation for Cancer Prevention and Treatment, Rabat, Morocco; Tata Memorial Centre Rural Cancer Project, Nargis Dutt Memorial Cancer Hospital (NDMCH), Barshi, Maharashtra, India
IARC-BELMED course: training course on principles, organization, evaluation, planning, and management of cancer screening programmes	Belarus	34	WHO headquarters, Switzerland; Public Health England, United Kingdom; Centro Javeriano de Oncología, Colombia
Introduction: training on Food Table GloboDiet	GoToMeeting	6	University College Dublin, Ireland
Train the trainers course on GloboDiet 24hDR interviews: data cleaning	GoToMeeting	5	GloboDiet collaborators, Malta
Train the trainers course on GloboDiet 24hDR interviews	GoToMeeting	8	GloboDiet collaborators, Brazil
ICAMA – Latin American Research Network in breast cancer: training in pathology and epidemiology	Costa Rica	15	PRECAMA collaborators in Latin America plus ICAMA colleagues from Guatemala
ABC-DO pathology training course	Uganda	22	
Training workshop for pathologists in cancer management	Côte d'Ivoire	24	West African Division of the International Academy of Pathology (WADIAP)
B3Africa webinars 1–3	GoToWebinar	23 + 60 + 22	Medical University of Graz, Austria; Uppsala University, Karolinska Institutet, Sweden
B3Africa face-to-face training course	South Africa	23	Stellenbosch University, Faculty of Medicine and Health Sciences, South Africa
2017			
Cancer registration workshop	Gabon	20	African Cancer Registry Network/Regional Hub for Cancer Registration in Sub-Saharan Africa
SurvCan-3: data collection for survival studies: follow-up using passive and active methods, live webinar	GoToWebinar	34	Cancer Institute (WIA), Chennai, India
Basic cancer registration course	Sri Lanka	60	Regional Hub for Cancer Registration in Southern, South-East, and Eastern Asia
Intermediate analysis cancer registration course	Ecuador	18	Regional Hub for Cancer Registration in Latin America; PAHO; INC Argentina; SOLCA Quito
Basic cancer registration course	Myanmar	70	National Cancer Institute Thailand; National Cancer Center Japan
Essential TNM: webinar sessions (3)	GoToWebinar	97 + 97 + 92	Regional Hub for Cancer Registration in Latin America; National Cancer Registry Uruguay
Cancer registration methods and strengthening cancer registries	Russian Federation	33	WHO Regional Office for Europe; Moscow Research Institute for Oncology; Regional Hub for Cancer Registration in Northern Africa, Central and Western Asia
Online regional transmission (Latin America) from Colombia National Cancer Institute coding course	Colombia (virtual for the region)	60	Regional Hub for Cancer Registration in Latin America; WHO/PAHO country office in Colombia
Cancer coding and staging masterclass	IARC	20	African Cancer Registry Network; WHO Regional Office for Europe
Hands-on training course in thermocoagulation for master trainer gynaecologists (participants from China)	India	4	Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS), Beijing, China; Christian Cancer Centre, Ambilikkai, India

Table 3. Specialized and advanced courses, 2016 and 2017 (continued)

Course title	Location	Number of participants	External collaborations
Hands-on training of pathology technicians for capacity development and strengthening of cytopathology, histopathology, and immunohistochemistry services in Bangladesh	Bangladesh	12	Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
Cervical cancer screening using VIA and management of premalignant lesions	Ecuador	6	Fundación Internacional Buen Samaritano Paul Martel Inc. (FIBUSPAM) and Instituto Nacional de Enfermedades Neoplásicas (INEN), Peru
Training course for master trainers in cervical cancer prevention, early detection, and management (participants from Bangladesh and India)	India	18	Directorate General of Health Services, Ministry of Health and Family Welfare, Government of Bangladesh; Tata Memorial Centre Rural Cancer Project, Nargis Dutt Memorial Cancer Hospital (NDMCH), Barshi, Maharashtra, India; WHO country office for Bangladesh
Training course for service providers in thermocoagulation and loop electrosurgical excision procedure (LEEP)	China	36	Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS), Beijing, China; Inner Mongolia Provincial Health Services
Training course for master trainers in cervical cancer prevention, early detection, and management	India	7	Chittaranjan National Cancer Institute
Training course in breast cancer awareness, prevention, early detection, and treatment	Ghana	130	Breast Care International
Training course on colposcopy and LEEP procedures in the management of abnormal cervical cancer screening results	Thailand	71	National Cancer Institute Thailand
CICAMS-IARC training course: planning and implementing cancer control programmes	China	36	Cancer Institute of the Chinese Academy of Medical Sciences (CICAMS), Beijing, China
Medical statistics for clinicians training course	India	50	Regional Cancer Centre, Trivandrum, India
Training course for master trainers in cervical cancer prevention, early detection, and management	India	15	Tata Memorial Centre Rural Cancer Project, Nargis Dutt Memorial Cancer Hospital (NDMCH), Barshi, Maharashtra, India
Training course for master trainers in cervical cancer prevention, early detection, and management	India	8	Regional Cancer Centre, Trivandrum, India
On-site visit to a recognized centre on breast cancer screening	United Kingdom	6	Public Health England, United Kingdom
ESTAMPA update on colposcopy training, within the First International Congress of Colposcopy and Pathology of the Lower Genital Tract	Peru	25	Peruvian League Against Cancer; Ministry of Health of Peru; PAHO; WHO; ESTAMPA sites around Latin America
Oncological screening	Russian Federation	20	Petrov Research Institute of Oncology, Saint Petersburg, Russian Federation
Training course on planning, feasibility, and piloting of the BELMED programme	Belarus	35	Public Health England, United Kingdom; WHO Regional Office for Europe
On-site training supplemented by a course	Belarus	20	Public Health England, United Kingdom; Loughborough University, United Kingdom
ICAMA – Latin American Research Network in breast cancer: training in pathology and epidemiology	Colombia	15	PRECAMA collaborators in Latin America plus ICAMA colleagues from Guatemala
B3Africa webinars 4–6	GoToWebinar	15 + 14 + 17	Medical University of Graz, Austria; Swedish University of Agricultural Sciences
Training course for master trainers in cervical cancer prevention, early detection, and management	Bhutan	20	Ministry of Health, Royal Government of Bhutan; Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan
BCNet/BBMRI-ERIC training workshop on biobanking for pathologists and pathology/histology technicians	Egypt	24	BBMRI-ERIC, Children's Cancer Hospital, Egypt
BCNet symposium: B3Africa in-person training	IARC	49	B3Africa consortium

Laboratory Services and Biobank Group (LSB)

Group head
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(until September 2017)
Dr Jiri Zavadil (Acting head)

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Data management assistant
Mr Ny Haingo Andrianarisoa

Biobank process management assistant
Dr Elodie Caboux

Laboratory services management assistant
Ms Brigitte Chapot
(until September 2017)

Biobank technicians
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Mr José Garcia
Ms Sophie Guillot
Mr Christophe Lallemand
Ms Gertrude Tchoua

Project assistant
Ms Dominique Meunier
(until September 2017)

Laboratory aide
Ms Nicole Farina

Students
Mr Marc Hellion
Ms Alyssia Marques
Mr Tiago Rambaud

The Laboratory Services and Biobank Group (LSB) liaises closely with the Administrative Services Office (ASO) and research Groups to provide core laboratory and biobanking services to support research activities across the Agency.

During the biennium, LSB expanded its role in supporting and advising biobanks in low- and middle-income countries (LMICs) and, in close collaboration with the Education and Training Group (ETR), conducted training courses and workshops on biobanking best practice principles for LMICs.

Laboratory Services

Common laboratory platforms

The focus of LSB is to ensure that the laboratory environment is conducive to work and that optimal laboratory services are provided for research. In conjunction with the Laboratory Steering Committee, Laboratory Services oversees the common laboratory platforms and ensures that the equipment is well maintained. Interactions between laboratory-based and epidemiological research are enhanced through the upgrading, updating, and acquisition of state-of-the-art scientific instruments and the provision of sufficient sample storage capacity. During the biennium, the shared platforms acquired new equipment.

Health and safety

Health and safety issues are managed in collaboration with the Occupational Health and Safety Committee (OHSC). Actions include (i) making available online the Safety Data Sheets of all reagents used or stored in IARC laboratories, (ii) installing “man-down” detectors for use in specific isolated rooms, (iii) presenting updates on chemical and biological risks to laboratory personnel, and (iv) organizing a pedometer challenge over a month, encouraging all personnel to be more physically active.

IARC Biobank

The IARC Biobank maintains biological sample collections from international collaborative studies and operates a service platform for sample retrieval, DNA extraction, and shipment of biological material worldwide. IARC’s facilities also serve as a custodian for collections from consortia and networks and for biological specimens from LMICs.

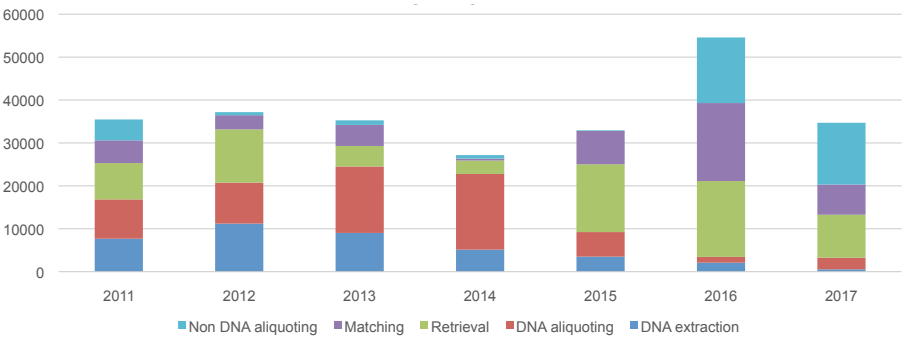
The IARC sample management system (SAMI) database stores information for

more than 5 million biological specimens, including more than 4 million from the European Prospective Investigation into Cancer and Nutrition (EPIC) study's collection. During the biennium, almost 200 000 new samples were imported into SAMI and more than 76 000 samples were accessed for internal or external collaborators. SAMI is continuously upgraded according to users' needs.

Standard practices and procedures are implemented across the Agency to govern sample transfer from and to the Agency and for the management of biological sample storage under optimal conditions. During the biennium, the Biobank secured additional funding from the Governing Council to replace obsolete equipment and purchase new units to increase cold storage capacity to cater for future needs and provide adequate backup facilities.

With regard to international biobanking, LSB led the revision of *Common Minimum Technical Standards and Protocols for Biological Resource Centres Dedicated to Cancer Research*, known as the "Green Book" (published by IARC in 2007). The new publication is known as the "Purple Book": *Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research*. The book provides best practice guidelines and recommendations for biobanks to facilitate collection, storage, and sharing of biological resources, including information on ethical, legal, and social issues (ELSI), with standard templates such as an informed consent form and Material Transfer Agreement.

Figure 1. Overview of the services provided by the IARC Biobank in a 7-year period. © IARC.

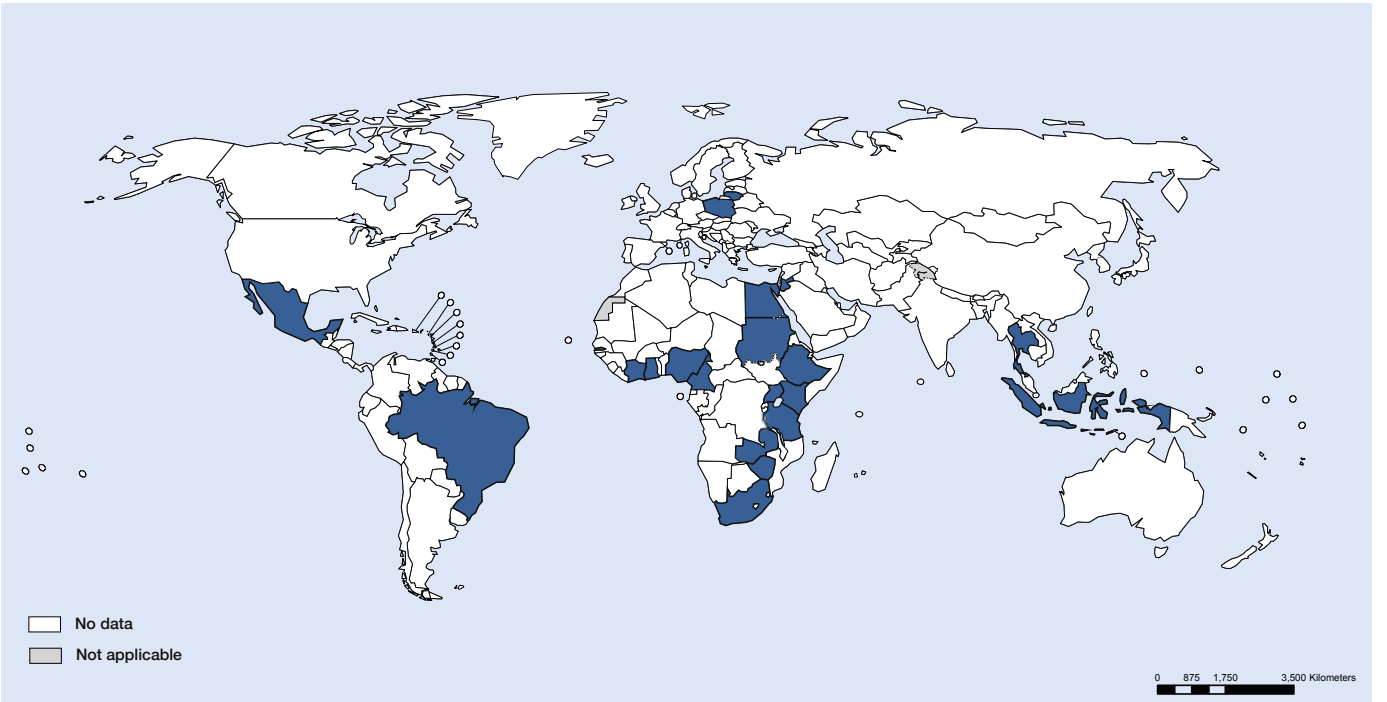


Biobank services

The Biobank provides pre-analytical services and operates on a cost-recovery basis, with a major contribution from the central IARC regular budget for infrastructure and salaries. During the biennium, a total of 21 projects were conducted relating to 26 requests from international institutions. This resulted in more than 32 000 sample retrievals from liquid nitrogen, 3400 DNA extractions, 6000 DNA aliquots, 39 000 non-DNA aliquots, and shipment of 165 parcels to 25 countries worldwide. Funds have been available for participation in research grants involving the use of biological samples.

An overview of the services provided in a 7-year period is presented in Figure 1.

Figure 2. BCNet members. © IARC.



World Health Organization

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: IARC
Map Production: IARC
World Health Organization (WHO)

Figure 3. Participants in the Second National Biobank Workshop, held in Yogyakarta, Indonesia, in November 2016. Courtesy of Faculty of Medicine, Gadjah Mada University, Yogyakarta, Indonesia.

The acquisition of equipment to extract nucleic acid from biological material other than blood has expanded the scope of the service platform to include extraction from tissue, saliva, and dried blood spots. Stringent quality control measures are in place to ensure high quality of samples, and the Biobank continues to participate in international proficiency schemes and scored very highly in the programmes of DNA extraction and DNA quantification from blood and tissue.

BCNet

Biobanking has evolved at a rapid pace to provide reliable infrastructure for high-quality research, but this is not the case in LMICs. In this regard, the LMICs Biobank and Cohort Building Network (BCNet) was created in 2013 to support the establishment of biobanks (http://bcnet.iarc.fr/). Activities have continued, and the network has developed into a focal point for LMIC biobanking. Currently, 34 institutions from 21 countries are members of BCNet (Figure 2). The network has established a catalogue programme (http://bcnet.iarc.fr/projects/biobank_catalogue.php) to register the biological resources of BCNet members. Information on available resources will be searchable via the BCNet website.

Training

International training workshops on Biobanking for Pathologists and Pathology/Histology Technicians were conducted in Côte d'Ivoire and in Cairo, Egypt, in partnership with the West African Division of the International Academy of Pathology and co-funded by the United States National Cancer Institute Center for Global Health (NCI-CGH) and the ADOPT-BBMRI project, within the framework of the European Union's Horizon 2020 (EU-H2020) programme. The workshops covered ELSI, quality, and information technology (IT). In-country workshops and training courses on biobanking were conducted by BCNet members in Indonesia (at Gadjah Mada University, in Yogyakarta) (Figure 3) and in Egypt (at the National Cancer Institute, in Cairo).

LSB is leading the Dissemination work package within the Bridging Biobanking and Biomedical Research across Europe and Africa (B3Africa) project. Project information is disseminated to biobank staff, researchers, ethics committee members, policy-makers, and the wider community through a website, newsletters, booths, presentations and posters at international events, open forums on ELSI, training sessions, and other meetings (Figure 4).

Collaborations

LSB represents IARC in the pan-European Biobanking and BioMolecular resources Research Infrastructure–European Research Infrastructure Consortium (BBMRI-ERIC) as an observer. IARC collaborates with BBMRI-ERIC

Figure 4. Participants in the B3Africa workshop on Ethics and Regulation in Biobanking, held in The Gambia in April 2016. Courtesy of Abdoulie Cham, Medical Research Council Unit, The Gambia.

members for international networking and interoperability issues to ensure that the structures and common services (CS) developed within Europe will be accessible to wider international communities. As a member of BBMRI-ERIC, IARC participates in various working groups – for CS-IT, CS-ELSI, and Quality Management – and participates in international projects.

LSB continues to support the African Organisation for Research and Training in Cancer (AORTIC), linking the organization with BBMRI-ERIC and BCNet and other biobanking organizations in Europe.

Grants

Three grant awards were received: (i) ADOPT BBMRI-ERIC (EU-H2020 no. 676550), which aims to expand BBMRI beyond Europe (October 2015–September 2018), (ii) B3Africa (EU-H2020 no. 654404), for which IARC is leading the Training and Dissemination work packages (July 2015–June 2018), and (iii) a grant for BCNet projects from NCI-CGH (NCI-CRDF-2016).

In addition, there are three research projects with budget allocation for biobank services: (i) HPV genomics, from Institut national du Cancer (INCa), France, (ii) Fat–ovarian, from INCa, and (iii) Impact of HBV genetic variability on liver disease in West Africa, from Agence nationale de recherches sur le sida et les hépatites virales (ANRS), France.

The Gambia Hepatitis Intervention Study (GHIS)

Group head
Dr Ramou Njie

Head of cancer registry
Mr Lamin Bojang

Trainee hepatologist
Dr Sheikh Omar Bittaye

Tumour registration officers
Mr Yusupha Bah
Mr Ebrima Bojang
Mr Modou Musa Sisawo
Mr Lamin Sanneh

Data entry clerk
Ms Mariatou Rahman

Senior project manager
Ms Mavis Foster-Nyarko

The Gambia Hepatitis Intervention Study (GHIS), now in its fourth decade, is a collaborative project undertaken by IARC, the government of the Republic of The Gambia, and the Medical Research Council (MRC), United Kingdom. GHIS was initiated in 1986 to evaluate the effectiveness of hepatitis B virus vaccination in childhood for the prevention of infection, chronic liver disease, and hepatocellular carcinoma in adulthood in a high-risk population. Led by the Director's Office, GHIS is a high-profile project of the Agency. At the beginning of GHIS, a population-based National Cancer Registry (NCR) was established.

The final phase of the project is under way. The focus is on identification of cases of liver cancer and chronic liver disease among patients who fall within the age range of the GHIS participants, and on establishing linkage of these patients to the GHIS database. The team of tumour registration officers, supported by the GHIS Group Head, is performing enhanced surveillance of liver cancer and chronic liver disease in hospitals and health centres across the country. Suspected cases of liver cancer are assessed clinically and by ultrasonography/computed tomography imaging and quantitative α-fetoprotein assay. Where possible, diagnosis has been strengthened by conducting histopathology at IARC, performed by Dr Behnoush Abedi-Ardekani (GCS); Dr Ousman Leigh, a Gambian pathologist, has been trained in liver pathology at IARC to provide a medium- to long-term improvement in capacity in The Gambia. All confirmed cases of liver cancer are recorded in the NCR, and cases of chronic liver disease are recorded in a linked database.

Efforts are ongoing to match the liver patients to the GHIS database on the basis of a number of identifiers. However, the variety of Gambian names, different spellings, and changes in names over time present major challenges to establishing this linkage more than 30 years after the study began. Evaluation of the palm prints and footprints offers one key linkage parameter, and this work is being conducted in collaboration with Interpol in Lyon.

An evaluation of GHIS, comprising a review of the NCR, liver cancer, and chronic liver disease data spanning the period 2012–2017, was carried out in a special one-day meeting held in Lyon on 24 October 2017. Among other issues, diagnoses (including pathology review), record linkage with vaccination status, and time to accrual of a sufficient number of cases for the statistical analysis plan were discussed. The meeting was attended by Dr Ramou Njie, Dr Ousman Leigh, IARC Director Dr Christopher P. Wild, Sir Andrew Hall, Professor Hazel Inskip, Professor Nick Day, Dr Behnoush Abedi-Ardekani, and Mr Morten Ervik.

Section of Support to Research (SSR)

Office of Director of Administration and Finance

Director of administration and finance
Mr David Allen (until April 2016)
Dr Tamás Landesz

Administrative officer
Ms Virginie Vocanson

Assistant (Documents)
Ms Agnès Meneghel

Administrative assistant
Ms Nathalie Lamandé

Administrative Services Office

Administrative services officer
Ms Elisabeth Françon

Administrative assistant
Ms Sophie Servat

Assistants (Procurement)
Ms Sandra Lejeune (until March 2017)
Ms Fabienne Lelong
Mr Didier Louis
Ms Sandrine Macé

Assistant (Registry)
Mr François Deloche

Assistant (Security and building management)
Mr Jean-Alain Pedil

Secretary
Ms Valérie Rut

Support staff
Mr Thomas Cler (Laboratory maintenance)
Mr José Garcia (Laboratory and administration)
Mr William Goudard (Space maintenance)
Mr Antoine Hernandez (Driver)
Mr Michel Javin (Reprography)
Mr Hafed Lamouchi (Electronic maintenance)
Ms Séverine Sarboni (Reception) (until August 2017)

Resource Mobilization, Budget, and Finance Office

Administration and finance officer
Ms Angkana Santhiprechachit

Resource mobilization and grant officer
Dr Olaf Kelm

Budget officer
Ms Editta Odame

Finance officers
Ms Julie Goux
Mr Rommel Nidea

Assistants (Budget)
Mr Thomas Odin
Ms Madeleine Ongaro
Mr Franck Rousset

Assistants (Accounts)
Ms Christine Abou-Rizk (until January 2016)
Mr Samuel Billard
Mr Pascal Binet
Mr Christian Mah
Ms Laurence Piau
Ms Adèle Séguret

Assistants (Resource mobilization)
Ms Véronique Chabanis
Ms Nathalie Lamandé (until January 2016)
Ms Claire Salignat

Support staff
Mr Olivier Badadan (until June 2016)

Trainees
Ms Eneried Jaramillo (until September 2017)
Ms Julie Muller (until June 2016)
Ms Mariam Safi (until June 2017)
Ms Anna Schmutz
Mr Valentin Sorgue (until June 2017)

Human Resources Office

Human resources officer
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Assistants (Human resources)
Ms Catherine Bassompierre
Ms Maud Bessenay
Ms Julianna Soos (Training)

Secretary
Ms Sophie Sibert

Central Secretarial Services (CSS)
Ms Dominique Bouchard
Ms Nandini Deleu
Ms Andreea Spanu

Staff physician
Dr Pierre-Olivier Dondoglio (until July 2016)
Dr Chantal Ferracin

Secretary to IARC Staff Association Committee and Staff physician
Ms Isabelle Poncet

Relocation assistant
Ms Christine Astier

Information Technology Services

Head, Information Technology Services
Mr Philippe Damiecki (until September 2017)
Mr Francisco Lozano

IT officers
Mr Philippe Boutarin
Mr Christopher Jack

Assistants (Informatics)
Ms Lucile Alteyrac
Mr Nicolas Tardy

Support staff
Mr Sébastien Agathe (Informatics technician)
Mr Théodore Cholin (Web development technician)
Mr Rémi Valette (SharePoint and .Net developer)

The role of the Section of Support to Research (SSR) is to support the achievement of IARC's scientific objectives through efficient and effective management of the Agency's resources and provision of administrative services, ensuring accountable risk mitigation and implementing strategies to strengthen capacities and maximize IARC's impact.

The Section is made up of the specialized administrative units that manage and provide services intrinsic to the successful implementation of the Agency's scientific programme in the areas of: (i) Resource Mobilization, Budgeting, and Financial Management; (ii) Human Resources Management; (iii) Procurement, Conference Services, Office Administration, and Building Management; and (iv) Information and Communications Technology. SSR ensures that the Agency's activities meet the highest standards of management, efficiency, and accountability in the use of the funding made available by its Participating States and donors.

In addition to the regular provision of services, during 2016–2017 the SSR team's achievements in four areas have contributed substantively to the continued efforts to maintain IARC's status as a leader in the ever-changing international research environment.

During the biennium, SSR spearheaded the review of IARC's key administrative processes in an effort to simplify, streamline, and re-engineer the workflows of the most frequently used contractual modalities. The resulting automated eWorkflows operating in a SharePoint environment aim to increase efficiency, accelerate clearance procedures, and reduce administrative burden across the Agency.

Notable progress has been made, in cooperation with our host country, in preparing for the construction of a new state-of-the-art IARC building in Lyon. The public tender for a combined design and build was launched by the Métropole de Lyon in May 2016. IARC has actively participated in the assessment, shortlisting, and decision-making process. The new building is scheduled to be inaugurated in 2021. Alongside working towards the construction of IARC's future premises, SSR continued to ensure that IARC's scientific activities were not interrupted by the continued technical failures experienced in the current premises. In view of several incidents with varying degrees of severity, a formal IARC Business Continuity Plan and Disaster Recovery Plan has been put in place to ensure a smooth response to anticipated and unexpected events. In addition, in view of the escalating international terrorist threat and specifically events in France during 2016–2017, significant efforts were made towards reinforcing IARC's security measures and response capacity.

Major efforts were made to mobilize additional external financial resources to deliver the approved programme of work in line with the IARC Medium-Term Strategy for 2016–2020. SSR continues to ensure effective management of resources entrusted to IARC, as consistently recognized by the WHO external auditors. Important efforts were made to further enhance IARC's project management capacity, reporting tools, and outreach. New data analytics tools were introduced during the biennium, such as an expanded Project Portal and a new Management Dashboard, helping to further enhance transparency, effective oversight, and financial reporting.

Several measures were implemented aimed at enhancing the development, motivation, and productivity of personnel. The revised IARC Learning and Development Framework comprises innovative approaches to ensure that IARC personnel are equipped with the right competencies to meet the current and future needs of the

Agency. Specialized training sessions were provided focusing primarily on technical requirements. To overcome budget constraints, face-to-face training sessions were complemented with online courses and novel group-based learning methods. IARC also implemented the revised compensation package for personnel in the professional and higher categories as from 1 January 2017. A new electronic recruitment system was introduced in 2017.

SSR remains committed to the principle of continuous quality improvement, striving to further improve the Agency's processes and support services, inter alia by collecting feedback through a yearly services survey. SSR also holds biannual town hall meetings to communicate the Section's objectives and planned activities, and holds information sessions when required to explain new policies and procedures.

Committees

Laboratory Steering Committee (LSC)

Laboratory research is essential to support various epidemiological projects conducted at IARC on the causes and mechanisms of cancer. It involves six Groups at IARC (BMA, EGE, GCS, ICB, LSB, and MMB). The IARC Laboratory Steering Committee (LSC) oversees the IARC core laboratory facilities and advises the Director on their most efficient use and requirements for future investment.

Significant tasks of the LSC over the biennium have concerned coordinating the acquisition of new equipment (sequencer, robot for chromatin extraction, freezers, and nitrogen tanks), defining priorities, and establishing a plan for replacement of obsolete small and medium-sized laboratory equipment. A plan for securing the power supply for critical laboratory equipment was set up. An inventory of all maintenance contracts for laboratory equipment was made, and priorities were established for coverage of the corresponding costs under the LSB budget. Some good practices for use of shared equipment and the procedure for reception of biological samples were revised. The Laboratory Services website on the intranet was reviewed and updated.

Biobank Steering Committee (BSC)

The role of the IARC Biobank Steering Committee (BSC) is to support biobanking activities at the Agency and advise the Director regarding the strategic development of the Biobank both internally and with external collaborators and projects, including the growing involvement in international biobanking capacity-building in low- and middle-income countries.

During the biennium, the structure of the committee was revised and the number of members reduced from 18 to 12 to better match the needs of the Agency.

The BSC advised and approved the request of LSB to apply to the Governing Council for new storage equipment for the Biobank. The requested purchase of new equipment was staggered over 3 years and was based on the evaluation of the future plans of the scientific Groups.

The BSC also participated in the preparation of *Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research*, which was published as an IARC Technical Publication (No. 44) in 2017. The information from the 2007 publication (IARC Working Group Report No. 2, known as the "Green Book") was updated, and a new section on ethical, legal, and social issues (ELSI) was included.

The BSC continued to participate in discussions about the design of the Biobank in the new IARC building, according to the future needs of the Agency, and participated in the development of the Business Continuity Plan for the Biobank. A document was circulated to laboratory groups for the prioritization of samples. The intended purpose was to evaluate the degree of priority for samples stored in freezers on the different laboratory floors.

Computational Biology, Bioinformatics, and Biostatistics (C3B) Steering Committee

The IARC Computational Biology, Bioinformatics, and Biostatistics (C3B) Steering Committee (formerly the Bioinformatics Steering Committee) continues to oversee IARC's activities in these relevant areas. IARC has recently reviewed and reinforced its capacity in terms of personnel and technical capabilities. The C3B, chaired by Dr James McKay (GCS) with support from vice-chairs Dr Jiri Zavadil (MMB) and Dr Pietro Ferrari (NMB), meets quarterly to consider strategic matters and developments and advise the Director accordingly.

The vibrant day-to-day activities happen within three Working Groups: on Bioinformatics, led by Dr Matthieu Foll (GCS) and Dr Magali Olivier (MMB); on Information Technology, led by Dr Matthieu Foll (GCS) and Mr Christopher Jack (ITS); and on Biostatistics, led by Dr Pietro Ferrari (NMB). These Working Groups promote and sustain a sense of community, and facilitate and foster across-Agency and interdisciplinary interactions, also involving collaborative partners. They organize seminars and discussion blogs, develop training sessions in collaboration with the Education and Training Group (ETR), and undertake expansions of IARC's high-performance computing capacity.

Ethics Committee (IEC)

The IARC Ethics Committee (IEC) ensures that research conducted or supported by IARC conforms to international ethical standards for research involving humans. The IEC ethical review is complementary to local/national ethical approval. Over the biennium, the IEC was composed of 11 senior individuals from diverse backgrounds and nationalities. The IEC is chaired by Dr Béatrice Fervers, supported by Dr Paolo Vineis as vice-chair and assisted by Dr Chiara Scoccianti as secretary. The Ethics Advisory Group provides guidance on an ad hoc basis on areas where specialist expertise is required.

During the 2016–2017 biennium (up to September 2017), the IEC evaluated 81 new projects and 39 resubmissions of projects previously reviewed by the IEC. To improve support to IARC scientists, the IEC developed simplified procedures and a template for informed consent. A platform for improved submission, processing, and review of projects was implemented. Training of IEC members and a course on biomedical research ethics for IARC personnel were organized. The IEC re-evaluated the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort (initial evaluation in 1995). A discussion paper on the ethical issues raised by incidental findings in genomic studies, prepared by the IEC, was submitted for publication.

Occupational Health and Safety Committee (OHSC)

The mission of the IARC Occupational Health and Safety Committee (OHSC) is to ensure, in close collaboration with the Staff Physician and the IARC administration, that optimal working conditions are provided to all IARC personnel.

The activities of the OHSC during 2016–2017 include (i) some developments for the easy visualization of Safety Data Sheets of all laboratory chemicals (collaboration with LSB), (ii) some preliminary work on risk assessment of all IARC activities, and (iii) regular and specific training, such as courses on chemical hazards and biological risks, as well as a first aid training course organized jointly with the Staff Association and attended by 43 participants.

As a fun way to fight sedentary behaviour at work, in spring 2017 the OHSC launched the first IARC pedometer challenge; it was a great success, with 270 participants and 57 782 323 steps recorded over a month. Finally, the OHSC drafted a code of good health and safety practice, which will be implemented at the end of 2017.

Governing and Scientific Councils

The International Agency for Research on Cancer (IARC) was established in May 1965, through a resolution of the Eighteenth World Health Assembly, as an extension of the World Health Organization, after a French initiative. Its governance is effected through the IARC Governing and Scientific Councils.

Governing Council

IARC's general policy is directed by a Governing Council, composed of the Representatives of Participating States and of the Director-General of the World Health Organization. It meets every year in ordinary session in Lyon, usually the week before the World Health Assembly. The Governing Council elects IARC's Director for a five-year term. The Council re-elected Dr Christopher P. Wild in May 2013 to serve for a second five-year term as from 1 January 2014. The chairperson of the Governing Council prepares the meetings together with the Secretariat and, together with the vice-chairperson, advises the Director throughout the year.

IARC was deeply saddened by the untimely death of Dr Chariklia Balas (1967–2017), who had served as the Representative of Germany on the IARC Governing Council since 2013.

Courtesy of Ulrich Dietz

Scientific Council

The Scientific Council consists of highly qualified scientists selected on the basis of their technical competence in cancer research and allied fields. Members of the Scientific Council are appointed as experts and not as representatives of Participating States. When a vacancy arises on the Scientific Council, the Participating State that nominated the departing member may nominate up to two experts to replace that member. Scientific Council members are appointed for four-year terms by the Governing Council. The Scientific Council reviews the scientific activities of the Agency and makes recommendations on its programme of permanent activities and priorities. The Scientific Council meets every year in ordinary session in late January/early February.

Budget

IARC activities are partially funded by the assessed contributions paid by its Participating States. In addition, substantial funding comes from extrabudgetary sources, mainly grant awards, both national and international. The regular budget for the 2016–2017 biennium was approved in May 2015 at a level of €43 413 599.

Participating States and Representatives at IARC Governing Council's Fifty-Eighth Session, 19–20 May 2016

United Kingdom of Great Britain and Northern Ireland

Dr Mark Palmer, Chairperson
Director, International Strategy
Medical Research Council
London

Dr Adam Babbs
Programme Manager – Cancer
Medical Research Council
Swindon

Australia

Professor Chris Baggoley,
Vice-Chairperson
Australian Government Chief Medical Officer
Department of Health
Canberra

Switzerland

Dr Diane Steber Büchli, Rapporteur
Federal Office of Public Health
Division of International Affairs
Bern

Austria

Dr Britta Kunert
Austrian Federal Ministry of Science, Research and Economy
Vienna

Belgium

Mr Lieven De Raedt
Attaché Relations Internationales
SPF Santé publique, Sécurité de la Chaîne Alimentaire et Environnement
Brussels

Brazil

No Representative

Canada

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Office of International Affairs for the Health Portfolio
Ottawa, Ontario

Denmark

Professor Mads Melbye
Director, Statens Serum Institute
Copenhagen

Finland

Professor Juhani Eskola
Director General, National Institute for Health and Welfare (THL)
Helsinki

Professor Sakari Karjalainen
Secretary General, Cancer Society of Finland and Cancer Foundation Finland
Helsinki

France

Dr Thierry Breton
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Institut national du Cancer (INCa)
Boulogne-Billancourt

Germany

Dr Chariklia Balas
Senior Advisor, Federal Ministry of Health
Bonn

India

Professor G.K. Rath (unable to attend)
Dr B.R. Ambedkar Institute Rotary Cancer Hospital (DBRAIRCH)
All India Institute of Medical Sciences (AIIMS)
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Ireland

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Cancer, Blood and Organs Policy Unit
Department of Health
Dublin

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Professor Walter Ricciardi (unable to attend)
Commissioner, Istituto Superiore di Sanità
Rome

Dr Pietro Comba
Research Director, Department of the Environment and Primary Prevention
Istituto Superiore di Sanità
Rome

Japan

Mr Hiroyuki Yamaya
Director, Office of International Cooperation
Division of International Affairs, Minister's Secretariat
Ministry of Health, Labour and Welfare
Tokyo

Dr Takuma Kato
Deputy Director, Division of International Affairs, Minister's Secretariat
Ministry of Health, Labour and Welfare
Tokyo

Dr Seiichiro Yamamoto
National Cancer Center Research Institute (NCCRI)
Tokyo

Morocco

Dr Rachid Bekkali (unable to attend)
Directeur général, Fondation Lalla Salma
Rabat

Dr Latifa Belakhel
Chef de Service de la Prévention et de Contrôle du Cancer
Direction de l'Epidémiologie et de Lutte contre les Maladies
Ministère de la Santé
Rabat

Netherlands

Dr Marianne Donker
Director, Public Health Department
Ministry of Health, Welfare and Sport
The Hague

Mr Marc Fakkel (unable to attend)
Policy Advisor, Public Health Department
Ministry of Health, Welfare and Sport
The Hague

Norway

Dr Edgar Rivedal
Senior Adviser, Norwegian Scientific Committee for Food Safety
Oslo

Dr Karianne Solaas
Senior Adviser, The Research Council of Norway
Lysaker

Qatar

Dr Al-Hareth M. Al-Khater
Deputy Medical Director, National Center for Cancer Care and Research
Hamad Medical Corporation
Doha

Republic of Korea

Dr Kyungwon Hwang
Deputy Director, Division of Disease Control Policy
Ministry of Health and Welfare
Seoul

Dr Yoon Jung Chang
Chief, Hospice and Palliative Care Branch
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Russian Federation

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WHO headquarters, Geneva

Ms Joanne McKeough
Principal Legal Officer
WHO headquarters, Geneva

Ms Françoise Mourain-Schut
Senior Legal Officer
WHO headquarters, Geneva

Dr Andreas Ullrich
Advisor to ADG/NMH, IARC Liaison Officer
WHO headquarters, Geneva

Dr Cherian Varghese
Coordinator, NVI/MND
WHO headquarters, Geneva

Observers

Scientific Council

Professor James F. Bishop
Outgoing chairperson

Professor Ellen Kampman (unable to attend)
Incoming chairperson

Union for International Cancer Control (UICC)

Dr Cary Adams
Chief Executive Officer, Union for International Cancer Control (UICC)
Geneva

External Audit

Mr Lito Q. Martin (unable to attend)
Director, International Audit and Relations Office
Commission on Audit
Quezon City, Philippines

Participating States and Representatives at IARC Governing Council's Fifty-Ninth Session, 18–19 May 2017

United Kingdom of Great Britain and Northern Ireland

Dr Mark Palmer, Chairperson
Director, International Strategy
Medical Research Council
London

Dr Adam Babbs
Programme Manager – Cancer
Medical Research Council
Swindon

Denmark

Professor Mads Melbye,
Vice-Chairperson
Director, Statens Serum Institute
Copenhagen

Ireland

Mr Keith Comiskey, Rapporteur
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Australia

Professor Brendan Murphy
Australian Government Chief Medical Officer
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Canberra

Austria

Dr Britta Kunert
Austrian Federal Ministry of Science, Research and Economy
Vienna

Belgium

Mr Lieven De Raedt
Attaché Relations Internationales
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Brazil

No Representative

Canada

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Ms Lucero Hernandez
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Italy

Professor Walter Ricciardi
Commissioner, Istituto Superiore di Sanità
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Mr Hiroyuki Yamaya
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Ministry of Health, Labour and Welfare
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Dr Hitoshi Nakagama
President, National Cancer Center
Tokyo

Dr Seiichiro Yamamoto
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Morocco

Dr Rachid Bekkali (unable to attend)
Directeur général, Fondation Lalla Salma
Rabat

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Chef de Service de la Prévention et de Contrôle du Cancer
Direction de l'Epidémiologie et de Lutte contre les Maladies
Ministère de la Santé
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Goyang-si, Gyeonggi-do

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Sweden

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Secretary-General, Medicine and Health
Swedish Research Council
Stockholm

Switzerland

Dr Diane Steber Büchli (unable to attend)
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Outgoing chairperson

Professor Giske Ursin
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Professor Béatrice Fervers
Chairperson, IARC Ethics Committee

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IARC Staff Publications 2016–2017

Achaintre D, Buleté A, Cren-Olivé C, Li L, Rinaldi S, Scalbert A (2016). Differential isotope labeling of 38 dietary polyphenols and their quantification in urine by liquid chromatography electrospray ionization tandem mass spectrometry. Anal Chem. 88(5):2637–44. http://dx.doi.org/10.1021/acs.analchem.5b03609 PMID:26814424

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