International Agency for Research on Cancer

World Health Organization

Scientific Council **SC/50/9**
Fiftieth Session 13/12/2013

Lyon, 29–31 January 2014
Auditorium

PRESENTATION OF CROSS-CUTTING THEMES

Sections have been asked to present three cross-cutting themes where the input of the Scientific Council would be valuable. These topics will be presented as follows:

Sections and Groups

Acronym	Full name of Section/Group	Responsible Officers
CIN	**Section of CANCER INFORMATION**	**Dr D. Forman** Deputy: Dr F. Bray
EDP	**Section of EARLY DETECTION AND PREVENTION**	**Dr R. Sankaranarayanan**
PRI	Prevention and Implementation Group	Dr R. Herrero
QAS	Quality Assurance Group	Dr L. Von Karsa
SCR	Screening Group	Dr Sankaranarayanan
ENV	**Section of ENVIRONMENT AND RADIATION**	**Dr J. Schüz** Deputy: Dr A. Kesminiene
GEN	**Section of GENETICS**	**Dr P. Brennan**
BST	Biostatistics Group	Dr G. Byrnes
GCS	Genetic Cancer Susceptibility Group	Dr J. McKay
GEP	Genetic Epidemiology Group	Dr P. Brennan
IMO	**Section of IARC MONOGRAPHS**	**Dr K. Straif** Deputy: Dr D. Loomis
INF	**Section of INFECTIONS**	**Dr M. Tommasino**
ICB	Infections and Cancer Biology Group	Dr M. Tommasino
ICE	Infections and Cancer Epidemiology Group	Dr S. Franceschi
MCA	**Section of MECHANISMS OF CARCINOGENESIS**	**Dr Z. Herceg**
EGE	Epigenetics Group	Dr Z. Herceg
MMB	Molecular Mechanisms and Biomarkers Group	Dr J. Zavadil
MPA	**Section of MOLECULAR PATHOLOGY**	**Dr H. Ohgaki**
NME	**Section of NUTRITION AND METABOLISM**	**Dr I. Romieu**
BMA	Biomarkers Group	Dr A. Scalbert
DEX	Dietary Exposure Assessment Group	Dr N. Slimani
NEP	Nutritional Epidemiology Group	Dr I. Romieu

Topic 1: Mutation spectra in experimental models and in humans (Jiri Zavadil, Head, Molecular Mechanisms and Biomarkers Group (MMB), Coordinator)

Participating Sections and Groups MCA/MMB, MCA/EGE; IMO; INF/ICB; GEN/GCS; GEN/BST

Key multidisciplinary activities at IARC aim to systematically identify, evaluate and classify chemical compounds for their carcinogenic risk, mainly through the Agency's flagship programme of the IARC Monographs (IMO). At IARC and elsewhere, the identification of chemicals posing carcinogenic hazards to humans has historically relied upon cancer epidemiology data and in vivo cancer bioassay studies in rodents. However, these studies have limitations in terms of interpretation and resource needs, which make them impractical as screens for the thousands of compounds people are exposed to during their lifetime. With the advent of high-throughput genome-wide studies, the emerging patterns of somatic mutations in human cancers offer some mechanistic insights into past carcinogenic exposures and cancer etiology, and a large amount of data on human somatic mutations is accessible via numerous public data portals. However, there is often a lack of experimental and mechanistic data linking the genome-wide mutation patterns to the specific effects of genotoxic compounds that can be used to classify them as carcinogens or suspected carcinogens in an evidence-based and timely manner.

In order to circumvent the need for costly and time-consuming animal models of cancer, and moving away from the single gene studies in classical in vitro assays, the MCA Section has initiated a novel cross-Section strategy based on experimental modelling of in vitro mutagenesis by select chemicals, during which genome-wide alterations and events that drive neoplastic disease can be assessed in a cellular phenotypic context that recapitulates key features of tumourigenesis (i.e. *initiation*, *promotion* and *progression*). To this end, MCA employs cultured primary mouse embryonic fibroblasts with humanized p53 knock-in, known as Hupki or HUF cells, in which exposures to cancer agents induce immortalization and transformation of cellular clones arising from senescing cultures. This process closely parallels the conversion of normal cells to tumour cells that occurs in vivo.

The MCA/MMB Group currently collaborates with the GEN/GCS Group and the BST Group to perform integrated genome-wide analysis using massively parallel sequencing to identify genetic alterations of primary HUF cells exposed to selected cancer agents, and to elucidate their specific mechanistic effects. Ongoing experiments with known strong mutagens including aristolochic acid (AA, IARC Group 1 carcinogen), N-methyl-N'-nitro-N-nitrosoguanidine (MNNG, IARC Group 2A carcinogen), UVC light, benzo(a)pyrene, aflatoxin B1, and nicotine-derived nitrosamine ketone (NNK) show impressive concordance with mutational signatures found in primary human tumours. Thus, the HUF experimental mutagenesis system has a high potential to replace traditional single-gene assays in successful testing hypotheses on environmental causes of human cancer, and on the role of specific driver events that underlie key stages of cancer development. Furthermore, its systematic and effective use may significantly enhance the speed and accuracy in generating mechanistic evidence needed for carcinogen classification.

In future experiments, dose-response data for mutational signatures in HUF cells will be added to the analysis pipeline, and additional questions will be addressed, such as how two chemically distinct carcinogens known to elicit the same class of base pair change show a different distribution and/or sequence context of the mutations across the genome (e.g. effects of chloroacetaldehyde

(CAA), derived from the human carcinogen vinyl chloride and known to induce A:T>T:A transversions, will be compared to the mutation profile found in AA-treated cells).

Various environmental agents have been implicated in cancer development by inducing *epigenetic alterations*; however, in the majority of cases the underlying mechanisms and exact gene targets have not been identified. Our HUF mutagenesis results reveal frequent occurrence of mutations in cancer driver genes involved in regulation of chromatin structure and of the epigenetic marks, recapitulating a feature of human cancers uncovered by recent genome-wide analyses of many cancer types. Novel mechanistic insights into the specific cancer agent effects will be generated in cooperation with the MCA/EGE Group by analysing changes in the HUF cells involving epigenetic regulation of genome activity, as profound in their functional significance as the alterations in the protein coding DNA. In both the genetic testing and epigenetic profiling stages, it will be important to examine numerous clones from each exposure tested to determine whether these initial observations prove to be consistent, and we will focus on investigating (a) the relationship between the induced mutation distribution and the chromatin organization of the parental cells; (b) the global remodelling of histone marks and DNA methylation patterns in the progression of the exposed cells through the senescence bypass towards immortalisation/transformation; and (c) the global impact of induced mutations on chromatin remodelling and on epigenome regulators.

A successful strategy for selecting the tested environmental agents is a key element in this cross-sectional project. An IARC meeting is to be held in April 2014 with an aim to establish priorities for compounds that IMO intends to review for carcinogen classification between 2015 and 2019. The list will consist of new compounds that have never been classified and for which there is emerging toxicological data of concern and of already classified compounds for which the toxicological or epidemiological data has changed. By working with IMO, MCA intends to use this list to select compounds that are currently classified as possible or probable human carcinogens (classification 2A and 2B) for evaluation using the HUF assays. We will apply additional selection criteria involving (a) evidence of human exposure; and (b) evidence or suspicion of carcinogenicity, for which the additional mechanistic data would be likely to assist in clarifying the classification when IMO brings them forth for review. In advance of any review, the MCA Section will work with IMO to develop guidance on the interpretation of the HUF assays and how existing results have been verified with known human carcinogens.

All the IARC Sections and Groups involved in the HUF mutagenesis project have the expertise to pursue these studies, and the (epi)genomic platforms available and those requested (Illumina MiSeq sequencer) will be directly applicable to this project. When conducted as a tightly coordinated cross-Section collaboration effort involving IMO, MCA, GEN/BST and ICB, the systematic experimental creation of data sets of genome-wide mutations and meta-analyses with the human tumour genome-wide mutation database contents will ultimately help identify the causal environmental factors that contribute to the mutation and epigenetic alteration load in human populations. Wherever applicable, the comparison will also be cross-validated against suitable experimental animal models currently under investigation, e.g. a skin carcinogenesis model developed at INF/ICB in which transgenic mouse lines expressing HPV38 E6 and E7 oncoproteins are studied by genome-wide methods to address mutation profiles resulting from the synergistic effects of chronic UV irradiation and viral oncogenesis. The HUF assay could ultimately be used to verify exposure:disease associations in epidemiology studies and to

strengthen the molecular science base for reliable carcinogen identification and classification by comparison with data obtained on human biospecimens in population-based studies.

Questions or areas of advice to be addressed by the Scientific Council

1) Is the HUF experimental system appropriate to address specific issues of tumour concordance between humans and experimental animals, another key aspect of the IARC Monographs Section activities?

2) Can this approach strengthen exposure analyses in epidemiological studies and their linkage to in vivo toxicology studies, key elements to the evaluation of carcinogenic hazards?

3) How should IARC best prioritize the selection of candidate compounds for analysis?

4) How can this cross-sectional effort uniquely distinguish itself from analogous large-scale projects such as Tox21 conducted at NIEHS?

Topic 2: Research into the causes and mechanisms of childhood cancer
(Joachim Schüz, Head, Section of Environment and Radiation (ENV), Coordinator)

Participating Sections: CIN, ENV, GEN, MCA, NME

Background

With an annual incidence rate around 150 per million children in developed countries and supposedly lower rates in developing countries, cancer before the age of 15 years is relatively rare. Most common subtypes are leukaemias, lymphomas and brain tumours with often distinct features and dissimilar from those diseases in adults. For some childhood cancers and in particular the most common type, acute lymphoblastic leukaemia, survival rates have dramatically improved over the last decades exceeding now 90% after five years in developed countries. Little is known about population based survival in low-resource settings. For other childhood cancers, however, five year survival is still poor and often below 50%, for instance acute myeloid leukaemia, medulloblastoma or hepatic carcinomas. Among survivors, several disease-related late effects have been described, including an increased risk of secondary malignancy and some social disadvantages. Therefore, identification of preventable risk factors, identification of high risk groups, and understanding the natural history of those cancers remain the preferred options for successful primary prevention despite the successes in treatment.

A number of modifiable risk factors have been linked with childhood cancer. It is likely that the effects of these risk factors are mediated through metabolic and gene regulatory pathways including epigenetic mechanisms. Exposure to these risk factors have been associated with some changes in metabolite levels in blood from adults and children, which notably participate in redox balance, lipid biosynthesis, amino acid metabolism, nucleotide biosynthesis, one-carbon metabolism and energy metabolism, and therefore have the potential to affect genetic pathways and in turn development of cancer. Adaptive responses during in utero life may also include epigenetic changes (including DNA methylation) in different developmental pathways (such as production and expansion of somatic stem/progenitor cells, metabolic changes, and production of and sensitivity to hormones), a combination of which may alter normal development of tissues and organs. These epigenetic changes may be evident at birth and thus could constitute powerful mechanism-based biomarkers that could be exploited in disease prevention and epigenetics-based therapy.

With the development of metabolomic and epigenomic assays using high resolution mass spectrometry and deep sequencing-based epigenomic profiling, it is now possible to perform comprehensive analysis of metabolome and DNA epigenome of cord blood samples collected at birth from cases and controls and explore potential links between “exposome” measures, early effect markers and exposures and childhood cancer. These technologies together with robust protocols to analyse the blood metabolome and epigenome offer new avenues to conduct metabolome-wide and epigenome-wide association studies in a similar way to genome-wide association studies.

In addition, there is accumulating evidence that fetal life and early childhood might have an important effect on health in adulthood, too. Early exposure to poor diet, lack of physical activity, tobacco smoke and other environmental exposures can alter infants and children growth pattern and may result in altered metabolism, obesity and risk of chronic disease in

adulthood. Epigenetic changes in the regulation of genes have been invoked as important mechanisms and could condition rapid growth, childhood obesity through premature changes in hormonal profiles and early maturation. However the role of specific nutrients and environmental exposure during fetal life and early childhood on epigenetic changes remain unclear. New development in exposomics, metabolomics and epigenetics can be applied in well-characterized ongoing birth cohorts to evaluate the impact of early exposure on intermediate markers of cancer.

Research situation

Being a rare cancer, research on childhood cancer has often been initiated by either enthusiastic individuals, in centres with a history and special support to address the disease, or networks often established ad hoc, rather than due to systematic funding frameworks. The scope and amount of research projects targeted at the etiology of childhood cancer differs greatly by country, often driven by childhood cancer charities, supporting small projects within their own country rather than research platforms. Few governmental initiatives exist and if so they are often related to specific exposures than childhood cancer as such.

With all these constraints there is still a wealth of information, however, it appears also to be of limited scope because most research comes from a relatively small number of developed countries and focuses on the most common subtypes. Many hypotheses have been put forward over the last decades, but there still seem to be few established risk factors, so that overall still less than 10% of all childhood cancers can be explained. In some countries particularly active in childhood cancer research, again due to the rarity of the disease, the same cases become enrolled in different studies, raising some doubts that this will truly lead to new knowledge. Three aspects therefore become extremely important for the future of successful childhood cancer research:

1) multicentre studies to overcome the problem of too small sample sizes; 2) learning from diversity and involving the yet unexplored regions of the world in the research – childhood cancer research needs to be globalized; 3) using new avenues to conduct metabolome-wide and epigenome-wide association studies to identify causal pathways. For all aims, IARC by default can play a key role. And indeed IARC is already involved or has initiated several childhood cancer research activities.

Activities at the Agency

Consortia

IARC Partners	**PI**	**Active**	**Theme**
ACCIS – Automated Childhood Cancer Information System			
CIN	IARC (CIN)	Yes	Descriptive analyses of childhood cancer registry data in Europe
CLIC – Childhood Leukemia International Consortium			
ENV (SG, SPL)	UC Berkeley	Yes	Consortium of >12 case-control studies on childhood leukaemia; few with biospecimens
I4C – International Childhood Cancer Cohort Consortium			
MCA (SG) ENV, MCA, NME (SPL)	U Melbourne (PI IARC VS)	Yes	Consortium of birth cohort studies with the ability to follow up for cancer; includes biospecimens

IARC Partners	PI	Active	Theme
GALnet – Global Acute Leukaemia Network			
ENV (PI, SPL)	IARC (ENV)	Pilot completed	Consortium of paediatric oncology centres (2-3 per continent)
ISET – International study on embryonal tumors			
GEN	GEN	Yes, on hold	Consortium in 12 countries on aetiology of non-CNS embryonal tumors; case-control design with sampling from index and parents

Main projects

PANCARE CHILDHOOD AND ADOLESCENT CANCER SURVIVOR CARE AND FOLLOW-UP STUDIES (PANCARESURFUP)			
CIN (SPL)	U Lund	2011-2016	IARC: Study of late effects of cancer among the long-term survivors
EUROPEAN NETWORK FOR CANCER RESEARCH IN CHILDREN AND ADOLESCENTS (ENCCA)			
CIN (SPL)	CCRI Vienna	2011-2014	IARC: Feasibility of collection of clinically relevant information through cancer registries
CEFALO – case-control study on childhood brain tumours in teenagers and adolescents			
ENV (SG)	SG	2005-2016	Case-control study in Denmark, Norway, Sweden, Switzerland; fieldwork completed in 2010
Metabolomics with I4C			
MCA (EGE)	U Melbourne	New	Identification of epigenetic precursors (DNA methylation) of childhood cancer and associated *in utero* determinants within I4C
NME (SPL)	SG	New	Epigenomics and metabolomics within the I4C cohort consortium

* SG (Steering Group), SPL (Subproject Leader), VS (Visiting Scientist), MB (Member)

With the platforms having no infrastructure funding but continuing based on small grants and individual's own contributions, this leads to variable progress over time and difficulties in following the outlined strategies. While within IARC there is information exchange, mutual invitations to meetings and efforts to join forces, especially the latter is challenging in practice given the insecure funding situation and the many stakeholders involved particularly for platforms where IARC is not in a leading role. It is notable, however, that IARC Groups already have the main or a co-leading role in some of the consortia, partnerships or projects, that could be even more strengthened with a broader strategic platform.

With regard to new avenues, metabolomics and epigenomics of cord blood specimens from cancer and control subjects in I4C cohorts will allow mapping the metabolic and early response pathways that can be linked with both known environmental risk factors and childhood cancer outcomes. Although a range of variables related to maternal exposure are already documented in birth cohorts, metabolic profiling of cord blood samples should provide novel information on causal risk factors and their identities.

Questions or areas of advice to be addressed by the Scientific Council

1) Does the Scientific Council regard childhood cancer research as a priority scientifically and is there potential for IARC to grow into a leading role, given the main aspects of the need of large-multicentre consortia with fair worldwide representation and integration of novel strategies such as epigenetics and metabolomics?

2) How does the Scientific Council recommend IARC to exert greater impact on the overall strategies? How can the limitation of lack of infrastructure funding be overcome given that funding sources most active in this area restrict support to smaller and more local activities?

Topic 3: HPV vaccination studies in advancing cervical cancer prevention in low- and middle-income countries (LMICs): opportunities and challenges (Rolando Herrero, Head, Prevention and Implementation Group (PRI), Coordinator)

Introduction

IARC has conducted research on the etiology and prevention of cervical cancer for almost 30 years, and our studies were essential to establish HPV as the cause of cervical and oropharyngeal cancers as well as the worldwide epidemiology of infection. Other studies established the utility of HPV testing for cervical cancer screening, and in recent years, IARC has participated in research on the efficacy of HPV vaccines, with emphasis on alternative delivery schedules aimed at reducing cost and facilitating delivery in developing countries.

Background

According to estimates of the IARC Section of Cancer Information (CIN), cervical cancer is the fourth most frequent female malignancy, with an estimated 528 000 new cases and 266 000 deaths in 2012. However, it remains the number one female cancer in several developing countries in Africa, Asia and the Americas, and some regions have observed recent increases in incidence and mortality rates, including several countries in Sub-Saharan Africa, Eastern Europe and Central Asia.

There is a strong inverse correlation between level of development and cervical cancer incidence and mortality and there are important survival differences by region. Well over four-fifths of cases (84%) and deaths (87%) in 2012 occurred in developing countries. The disease affects relatively young women, and a recent analysis from CIN ranked cervical cancer highest among cancers in several regions in terms of disability-adjusted life years (DALYs), with age-adjusted estimates ranging from 84 per 100 000 in areas of very high human development index (HDI) to 595 per 100 000 in areas of low HDI.

Research opportunities

Modelling the long-term effects of vaccination and screening

Infection transmission models coupled with models of cancer natural history play a crucial role to assess the long-term consequences of introducing HPV vaccination in LMICs. These models are useful to clarify infection transmission patterns, to estimate the key parameters that govern the natural history of infection and cancers, and to project the effectiveness of different vaccination strategies. Model-based estimates of effectiveness can also be related to the social and economic costs of each vaccination strategy. Empirical data from trials or high-quality observational studies are essential both to parameterize these models and to assess the validity of their estimates.

Two modelling initiatives are proposed: a joint collaborative project with the Lowy Cancer Research Centre (Professor Karen Canfell) and the development of a set of models of HPV infection and related cancers. For the collaborative project a mixed-methods approach is proposed involving detailed dynamic modelling of sexual behaviour, HPV transmission, prevalence, persistence and progression to HPV-related cancers, as well as cervical screening, diagnosis, pre-cancer treatment, test-of-cure after treatment and cancer stage-specific survival, in selected high- and medium-income countries for which extensive data for parameterization,

calibration and validation of the models are available. Based on these results and population projections, national and regional scenarios of the HPV-related future burden will be developed. In addition, a population-based model has been recently developed at IARC. Model parameterization and validity assessment were performed using data from a large population-based trial on HPV testing and cross-checked for reproducibility in Italy and Sweden. The model was then adapted to assess the benefits of catch-up in vaccination against HPV in LMICs and of adding boys' vaccination to programmes routinely targeting young adolescent girls. The same model has also been used to quantify the expected herd-immunity effect in the context of community-based vaccination trials and of national HPV vaccination programmes. The development of an individual-based model analogous to the current population-based one is now essential in order to account better for heterogeneity in sexual behaviours, natural history of HPV infection and individual responsiveness to preventive measures.

There are major opportunities for collaborations with a broad range of experts including cancer modellers to provide the evidence base for the long-term impact of interventions. Work within CIN involves quantifying the HPV-related cancer burden according to various prevention/screening scenarios. The focus will be on cervical (and other HPV-related) cancers, and the collective impact of the national implementation of the HPV vaccine alongside cervical cancer screening programmes. The aim of this project will be to develop comprehensive estimates of the global burden of HPV-related cancers in 2012–2060, providing the annual number of cancer cases, deaths and DALYs, by country, geographic region, and level of development over this period.

IARC has previously quantified the declines in cervical cancer rates from the late 1980s to the early 2000s. This scenario coupled with population projections still leads to an overall global increase in the number of cervical cancers expected by 2030. However, this will be partially countered by screening and improvements in human development and health services. Over the last seven years, prophylactic vaccination against HPV in pre-adolescent females has been introduced in most developed countries, supported by modelled evaluations of its cost-effectiveness.

Vaccination studies

The Guanacaste Project (PEG) is a long-term collaboration with the US National Cancer Institute (NCI) to investigate natural history and prevention of HPV infections and associated neoplasia, with participation of IARC's Prevention and Implementation Group (PRI). Between 2004 and 2005, the Costa Rica Vaccine trial (CVT) recruited approximately 7500 women aged 18–25 in a randomized controlled trial of the bivalent HPV vaccine (HPV 16/18) to evaluate its efficacy against cervical infections and CIN2+. The trial has demonstrated the efficacy of the vaccine to prevent persistent cervical HPV infections with HPV 16/18 and phylogenetically related HPV types as well as impact of vaccination on cervical cytology screening, colposcopy and treatment in the first four years after vaccination. In addition, the trial has shown the duration of immune response (up to four years) was similar among women who received one, two, or the recommended three doses of the vaccine. We have also demonstrated vaccine efficacy for prevention of prevalent anal and oral HPV 16/18 infections four years post-vaccination. Long-term follow-up of vaccinated cohorts continues to evaluate long-term protection, safety, immunogenicity and HPV type-replacement.

The Screening Group (SCR) initiated a multicentre cluster randomized trial in India in 2009 to compare efficacy of two versus three doses of quadrivalent HPV vaccination (types 6, 11, 16, 18) for preventing persistent HPV infection and cervical neoplasia. The study aimed to recruit 20 000 unmarried girls aged 10–18 years and randomly allocate them to two or three doses of vaccine. Study outcomes include immunogenicity as well as infection and disease. Suspension of vaccination occurred under instruction from the Indian Council of Medical Research (ICMR). At that time, of the 21 258 eligible girls identified, 17 729 had received one or more doses of HPV vaccine: 4955 only one dose; 3963 two doses on days 1 and 60; 4920 two doses on days 1 and 180 or more; and 4337 three doses on days 1, 60 and 180 or more. As foreseen in the protocol, we are conducting yearly visits with our participants providing clinical care and collecting blood and cervical cells among those who report having married. A cohort of 2000 age matched unvaccinated girls has been recruited recently to facilitate comparison between vaccinated and unvaccinated girls. The analysis of plasma samples at baseline, 7, 12 and 18 months has demonstrated that sero-conversion rate at one-month after the last dose exceeded 99% for all targeted HPV types for both those who had received two and three doses over 180 days or more. Immunogenicity after two doses on days 1 and 180 or more was non-inferior to three-doses on days 1, 60 and 180 or more; immunogenicity among 15–18 year-old girls was non-inferior to that of 10–14 year-olds. Immunogenicity of one dose and two doses on days 1 and 60 were significantly inferior to two and three doses. Analysis of 24- and 36-month plasma and cervical cell samples are underway.

Bhutan was the first low-income country to introduce HPV vaccination. The Ministry of Health (MOH) developed a national vaccination programme recommending immunization with quadrivalent (HPV 6, 11, 16, and 18) vaccine for 12-year-old girls and a “catch-up” campaign for girls 13–18 years in the first year. In 2010, a pharmaceutical company provided the vaccine for all girls, and for the next five years the Australian Cervical Cancer Foundation funded vaccine for 12-year-olds. Health workers administered vaccine in schools or health facilities and in 2010, reached 92% coverage, providing an example for other low-income countries considering HPV vaccination. Monitoring of HPV vaccination is challenging given the long latency of cervical cancer. In the short-term, it is possible to measure decreases in infection prevalence and variation in the ratio between HPV types in sentinel populations. In 2012 the Ministry of Health of Bhutan, in collaboration with the IARC Section of Infections (INF) started a study to evaluate HPV prevalence in women aged 18 years or older. By 2016, the early impact of vaccination will start to be detectable in women 25 years or younger. An expansion of cervical screening and introduction of HPV-based screening is also part of the same project, potentially improving cervical cancer prevention and ultimately serving as the basis for long-term vaccination monitoring. In Rwanda in 2010, the Ministry of Health developed a National Strategic Plan for the Prevention, Control, and Management of Cervical Cancer, including vaccination of girls in primary grade six, with additional outreach to 12-year-old girls not at school, with coverage of 93.2%. Collaboration with IARC is under way to provide timely data on the impact of the vaccination programme on the prevalence of HPV infection.

In September 2013, in collaboration with NCI, IARC organized a meeting of experts to define the best outcomes for trials of new HPV vaccines under development as well as new applications of current vaccines. In general, the group recommended a shift to virologic and immunologic outcomes to facilitate future trials. The results of the meeting will be instrumental for new WHO guidelines to be developed next year.

Questions or areas of advice to be addressed by the Scientific Council

1) What are the priorities for modelling of HPV vaccination and screening?

2) Can the uncertainty in the key parameters used in HPV modelling be addressed by new information from the current cohorts and clinical trials?

3) Should we explore further in clinical trials the utility of less than three HPV vaccine doses?

4) What should be the role of IARC in evaluating routine national immunization programmes in LMICs?