International Agency for Research on Cancer

World Health Organization

Governing Council
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ACCEPTANCE OF GRANTS AND CONTRACTS – REVISION 1

1. Post facto reporting

The Governing Council is invited to note the post facto reporting of grants and contracts accepted by the Director over €100 000 per annum, including sums passed to third parties, for the period 16 March 2022 to 22 March 2023, as detailed below.

Cancer Surveillance Branch (CSU)

1.1 Project title: **IARC's Cancer and Covid 19 initiative**

The COVID-19 pandemic has markedly impacted cancer services and therefore cancer burden globally. Countries have implemented diverse mitigation strategies during the crises to reduce its impact on cancer outcomes. Yet the impact caused by disruptions of the health system and cancer services varied widely across countries and populations, creating a large inequality in cancer burden. The aim of this initiative is to provide a surveillance framework for the evaluation of the potential impact of pandemics and other emergencies on cancer diagnosis and outcomes in the short and longer term using the most up-to-date population level data. Ultimately it aims to enable countries prioritize cancer control and recovery strategies during and following the severe social and health services disruptions during crises. More precisely C-19 Initiative will: (i) examine national policy responses and public health practice during crises such as the COVID-19 pandemic to draw on best practice via review and data collection; (ii) improve health system resilience of countries through provision of guidance in building back better. This will be done by development of a dynamic evidence-based decision-making platform, with a dashboard of detailed and systematic mapping of policy responses and their potential impact on cancer outcomes; and (iii) provide technology transfer between Participating States and partner countries from low- and middle-income countries (LMICs) including opportunities to second staff to IARC to be directly involved in the Initiative via dedicated fellowships.

Donor:	Medical Research Council (GB)
Duration:	24 months
Funds for IARC:	€874 350.00
Funds for partner:	N/A
Total:	€874 350.00
Partner:	Cancer Council New South Wales (AU)

1.2 Project title: **Supporting the Cancer Inequalities Registry to map disparities and inequalities between Member States and regions, with a focus on socio-economic inequalities**

The EU-CanIneq aims to coordinate a research and data framework that will develop and expand relevant indicators of socioeconomic inequality in cancer in the EU to be integrated into the European Cancer Inequalities Registry, the flagship initiative of Europe's Beating Cancer Plan. The project is coordinated by IARC with the following objectives: 1) To enable the logistic framework on the collection and harmonization of data on socioeconomic inequalities in cancer in the EU; 2) To produce indicators on socioeconomic inequalities in cancer to be integrated into the European Cancer Inequalities Registry; 3) To analyse, map, compare and critically discuss socioeconomic inequalities in cancer in the EU; 4) To provide country-specific information and insights on socioeconomic inequalities in cancer in Europe; 5) To disseminate core findings in Europe and across Member States. The data collection and harmonization will rely on the longstanding logistic infrastructure based at the Erasmus MC, the Netherlands, which have continued collaboration with national data providers, and have unique expertise in the area of social inequalities in health. The project will focus on total cancer mortality as well as on mortality from the most frequent cancers (breast, cervix, colorectum, lung, prostate and stomach). With respect to the dimensions and indicators of socioeconomic condition, the project will focus on educational level, gender, age and geographical area (including the East-West divide). Ad hoc scientific and methodological workshops will be organized at IARC in a timely fashion with experts to discuss the development, application and outcomes of projection and extrapolation methods necessary to overcome the current data gaps. The project also envisages a strong dissemination component, with scientific reports combined with a high-level summit that intends to raise awareness about socioeconomic inequalities in cancer and support policy directions that can reduce them.

Donor:	European Commission - European Health And Digital Executive Agency / EU4H (BE)
Duration:	30 months
Funds for IARC:	€600 000.00
Funds for partner:	N/A
Total:	€600 000.00
Total budget cost:	€1 000 000.00
Partner:	N/A

Environment and Lifestyle Epidemiology Branch (ENV)

1.3 Project title: **Scientific-Based Exposure and Risk Assessment of Radiofrequency and mm-Wave Systems from children to elderly (5G and Beyond)**

The pervasiveness and social-economic dependence on wireless technology has steadily increased over the last three decades. Currently, the 5th generation (5G) New Radio (NR) cellular system is being deployed to unlock the potential of new applications that require the better connection of many more devices (Internet of Things), higher data rates and low latency (autonomous driving, 'Factory of the Future'). 5G operates in two frequency bands, 5G NR FR1 and 5G NR FR2. Many exposure parameters of 5G are similar to those of 2G-4G.

However, there are also many differences that lead to major knowledge gaps regarding possible adverse health effects, of which the major one will be addressed by the SEAWave project. SEAWave will (i) quantify

the differences in exposure patterns between 2G-4G and 5G for the entire population including children; (ii) provide new tools and instruments for reliable exposure evaluation of base stations, local networks in factories, and end-user devices; (iii) provide the means to minimize exposure; (iv) generate important new scientific data for assessing the health risk from exposure to the new frequency bands (FR2), especially with regard to the potential (co-)carcinogenicity of skin exposure and other hazardous effects; and (v) provide knowledge for effective health risk communication and dissemination to various stakeholders. To achieve these ambitious objectives, the interdisciplinary consortium consists of highly experienced partners with leading expertise in the field who ideally complement each other to achieve maximum impact. European citizens, workers, national public health authorities, European Commission services, regulators, and standardization bodies will all benefit from the SEAWave results as they will support science-based decisions and policies for the safe deployment and use of 5G and future wireless networks. IARC is the Work Package Leader for the Risk Assessment and participates also in the risk communication part, as well as informing the consortium about epidemiological studies outside the project. Project SEAWave is part of the European cluster on EMFs and health.

Donor:	European Commission - European Health And Digital Executive Agency / Horizon Europe (BE)
Duration:	36 months
Funds for IARC:	€424 406.00
Funds for partners:	€6 893 371.00
Total:	€7 317 777.00
Partners:	Aristotle University of Thessaloniki (GR), Institute Mines-Télécom Paris (FR), French Alternative Energies and Atomic Energy Commission (FR), Institute of Non-Ionizing Radiation (SI), Italian National Agency for New Technologies, Energy and Sustainable Economic Development (IT), Fraunhofer Institute for Toxicology & Experimental Medicine (DE), Greek Atomic Energy Commission (GR), International University of Applied Sciences (DE), National Frequency Agency (FR), Federal Office for Radiation Protection (DE), Interuniversity Microelectronics Centre (BE)

1.4 Project title: **Investigating exposure to pesticides and the risk of female breast cancer in an international consortium of agricultural cohorts (AGRICOH)**

Breast cancer is the most common cancer and leading cause of cancer death among women in the world. An emphasis on primary prevention is needed to tackle this global epidemic of breast cancer which is expected to reach 3 million new cases per year by 2040. In addition to the established risk factors, such as hormone replacement therapy, obesity, and alcohol consumption, endocrine-disrupting chemicals have been suspected to promote tumour growth through estrogen-, progesterone-, or other hormone-mediated pathways. Several widely used pesticides are known or suspected endocrine-disruptors, yet very few studies have investigated breast cancer risks associated with the use of specific pesticides. Use of the insecticides chlorpyrifos and terbufos was associated with 40–50% higher risks of breast cancer among thirty thousand farmers' wives in the Agricultural Health Study (AHS). These findings need replication, and even greater sample size will be needed to further investigate associations by hormone receptor and menopausal status, which may modify risks given the heterogenous nature of breast cancer and the endocrine mechanisms implicated. This is why the question is now addressed in the AGRICOH consortium pooling data from three large cohorts (USA, France, Norway) of female applicators and farmers, as well as

spouses of farmers, and in addition to the initial application estimates exposure from re-entry of pesticides.

Donor:	The Dutch Cancer Society (NL)
Duration:	35 months
Funds for IARC:	€305 669.00
Funds for partners:	€197 261.60
Total:	€502 930.60
Partners:	Institute for Risk Assessment Sciences (NL), Université de Bordeaux (FR), Université de Caen Normandie (FR), National Institutes of Health - National Cancer Institute (US), National Institute of Occupational Health – STAMI (NO)

1.5 Project title: **ABC-DO Ghana – Mentoring Supplement**

The primary aim of the supplement is to fund a LMIC researcher and pay their salary and research costs to conduct research locally, under the mentorship of the parent R01. The funding allocation is heavily biased towards the LMIC institution as per the call's remit. With the need to improve breast cancer survival across sub-Saharan Africa, the present supplemental proposal will develop a linked project in Ghana, where Dr Clement Narh is based. ABC-DO Ghana will examine breast cancer in a Ghanaian regional setting, focussing on the breast cancer experience of women who are much further from the oncology facilities in capital cities. The study will follow breast cancer patients diagnosed at six district hospitals spanning the length of the Volta region, and follow them to examine their access to treatment, willingness to accept treatment and travel to regional hospitals to undergo treatment. We will assess who is making the decisions for treatment continuation, what are the barriers, use of traditional medicine.

Donor:	National Institutes of Health - National Cancer Institute (US)
Duration:	8 months
Funds for IARC:	€16 759.57.87 (US$ 16 810.00)
Funds for partner:	€107 245.30 (US$ 107 568.00)
Total:	€124 004.87 (US$ 124 378.00)
Partner:	University of Health and Allied Sciences, Hohoe (GH)

Early Detection, Prevention and Infections Branch (EPR)

1.6 Project title: **HPV serologic correlates and extended vaccine durability**

The IARC-India HPV vaccine study to evaluate the safety and efficacy of 2 versus 3 doses of the quadrivalent HPV vaccine was initiated in 2009 as a randomized clinical trial. Overall, 17 729 girls were vaccinated, with 4348 (25%) girls receiving three doses on days 1, 60, 180 or later (3-dose group), 4979 (28%) receiving two doses on days 1 and 180 or later (2-dose group), 3452 (19%) receiving two doses at days 1 and 60 by default (2-dose default group), and 4950 (28%) receiving one dose by default (single-dose default group). Follow up of the recipients of single, two and three doses is ongoing for over last 12 years.

The present study nested in the IARC-India HPV vaccine study has the following two components:

1. Assessing Month 18 Immune Responses as Correlates and Signatures of Risk of Subsequent Type-Specific HPV Endpoints. Immune correlated of protection assesses the lowest level of antibody following

vaccination that helps to continue with protection and prevents breakthrough infections. This information is crucial to understand the durability of protection from the different doses of HPV vaccine.

2. Assessment of long-term immunogenicity of the recipients of a single dose of HPV vaccine.

Our study will be the only large study that will provide information of the antibody levels against HPV 15 years post-vaccination in different dose groups.

Donor:	Bill & Melinda Gates Foundation (US)
Duration:	29 months
Funds for IARC:	€530 442.88 (US$ 532 039.00)
Funds for partners:	N/A
Total:	€530 442.88 (US$ 532 039.00)
Partners:	German Cancer Research Center (DE), Rajiv Gandhi Centre for Biotechnology (IN)

1.7 Project title: **Implementation of an affordable and equitable integrated multi-cancer early detection package to improve cancer outcomes in resource-constrained settings**

Primary aim of the study is to design and evaluate a new multi-level strategy, integrated to the local health system, contextualized to the local settings and co-developed through stake-holder engagement to improve access to the early detection and downstream care continuum for oral, breast and cervical cancers in vulnerable, rural populations in India.

Secondary aims are to:

- Understand and (re)design upstream and downstream pathways both to access interventions and downstream, where necessary, to access definitive care.
- Investigate scale up costs (capital and recurrent) and design affordable programmes within a UHC framework through social insurance and free-at-point of care models.
- Develop models for embedding scaled up interventions in state and national cancer control plans through a health-systems strengthening approach.

Study settings: We propose to conduct our implementation research study in three different states in India (Kerala, Tamil Nadu & Rajasthan), targeting the rural population in each state. The states were selected not only because of the differences in their population characteristics, but also in their burden of common cancers and variations in the structure and organization of the health system.

The aims will be delivered through 6 integrated work packages WP 1. Creating & engaging a stakeholder's team; WP 2. Assessing the contextual factors that create barriers for the population to access early detection and treatment services; WP 3. Assessment of capacity of the local health systems catering to cancer early detection and treatment pathway; WP 4. Designing and costing a multi-level intervention strategy to improve participation of the rural populations to early detection care continuum; WP5. Pilot implementation and evaluation of intervention strategies; WP6. Assessment of settings readiness and capacity to sustain and scale up interventions.

Donor:	Medical Research Council (GB)
Duration:	48 months
Funds for IARC:	€466 781.90 (GBP£ 403 064.00)
Funds for partners:	€1 622 178.98 (GBP£ 1 400 744.00)

Total:	€2 088 960.88 (GBP£ 1 803 808.00)
Partners:	King's College London (GB), Research Triangle Institute International (US), GBH American Hospital (IN), Karkinos Healthcare Pvt. Ltd (IN), Tata Memorial Hospital (IN), Cancer Institute WIA Chennai (IN)

1.8 Project title: **HPV Context-specific Modelling**

Currently, catch-up (CU), i.e. multi-age cohort, HPV vaccination of girls is recommended by WHO up to 14 years of age. Nevertheless, multiple sets of evidence from both high and low/middle-income countries (HICs and LMICs) strongly suggest that CU vaccination of young women up to between 18 to 25 years of age, can be highly effective in reducing HPV prevalence and cervical cancer incidence in the targeted birth cohorts. A wide age-range CU vaccination may also enhance herd protection to younger birth cohorts. On the other hand, in many countries the adoption of CU up to 14 years of age as recommended has been substantially constrained by current vaccine shortage and costs, especially in LMICs. Several published modelling studies indicate that the return of CU vaccination diminishes with increasing women's age as these are more likely to be already infected by HPV due to previous sexual exposure. However, since behavioural norms differ across countries and populations, the diminishing return function and the optimal maximum age for CU are inherently context specific. Other factors affecting the occurrence of HPV and cervical cancer in the population, such as HIV prevalence, are also context specific. At IARC, over the years and across multiple projects in both HICs and LMICs, we have been developing a range of open-source HPV transmission and progression models: some of the models are fully implemented and published or submitted for publication, others are in an advanced stage of development and working versions of these tools are planned to be available within months.

Donor:	Bill & Melinda Gates Foundation (US)
Duration:	38 months
Funds for IARC:	€807 889.10 (US$ 848 623.00)
Funds for partner:	N/A
Total:	€807 889.10 (US$ 848 623.00)
Partner:	N/A

1.9 Project title: **Monitoring impact of hepatitis elimination**

Since 2016, the WHO Global Health Sector Strategy on hepatitis calls for elimination through scaled up prevention, testing and treatment. Elimination of hepatitis as a public health threat is defined as -90% reduction in incidence and -65% reduction in mortality compared with the 2015 baseline. Modelling studies suggest that diagnosing 90% of those infected and treating 80% of those diagnosed would lead to the mortality reduction goal. However, such studies are limited by the absence of reliable, empirical data on the population-based prevalence of the stage of severity of persons with HBV or HCV infection. Empirical data measuring directly how testing and treatment affects the fractions of cirrhosis and hepatocellular carcinoma (HCC) from HBV and HCV are essential for data validation. IARC is in a unique position to conduct that role given its expertise in the measurement of (a) the incidence of HCC and (b) the fractions of cirrhosis and HCC associated with HBV, HCV and other etiologies.

Donor:	World Health Organization - Headquarters (CH)
Duration:	10 months

Funds for IARC:	€124 608.00 (US$ 132 000.00)
Funds for partner:	N/A
Total:	€124 608.00 (US$ 132 000.00)
Partner:	N/A

Evidence Synthesis and Classification Branch (ESC)

1.10 Project title: **Mapping the Evidence for the WHO Classification of Tumours: a Living Evidence Gap Map by Tumour Type**

Decisions for the WHO-Classification-of-Tumours (WCT) as global reference tool should be informed by best available evidence, minimizing risk of incorporating misinformation into clinical decision's pathway. We aim to map the evidence-base of the WCT, identifying gaps and pockets of low-level-evidence. The WCT-EVI-MAP project will apply a mixed-method, stepwise approach to adapt Evidence-Gap-Map (EGM) methodology to the WCT. Steps include -development of a framework through expert consultation (e-Delphi study), -retrieving of evidence applying a living approach (continuous search for new evidence), -mapping of evidence in Mega-maps of group of tumour types using EPPIReviewer®, and descriptive analysis of WCT pre-post WCT-EVI-MAP. The resulting EGMs will describe the body of evidence for single tumour types, by research field and evidence-level in an easy-to read visual representation. Mega-maps will be combined to provide an open-access online tool with living EGMs of the WCT. Dimensions of the map defined through the first phase of expert consensus will include evidence on epidemiology, molecular pathology, prognosis, as defined in the 5th edition of the WCT and three levels of evidence (low, medium and high) as defined by the current evidence pyramid. A strict multidisciplinary approach will be applied, and the results will be integrated into the strategic planning of the WCT 6th edition. The WCT-EVI-MAP will represent a ground-breaking advance for the WCT and research in the field, positively impacting cancer diagnosis and management. The online tool will increase the discoverability and use of studies by the WCT decision-makers, research commissioners and stakeholders. Such long-term, positive impact has been already observed in other specialized fields with and constitutes an additional step towards evidence-based pathology.

Donor:	European Commission - Research and Innovation (BE) / Horizon Europe
Duration:	48 months
Funds for IARC:	€844 712.00
Funds for partners:	€1 923 528.00
Total:	€2 768 240.00
Total budget cost	€3 500 000.00 (including the UK contribution for the UK-based Associated Partners)
Partners:	Maria Sklodowska-Curie National Research Institute of Oncology (PL), National Center for Epidemiology, Carlos III Institute of Health (ES), Institute of Laboratory Medicine, German Heart Center (DE), Singapore General Hospital (SG), University of Oxford (GB), University of Newcastle upon Tyne (GB)

1.11 Project title: **IARC Handbooks of Cancer Prevention Vol. 20 - Reduction of alcohol consumption**

Consumption of alcoholic beverages is a major risk factor for cancer, causing cancers of the oral cavity, pharynx, larynx, oesophagus, liver, colorectum and female breast, and possibly of other sites. In 2010, WHO agreed on a global strategy to reduce the harmful use of alcohol. Yet a recent study estimated that in 2020 approximately 4% of all new cases of cancers worldwide were due to alcohol consumption, with cancers of the oesophagus, liver and breast representing close to 60% of all cases. Thus, prevention of alcohol-associated cancers remains an important public health challenge. The IARC Handbooks of Cancer Prevention programme performs comprehensive reviews and evaluations of the evidence on the effectiveness of interventions and strategies to reduce cancer incidence or mortality. The process engages international Working Groups of independent, interdisciplinary scientific experts who perform a transparent review and synthesis of the available evidence, which is then translated into an evaluation according to set criteria. This Handbook will provide a first-time evaluation of the evidence of the impact of reducing alcohol consumption, or quitting the habit, in reducing the risk of alcohol-attributable cancers and mortality thereof. Three streams of evidence will be reviewed and evaluated: studies in humans, studies in experimental animals, and mechanistic studies. For each stream of evidence, an evaluation will be made of the strength of the evidence that reducing alcohol consumption reduces the risk of cancer. Preliminary evaluations will be combined into an overall evaluation. A summary of the outcomes will be published in a peer-reviewed journal after the meeting, and the full volume of Handbook will be published online and in print after scientific and technical editing. The evaluations of the IARC Handbooks are widely used by national and international health agencies to develop evidence-based interventions or policy recommendations for reducing cancer risk at the population level.

Donor:	Institut National du Cancer (FR)
Duration:	36 months
Funds for IARC:	€419 569.00
Funds for partner:	N/A
Total:	€419 569.00
Partner:	N/A

1.12 Project title: **IARC Handbooks on Cancer Prevention Programme**

The IARC Handbooks of Cancer Prevention provide an evidence-based approach to identify which interventions or strategies can prevent cancer or detect cancer at an early stage. The evaluations of the IARC Handbooks are widely used by national and international health agencies to implement evidence-based interventions or develop policy recommendations to reduce cancer risk at the population level. To date, the Handbooks Programme has produced 19 volumes, including evaluations of chemopreventive agents, behavioural interventions, cancer screening, and policies and taxation. To accomplish its mission, the Programme performs comprehensive systematic reviews of the available evidence on the effectiveness of preventive interventions or strategies in reducing cancer incidence or mortality. The process engages independent, interdisciplinary Working Groups of international scientific experts who perform a transparent synthesis of different streams of evidence, which is then translated into an overall evaluation according to set criteria.

During the five-year period of performance, we will build on the achievements of the current period. We will organize at least three Handbook meetings to evaluate interventions targeting cancer-related public health issues of high concern. This involves monitoring the literature to identify relevant topics; selecting a Working Group of international experts; convening the Working Group and coordinating the systematic review and consensus evaluations; publishing the resulting evaluations and the final Handbook; and disseminating the outcomes. When required, we will convene a Scoping Meeting as a first step in the preparation, to define the outline, identify potential participants and determine key and controversial issues. This preparatory step will enhance the focus of the Handbook and better target users' needs. Also, we may develop supplementary products based on the outcomes of the main Handbook, which will help decision-makers use the evaluations in their specific settings. The types of products will depend on the intervention(s) evaluated, the outcome of the evaluations, and specific needs related to the interventions or the cancer burden. They may include, but are not limited to, cost-effectiveness modelling studies, mapping of evidence gaps, or analyses of population-attributable fractions. Finally, we will expand our means of communication and dissemination of the results to a wider audience, using various social media channels and pictorial information posted on our website. Also, the Programme will strengthen exchanges with other IARC Branches, with WHO, and with other national and international organizations to share resources, optimize efficiency, and increase the visibility and impact of the Programme.

Donor:	Center for Disease Control and Prevention (US)
Duration:	60 months
Funds for IARC:	€947 000.00 (US$ 1 000 000.00)
Funds for partner:	N/A
Total:	€947 000.00 (US$ 1 000 000.00)
Partner:	N/A

Genomic Epidemiology Branch (GEM)

1.13 Project title: **Opioid Cohort Consortium (OPICO) to investigate the determinants and long-term health consequences of opioid medication use**

Recently, opium consumption was classified as "carcinogenic to humans" by IARC Monographs, which raise concerns about opioid medications that are either derived from opium or synthesized in laboratories to mimic its chemical structure and effects. Current evidence on opioid medications and cancer is primarily from ecologic and registry data linkage studies. Analyses of records from national health insurance or addiction registry programmes across different countries showed increased cancer incidence or mortality amongst opioid medication users. However, it has been impossible to rigorously evaluate whether using opioid medications is associated with future cancer risk due to paucity of data on opioid use and insufficient statistical power in prospective cohort studies. To overcome the limitations that have hindered reliable studies in humans, we initiated the Opioid Cohort Consortium (OPICO) with pilot funding in 2020. OPICO brings together large-scale prospective cohort studies that have either gathered data on medication use or have linked participant data to medication dispensing records.

In this project, we will build on the pilot phase to harmonize and pool data from 8 cohorts in France, Australia, United States of America, United Kingdom, and Iran, yielding a large-scale data resource with one million participants. This resource would allow an accurate assessment of the relationship between opioid medication use at baseline and during follow-up, with cancers. The assessment will include details

on the type, strength, duration, and dose of opioid medications used, which might differently affect any potential relationship between using opioid medications and cancers. In line with IARC's mission, this project brings together collaborators and resources from around the world to enhance understanding an emerging cancer risk factor.

Donor:	Institut National du Cancer (FR)
Duration:	48 months
Funds for IARC:	€510 976.00
Funds for partners:	N/A
Total:	€510 976.00
Partners:	Institut National de la Santé et de la Recherche Médicale (FR), University of New South Wales Sydney (AU), University of Sydney (AU), Tehran University of Medical Sciences (IR), National Cancer Institute (US)

1.14 Project title: **Reconciling lung carcinoids histopathological and molecular classifications**

Lung neuroendocrine tumours (LNET) are rare tumours comprising low-grade (typical) and intermediate-grade (atypical) carcinoids. Typical carcinoids exhibit good prognosis, although 10–23% metastasize to the regional lymph nodes, while 40–50% of atypical carcinoids present metastasis, reducing the five-year overall survival rate to 50%. Recently, we have performed the first comprehensive molecular characterization of lung carcinoids and identified clinically relevant molecular groups named A1, A2 and B. Parallel efforts have been made to identify prognostic immunohistochemistry (IHC) and molecular imaging markers (PET scans) to refine the current 2021 WHO histological classification. Despite promising concordant results, there is still no consensus on the optimal approach for LNET differential diagnosis. Classification or grading schemes for pulmonary carcinoids have been generally proposed in a specific area of research (histopathology, molecular biology, or nuclear medicine) independently of the others, and there is a strong need to unify them to improve the diagnosis and clinical management of patients. In this proposal, we aim to reconcile the histopathological and molecular LNET classifications, ranging from morphology, IHC, molecular imaging, and multi-omics data. To achieve this, we will pursue the following specific aims: (1) evaluate IHC markers and molecular imaging phenotypes across our molecular (multi-omics) groups; (2) identify morphological features in the three molecular groups using Artificial Intelligence applied to whole-slide images; and (3) understand the link between the molecular and morphological features identified using spatial proteomics. By using a multidisciplinary approach to LNET classification, this project will generate the knowledge to overcome the existing barriers to integrate the molecular findings in the classification of tumours. Altogether, this will pave the way to a more robust and prognostic based LNET classification and provide the opportunity to identify new treatments and optimal therapeutic combinations.

Donor:	Neuroendocrine Tumor Research Foundation (US)
Duration:	24 months
Funds for IARC:	€247 860.00 (US$ 270 000)
Funds for partners:	N/A
Total:	€247 860.00 (US$ 270 000)
Partners :	Centre Leon Bérard (FR), Ecole Centrale de Lyon (FR), Aix-Marseille Université (FR), Hospice Civil de Lyon – HCL (FR), Maimonides Biomedical Research Institute of Cordoba (ES)

1.15 Project title: **Discovering the molecular signatures of cancer Promotion to Inform Prevention**

The cancer research community is on the verge of a major leap in our understanding of the factors that contribute to human cancer risk. While it is clear that mutations in DNA, either spontaneous or environmentally induced, are essential for cancer development, recent advances have highlighted the importance of non-mutagenic factors as rate-limiting determinants of cancer risk in human populations and in mouse cancer models. The root causes of human cancer have been widely debated, but most of the emphasis has been on the origins of the "driver" mutations that are ubiquitous in human tumours. Although epidemiology studies have highlighted the possible roles of lifestyle factors such as obesity, alcohol consumption, inflammation and poor diet in cancer risk, it has generally been assumed that these act directly or indirectly to cause mutations in DNA, thus contributing to tumour mutational burden resulting in increased cancer risk. In contrast, recent sequencing studies have uncovered abundant mutations in normal human tissues, suggesting that even strong cancer driver mutations are not sufficient for cancer formation. These results were presaged by studies of mouse tumour models, some carried out more than 50 years ago, showing that promotion is the rate-limiting step in tumour development. To identify the mechanisms that control mutated normal cells, and to elucidate the precise mechanisms by which promoting factors stimulate the conversion of these cells to neoplastic growth, we have assembled a multidisciplinary team of investigators with wide-ranging experience in epidemiology, genetics, computational network analysis and machine learning, tissue imaging of gene expression, single cell transcriptomics, and genome-wide CRISPR functional screens. We will focus on a unique collection of several thousand human normal and matched tumour samples from >20 countries, including regions of both high and low cancer risk. Detailed risk factor information and whole genome sequence data is available from all these samples as part of the Mutographs study. Analysis of these samples, together with detailed intervention studies in human populations, mouse models and human organoids, will allow us to develop a roadmap of tumour promotion from single normal cells carrying driver mutations, through to malignant progression. These studies will facilitate identification of the causative environmental factors that promote cancer and provide routes to new methods and approaches to cancer prevention based on a deeper understanding of the process of initiated cell selection by tumour promoting agents.

Donors:	Cancer Research UK (GB) and National Institute of Health (US) *[Cancer Grand Challenge programme]*
Duration:	60 months
Funds for IARC:	€3 698 682.81 (GBP£ 3 169 748.00) [funded in half by two donors]
Funds for partners:	€19 638 590.48 (GBP£ 16 830 149.04) [funded in half by two donors]
Total:	€23 337 273.28 (GBP£ 19 999 897.04) [funded in half by two donors]
Partners:	University of California San Francisco (US); Institute for Research in Biomedicine (ES); Duke University (US); Stanford University (US); KTH Royal Institute of Technology (SE); Imperial College London (GB)

Nutrition and Metabolism Branch (NME)

1.16 Project title: **Providing Cutting Edge Cancer Research Services Across Europe**

canSERVs mission is to make cutting-edge and customized research services available to the cancer research community EU wide, enable innovative R&D projects and foster precision medicine for patients benefit across Europe. By connecting, coordinating, and aligning existing oncology and complimentary

research infrastructures (RIs) and providing services in a synergistic way transnationally, canSERV will capitalize on the critical mass of experts and cutting-edge services offered by canSERVs RIs and their extended network. canSERV brings together world-class European life science RIs (BBMRI, EURO-BIOIMAGING, ELIXIR, EU-IBISBA, EuroPDX, EU-OPENSCREEN, INSTRUCT, EATRIS, INFRAFRONTIER, EMBRC, ECRIN, EATRIS, MIRRI, ARIE, CCE, EORTC and IARC) that collectively not only covers all aspects along the development pipeline for oncology, but is also capable of interconnecting these technologies providing users with a guidance for navigating them through the entire translational value chain. The patient organization ECPC will bring the patient's perspective, while the two SMEs, ARTTIC and ttopstart, will provide valuable input regarding stakeholder engagement, and project management activities. A common access management system (CAMS) will be developed based on mature solutions from INSTRUCT and BBMRI. The CAMS will provide a method for selection of services, construction and submission of research proposals, multi-step review of research proposals, and tracking of the access process from approval through delivery to conclusion. Through a united user-intuitive transnational access where a united catalogue of oncology services will be offered, our users will have access to a comprehensive service portfolio. As our ambition is to scale up canSERV to a pan-European collaboration of RIs for accelerating the development and implementation of solutions for the cancer patient community, the sustainability of this network beyond the end of the project will also be addressed.

Donor:	European Commission - Research and Innovation (BE) / Horizon Europe
Duration:	36 months
Funds for IARC:	€313 255.31
Funds for partners:	€14 553 185.19
Total:	€14 866 440.50
Partners:	Biobanking and BioMolecular resources Research Infrastructure - European Research Infrastructure Consortium (AT), European advanced translational research infrastructure in medicine (NL), European Clinical Research Infrastructure Network – ECRIN (FR), ELIXIR (GB), European Marine Biological Resource Centre (FR), European high-capacity screening network - EU-OPENSCREEN-ERIC (DE), Euro-BioImaging ERIC (FI), EurOPDX (BE), Infrastructures de recherche en biologie, santé et agronomie (FR), Analytical Research Infrastructures of Europe (BE), ARTTIC (FR), Cancer Core Europe (BE), European Organisation for Research and Treatment of Cancer (BE), European Cancer Patient Coalition (BE), Microbial Resource Research Infrastructure – ERIC (PT)

1.17 Project title: **Collaborative project between IARC and WCRF: Evaluation of Biological Mechanisms linking Diet, Lifestyle and Cancer within the CUP-2.0**

World Cancer Research Fund International's Global Cancer Update Programme (CUP) analyses global research on how diet, nutrition and physical activity affect cancer risk and survival. The CUP mechanisms component aims to develop a clearer understanding of the biological processes that underpin associations between diet, nutrition, physical activity and cancer. In the CUP transition phase, an expert panel developed a framework for evaluating mechanistic data to support the conclusions of the CUP. Recognizing the heterogeneity (experimental, animal, genetic, human molecular epidemiologic) and complexity of mechanistic data, a pragmatic approach was proposed in which molecular and genetic epidemiology data would be meta-analysed (in a manner analogous to how epidemiologic data is analysed and synthesized in the CUP) while experimental data would be evaluated using a more qualitative approach using a

protocol developed by the IARC Handbooks of Cancer Prevention programme. To take this work forward into the CUP 2.0, we propose a joint collaboration between IARC involving Dr Gunter (Head, Nutrition and Metabolism Branch), Dr Dossus (NME scientist), and Dr Béatrice Lauby-Secretan (Head, Handbooks) and WCRF with input from an assembled expert panel of diverse scientific disciplines.

Donor:	World Cancer Research Fund International (GB)
Duration:	36 months
Funds for IARC:	€402 944.57 (GBP£ 350 000.00)
Funds for partner:	N/A
Total:	€402 944.57 (GBP£ 350 000.00)
Partner:	N/A

1.18 Project title: **Identifying the risk factors underlying the rising rates of colorectal cancer in younger adults: observational and Mendelian randomization analyses**

In contrast to declining incidence and mortality rates, since the mid-1980s, rates of early-onset colorectal cancer (EOCRC, diagnosed <50 years) have increased in many countries. This rising incidence has occurred over a relatively short period and cannot be explained by population genetics. Few epidemiological studies have adequately examined the etiology of EOCRC as most evidence is from case-control studies, small-scale cohort analyses, or clinical database studies lacking high-quality data on lifestyle risk factors and covariates. It is currently unknown if any lifestyle-related risk factors are causally associated with EOCRC. In the first objective of this project, we will prospectively examine associations between multiple lifestyle-related risk factors and EOCRC risk in pooled analyses of up to 24 prospective cohort studies including >3100 incident EOCRC cases. In the second objective we make causal inferences for the associations between lifestyle-related risk factors and EOCRC by conducting a series of Mendelian randomization analyses in 6000 cases/65 000 controls from three genetic consortia. In this project, we expect to identify lifestyle-related risk factors robustly associated with EOCRC development. Such information informs on the etiology of EOCRC, sheds light on possible lifestyle behaviours that can be intervened upon, and could be used by clinicians to risk stratify young-adults who may present with non-specific CRC symptoms for early screening.

Donor:	Institut National du Cancer (FR)
Duration:	48 months
Funds for IARC:	€492 642.00
Funds for partners:	N/A
Total:	€492 642.00
Partners :	Albert Einstein College of Medicine of Yeshiva University (US), Fred Hutchinson Cancer Center (US)

1.19 Project title: **Circulating Proteins and Risk of Cancer, Type 2 Diabetes, Cardiovascular Diseases, Neurological Diseases and Premature Death in EPIC**

The overall objective of the proposed collaboration is to establish a research programme aimed at the identification of circulating proteins as biomarkers of common chronic diseases and premature death within the EPIC cohort. This will be the first large-scale research undertaking to discover novel biomarkers

of cancer, diabetes, cardiovascular diseases, neurodegenerative diseases and mortality using new proteomics technology developed by Somalogic (SomaScan) that can accurately measure approximately 7000 proteins in a single plasma sample. The proposed study will apply the SomaScan technology to ~29 000 EPIC baseline plasma samples stored at IARC. This collaborative project has the potential to be transformative for EPIC and for cancer and chronic disease population research generally, with new opportunities to identify biomarkers of chronic disease risk and early detection.

Donor:	Imperial College of Science, Technology and Medicine London (GB)
Duration:	24 months
Funds for IARC:	€499 048.51 (GBP£ 437 437.58)
Funds for partner:	N/A
Total:	€499 048.51 (GBP£ 437 437.58)
Partner:	Imperial College of Science, Technology and Medicine London (GB)

1.20 Project title: **Discovering the causes of three poorly understood cancers in Europe**

The overall goal of DISCERN is to understand the causes of three poorly understood cancers in Europe; renal, pancreatic and colorectal cancer, and help to explain their geographical distribution, including their high incidence in central and eastern Europe. This will be achieved by combining large-scale European biorepositories comprising population-based cohorts and tumour case-series with state-of-the-art molecular profiling techniques and machine learning approaches. In particular, DISCERN will identify potential new causal risk factors for the three cancers using novel exposomics and proteomics scans, as well as detailed geospatial and environmental exposure information from 16 large-scale epidemiological cohorts including almost 900 000 individuals. It will also explore biological mechanisms on how these risk factors are potentially causing these cancer types with a focus on promoting factors in normal tissues using deep sequencing, single cell multi-omics and spatial proteomics. The causal effects of identified cancer risk factors and the cellular signalling responses they trigger will be further evaluated using a panel of stem cells and colon, renal and pancreatic 3D organoids. The results from DISCERN will be disseminated to citizens, patients and policy makers through collaborating patient and participant organizations. DISCERN will provide the critical evidence base required to develop new prevention strategies to tackle the growing burden of renal, pancreatic and colorectal cancer in Europe. This action is part of the Cancer Mission cluster of projects on "Understanding".

Donor:	European Commission - Research and Innovation (BE) / Cancer Mission
Duration:	60 months
Funds for IARC:	€2 147 553.75
Funds for partners:	€6 710 259.25
Total:	€8 857 813.00
Total budget cost:	€10 043 030.00 including the UK contribution for the UK-based Associated Partners
Partners :	University of Utrecht (NL), Masaryk University (CZ), IRB Barcelona - Institute for Research in Biomedicine (ES), National Research Institute for Agriculture, Food and Environment - Institut national de la recherche agronomique (FR), Leiden University (NL), Royal Institute of Technology – KTH (SE), University of Tartu (EE), International Kidney Cancer Coalition (NL), Digestive Cancers Europe (BE), University of Turin (IT), Research Institute Bellvitge Biomedical Foundation (ES),

Nofer Institute of Occupational Medicine (PL), Maria Skłodowska-Curie Institute of Oncology (PL), IRCCS Bari Cancer Hospital (IT), Arctic University of Norway / UiT (NO), Pancreatic Cancer Europe (BE), University of Oxford (GB), Imperial College of Science, Technology and Medicine London (GB)

1.21 Project title: **Identification of aggressive differentiated thyroid cancers: a metabolomics approach**

Thyroid cancer (TC) is the most common endocrine malignancy with differentiated thyroid carcinomas (DTC) accounting for 90% of TC. Most patients with DTC have excellent prognosis. However, some patient subsets suffer from more aggressive cancers, and may need extensive surgery and treatment. Being able to identify these patients and predict the risk of developing an aggressive cancer would help stratify patients for proper treatment. Metabolomics uses new state-of-the-art analytical techniques to measure the metabolome, which is the final downstream product of gene expression, and close indicator of phenotypes. This technique represents a very useful tool for the identification of new biomarkers associated to different endpoints.

In this project, we will: a) Apply untargeted metabolomics to prospectively collect plasma samples from subjects with benign thyroid conditions, indolent T1, and T2-T4 DTC cases and from their matched controls, to identify biomarkers specifically associated to each thyroid condition; b) Replicate and validate the results observed; c) Develop risk prediction models that will identify subjects at risk of aggressive vs indolent DTC; d) Examine whether other available biomarkers (thyroid hormones, inflammation), genetic variants and lifestyle risk factors may increase sensitivity and specificity of associations.

We propose to set up a study within the French E3N cohort, and the large EPIC (European Prospective Investigation into Cancer and nutrition) cohort and validate/replicate the main findings on metabolomics in samples from the American Sister Study.

We expect to be able to identify biomarkers/metabolic pathways that are specifically associated with different thyroid conditions that would ultimately provide the basis for stratifying patients into suitable treatment strategies.

Donor:	Institut National du Cancer (FR)
Duration:	48 months
Funds for IARC:	€429 694.00
Funds for partners:	€89 532.00
Total:	€519 226.00
Partners :	Institut National de la Santé et de la Recherche Médicale (FR), National Institutes of Health - National Cancer Institute (US)

2. Prior approval for projects in collaboration with the private sector

There are no projects to be considered for prior approval this year.

3. Prior approvals

The Governing Council is invited to consider, for approval, projects submitted over €500 000 per annum, excluding sums passed on to collaborating institutions, and projects that require more than €100 000 per annum, excluding the principal investigator's staff costs, from the IARC regular budget.

Please note the following projects have been provisionally approved by the Chairperson of the Governing Council.

Environment and Lifestyle Epidemiology Branch (ENV)

3.1 Project title: **Revision and update of the European Code against Cancer**

In the ECAC5 project we will develop the 5th edition of the European Code against Cancer (ECAC), updating the previous version based on the most recent scientific evidence, expanding to population level prevention measures, and tailoring to different target audiences. ECAC5 is a key EU cancer prevention instrument contributing to successfully achieve the Europe Beating's Cancer Plan's goals. A multidisciplinary approach will be followed to revise and update the evidence base, guided by an established methodology, and to develop recommendations and supporting information on cost-effective cancer prevention measures at the individual and population levels, in synergy with other noncommunicable diseases' preventive messages. Behavioural science approaches, new technological innovations and modern ways of communication will be also regarded in order to improve health literacy, and more specifically cancer prevention literacy, across European populations and target groups. ECAC5 builds on a set-up, experiences, methodology and terms of references for the different pan-European Committees that have been put in place for the development of the 4th edition of the ECAC, ensuring the quality standards and making the project very cost effective. ECAC5 aims to make an impact in the cancer prevention arena in the short-, medium- and long-term by promoting effective communication of critically appraised and scientifically established evidence in cancer prevention, by providing strategies to steer national health policies in cancer prevention and by providing a united EU voice to call for cancer prevention.

This is aligned with the IARC project tree objective 4.3 – 'Strengthen global knowledge and global and national capacities to implement effective, quality assured, affordable interventions'.

Donor:	European Commission - European Health And Digital Executive Agency / EU4H (BE)
Duration:	48 months
Funds for IARC:	€1 500 000.00
Funds for partner:	n/a
Total:	€1 500 000.00
Total budget cost:	€2 500 000.00

Early Detection, Prevention, and Infections Branch (EPR)

3.2 Project title: **Strengthening cancer screening data collection to update European Cancer Information System and improve quality and coverage of cancer screening programmes in Europe**

Europe's Beating Cancer Plan is expected to put forward a new EU-supported Cancer Screening Scheme to help Member States ensure that 90% of the EU population who qualify for breast, cervical and colorectal cancer screenings are offered screening by 2025. To guide further EU action on cancer screening with the most recent evidence, the Commission is already committed to support EU Member States (MS) to collect data related to performance of cancer screening programmes and utilize the same for improvement of quality and equity. The European Cancer Information System (ECIS) has been created and is maintained by the Joint Research Council to collect data related to cancer uniformly across the MS. While the ECIS has been customized to collect data from cancer registries, it is not yet functional to collect cancer screening data. IARC with support from various European Institutions and European Cancer Leagues aim to submit a proposal to develop the functionalities of ECIS for screening data collection, collect data from selected MS in a harmonized manner, share the same with ECIS and finally support MS to utilize the analysed data from programme quality improvement. Our proposal will support the Commission to achieve the objectives under the Flagship Initiative for improving cancer screening in Europe.

This is aligned with the IARC project tree objective 3.2 'Enhance the implementation of cancer prevention and control programmes', as the project will develop indicators, data tools and guidelines for monitoring and evaluation of cancer screening programmes globally.

Donor:	European Commission - European Health And Digital Executive Agency / EU4H (BE)
Duration:	18 months
Funds for IARC:	€580 483.00
Funds for partners:	€1 079 744.00
Total:	€1 660 227.00
Total budget cost:	€2 767 051.03
Partners:	Reference Centre for Epidemiology and Cancer Prevention in Piemonte (IT), Association of European Cancer Leagues (BE), Cancer Society Of Finland - CSF (FI), Sciensano (BE), Norwegian University of Science and Technology – NTNU (NO), Erasmus University Medical Center Rotterdam (NL), Center for Cancer Detection – CvKO (BE).

4. Interest income from grants

In accordance with the standing authorization provided to the Director under resolution GC/55/R23 and the conditions set forth in the signed agreement, interest income amounting to €4790.98 was apportioned to the below grant in 2022.

Grant No.	Project	Donor	Interest (in euros)
100639	Extended Follow-up of the Participants of IARC-INDIA HPV Vaccination Study to Evaluate the Effectiveness of one, two and three Doses of Quadrivalent HPV Vaccine in Preventing Cervical Neoplasia	Bill and Melinda Gates Foundation	4790.98