

ACCEPTANCE OF GRANTS AND CONTRACTS

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, as detailed below.

Section of Cancer Surveillance (CSU)

1.1 Project title: **Uncovering international disparities in metastatic breast cancer outcomes**

Out of all US women diagnosed with breast cancer, 5–9% are diagnosed with metastatic breast cancer (MBC) as compared to 3–5% reported in Northern European countries. Survival from breast cancer declines significantly with worsening stage at diagnosis, and a large part of the survival gap between populations, within or across countries, can be attributed to a lower or higher burden of MBC. This suggests that differences in (access to) diagnostics and treatment may play an important role in outcomes of MBC. Using high-quality data from selected high-income countries (HIC) to benchmark the US to Europe, Australia and Canada, this project aims to investigate the causes of international disparities in metastatic breast cancer outcomes on the population-level.

Donor: Susan G. Komen Breast Cancer Foundation (USA)
Duration: 36 months
Funds for IARC: €381 838.28 (US\$ 448 167.00)
Funds for partners: -
Total: €381 838.28 (US\$ 448 167.00)
Partners: n/a

Director's Office (DIR)

1.2 Project title: **Financial contribution to the IARC Nouveau Centre project**

Mr Alain Mérieux has made a designated voluntary contribution to support the IARC Nouveau Centre project.

Donor: Compagnie Mérieux Alliance (FR)
Duration: 27 months
Funds for IARC: €1 000 000.00
Funds for partners: -
Total: €1 000 000.00
Partners: n/a

Section of Early Detection and Prevention (EDP)

Prevention and Implementation Group (PRI)

1.3 Project title: **Exploring metabolic disturbances associated with gastric cancer development: comparing French, European and high-risk populations**

Gastric cancer (GC) mortality in France remains high due to late diagnosis and poor survival. Moreover, GC burden in the overseas French territories is substantial. Global burden is increasing due to population growth, aging and unhealthy lifestyles, highlighting the importance of early intervention and prevention. The geographical variation in GC incidence does not correlate as expected with the prevalence of *Helicobacter pylori* (*H. pylori*), a known GC carcinogen, suggesting a complex etiology involving other modifiable risk factors. GC is thought to develop through a complex sequence of abnormal tissue changes, likely accompanied by metabolic changes. A comprehensive analysis of metabolic changes along the continuum of GC development would enhance our understanding of GC and guide preventive strategies.

Objectives: To (1) investigate plasma metabolite profiles for GC development prospectively through an untargeted metabolomics approach, and (2) generate evidence on modifiable GC risk factors with a careful examination of the interactions of unhealthy dietary/lifestyle patterns with metabolic pathways as part of the underlying mechanisms of GC etiology.

Expected results: Our findings will identify metabolic perturbations that potentially elucidate underlying mechanisms of GC development involving lifestyle factors and *H. pylori* infection.

Donor: Institut National du Cancer (FR)

Duration: 36 months

Funds for IARC: €294 941.00

Funds for partners: €36 291.00

Total: €331 232.00

Partners: Inserm U1018, France.

Section of Environment and Radiation (ENV)

1.4 Project title: **African Breast Cancer – Disparities in outcomes Plus (ABC-DO-Plus)**

The proposed study concerns a high-quality multidimensional study of survival in sub-Saharan African women with breast cancer, its determinants, as well as of health-related quality-of-life in survivors. Apart from information on the relatively low breast cancer survival in the very short-term in sub-Saharan Africa, little is known of five-year survival, its determinants, or of breast cancer survivorship in this setting. Early deaths from breast cancer are deservedly priority areas to be tackled, but additionally, research needs to extend to longer timescales and to wider health domains including the hitherto neglected health-related quality-of-life of survivors. A central consideration to all breast cancer research is the molecular heterogeneity of this tumour, not yet robustly characterized in sub-Saharan Africa, nor studied in relation to survival in this setting.

Donor: National Institutes of Health - National Cancer Institute (USA)

Duration: 45 months

Funds for IARC: €703 352.32 (US\$ 799 264.00)
Funds for partners: €605 511.28 (US\$ 688 081.00)
Total: €1 308 863.60 (US\$ 1 487 345.00)

Partners: Chris Hani Baragwanath Academic Hospital, South Africa; University of North Carolina at Chapel Hill (UNC), Zambia; Makerere University College of Health Sciences, Uganda; Federal Medical Centre Owerri, Nigeria; Abia State University Teaching Hospital, Nigeria; Halle University, Germany; Windhoek Central Hospital, Namibia; London School of Hygiene and Tropical Medicine, UK.

Section of Evidence Synthesis and Classification (ESC)

IARC Handbooks Group (IHB)

1.5 Project title: **IARC Handbooks of Cancer Prevention Vol. 19 – Oral Cancer Screening and Prevention**

Oral cancer is one of the most prevalent cancers, particularly in South-East Asia where it ranks number one cancer killer. The main risk factors for oral cancer are tobacco in all forms, betel-quid and other areca-nut related products, alcohol consumption, and human oncogenic papillomaviruses. All these factors are preventable, and it has been estimated that at least three-quarters of oral cancers may be prevented through primary and secondary prevention (reducing exposure, screening and early detection). Volume 19 of the IARC Handbooks will address for the first time primary and secondary prevention of oral cancers, with a special emphasis on smokeless tobacco/areca nut consumption. With reference to primary prevention, the programme will evaluate (1) the benefit of reducing exposure to each risk factor in reducing oral cancer incidence and/or mortality, and (2) the effectiveness of interventions in reducing consumption of smokeless tobacco, betel quid and other tobacco-related products, including implementation of bans on sale and other policies. For secondary prevention, this project will evaluate the effectiveness of oral cancer screening. Each volume of the Handbooks is developed by an ad hoc, specifically convened Working Group of international scientists with expertise in the topic of interest.

Donor: Institut National du Cancer (France)
Duration: 36 months
Funds for IARC: €371 657.00
Funds for partners: -
Total: €371 657.00
Partners: n/a

Section of Genetics (GEN)

Genetic Epidemiology Group (GEP)

1.6 Project title: **Integrative Cancer Epidemiology Programme: Towards improved causal evidence and enhanced prediction of cancer risk, progression and survival**

Cancer prevention and improved survival are strategic priorities for Cancer Research UK (CRUK). Life-style changes to augment conventional treatments in people with cancer were identified as a

UK research priority by the James Lind Alliance. These priorities reflect the rising global burden of disability and death attributable to cancer and can be ascribed in large part to increases in common and preventable factors (e.g. overweight, insulin resistance) and related risk behaviours (e.g. unhealthy diet and sleep, physical inactivity, tobacco use). This programme builds on our world-leading expertise in the application of causal analysis methods (specifically, Mendelian randomization) and population-based bioinformatics and genomic sciences. These methods facilitate robust discrimination between exposures that are causal in cancer risk or progression, and hence are possible targets for behavioural or therapeutic interventions, from non-causal biomarkers which may nevertheless act as early-detection or predictive biomarkers. The large quantity of publicly available GWAS data can be harnessed for causal analyses, and combined with increasingly accessible multi-omic data, to fuel improved understanding of molecular causes, mechanisms and predictors of cancer risk and progression. We have identified six major research themes indicative of contemporary challenges in cancer research that can be addressed through the application of innovative epidemiological approaches and that will form the focus of this programme: i) Metabolic health; ii) Sleep and physical activity; iii) Smoking cessation; iv) Systemic responses; v) Somatic mutations; and vi) Cancer progression, novel treatment and survival. These research themes will be tackled by integrating state-of-the-art methodological approaches coordinated across four Work Packages (WPs): WP1 Mendelian randomization for robust causal inference; WP2 Molecular mechanisms; WP3 Predictive biomarkers; and WP4 Designing and evaluating interventions. The programme will be underpinned by cross cutting strands in Training and capacity building; Bioinformatics, artificial intelligence and data mining; Evidence synthesis (including data sharing and reproducibility); and Patient and Public Involvement and Engagement.

Donor: Cancer Research UK (GB)

Duration: 60 months

Funds for IARC: €702 892.35 (GB£ 621 855.00)

Funds for partners: €8 000 537.01 (GB£ 7 078 145.00)

Total: €8 703 429.36 (GB£ 7 700 000.00)

Partners: Bristol University, UK; National Institute for Health Research (NIHR), UK; McGill University, Canada; Imperial College of London, UK; Braintrust UK; University of Exeter, UK; Quadram Institute, UK.

Section of Genetics (GEN)

Genetic Epidemiology Group (GEP)

1.7 Project title: Facilitating data sharing within the Lung Cancer Cohort Consortium (LC3)

Lung cancer causes 1.6 million deaths annually and is the most common cause of cancer death worldwide, including in the US. The Lung Cancer Cohort Consortium (LC3) was established in 2011 with three overarching aims; (i) to investigate etiological factors of lung cancer beyond tobacco exposure, (ii) to evaluate biomarkers for use in lung cancer risk prediction, and most recently also (iii) to establish valid questionnaire-based risk prediction models. The purpose of the administrative supplement is to leverage the rich and unique data resources developed within LC3 to support the development of a centralized data repository and analytical platform for LC3 data

that facilitates data sharing and remote analysis within the consortium, thereby accelerating lung cancer research within the NCI Cohort Consortium.

Donor: National Institutes of Health - National Cancer Institute (USA)
Duration: 12 months
Funds for IARC: €196 956.13 (US\$ 239 606.00)
Funds for partners: -
Total: €196 956.13 (US\$ 239 606.00)
Partners: Baylor College of Medicine, USA.

Section of Infections (INF)

Infection and Cancer Epidemiology Group (ICE)

1.8 Project title: **Measurement of Human Papillomavirus (HPV) vaccine introduction impact**

The activities will be conducted within the framework of Work Area 8 – Improved availability of HPV impact data – of the WHO BMGF Umbrella grant for Global Health 2020-2023 [Grant number: INV-005318]. Measuring the impact of HPV vaccination is technically complex and requires a long timeframe making it challenging for middle- and low-income countries (LMICs). IARC therefore implemented two large scale impact studies in Bhutan and Rwanda, both early adopters but also atypical countries. Results from both countries show that HPV vaccination with optimal population coverage has an excellent impact in reducing HPV burden in vaccinated populations in middle- and low-income countries. Further results from impact studies from additional settings and context-specific approaches are needed to give governments in LMICs confidence that their large investments in HPV vaccination will have a sizeable impact on local cervical cancer burden.

Objectives: To conduct baseline HPV prevalence surveys to set the benchmark for future vaccination impact assessment. This will generate further context-specific evidence of population-level HPV effectiveness from selected middle- and low-income settings.

Planned Activities: Based on consultations with EPI at WHO headquarters, to improve availability of HPV impact data globally, IARC/EPR¹ will develop the following areas of activity as part of its workplan: Baseline surveys HPV prevalence surveys in two selected settings in LMICs; Tools to standardize the measurement of the impact of HPV vaccination in LMICs.

Donor: Bill and Melinda Gates Foundation (USA) through World Health Organization - Headquarters (CH)
Duration: 34 months
Funds for IARC: €751 698.82 (US\$ 920 072.00)
Funds for partners: -
Total: €751 698.82 (US\$ 920 072.00)
Partners: n/a

¹ Early Detection, Prevention and Infections (EPR) Branch.

Section of Mechanisms of Carcinogenesis (MCA)

Epigenetics Group (EGE)

1.9 Project title: **Epigenetic mechanisms at the origin of childhood leukaemia: from birth to diagnosis**

Childhood cancer (CC) is the first cause of death by disease in children, but little is known about its causes. Because CC is rare, it is important to combine data from many countries and collect it at several critical periods during the child's life in order to unearth the roots of this cancer. This project brings together detailed data and unique biological samples from large international CC consortia, focusing on childhood leukaemia, the most common form. Using cutting-edge technologies, we will create a molecular map of the patients' genomes from birth to diagnosis in order to identify cancer biomarkers detectable in the blood of patients since the time of birth. This will also enable us to discover driver genes which underlie the causes of childhood leukaemia and which affect clinical outcomes, such as survival and risk of recurrence. This work proposes a novel approach that can trace back this cancer to its early origins, which may stem from the pregnancy period, and offers promising biomarkers for early-detection several years before diagnosis as well as driver molecular events that can be exploited in targeted therapy.

Donor: Institut National du Cancer (France)

Duration: 18 months

Funds for IARC: €150 000.00

Funds for partners: -

Total: €150 000.00

Partners: Norwegian Institute of Public Health, Norway; Oslo University Hospital, Norway; National Cancer Institute, Brazil; Statens Serum Institut, Copenhagen, Denmark; University of Southern California, USA; Oxford University, UK; Inserm, France.

Section of Nutrition and Metabolism (NME)

Biomarkers Group (BMA)

1.10 Project title: **Triple negative breast cancer: improving prevention and survival by the identification of new metabolic pathways**

In France in 2017, close to 59 000 women were diagnosed with breast cancer and approximately 12 000 died from the disease. Only a few modifiable risk factors have been identified for breast cancer and primary prevention strategies are urgently needed. Breast cancer is a heterogeneous disease with different molecular subtypes that are characterized by different etiology and survival rates. Triple negative breast cancers represent around 10–15% of newly diagnosed cases and are characterized by the absence of estrogen and progesterone receptor expression and lack of overexpression or gene amplification of human epidermal growth factor receptor. Therefore these patients are not eligible for hormonal or targeted therapies and generally have poorer survival (76% 5-year survival vs 88% for hormone positive cancers, SEER data) and a higher risk of distant metastases. Some epidemiological data are starting to emerge suggesting that risk factors for triple negative breast cancers may differ from those identified for other subtypes. A large pooled analysis of prospective cohorts indicated that the risk of triple negative breast cancer was higher

in parous vs nulliparous women and was not related to excess weight or obesity, contrary to what is observed for other subtypes. Given the lack of knowledge on the etiology of triple negative breast cancer, there is an urgent need to identify biological pathways associated with its development that could be targeted for primary prevention as well as to prevent recurrence and improve survival. High-resolution mass spectrometry is a powerful bioanalytical technique which allows the characterization and quantification of a large number of small molecules in biological samples. Metabolomics based on high-resolution mass spectrometry can detect subtle changes in the metabolic network which may be related to disease development, including cancer. Its application in population-based prospective studies has recently started to be implemented to increase our understanding of the metabolic changes associated with exposure to cancer risk factors and their role in cancer etiology. Currently, mutational signatures have been identified in many tumour types, including breast tumours, some of which have been linked to specific exposures or mechanisms; however, for the majority we have no clear understanding. Most studies on metabolic pathways in triple negative breast cancer have been based on cell lines, animal models of very limited number of human subjects. To acquire novel data on biological pathways that lead to triple negative breast cancer, we propose to use untargeted metabolomics to identify new metabolic pathways associated with risk and survival of triple negative breast cancers using plasma samples from the European EPIC cohort (250 triple negative breast cancer cases with prediagnostic blood samples and 250 matched controls) and tissue samples from the French-EPIC cohort (E3N, N=25 tumour + 25 normal breast tissue samples).

Donor:	Institut National du Cancer (France)
Duration:	48 months
Funds for IARC:	€319 866.00
Funds for partners:	€83 894.00
Total:	€403 760.00
Partners:	Inserm, France.

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 approval for projects over €500 000 per annum

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.

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

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 €3497 was apportioned to the below grant in 2020.

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	3497

5. For information reporting

The Governing Council is invited to note that contracts for a total of over €100 000 per annum have been accepted by the Director for the initiative below. However, the funds are originating from various donors therefore no formal post facto reporting is required.

Section of Evidence Synthesis and Classification (ESC)

WHO/IARC Classification of Tumours Group (WCT)

5.1 Project title: **Consortium Agreement for the International Collaboration for Cancer Classification and Research (IC3R)**

The WHO Classification of Tumours series published by IARC are known worldwide as the WHO Blue Books. This series offers a valuable contribution to cancer research and surveillance and fulfils an important role in scientific evidence synthesis and international standard setting. However, the multidimensional nature of cancer classification, the way in which the WHO Classification of Tumours is constructed, and the scientific information overload in the field constitute a huge challenge for the future of tumour classification and cancer diagnosis. We have setup the International Collaboration for Cancer Classification and Research (IC3R) to provide a forum for the coordination of efforts in evidence generation, standards setting and best practice recommendations in the field of tumour classification. The first IC3R meeting, held in Lyon (France) in January 2019, gathered representatives of major institutions involved in tumour classification and related fields to discuss and identify challenges in data comparability, standard setting, quality management, evidence evaluations, copyright(s) and develop a collaborative plan to address these challenges. The major outcomes of the meeting, as well as the work plan of the IC3R collaboration defined the following actions: creation of a consortium, adoption of ISO standards for cancer research laboratories, the development of Evidence-based Pathology and provision of knowledge and data sharing media.

Donor: Several partners contributing through membership fees

Duration: 12 months (renewable)

Funds for IARC: €110 000.00
Funds for partners: -
Total: €110 000.00

Partners: Centre Léon Bérard, France; INT-Fondazione Pascale, Italy; Sciensano Belgium Institute of Health, Belgium; Office of Science and Engineering Laboratories, US Food and Drug Administration, USA; Peter MacCallum Cancer Institute, Australia; National Cancer Center, Japan; Singapore General Hospital, Singapore; Bambino Gesù Children's Hospital, Italy; Pathology Queensland, Australia; University of Waterloo KIMIA Lab, Canada; German Heart Centre of the Free State of Bavaria, Germany; Northwell Health, USA.