

SECTION OF NUTRITION AND METABOLISM (NME)

Section head
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DIET, NUTRITION, METABOLIC/HORMONAL IMBALANCES, EXCESS ENERGY CONSUMPTION, OBESITY AND PHYSICAL INACTIVITY ARE THOUGHT TO BE IMPORTANT CONTRIBUTORS TO INCREASING CANCER INCIDENCE RATES WORLDWIDE. HOWEVER, THE MECHANISMS OF ACTION OF THESE FACTORS REMAIN POORLY UNDERSTOOD. IN ADDITION, THE CONTRIBUTING INFLUENCE OF DIETARY TRANSITIONS FROM TRADITIONAL TO WESTERN-TYPE DIETS, WHICH IS TAKING PLACE IN LOW- AND MIDDLE-INCOME COUNTRIES (LMICs) (E.G. LATIN AMERICA), AND EXPOSURES IN UTERO AND DURING EARLY INFANCY ARE NOT WELL STUDIED.

The main objective of the Section of Nutrition and Metabolism (NME) is to address these issues by evaluating the association between diet (including dietary patterns), nutrition, physical activity and energy imbalance with cancer risk in high- and low-to-middle-income countries using cohort and case-control designs or human intervention studies. Among other responsibilities, this Section plays a leading role in the coordination and maintenance of the European Prospective Investigation into Cancer and Nutrition (EPIC), a large ongoing prospective cohort initiated by IARC.

Emphasis is on improving the accuracy, understanding and interpretation of dietary exposures; developing, validating and disseminating standardized dietary methodologies relevant to international study settings; applying biomarkers and metabolomics to study cellular, biochemical and physiological changes and consideration of gene–diet/nutrient/ environment interactions. This approach will allow for a better understanding of the mechanisms/metabolic pathways by which diet, contaminants and hormones affect cancer and intermediate endpoints.

Ultimately, the translation of findings into public health recommendations and the development of appropriate cancer prevention strategies are of major importance to the Section.



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Research in the Nutritional Epidemiology Group (NEP) complements work conducted in the Dietary Exposure Assessment Group (DEX) and the Biomarkers Group of the Section of Nutrition and Metabolism (NME). Our research focuses on the role of diet, nutrition, metabolic/hormonal imbalances, excess energy consumption, obesity and physical inactivity on the incidence of cancer, and other metabolic diseases related to cancer, with emphasis on biomarkers and gene-diet/nutrient/environment interactions. We are developing a lifespan approach by conducting epidemiological studies to evaluate risk factors that begin in pregnancy and early infancy and continue through young adulthood, midlife and older adulthood.

Our approach includes studies conducted in both high-income countries and LMICs where epidemiological transition offers a unique opportunity to study the occurrence of chronic disease and the associated risk factors related to rapid change in lifestyle.

STUDIES IN HIGH-RESOURCE SETTINGS (THE EPIC PROJECT)

Over the last two years, NEP has ensured the cyclic endpoint and vital status update of the EPIC database, with the centralization of the most recent information on incident cancer events and on mortality from collaborating centres. Accordingly, new versions of project-specific databases were made available to the EPIC working group network, including the preparation of nested case-control datasets. The Group provided computing support to the Laboratory Information Management System (LIMS) for the retrieval of biological samples, in collaboration with the IARC Laboratory Services and Biobank Group.

NEP is active in several cancer site-specific EPIC working groups. For colorectal cancer, recent publications include: a study of blood levels of parathyroid hormone, which showed a positive risk association at very high levels, particularly among men (Fedirko *et al.*, 2011a); blood lipid and lipoprotein concentrations, which demonstrated that high concentrations of serum HDL are associated with a decreased risk of colon

cancer (van Duijnhoven *et al.* 2011); metabolic syndrome (Aleksandrova *et al.*, 2011); plasma folate, B-vitamins and related genetic variants (Eussen *et al.*, 2010a; Eussen *et al.*, 2010b); C-reactive protein (Aleksandrova *et al.*, 2010) and biomarkers of oxidative stress (Leufkens *et al.*, in press). Also, research is ongoing to more fully assess the biologically plausible lifestyle, dietary, metabolic and genetic effect modifiers of the vitamin D-colorectal cancer (CRC) association. Furthermore, the Group has been collaborating on a vitamin D-CRC project within the Vitamin D Pooling Project Consortium, which is comprised of more than 15 cohort studies from around the world. Finally, NEP has extended its previous vitamin D work on colorectal cancer survival showing that higher vitamin D status before cancer diagnosis improves survival of patients with colorectal cancer, but selected genetic polymorphisms in the vitamin D pathway genes do not have an effect on survival and do not modify the inverse association with vitamin D.

In 2010, the Group received funding from the World Cancer Research Fund for a project to explore the role of advanced glycation end products, colonic barrier function and endotoxin exposure on risk of colorectal cancer. The project intends to combine biomarker measures and dietary/lifestyle data to perform pathway analyses for multiple determinants of colorectal cancer risk.

For liver cancer, biomarker and data analyses are ongoing for several studies exploring dietary, lifestyle and hormonal determinants of risk. The Group is leading the analyses on dietary factors (e.g. glycemic index, glycemic load, dietary fibre and red and processed meats) and nutritional biomarkers (e.g. total iron and ferritin) in relation to cancers of the liver, intra- and extra-hepatic bile ducts and gallbladder. They are also contributing to the ongoing analyses on causes and the burden of hepatocellular carcinoma (HCC) (Trichopoulos *et al.*, in press), the role of obesity and hormones in the development of HCC and identification of proteomic and metabolomic biomarkers of HCC.

Other recent NEP publications relate to gastric cancer (Balassiano *et al.*, 2011;

Jakszyn *et al.*, 2011a; Sala *et al.*, 2011; Campa *et al.*, 2011a; Duell *et al.*, 2010; Eussen *et al.*, 2010c), prostate cancer (Campa *et al.*, 2011b; Price *et al.*, 2010), pancreatic cancer (Grote *et al.*, 2011; Chuang *et al.*, 2011; Petersen *et al.*, 2010), bladder cancer (Jakszyn *et al.*, 2011b; Büchner *et al.*, 2011), lung cancer (Johansson *et al.* 2010; Menvielle *et al.*, 2010), endometrial cancer (Dossus *et al.*, 2010; Allen *et al.*, 2010), ovarian cancer (Gram *et al.*, 2011), lymphoma (Neasham *et al.*, 2011) and all cancer sites (Elliott *et al.*, 2010; Boffetta *et al.*, 2010).

BREAST CANCER EPIDEMIOLOGY IN HIGH- AND LOW- AND MIDDLE-INCOME COUNTRIES

Breast cancer is the most frequent cancer among women worldwide, with an estimated 1.38 million new cancer cases diagnosed in 2008 (10.9% of all cancers), and the most frequent cause of mortality in both developed and developing countries. Except for reproductive factors, little is known about lifestyle risk factors. In addition, few studies have focused on premenopausal breast cancer, which is associated with greater severity of disease and shorter survival.

NEP is focusing on studying breast cancer risk in both developed and developing countries. As part of the Breast Cancer Working Group of the EPIC Project, we have evaluated the role of specific nutrients in relation to breast cancer in both pre- and postmenopausal women, in particular the role of glycemic load and glycemic index (Romieu, submitted) and the role of fibre (Ferrari, submitted). Results suggest a role of the insulin pathway in the risk of breast cancer and a protective effect from fibre on breast cancer risk. We are currently evaluating the role of folate and its interaction with alcohol intake, specific gene polymorphisms and epigenetics. To provide integrated recommendations for breast cancer prevention, we are working on the development of a healthy lifestyle index using the large EPIC database (Ritte *et al.*, 2011; Key *et al.*, 2011; Campa *et al.* 2011b; Menvielle *et al.*, 2011; Campa *et al.*, 2010; Key *et al.*, 2010; Bakken *et al.*, 2011).

In LMICs, we are collaborating on the EsMaestras study, a large cohort study of Mexican teachers recruited in 12 Mexican states (close to 80 000 women), which was developed to investigate the role of lifestyle factors in relation to chronic disease in women, particularly breast and cervical cancer. In this population we observed a strong link between obesity and a diet rich in carbohydrates, sweet drinks and processed food (Romieu *et al.*, 2011a). We also observed a positive association between metabolic syndrome and breast density, a strong predictor of breast cancer among premenopausal women (Romieu *et al.*, 2011b). Further analyses are ongoing to determine the role of hormones, IGF1, IGFBP3, leptin, adiponectin, other cytokines and nutrient biomarkers in relation to breast density.

In a large, multicentre case-control study of breast cancer conducted in three states of Mexico, we explored the association of fatty acid (Chajes, submitted) and vitamin D (Fedirko, submitted), a nutrient with high prevalence of deficiency among Mexican women in relation to breast cancer. This work was developed in collaboration with the National Institute of Public Health (NISP) and the National Institute of Cancerology (INCAN) in Mexico and the Ministry of Health (Mexico).

Recently, we have initiated a multicountry study (Brazil, Chile, Colombia, Costa Rica and Mexico) of molecular subtypes of premenopausal breast cancer in Latin American women. The objective of the PRECAMA study is to evaluate the distribution of specific molecular cancer subtypes and identify the role and mechanisms of diet, physical activity, obesity and metabolic disorders in breast cancer incidence and survival. The pilot phase is ongoing. A similar project is planned in South Africa.

THE ROLE OF EARLY LIFE EXPOSURE ON LATER HEALTH EVENTS: LATIN AMERICAN BIRTH COHORT CONSORTIUM ON HEALTHY GROWTH AND DEVELOPMENT

The role of fast nutritional transition and changes in lifestyle on children's growth and development, as observed in LMICs, is not well established. Early exposure to poor diet, a sedentary

lifestyle, tobacco smoke and other environmental exposures can change infants' and children's growth pattern and may result in altered metabolism, obesity and risk of chronic disease in adulthood. The objectives of the Latin American Birth Consortium on Healthy Growth and Development are to combine Latin American birth cohorts from three major Latin American countries, Brazil, Chile and Mexico, to evaluate early life factors associated with optimal growth patterns and development and the prevention of obesity and metabolic disorders.

Obesity is a global epidemic and an increasing number of children are affected, which is often associated with co-morbidities in childhood and adulthood. Worldwide, close to 42 million preschool children (under the age of five) are overweight or obese and 35 million of them are living in developing countries. One of the first activities of the consortium will be to explore the role of maternal anthropometry with the health and growth in offspring.

GENE-NUTRIENT INTERACTIONS

Exploration of gene-nutrient interactions is of interest to the Group. Recent activities include involvement in the Micronutrient Genomics Project, an international collaboration. Investigations are currently underway on body iron status, hemochromatosis gene mutations, the variation in the vitamin D receptor gene (Hughes *et al.*, 2011) and genes involved in the vitamin D signalling (grant application pending) and risk of colorectal cancer. The interaction of folate with alcohol and folate metabolism genes, particularly for breast cancer, is also an area of active study, as well as the role of nutrients on epigenetics (Teegarden D *et al.*, submitted).

ALCOHOL AND CANCER

The Group initiated, in collaboration with the French Direction Générale de la Santé, an exhaustive evaluation of the role of alcohol and tobacco on the incidence and mortality of cancer, cardiovascular disease and diabetes, using scientific evidence produced from EPIC.

NEP is participating in a collaborative effort to perform a comprehensive review and meta-analysis of alcohol consumption and risk of cancers, particularly those cancer sites for which collective information is still unavailable or insufficient. A particular focus for this effort is the effect of low-dose intakes of alcohol. A recent publication from this project shows an increased risk of colorectal cancer for consumption of >1 drink per day (Fedirko *et al.*, 2011b). Also, the Group has contributed to the preparation of manuscripts on alcohol consumption and lung cancer in never smokers (Bagnardi *et al.*, 2011), oesophageal squamous cell carcinoma (Islami *et al.*, 2011; Rota *et al.*, 2010) and laryngeal cancer (Islami *et al.*, 2010), and on the effects of low-dose alcohol consumption (≤ 1 drink/day) on all cancer sites (Bagnardi *et al.*, submitted).

The Group was also involved in a project based on the EPIC study on the attributable burden of alcohol consumption on cancer risk. It showed that alcohol is responsible for a large proportion of cancers in Europe (Schütze *et al.*, 2011).

DETERMINANTS OF HEALTHY AGEING

The Group leads the cancer-specific 'work package' as a partner in the European project entitled Consortium on Health and Ageing Network of Cohorts in Europe and the United States (CHANCES). The project brings together 13 international cohorts and aims to conduct pooled analyses of risk determinants for various diseases of aging, particularly cancer risk and survival in elderly populations.

NUTRITIONAL METABOLOMICS

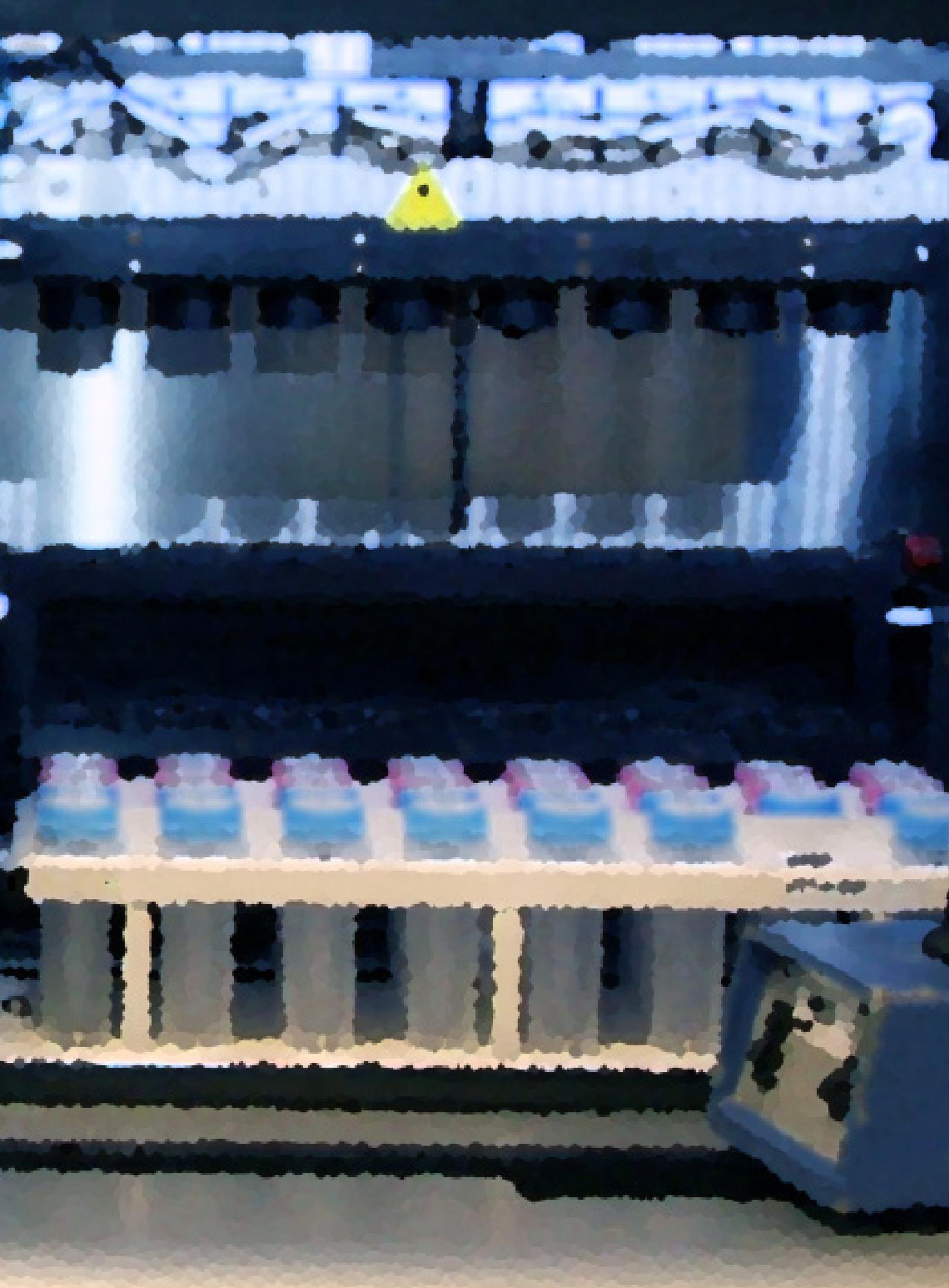
Recently, NEP suggested that metabolomics could play a key role in future assessments of novel biomarkers of dietary intake (Primrose *et al.*, 2011; Chadeau-Hyam *et al.*, 2011; Jenab *et al.*, 2009a). We are leading a collaboration to explore metabolomic profiles specific to dietary patterns and lifestyle habits. The Group is also involved in conducting nested case-control studies of NMR metabolomic analyses for pancreatic and liver cancers, in collaboration with a leading center, the European Center for High Field NMR in Lyon, France (<http://www.ens-lyon.fr/crmn/crmn/index.html>).

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The Biomarkers Group (BMA) was created in 2010. The major objective of the BMA is to identify new biomarkers of dietary exposure, food contaminants, environmental toxicants and hormones and metabolism, and to apply them to large cohort and case-control studies in relation to cancer risk, as well as to small-scale interventions in humans. The Group will work closely with DEX and NEP. This approach will allow a better understanding of the mechanisms/metabolic pathways by which diet, contaminants and hormones affect cancer and intermediate endpoints.

Two major approaches are in place to attain these goals:

1. DEVELOPMENT OF NEW ANALYTICAL METHODS TO CHARACTERIZE THE HUMAN METABOLOME

The human metabolome (all small molecules contained in a biological sample) carries considerable information that reflects the physiology of an individual. Recent progress in analytical techniques allows one to capture an increasing amount of this information.

Within the Group, high-throughput and highly sensitive methods, including mass spectrometry and immunological methods, have been developed to discover, validate and implement biomarkers of dietary and environmental exposure, physical activity and physiological status. These methods can be specific for a compound. During this biennium, we have developed a reference method for the analysis of Bisphenol A, a major endocrine disruptor among food contaminants. The method has been validated on blood cord samples in collaboration with the Hôpital Neurocardiologique, Bron (Harthe *et al*, submitted).

Special emphasis is given to metabolomics, a powerful and innovative approach able to measure hundreds of metabolites in human biospecimens. Such an approach, only recently applied to molecular epidemiology in metabolome-wide association studies, will contribute to our understanding of the role of diet and lifestyle on cancer risk. A new in-house research capacity has been set up with the acquisition of

two highly sensitive mass spectrometers coupled with liquid chromatography (LC-MS) and a new generation gas chromatograph (GC), which is used to characterize and quantify large sets of molecules from complex families, like fatty acids or polyphenols.

Targeted metabolomics is applied to the quantification of specific portions of the metabolome such as dietary polyphenols, major antioxidants of the diet with over 400 compounds known in various foods, or phthalates also known for their large structural diversity. Fractions of the metabolome sharing a similar functionality (e.g. phenols, carboxylic acids or amines) are labelled with deuterated or ¹³C-labelled reagents to form characteristic derivatives. The formation of such derivatives (metabolite coding) greatly improves sensitivity, selectivity and reduces analytical variability for quantification of compounds often present in trace amounts. These methods are developed in collaboration with the Service Central d'Analyse, Solaize, Lyon (CNRS) and the Chemistry Department of the University of Alberta. They are applied to samples of low volume (a few uL) compatible with cohort studies, where sample volume is often a limiting factor. A GC methodology has been developed and validated in collaboration with the Institut Gustave Roussy for the separation and quantification of 60 fatty acids, including 12 trans fatty acid isomers, some of them are being validated as biomarkers of industrially processed foods (Chajès *et al*, in press, 2011a).

Non-targeted metabolomics is used for biomarker discovery. Metabolic fingerprints obtained by high-resolution mass spectrometry in subjects differing in their lifestyle or diet, are compared by multivariate statistics to identify biomarkers characteristic of a specific food or diet. These methods are applied to the identification of novel biomarkers of food intake or environmental exposure in collaboration with the University of Alberta (Department of Computing Science), Imperial College London, INRA Clermont-Ferrand and University College Dublin.

2. IMPLEMENTATION OF BIOMARKERS IN COHORT STUDIES

Biomarkers have been implemented to explore associations with cancer risk in a few particularly relevant areas:

Fatty acids and cancer. New associations between specific fatty acid profiles and the risk of gastric cancer (Chajès *et al*, 2011b) and breast cancer (Chajès *et al*, 2011c) have been revealed. The gas chromatography has been improved and sixty fatty acids from plasma phospholipids have been identified and quantified in the EPIC study. The Group is currently undertaking a large nested case-control study (5000 breast cancer cases), in collaboration with the Lipidomic Platform from the Institut Gustave Roussy, to investigate associations between biomarkers of exposure to dietary trans fatty acids characteristic of industrially processed foods and dietary trans fatty acids characteristic of ruminant-derived foods, along with other fatty acids from the lipidome, and breast cancer risk within the EPIC cohort.

Several studies on the association between fatty acid biomarkers and cancer risk are ongoing within both the EPIC cohort and the Mexican EsMaestras and CAMA cohorts. The goal is to better understand interactions between fatty acids with specific gene and pathways in relation to gene methylation and cancer outcomes.

Hormones and cancer. The BMA has vast experience investigating hormones as risk factors for various cancers. Over the last biennium, the activities of the Group have focused on the validation of commercially available assays for measurements of hormones (growth factors, sex steroids, c-peptide, adiponectin, leptin and thyroid hormones) for large-scale epidemiological studies. We have undertaken hormone analyses for different case-control studies nested within EPIC to characterize associations between endogenous hormones and cervical cancer risk (Rinaldi *et al*, submitted) and between thyroid hormones and thyroid cancer risk. The BMA has also undertaken analyses of estrogens on samples from the New York University Women's Health study

and the Northern Sweden Health and Disease study within the framework of a collaborative project on breast cancer, and is currently initiating the analyses of several hormones on samples from the Mexican EsMaestras cohort for a project exploring the associations between hormone levels and breast density in women. The Group has a special interest in exploring the relationship between endogenous hormones (sex steroids, growth factors, insulin and cytokines) and environmental risk factors, including physical activity, in the EPIC cohort (manuscript in preparation).

The scientists of the Group are also involved in the activities of several cancer-related EPIC working groups (breast, ovary, endometrial) in close collaboration with NEP. We are coordinating the activities of the EPIC thyroid cancer working group (in collaboration with Dr. Silvia Franceschi, ICE), and leading a study on obesity, reproductive factors, thyroid hormones and thyroid cancer risk. The Group is also collaborating on case-control studies on breast cancer risk in women in Latin America and South Africa, led by NEP. For all these projects, the collection of different biospecimens (blood, urine, tumor tissues) and measurement of different biomarkers for nutritional, hormonal and metabolic status are foreseen, to improve the understanding of the mechanisms involved.

Polyphenols and cancer. Polyphenols are the most abundant antioxidants in the diet and are thought to play a role in cancer prevention. In collaboration with the University of Alberta and the University of Barcelona, the BMA has developed a comprehensive database on polyphenols in foods and their metabolites (Phenol-Explorer 2.0; Perez-Jimenez *et al.*, 2010b,c). In collaboration with NEP, a food composition table for polyphenols for the EPIC cohort has been constructed based on this data and is being used to study associations with cancer risk. Data on polyphenol metabolism is used to identify candidate biomarkers of exposure (Perez-Jimenez *et al.*, 2010a) which will be validated in the EPIC cross-sectional study.

Food metabolome. Over 20 000 chemical constituents have been described in foods. Ingested with food intake and absorbed through the gut barrier, they are present in blood and urine and form what we have called the food metabolome. A number of these metabolites reflect consumption of foods that may influence cancer risk. Over the last year, the Group has identified a specific fatty acid profile in pre-diagnostic plasma samples as a biomarker of both dietary fatty acids and fatty acid metabolism. In close collaboration with DEX, we have investigated new biomarkers of processed foods in a cross-sectional study nested in the EPIC cohort, and have identified plasmatic trans elaidic acid as a biomarker of highly processed foods (Chajès *et al.*, in press, 2011a).

We also undertook, in collaboration with DEX, the construction of a new database on the food metabolome and on biomarkers of food intake. Applying metabolomics to the EPIC cross-sectional study, we will compare groups of consumers and non-consumers of various foods and identify characteristic biomarkers of consumption for these foods. These new biomarkers will be applied to large cohort studies to look for new associations with cancer risk.

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The overall goal of the Dietary Exposure Assessment Group (DEX), within the Nutrition and Metabolism Section (NME), is to improve the accuracy, understanding and interpretation of (changes in) dietary exposure in studies on diet and cancer and other intermediate diseases. This Group has a leading role in the development of standardized dietary assessment methodologies and in improving their integration in dietary monitoring and diet-disease analyses, particularly in international study settings.

DEVELOPMENT OF STANDARDIZED DIETARY ASSESSMENT METHODOLOGIES

Great interest has been expressed for using the computerized 24-hour dietary recall method EPIC-Soft, initially developed as a reference calibration method within the EPIC study, in various other national and international nutritional studies. This justified further investments in its development and validation.

In the recently completed European Food Consumption Validation (EFCOVAL) project, EPIC-Soft was successfully adapted, further developed and validated on various aspects expected to fulfil specific needs of pan-European dietary monitoring and risk assessment (Slimani *et al.*; 2011, Crispim *et al.*, 2011, Huybrechts *et al.*, 2011). Figure 1 shows a typical interview screen of the food/recipe description and quantification step using EPIC-Soft. Figure 2 illustrates distributions of usual protein intake as estimated by an EPIC-Soft 24-hour recall interview and by biomarker measurements.

To respond to the need for wide dissemination of the EPIC-Soft application, while preserving its core concepts of standardization and integrity, a centralized web-based platform (EPIC-Soft Methodological Platform (EMP)) hosted at IARC is under development (the concept has been finalized and the technical implementation is ongoing). This comprehensive platform will provide full support to conduct international nutritional studies in Europe and elsewhere, using common tools and procedures to collect, control and handle dietary interview data.



Figure 1. Typical screen of a 24-hour recall interview of the food/recipe description and quantification step using EPIC-Soft

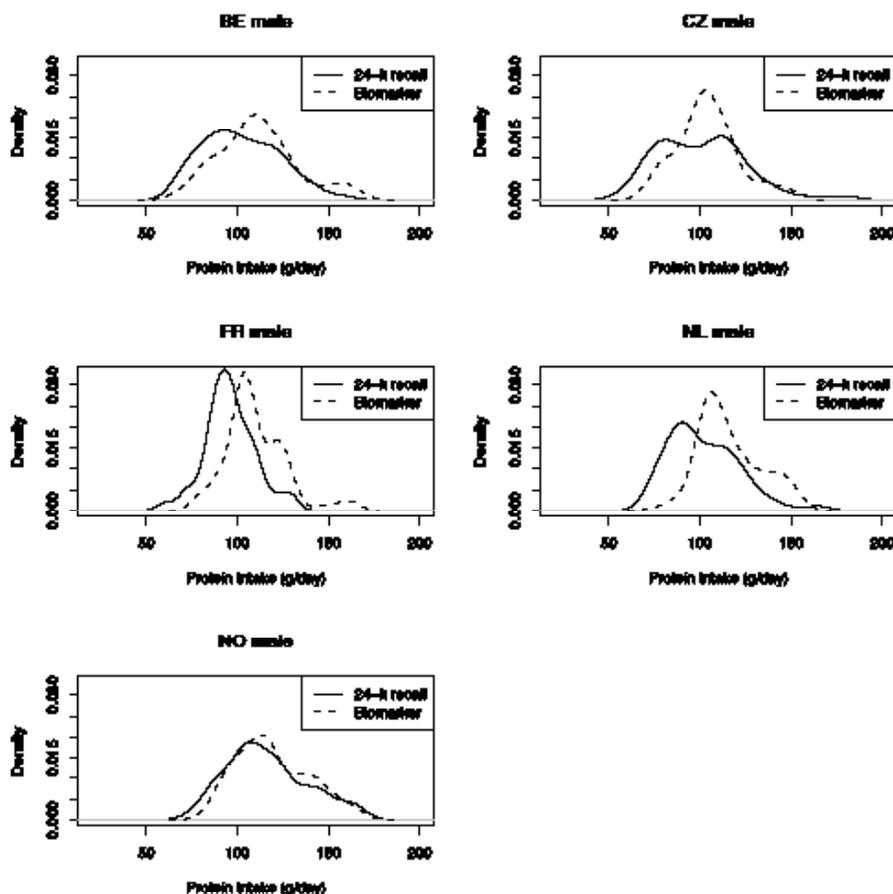


Figure 2. Estimated distribution of usual protein intake in men in the EFCOVAL study, based on two 24-hour dietary recall interviews (EPIC-Soft) and biomarkers for five European countries (BE, Belgium; CZ, the Czech Republic; FR, France; NL, the Netherlands; NO, Norway)

The decision by the European Food Safety Authority (EFSA) to launch the first pan-European monitoring survey, while recommending EPIC-Soft as the reference method to be used across the EU Member States, acknowledges the Group's methodological activities and endorses the recommendations and conclusions of the EFCOVAL project (<http://www.efsa.europa.eu/en/press/news/datex100212.htm>).

Additional related software has been successfully developed or is under development: (1) A data entry version of EPIC-Soft (PANCAKE project) has been created and is better suited and more user-friendly for data entry of repeated consecutive measures of food consumption collected by food diaries among children and the elderly. Currently, it is being tested in a pilot study in the Czech Republic and Belgium (manuscript in preparation); (2) The conceptual specifications of a new EMP module for matching food consumption data from EPIC-Soft with nutrient and other databases in international studies, is currently being developed by DEX within the EU-funded project EuroFIR Nexus.

DEX was also involved in the evaluation of measurement properties of dietary assessment tools (Illner *et al.*, 2011). A review paper of the applicability of new technologies in dietary assessment for large-scale epidemiological studies is in preparation.

The development of new dietary tools also includes the extension of the standardized EPIC Nutrient Databases (ENDB) developed by DEX (Slimani *et al.*, 2007). A new folate database has been compiled (manuscript in preparation) based on an in-depth inventory and evaluation of the available concentration data (Bouckaert *et al.*, 2011).

STUDIES ON DIETARY EXPOSURE (INCLUDING BIOMARKERS OF DIET)

In collaboration with researchers within the NME, descriptive analyses have been completed or are ongoing related to dietary exposure, such as the first standardized comparison of dietary folate intake across 10 European countries (Park *et al.*, 2011) and dietary

acrylamide exposure in the EPIC study (manuscript in preparation) and the related biomarkers including plasma fatty acids (Chajès *et al.*, 2011).

In the EFSA-funded EMP-PANEU project (Food Consumption Data Collection Methodology for the EU-Menu Survey), and in light of the future pan-European food consumption survey, DEX is currently implementing five country-specific versions of EPIC-Soft (Bulgaria, Finland, Hungary, Poland and Portugal). Furthermore, a new training module with e-learning components as a possible future part of the EMP platform will be tested.

STUDIES ON DIET AND CANCER AND OTHER (INTERMEDIATE) CHRONIC DISEASES

DEX is also involved in projects concerning the role of diet and biomarkers of diet in relation to cancer (EPIC) and other chronic diseases, such as obesity and diabetes (EPIC-PANACEA, INTERACT projects). A particular focus is on industrial foods (industrial trans fatty acids, acrylamide, excess energy consumption and glycemic index/glycemic load dense foods). This work is in collaboration with other researchers from the NME. Within the EPIC-PANACEA project on obesity and lifestyle factors, DEX is coordinating published findings on the relationship between diets rich in foods with high glycemic index/glycemic load and plasma fatty acids and obesity (Huybrechts *et al.*, Chajès *et al.*, both in preparation), as well as a methodological work on underreporting among obese subjects using both dietary and biomarker data (Freisling *et al.*, 2011).

DEVELOPMENT AND APPLICATION OF NEW METHODOLOGIES TO ANALYSE DIETARY PATTERNS

One of the Group's new research interests is dietary pattern analyses - a promising approach for better depicting the complexity of diet and improving the understanding of its association with diseases, particularly cancer. DEX, in collaboration with researchers from other Sections (BST, NEP) and external partners, initiated a project on analysing nutrient and biological patterns in international studies with applications in

colorectal cancer (ongoing grant), breast cancer (ongoing grant) and diabetes (INTERACT project). As a starting point of these activities, research has been published on the diversity of nutrient patterns in the EPIC study at a population level using a multidimensional graphical representation of the patterns (*Freisling *et al.*, 2010).

GOALS AND FUTURE PROJECTS

Already under discussion are two European projects which will make use of the improved EPIC-Soft methodology: the first pan-European monitoring survey involving the 27 Member States (direct institutional contract between EFSA and IARC to support its implementation already in place), and a second dietary measurement on a large subsample of the EPIC cohort. Using a common standardized methodology (EPIC-Soft) will provide a unique opportunity to bridge two major areas of nutritional surveillance (EU Menu project) and epidemiology (EPIC) in Europe, open new avenues for cancer and other research, and facilitate translation of scientific evidence into public health, policy and other actions.

Discussions have been initiated about developing versions of EPIC-Soft for Brazil, Mexico (Latin America) and South Korea, which would support new NME projects and provide greater insight on dietary changes in non-European countries and those countries undergoing nutritional transition.

Finally, an ambitious project ('Nutrition and physical (in)activity as determinants of cancer risk in Africa: data for formulating new research strategies and targeted regional prevention guidelines'), funded by IARC's Fellowship Programme, will commence with the arrival of Dr Pisa (postdoctoral fellow). This project aims to perform an unprecedented inventory of the current available data related to nutritional cancer research in Africa. It will consider crucial methodological and logistical aspects (e.g. available/needed dietary and physical activity assessment methodologies, cancer prevention guidelines and cancer registries). This evaluation is expected to create opportunities to support and develop further nutritional and cancer research activities in African countries.

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