CREAL
REPORT
2012-2013

centre for research
in environmental
epidemiology

CREAL
REPORT
2012-2013

CREAL REPORT 2012/2013

SUMMARY

DIRECTOR'S WELCOME

Dear Sir/Madam,

Once again we have the pleasure of presenting CREAL's annual report, for the period 2012-2013. CREAL is approaching the tenth anniversary of its creation, an appropriate moment to show not only our activities during this time, but also how we have developed as a centre and some of the challenges we face.

The centre's Strategic Plan, which was approved by the Board in 2009, was in effect up until December 2013, and for this reason, we worked on updating it for the period 2013-2015. The highlights of this last period include the centre's evaluation by the ***Scientific Advisory Committee (SAC)*** and **iCERCA**. The SAC's visit, its third since CREAL's creation, was also a very special visit, in that most of its members were new following the renewal process in 2012. In parallel with the SAC's evaluation, the iCERCA evaluation was also carried out by a committee comprised of specialists in the fields of research, management and auditing, and which also included two members of the SAC. The reports from these two evaluations have been reviewed in detail by CREAL management and their recommendations have been included in the Strategic Plan.

One of CREAL's highlights is its international competitiveness. CREAL researchers are conducting 29 international research projects, 9 of which are led by researchers from the centre (including an ERC Advanced Grant). One such project, coordinated by Dr. Martine Vrijheid is HELIX "The Human Early-Life Exposome - novel tools for integrating early-life environmental exposures and child health across Europe", which has received funding to develop the concept of the exposome during the early stages of life. The exposome is a new paradigm in environmental health and one of CREAL's most important scientific challenges. It is not a coincidence that members of CREAL lead the organization of conferences and international scientific meetings. During this period we have organized three international workshops funded by the European Science Foundation and the B.Debate initiative. In 2013, the annual congress of the European Respiratory Society was held in Barcelona, with 18,000 attendees, and with Dr. Judith Garcia-Aymerich from CREAL as the co-chair of the Scientific Committee.

Scientific production is a good reflection of CREAL's commitment to international leadership. A few months ago the SCIMAGO report became available, including a total of 4702 centres worldwide. Examining the indicators that allow us to compare centres independently of their size, CREAL falls within the top 100 worldwide for most indicators. In 2013, these positions were as follows: 25th in excellence, 66th in leadership of excellence, 155th in international collaboration, 61st in normalized impact factor, and 52nd in the percentage of publications in the first quartile of impact. These data place CREAL among the top centres in Spain (1st and 2nd in normalized impact and excellence, respectively).

Another important feature of this period has been the development of a professional career model for researchers, including both the centre's policies in this area, as well as the external evaluation of promotions. For the first time since its inception, the centre has evaluated the promotion of eligible researchers, which has been carried out through AGAUR and with the supervision of the SAC. Another important milestone is the recognition of CREAL as a **university research institute attached to UPF**, which was published in the official bulletin of the Government of Catalonia on 22 April, 2013. This recognition helps to strengthen collaboration and CREAL's commitment to UPF.

The centre continues to enhance its **knowledge transfer and enrichment activities**. Noteworthy local activities during the period 2012-13 include CREAL's collaboration with the Barcelona Metropolitan Area Mobility Master Plan (Pla Director de Mobilitat) and Catalan Inter-Departmental Plan for Public Health (PINSAP). International translational activities include participation in the review of WHO standards for air pollution 2012.

In the area of **financial management**, and within the context of the economic crisis, CREAL continues its efforts to improve efficiency and cost containment. In addition, and despite current restrictions on some of the calls for external resources, the current percentage of external financing is 66%.

We leave until last what is possibly CREAL's most important strategy in order to build a sustainable future within the current context of funding and international competitiveness, namely the development of our Alliance with ISGlobal, which we discussed in the previous report. During this period, this Alliance has developed with the support of all sponsors, and of two grants from the SUMA 1 and 2 calls, while carrying out the strategic actions designed upon the alliance's strategic foundation. We expect that this process will lead to complete integration in a centre with sufficient critical mass and excellence to become a world leader in the field of research, translation and education in global and public health.

As always, we reserve our final words to thank the generous commitment of all members of CREAL, of the Scientific Advisory Committee, and of its president, Professor Jonathan M. Samet, and the unwavering support of our sponsors, the departments of Health, Economics and Knowledge, and of Planning and Sustainability of the Government of Catalonia, Mar Health Park, and Pompeu Fabra University.

Josep M Antó, Jordi Sunyer, Manolis Kogevinas

Directors

BASIC DATA 2012-2013

- 13 RESEARCH GROUPS
- 33 RESEARCHERS
- 21 PREDOCTORAL RESEARCHERS
- 15 STATISTICIANS
- 31 RESEARCH TECHNICIANS
- 17 MANAGEMENT AND ADMINISTRATION PROFESSIONALS

CREAL REPORT 2012/2013

SCIENTIFIC ACTIVITY 2012-2013

260 ORIGINAL SCIENTIFIC PUBLICATIONS IN INTERNATIONAL JOURNALS

- **47** % D1 JOURNALS
- **68** % INTERNATIONAL COLLABORATIONS
- **3,065** RCI 2012
- **20** ORIGINALS IN ENVIRONMENTAL HEALTH PERSPECTIVES

95 ONGOING COMPETITIVE GRANTS

- **29** ONGOING INTERNATIONAL PROJECTS
  - **9** COORDINATED BY CREAL
- **29** ONGOING NATIONAL PROJECTS
- **31** ONGOING COMPETITIVE CONTRACTS
- **6** ONGOING STRUCTURAL GRANTS

BOARD OF TRUSTEES

(2013, December 31st)

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Generalitat of Catalonia

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MEMBERS

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Vice-Rector for Science Policy
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Balbina Ugena i Villalobos
Managment Director
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Lluis Rovira i Pato
Director of CERCA Institution
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Isabel Hernández i Cardona
Assistant Director of Prevention and Control of Pollution
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CERCA Institute
Legal Advice

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Vice-Rector for Science Policy
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Marta Aymerich Martinez
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PROGRAM MANAGER

Susana Gros

CREAL RESEARCH PROGRAMMES

CREAL RESEARCH
PROGRAMMES

CREAL's research is organized into 6 research programs, three focused on health outcomes (respiratory disease, cancer and children's health), and three on important environmental exposures (air pollution, water pollution and radiation).

The centre places an important emphasis on collaboration between programmes, which is strongly supported by all our researchers, who encourage cohesion and synergy, and promote the role of CREAL as a leading international centre by fostering multidisciplinary networking.

RESPIRATORY PROGRAMME

PROGRAM SUMMARY

Among respiratory diseases, asthma and Chronic Obstructive Pulmonary Disease (COPD) are among the main causes of disability-adjusted life years (DALYs) worldwide, according to the 2010 Global Burden of Disease (GBD) study (Murray JL *et al*. Lancet 2012). These disease are the main focus of the Respiratory Programme at CREAL, with several active projects devoted to elucidating both their causes and their characteristics.

Regarding causes, several projects focus on the study of environmental risk factors: The PRESTIGE study reported the persistence of respiratory symptoms 5 years after exposure to the clean–up work of a large oil-spill. The HiTea study examines the respiratory effects of exposure to biological agents in the indoor environment of schools. The ECRHS and EPIASLI-2 studies have continued to provide relevant information about the role of air pollution and occupational exposures in the incidence, control and severity of asthma. The URBAN training project is taking an important step beyond previous observational research, in studying the effects of a population-based intervention on physical activity and health in COPD patients. Other initiatives that assess physical activity in patients with chronic respiratory diseases include the PROACTIVE and the Exercise Equations projects.

Regarding the characteristics of these diseases, we carry out intensive research to develop new phenotyping methods. The PAC-COPD and MeDALL projects are pioneering the use of unsupervised statistical methods to understand the heterogeneity of asthma and COPD, and have provided new insights into alternative disease classifications including the comorbidity of allergic diseases during childhood. The ECRHS study continues to be a source of new knowledge on the genetic and molecular mechanisms of respiratory diseases and their interaction with the environment. The early diagnosis of these diseases is an important challenge that is being addressed by the BioLUNG project on predictive biomarkers.

The summaries of these and other studies included in this section highlight the main findings of research conducted in 2012-2013, and ideas leading to new projects. It is worthwhile noting that the respiratory research program at CREAL covers all age groups, from childhood to old age, including studies in young adults with many fluid interactions with other CREAL research programmes.

PROJECTS

MeDALL

TITLE: Mechanisms of Development of Allergy (http://medall-fp7.eu/)
PI: Josep M Antó
PERIOD: 2010-2014
FUNDING SOURCE: EU-FP7-Health (1.493.456€), co-coordinators

The *Mechanisms of the Development of ALLergy* study aims to generate new knowledge on mechanisms of initiation of allergy from childhood to adolescence, integrating birth cohort studies with experimental and mechanistic studies (Bousquet J and Antó JM. *Allergy*, 2011). A protocol for the systematic review of classical allergic phenotypes has been prospectively registered (CRD42012002443) with the International Prospective Register of Systematic Reviews (PROSPERO) (http://www.crd.york.ac.uk/prospero/display_record.asp?ID=CRD42012002443) and the methodology for the conduct of this systematic review has been published (Pinart *et al*., WebmedCentral *Allergy*;3:WMC003408). A manuscript reporting the findings of the systematic review is in preparation. A study of classical phenotypes using cross-sectional and longitudinal analysis revealed that asthma, rhinitis and eczema are not independent but co-occur at an early age (4 years), and that co-occurrence persists until age 8 and is similar in IgE positive and negative children (Pinart M *et al. Lancet Resp Med* 2014). K-means cluster analysis has been used to identify unsupervised phenotypes showing that children can be classified into two groups at 4 and 8 years of age, one group with low prevalence of allergic diseases, and one with higher prevalence of all three allergy-related diseases, suggesting the existence of a unifying allergy phenotype (Garcia-Aymerich J *et al. submitted*). Again, clusters were very similar regardless of whether information on IgE sensitization was included or excluded. In an historical serum samples from the INMA-Sabadell and BAMSE birth cohorts, we have measured a limited number of analytes via ELISA (including YKL-40 and IL1RL1-a), and a test panel of approximately 80 biomarkers via the Luminex-based multi-analyte profiling (MAP) technology. Regarding follow up (PI J Sunyer), a MeDALL core questionnaire and a set of Standard Operating Procedures (SOPs) have been developed (Hohmann *et al., Int Arch Allergy Immunol*, 2014) and follow-up of almost 1200 children from the INMA cohorts has been completed. Phase 2 studies are in progress to validate biomarkers that are predictive of allergic diseases and to integrate biomarkers with epigenetics, and transcriptomics with phenotypes.

ECRHS III

TITLE: European Community Respiratory Health Survey 18 year of follow-up of the Spanish cohort
PI: Josep M Antó; Co-PI: Jan-Paul Zock
PERIOD: 2010-June 2013
FUNDING SOURCE: FIS-ISCIII (77.440 €), SEPAR (12.000€)

The *European Community Respiratory Health Survey* (ECRHS) is an international respiratory health study in young adults mainly from Western Europe, including 5 areas in Spain (www.ecrhs.org). The first two ECRHS surveys (I and II) were conducted in 1990-1992 and 2001-2, and ECRHS III began in 2011. ECRHS has been highly productive to date, with more than 300 articles published in peer reviewed journals. During 2011-12, relevant findings reported by CREAL researchers included the fact that COPD may start early in life as a result of smoking and other determinants like airway responsiveness and respiratory infection in childhood (de (Marco R *et al. AJRCCM* 2011), that the use of latent class revealed four distinct asthma phenotypes (Siroux V, ERJ 2011) and that people who clean their homes with hypochlorite bleach are more likely to have respiratory symptoms (Zock JP *et al. JACI* 2011). Regarding ECRHS III in Spain, the fieldwork was completed with a response rate for the short questionnaire of 82% (n:1551), of whom 73% agreed to participate in a clinical visit including a detailed face-to-face interview, and measurements of

ECRHS III

biometry, forced spirometry with a bronchodilator test, bioimpedance and fractional exhaled nitric oxide, serum total and IgE specific to common allergens. Skin prick testing was carried out, and peripheral blood and urine samples were collected and stored for future biomarker and DNA analysis. Additional questionnaires including items on diet, gender, physical activity, quality of life and asthma control, among others were self-administered. At the European level, 60.9% (8,373/13,747) of adults who completed the clinic investigations in ECRHS I also completed the postal survey in ECRHS 3.

BIOLUNG

TITLE: Molecular Epidemiology of Lung Function: an Integrated Approach
PI: Stefano Guerra
PERIOD: 2010-2012
FUNDING SOURCE: FIS-ISCIII (207.515 €)

BACKGROUND AND AIMS

It has been long known that reduced lung function is a strong predictor of functional impairment, reduced quality of life, and overall mortality. These associations are mostly related to the deleterious health effects of COPD. Although most COPD patients develop the disease in middle to late adult life, the accelerated decline in lung function that leads to the development of the disease usually starts in young adulthood. Thus, the identification of systemic biomarkers of lung function decline in young adult life could provide insights into the molecular mechanisms of early susceptibility to COPD, and have critical implications for prevention.

METHODS

In this project, we used the Spanish branch of the prospective population-based ECRHS study, which provides detailed information on respiratory phenotypes and an extensive collection of serum samples and DNA. Using the Luminex-based MAP technology and ELISA in serum, we tested a panel of approximately 20 biomarkers variably involved in inflammation, innate immunity, proteolysis, auto-immune responses and other pathways (YKL-40, CC-16, SP-D). For most of these biomarkers, haplotype-tagging single nucleotide polymorphsims (SNPs) from the encoding genes have been also genotyped, with the ultimate goal of testing levels of biomarkers and genetic variants together against levels and decline of lung function.

MAIN FINDINGS

Biomarkers were measured in 850 Spanish ECRHS participants and nearly 200 SNPs in the genes of interest were genotyped in approximately 800 participants. CC-16 was associated with deficient lung function and airflow limitation as described in Rava *et al*. (Rava *et al*. 2013). YKL-40 was found to be associated with deficient lung function and smoking-related lung function decline. These findings were consistent with those obtained in an independent cohort in the TESAOD study in Tucson, and a collaborative study has been published (Guerra, Halonen *et al*. 2013). A number of pro-inflammatory molecules were also found to be related with deficient lung function. Interestingly, variation in the encoding genes was frequently found to be associated with serum levels of the corresponding biomarkers. Despite the fact that the association between genes and corresponding protein levels were sometimes extremely strong, both in terms of statistical significance and the percentage variability of serum levels explained by genetic variation,

References*:* Guerra, S., M. Halonen, *et al*. (2013). "The relation of circulating YKL-40 to levels and decline of lung function in adult life." Respir Med 107(12): 1923-30.

Rava, M., L. Tares, *et al*. (2013). "Serum levels of Clara cell secretory protein, asthma, and lung function in the adult general population." J Allergy Clin Immunol 132(1): 230-2.

PROJECTS

BIOLUNG

we did not find strong genetic associations with complex phenotypes such as lung function (Rava *et al.*, in preparation). These findings support the value of protein biomarkers in association and prediction studies of complex diseases/traits. In line with this, we have completed a study including ECRHS, TESAOD, and the Swiss SAPALDIA cohort, in which baseline serum CC-16 levels were found to predict subsequent lung function decline in all three cohorts (Guerra *et al.*, in preparation).

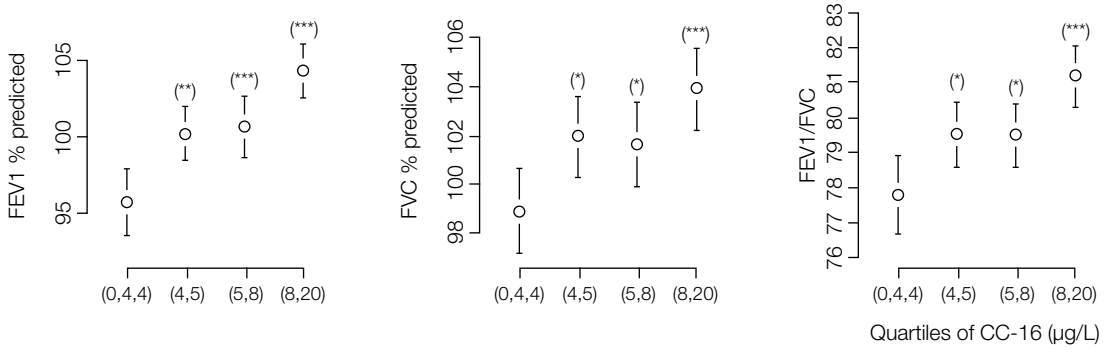

Figure 1: *Strong correlation between increasing levels of serum CC-16 (x axis) and increasing levels of lung function among Spanish ECRHS participants(Rava, Tares et al. 2013).*

PROactive

TITLE: Physical Activity as a Crucial Patient Reported Outcome in COPD
(http://www.proactivecopd.com/)
PI: Judith García-Aymerich
PERIOD: 2009-2013
FUNDING SOURCE: Innovative Medicines Initiative (IMI) (433.568 €), partner

Physical Activity as a Crucial Patient Reported Outcome in COPD - Innovative Medicines Initiative, Grant IMI-115011; partner

The PROactive project combines data from systematic reviews of the literature, interviews with patients, and expert opinion to construct a final 'draft item list' for PRO instruments, and program them into an electronic (e)PRO. The draft list has been tested in a multicentre study led by CREAL and involving over 250 COPD patients from five European countries, in parallel with two physical activity monitors that were selected on the basis of a set of stringent validation studies of six devices. The resulting pre-final tools show good instrumental properties in terms of dimensionality, construct validity, and reliability. The main manuscript of the PROactive study, led by CREAL, is in preparation. CREAL has also led two systematic reviews (Gimeno-Santos, HQLO 2011; Gimeno-Santos, Thorax 2014); the second reviewed and summarised all evidence available so far on determinants and outcomes of physical activity in COPD patients (see Figure 2)

PROactive

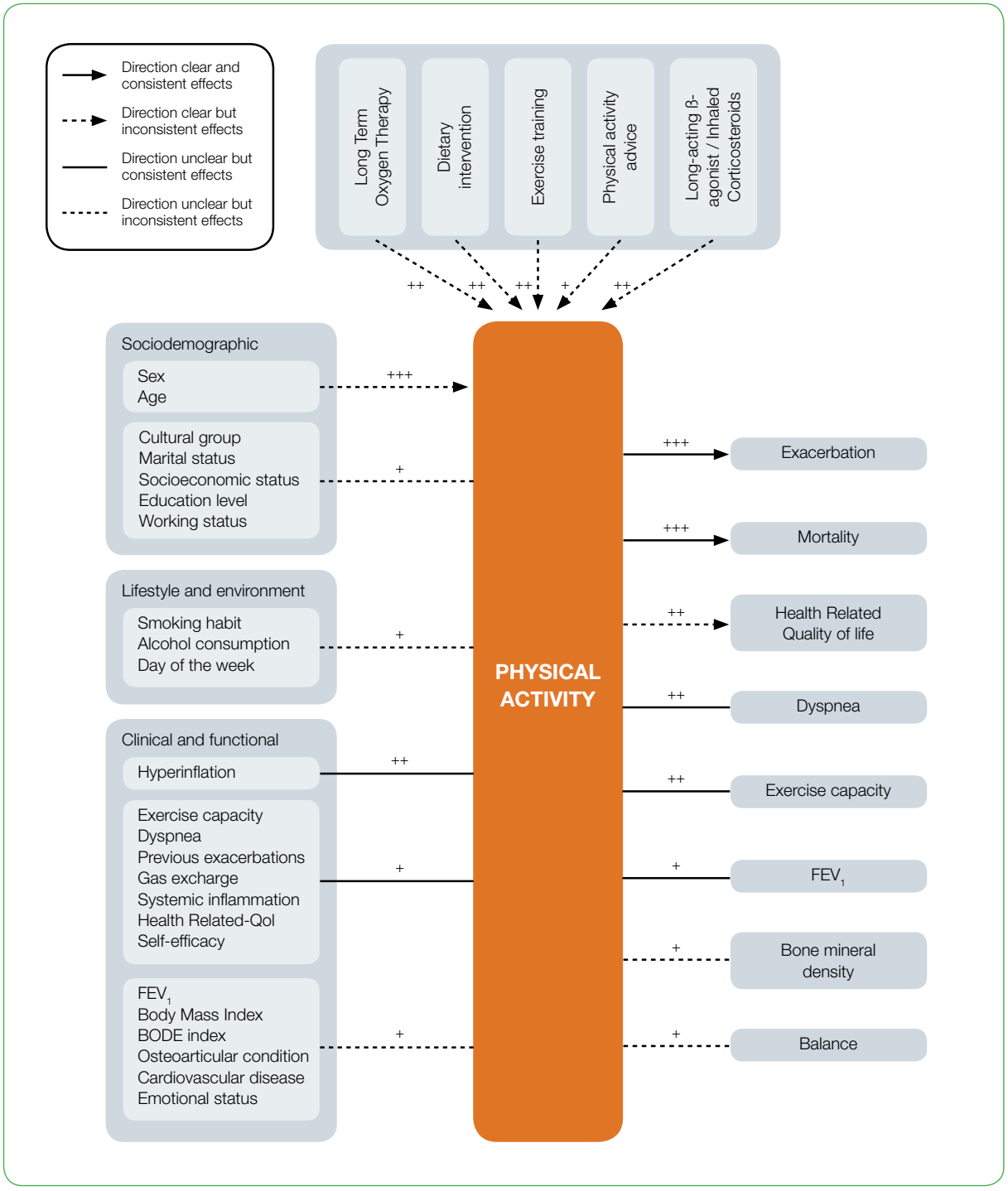

Figure 2: *Conceptual model of physical activity in patients with COPD.*

PROJECTS

EXERCISE EQUATIONS

TITLE: Elaboració de les equacions de referència per a les proves de marxa de 6 minuts i de llançadora (shuttle test) en població espanyola adulta
PI: Judith Garcia-Aymerich / Elena Gimeno
PERIOD: 2012-2013
FUNDING SOURCE (and total amount):
SOCAP (4.000€)

Development of reference equations for the 6-min walking test and shuttle test in the Spanish adult population - SEPAR 269/2010; SOCAP.

This study aims to develop equations for 6-minute walk and shuttle tests for the Spanish population. During 2012-13, we recruited a total of 583 subjects from 17 hospitals, universities and community centres in 9 areas of Spain. Subjects were characterized and performed exercise tests. The sample was evenly distributed with respect to gender (49% men, 51% women); their mean (SD) age was 62 (11) years, height 164 (11) cm, weight 74 (14) kg and BMI 28 (20) kg/m2. The median distance walked in the 6-min walking test was 621 m for men and 551 m for women, and 645 m and 485 m in the shuttle test, respectively. Sex-stratified statistical analysis is currently ongoing. We will study factors associated with exercise capacity using linear regression, and obtain the coefficients and the percentage of variance explained. We hope that our equations will be useful not only for Spanish population but also for other populations in the Mediterranean region, where populations share similar characteristics and reference equations have not yet been developed.

SESAP

TITLE: Socio-Economic Status and Air Pollution in three European cohorts, EGEA, SAPALDIA and ECRHS
PI: Benedicte Jacquemin
PERIOD: 2012-2016
FUNDING SOURCE: ANSES (170.768 €)

The main objective of SESAP is to assess whether socio-economic status (SES) is associated with air pollution exposure in Europe (ECRHS, SAPALDIA and EGEA). The secondary objectives are to assess if such associations are modified by asthma or obesity.

In the past year, we have worked on collecting and homogenizing data for individual- and area-level SES variables, and preliminary analysis show that Europeans with higher SES are more exposed to air pollution, regardless of the SES of the area where they live. However there is some heterogeneity in these patterns, as in cities with a more industrial history or activity, where participants with lower SES are more exposed. We plan to submit a first paper on the main objective by summer 2014, and the other two papers at the beginning of 2015.

URBAN TRAINING

TITLE: URBAN trainign in COPD- Effectiveness of an intervention of urban training in patients with chronic obstructive pulmonary disease (COPD): a randomised controlled trial

PI: Judith Garcia-Aymerich

PERIOD: 2012-2014

FUNDING SOURCE (and total amount):

Several sources of competitive funding [FIS-ISCII (114.126€), SEPAR (12.000€)

The Urban Training project is a multicentre controlled clinical trial that aims to assess the effectiveness and cost-effectiveness of an urban training intervention after 12 months follow-up in 600 COPD patients from five municipalities (Barcelona, Badalona, Mataró, Viladecans and Gavà). During 2012-2013, we developed a manual to standardize classification of the trails, and have marked trails in a total of 34 areas from the five municipalities. Each area includes three intensity trails: mild (green), moderate (orange) and vigorous (red), to be used by patients with different physiological and personal needs (figure 3). We conducted an experimental study with volunteer COPD patients (n=12) and healthy subjects (n=10) to assess physiologic response during urban training using a gas analyser (Metamax®, Cortex Medical, Germany); the manuscript is in preparation. We designed the intervention which includes motivational interviewing, access to a telephone number, periodic texting to patients' phones, a web page (www.entrenament-urba.cat), a pedometer to obtain daily feedback and a calendar. In November 2013 we started data collection and a total of 116 COPD patients have been included and are being followed up. The first results on effectiveness of the intervention will be available by the end of 2014.

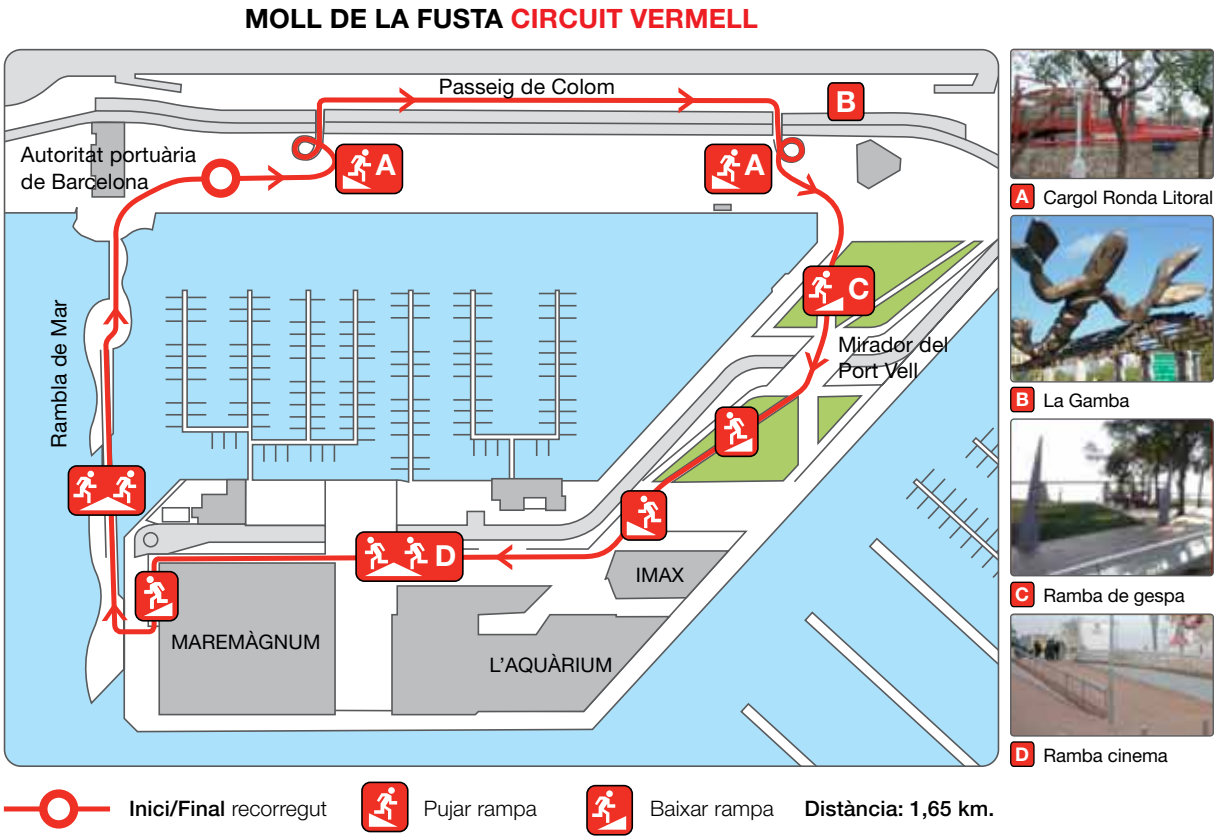

Figure 3: *Strong correlation between increasing levels of serum CC-16 (x axis) and increasing levels of lung function among Spanish ECRHS participants(Rava, Tares et al. 2013).*

MEMBERS

PROGRAMME LEADER

Josep M Antó

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PUBLICATIONS

RESPIRATORY PROGRAMME PUBLICATIONS 2012-2013

- Vollenweider DJ, Jarrett H, Steurer-Stey CA, Garcia-Aymerich J, Puhan MA. Antibiotics for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012; 12: CD010257.

- Puhan MA, Hansel NN, Sobradillo P, Enright P, Lange P, Hickson D, Menezes AM, Riet GT, Held U, Domingo-Salvany A, Mosenifar Z, Anto JM, Moons KG, Kessels A, Garcia-Aymerich J. Large-scale international validation of the ADO index in subjects with COPD: an individual subject data analysis of 10 cohorts. BMJ Open 2012; 2(6).

- Millares L, Marin A, Garcia-Aymerich J, Sauleda J, Belda J, Monso E. Specific IgA and metalloproteinase activity in bronchial secretions from stable chronic obstructive pulmonary desease patients colonized by Haemophilus influenzae. Respir Res 2012; 13(1): 113.

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CANCER PROGRAMME

PROGRAM SUMMARY

Cancer is a major cause of death worldwide and has been shown to be caused by numerous environmental and occupational exposures. Cancer research at CREAL is carried out in 3 programs, the Cancer, Radiation and Water Pollution programs. The main aim of the Cancer Program is to identify and prevent environmental and occupational causes of cancer, and to evaluate the role of genetic factors and their interaction with environmental exposures. Molecular and genetic techniques are regularly used in the cancer studies. Several studies conducted at CREAL participate in international consortia, and CREAL researchers regularly participate in international expert committees, such as the IARC/WHO Monographs. The main research effort in the Cancer program is the MCC-Spain study, which is a population-based multicase-control study conducted throughout Spain and coordinated by CREAL and the ISCIII, Madrid. In MCC-Spain we examine environmental and genetic factors associated with colorectal, breast, prostate and stomach cancers and Chronic Lymphocytic Leukaemia. CREAL researchers focus their research in MCC-Spain in the evaluation of circadian disruption including shift work and sleep disruption, chemical contaminants in water, endocrine disruption, occupation, infection, diet and cooking methods, air-pollution and greenness, and genetic variation. Research in bladder cancer has historically been a major area in the cancer programme, and the Spanish bladder cancer study (EPICURO study) was initiated in the late 1990s in close collaboration with the US NCI. Currently, genetic factors are examined mostly through participation in the International Bladder Cancer Consortium. Other research activities of the program include the evaluation of genotoxic risks in children, research on lymphomas, and smaller biomarker-based studies on specific exposures. Finally, pilot work is underway with researchers at CRESIB (Centre for International Health Research of Barcelona) and ICO (Catalan Institute of Oncology) to develop cancer research in Africa on infection and environmental exposures.

PROJECTS

MCC-SPAIN

TITLE: Multicase-control Population-Based Study on High Incidence Tumours in Spain (MCC-SPAIN study) - Colorectal, breast, prostate, stomach cancers and chronic lymphocytic leukaemia (CLL)

PI: Manolis Kogevinas

PERIOD: 2008-ongoing

FUNDING SOURCE: CIBER-ESP-Strategic Action (850.000 €); FIS-ISCIII (397.900 €)

Together with the Instituto de Salud Carlos III (Madrid), CREAL is coordinating a large population-based case-control study of 5 common tumours in Spain (MCC-Spain) that evaluates environmental exposures and genetic factors. 10,137 subjects aged 20-85 years were enrolled, including 1,115 cases of prostate cancer, 1,749 cases of breast cancer, 2,172 cases of colorectal cancer, 492 cases of gastro-esophageal cancer, and 550 cases of chronic lymphocytic leukaemia (CLL). Subjects were enrolled in 23 hospitals in 12 provinces in Spain between 2008 and 2013. Participants completed a computerized face-to-face interview on sociodemographic factors, environmental exposures, occupation, medication, lifestyle, and personal and family medical history. This was supplemented by a self-administered food-frequency questionnaire and additional telephone interviews. Blood samples were collected from more than 95% of subjects, and saliva samples were collected for CLL cases and participants who refused to give blood. Clinical information was collected for cases and paraffin blocks and/or fresh tumour samples are available for most collaborating hospitals. Samples were genotyped using an exome array enriched with genetic markers in specific pathways. Multiple analyses are planned to assess the association between environmental, personal and genetic risk factors for each tumour. The first sets of results will be published in 2014.

CIRCADIAN

TITLE: Epidemiological study on shift work, disruption of circadian rhythm, genetic susceptibility and risk of breast and prostate cancer

PI: M Kogevinas

PERIOD: 2012-2014

FUNDING SOURCE (and total amount):
FIS-ISCIII (219,120 €)

In 2007 the IARC/WHO classified shift work involving disruption of circadian rhythms as a probable human carcinogen. While sufficient evidence was available from animal studies, the epidemiological evidence was found to be limited. Our work on circadian rhythms involves two main projects, MCC-Spain and the Circadian Disruption Biomarker study. The main objective of the MCC-Spain project (see above) is to investigate whether shift work is associated with risk of breast, prostate or colorectal cancer. It also assesses whether nutritional and other exposures within the context of circadian disruption are associated with risk of breast cancer or prostate cancer, taking genetic susceptibility into account. Finally, it assesses whether “chronotype” (a human attribute reflecting the time of day when physical functions are active) is associated with risk of breast or prostate cancer, and whether it modifies the effect of shift work or more generally of time-shift in activity. The CIRCADIAN biomarker sub-study evaluates differences in melatonin and other sex hormones between night and day workers, and studies the relationships between light exposure and hormone rhythms in shift workers. Results from both studies will be published in 2014.

EXPOSOMICS

TITLE: Individualized exposure assessment and omic profiling for life-course epidemiology in Europe
PI: Manolis Kogevinas and Mark Nieuwenhuijsen
PERIOD: 2012-2016
FUNDING SOURCE: FP7-Env (1.2M€), partner

This European project uses a novel approach to assess exposure to high priority environmental pollutants by characterizing the external and the internal components of the exposome, focusing on air and water contaminants during critical periods of life. To this end, the project will centre on, 1) exposure assessment at the personal and population level within existing European short- and long-term population studies, exploiting available tools and methods that we will develop for personal exposure monitoring (PEM) (e.g. portable sensors, smartphone-based technologies, high-resolution chemical analysis), and 2) multiple "omics" technologies for the analysis of biological samples (internal markers of external exposures). Exploration of the relationships between external exposures (as measured by PEM, which has not previously been used in large scale studies) and global profiles of molecular features (as measured by omics) in the same individuals constitutes a novel advance towards the development of "next generation exposure assessment" for environmental chemicals and their mixtures. The link with disease risks paves the way to what are defined here as 'exposome-wide association studies' (EWAS). At CREAL, we will conduct the exposomics part of this project focused on water contaminants in swimming pools and drinking water among children and adults, and will also actively participate with short- and long-term studies on air pollution. tion and prediction studies of complex diseases/traits. In line with this, we have completed a study including ECRHS, TESAOD, and the Swiss SAPALDIA cohort, in which baseline serum CC-16 levels were found to predict subsequent lung function decline in all three cohorts (Guerra *et al.*, in preparation).

STATMET-NGS

TITLE: Statistical methods in next generation sequencing
PI: Juan Ramón González
PERIOD: 2012-2015
FUNDING SOURCE: MINECO (28.193 €)

Epidemiology has moved towards genetic epidemiology to study the role that genetic factors and their interaction with the environment play in risk of complex disease. In recent years, several new sequencing technologies have begun to provide huge amounts of genetic information, which demands the development of new statistical methods and bioinformatics tools for analyzing the association between genes and diseases. This project focuses on developing methods to predict structural variants such as CNVs, inversions or mosaicisms, and assesses their relationship with common diseases such as cancer, asthma and obesity. This project has already created several bioinformatics tools (including tweeDEseq, inveRsion, invClust and MAD) that have allowed us to demonstrate, for example, that the appearance of genetic mosaicisms is related to age, and that these alterations can be used as an early marker of disease. Another recent finding is that a common 16p11.2 inversion polymorphism is associated with asthma and obesity, representing the first evidence to date for joint susceptibility to asthma and obesity.

MEMBERS

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PUBLICATIONS

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CHILD HEALTH PROGRAMME

PROGRAM SUMMARY

The Child Health programme has achieved the following: 1. Leadership in international projects; 2. A reference centre on the coordination of birth cohorts; 3. Maintenance and growth of the INMA birth cohort project throughout Spain and of the RHEA cohort in Greece; 4. Establishment of a leading centre on neurodevelopmental epidemiology; 5. Development of a research plan on epigenetics; 6. Development of a research plan on childhood obesity and the environment; 7. Development of a research plan on the early life exposome, integrating novel exposure assessment and omics techniques; 8. Development of research on "new" exposures in children, including chemicals, EMF/mobile phones, and green spaces (together with the Radiation and Air Pollution programmes). The programme has coordinated three European projects (ENRIECO, CHICOS and HELIX) and one ERC advanced grant (BREATHE), and is leading work-packages in several international projects (HITEA, MEDALL, ESCAPE, EUROCAT). It also coordinates the European birth cohorts within the CHICOS EU-FP7 project, MEDALL on allergy and asthma, PHENOTYPE on building environment, and HELIX on 'exposome', as well as the ERC BREATHE project on neurodevelopment and school air, in which we provided several joint analyses across European birth cohorts, such as on the effects of air pollution on reproductive outcomes and neurodevelopment, and the role of PCB153 and DDE on birth weight. During the period 2012-13, the group has published 76 papers with data from the INMA cohort (81% in the first quartile). The INMA project has published important results on the effects of persistent organic pollutants (POPs) on neurodevelopment and respiratory health, the effects of maternal obesity, Vitamin D and the interaction between breastfeeding, PUFAs and genetic variation on neurodevelopment. Participation in the EGG and EAGLE consortia on genetics in birth cohorts has resulted in the coordination of several meta-analyses.

PROJECTS

INMA

TITLE: INMA Project (http://www.proyectoinma.org/en_index.html)
PI: Jordi Sunyer
PERIOD: 1997 - ongoing
FUNDING SOURCE: CIBERESP-Strategic Action, several national and international competitive and non-competitive sources of funding

The *INfancia y Medio Ambiente [Environment and Childhood]* Project is a research project that aims to study the role of environmental pollutants during pregnancy and the early stages of life and their effects on children's growth and development.

Birth cohorts are a powerful platform for etiological research. The INMA birth cohorts, which performs follow-up in a series of more than 3,000 children in Spain at weeks 12, 20, and 32 of pregnancy, at birth, and at ages 1, 2, 4, 7 and 9 (latest follow-up). Detailed environmental measurements were carried out during pregnancy and the first years of life, including air pollution, water pollution, pesticides, metals, hormone disruptors, diet, nutrients and fatty acids, GWAS, EWAS, socio-demographics, co-morbidities and mental health; and repeated measures of cognitive development and behaviour, anthropometry and metabolic syndrome, and asthma, allergy and lung function are being taken during subsequent follow-up. Biological tissue has been collected during each follow-up.

The INMA birth cohort project has seen the development of successful new rounds of follow-up in each of the sub-cohorts (at age 4 and 6-7 years). It has also initiated a new project to include siblings; is participating in many European collaborations; has published important results on the effects of POPs on neurodevelopment and respiratory health, and on the interaction between breastfeeding, PUFAs and genetic variation on neurodevelopment; and the effects of air pollution on reproductive outcomes and neurodevelopment. During the period 2012-13 the group has published 76 papers including data from the INMA cohort. A new study (MINECO) will recruit siblings of the INMA cohort, and new exams are planned within INMA at age 9.

EUROCAT

TITLE: Surveillance of Congenital Anomalies in Europe
PI: Martine Vrijheid
PERIOD: 2011-2013
PARTICIPANTS: www.eurocat-network.eu
FUNDING SOURCE: DG SANCO Joint Action

The EUROCAT network of population-based con-genital anomaly registers has been in existence since 1979, and has been co-funded by DG Sanco's Rare Diseases and Public Health Programmes and Joint Actions for the past ten years. It monitors 1.5 million births per year, representing 28% of all births in the European Union as well as some non-EU European countries, through 38 registries in 21 countries (www.eurocat-network.eu/). The current Joint Action aims to facilitate reduction of the public health burden of congenital anomalies by epidemiological surveillance through the EUROCAT network. One Work Package (WP6), led by the Martine Vrijheid at CREAL, has evaluated the feasibility of linking registry data with environmental pollution maps through a pilot study in Barcelona and other European regions. We also carried out a systematic review and meta-analysis of previous literature on this topic and found evidence suggesting that ambient air pollutants modulate risk of congenital cardiac anomalies. NO_2 and SO_2 exposure was related to increased risk of coarctation of the aorta and tetralogy of Fallot, and PM10 exposure to increased risk of atrial septal defects (Vrijheid *et al*., EHP 2011). In the Barcelona case study, which included 2,247 non-chromosomal cases of

EUROCAT

congenital anomaly and 2,991 controls, we found an increased risk of coarctation of the aorta in relation to NO_2 and NO_x which was consistent with the results of a published meta-analysis (Schembari *et al*. 2014). The observation of increased risks of digestive system anomalies in relation to NO_2 and NO_x, and of abdominal wall defects related to coarse PM are novel and require confirmation. The pilot study in Barcelona shows that EUROCAT registry data can be used for investigation of congenital anomaly risks associated with environmental pollutants/hazards that vary on a small spatial level within cities. Subject address data, local GIS expertise, and local environmental exposure assessment expertise are needed, but these are not currently well developed in many registries.

CHICOS

TITLE: Developing a Child Cohort Strategy for Europe (http://www.chicosproject.eu/)
PI: Martine Vrijheid
PERIOD: 2010-2013
FUNDING SOURCE: EU-FP7-Health (409.440 €), coordinators

CHICOS, an FP7 action coordinated by Dr Martine Vrijheid at CREAL, published its recommendations in 2013 (www.birthcohorts.net). CHICOS developed a comprehensive inventory of birth cohorts, evaluated existing data on child health outcomes and risk factors, and assessed how the contribution of cohort data to policy may be improved. Thirteen working groups reviewed cohort data on child health outcomes and risk factors. Eight case studies on topics of interest for policy, such as social class, alcohol consumption during pregnancy, obesity and fish consumption, were set up to evaluate data harmonisation and pooling issues; they pooled and compared data from many cohorts. More than 70 birth cohorts across Europe are prospectively studying more than 500,000 mothers, fathers and children at repeated time points and over long time periods (Fig 4). Within the existing European birth cohorts, CHICOS found that there is lack of data for minority groups, southern and eastern European countries, and older children and adolescents. CHICOS has shown that pooling cohort data between countries is possible and valuable, but that there are still substantial practical obstacles in international collaborative initiatives. There is currently no common European database with longitudinal, individual-level, data on child health and its determinants. Improved collaboration throughout Europe will enhance research and the knowledge obtained from individual birth cohorts and their ability to contribute policy-relevant findings, and to respond rapidly to new policy concerns. Therefore, CHICOS recommends establishing a European Birth Cohort Infrastructure using data from existing and new cohorts. It should build a permanent Europe-wide data infrastructure containing a minimum set of prospective, individual-level variables regarding child health in Europe, which will provide key statistics on child health and its determinants and will enable health surveillance and act as a basis for aetiologic research.

PROJECTS

BIOLUNG

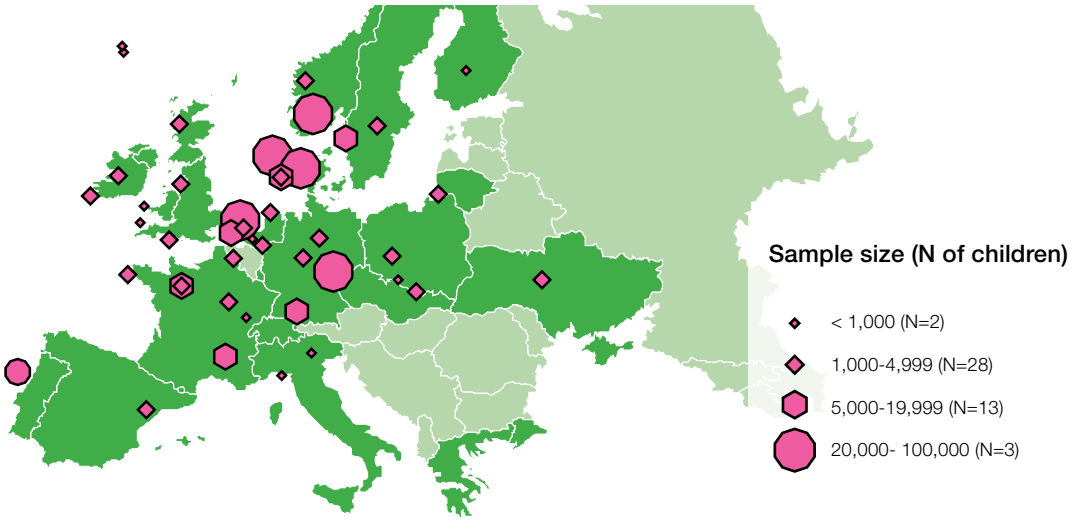

Fig. 4. *Location and sample size (N of children) of European birth cohorts included in the CHICOS inventory (Larsen et al. 2013)*

HELIX

TITLE: The Human Early-Life Exposome – novel tools for integrating early-life environmental exposures and child health across Europe (www.projecthelix.eu)
PI: Martine Vrijheid
PERIOD: 2013-2017
FUNDING SOURCE: EU-FP7- Environment (2.3M€), coordinators

The "exposome" concept was proposed to encompass the totality of exposures from conception onwards, complementing the genome. HELIX is a new FP7 collaborative research project commissioned by the EU exposome programme (Vrijheid *et al., EHP* 2014, doi:10.1289/ehp.1307204). HELIX aims to use novel exposure assessment, biomarkers, and statistical tools to characterise early-life exposure to multiple environmental hazards and evaluate their association with child health outcomes, thus developing an "Early-Life Exposome" as a first step towards the full exposome. HELIX uses six existing prospective birth cohort studies throughout Europe (France, Greece, Lithuania, Norway, Spain, UK). A first step is to measure the external exposome (robust exposure estimates for a broad range of chemical and physical exposures, both pre- and post-natal, in 1,200 mother-child pairs). A second step will measure the internal exposome (molecular signatures) and integrate multiple dimensions of the exposome (multiple exposures, multiple time points, individual variability and behaviour, molecular signatures). A third step will develop the tools and methods required to evaluate the exposome's impact on child health, including nested repeat-sampling panel studies to collect data on individual, temporal, and toxicokinetic exposure variability, and thereby characterise uncertainty in exposure estimates (e.g. using exposure devices linked to new smartphone technology for outdoor exposures). HELIX will also determine molecular profiles and biological pathways associated with certain exposures using new omics tools (metabolomics, transcriptomics, and epigenomics). Statistical methods (including Bayesian and structural equation models) will be developed to provide exposure-response estimates for multiple exposures and child health responses (growth and obesity, neurodevelopment, immune system outcomes). Finally, a health impact assessment model will be built for multiple early-life exposures. HELIX was presented at the launch event of the EU Exposome programme at IARC in Lyon in November 2012 (Nature News: 491, 647, 29 November 2012, DOI: doi:10.1038/491647a). The HELIX Kick-Off meeting was held on 11-13 March 2013 in Barcelona. It will run for 4 and half years.

ESCAPE

TITLE: European Study of Cohorts for Air Pollution Effects (http://www.escapeproject.eu/)
PI: Jordi Sunyer
PERIOD: 2009 - 2012
FUNDING SOURCE: EU-FP7-Environment (708.431 €), partner. MICINN (90.900 €)

The objective of ESCAPE is to develop precise home and outdoor long-term air pollution exposure estimates for subjects participating in pre-existing European cohorts, with the aim of assessing health effects in four main domains: cardiovascular disease, chronic respiratory disease, cancer, and mortality and perinatal outcomes. The project was coordinated by B. Brunekreef (Institute for Risk Assessment Sciences, Utrecht, The Netherlands). CREAL researchers have been actively involved in all areas of this project. In the past year, seven papers describing methods to develop air pollution exposure models, 10 papers assessing the impact of long term air pollution on health have been published, and 14 more have been submitted. The most important results to date include the observation that air pollution is associated with mortality, lung cancer and low birth weight, even at levels below those recommended by the European Union or even the World Health Organization.

BREATHE

TITLE: BRain dEvelopment and Air polluTion ultrafine particles in scHool children (http://www.creal.cat/projectebreathe/)
PI: Jordi Sunyer
PERIOD: 2011 - 2016
FUNDING SOURCE: European Research Council – Advanced Grant (2.5M€)

The *BRain dEvelopment and ultrafine particle Air polluTion in scHool childrEn (BREATHE) Project* is a population-based neuroscience study assessing whether exposure to traffic-related air pollutants (TRAPs) in schools adversely affects children's neurodevelopment. Children (n=2,907) aged 7 to 10 years from 39 schools in Barcelona (Catalonia, Spain) with high and low TRAP levels, paired by socio-economic status, were tested using a series of four computerized tests between January 2012 and March 2013 to evaluate development of working memory, executive attention, impulsivity, and selective attention. Behavioural problems (strengths and difficulties questionnaire) and Attention Deficit and Hyperactivity Disorder status (ADHD_DSM IV) was reported by parents. MRI scans (T2, flair, spectroscopy and DTI) and fMRI (resting, visual and audition stimuli) were conducted in ~300 children. To search for gene-environment interactions, a GWAS was conducted in 80% of children. Air pollution (nitrogen dioxide (NO_2), ultrafine particle number (UFP), and particulate matter content (PM) ≤0.25 µm (quasi-ultrafine), 0.25-2.5 µm (accumulation mode), 2.5-10 µm (coarse mode) and ≤2.5 µm ($PM_{2.5}$)) was measured simultaneously in each school pair in both the classroom and the courtyard during two week-long campaigns in 2012. A total of 1,092 PM filters were collected and elements and hydrocarbons were analysed. Traffic noise in the classroom and traffic intensity at the school entrance was directly measured. Residential air pollution exposure was based on modelled geographical estimates. Data from 10,973 cognitive tests showed a notable increase in cognitive function (~10%/yr) during the primary school years. TRAP levels varied considerably between schools. Some TRAPs showed a high indoor penetration. PM levels were higher indoor than outdoor due to continuous re-suspension of soil particles and a mixed indoor source, largely including organic and Ca-rich particles. Analyses of the effects of traffic-related air pollution in schools, largely diesel pollutants such as UFP, on cognitive development, fMRI and the gene-air pollution interaction are underway. Results will likely indicate cost-benefit interventions in schools to boost the protection of brain maturation among children.

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PUBLICATIONS

CHILD HEALTH PROGRAMME PUBLICATIONS 2012-2013

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AIR POLLUTION PROGRAMME

PROGRAM SUMMARY

The air pollution programme includes epidemiological, exposure assessment, and health impacts studies of air pollution. The main aims are to better understand where exposure to air pollution takes place, what are the relationships between health and indoor and outdoor exposure, what are the potential modifying factors (e.g. green spaces), and what are the health impacts of air pollution policies. Our work uses new tools such as geographical information systems, satellite data and smartphone technology to estimate individuals' exposure to air pollution, and more recently this has been extended to the effects of temperature, green spaces and noise on health.

Over the past few years we have participated in the large EC funded ESCAPE study, and have led a number of outcome groups (cognitive function and birth outcomes). The project has come to fruition with a number of important publications in various journals such as The Lancet, Lancet Respiratory Medicine and Lancet Oncology. Other projects such as REGICOR, APHEKOM, ARIBA and MED-Particles have come to an end and are providing new insights into the effects and impact of air pollution. REGICOR-AIR reported an association between subclinical atherosclerosis and traffic and air pollution exposure. MED-Particles explored the short-term effect of particles on mortality and hospital admissions in 12 Mediterranean cities. While both coarse and fine particles had an effect on health, the effect of fine particles was stronger. The ARIBA study provided new insights into personal exposure among pregnant women, and the effects of air pollution, green spaces and temperature on complications during pregnancy and adverse birth outcomes. A recent international collaboration on air pollution and birth outcomes (ICAPPO) produced a milestone paper on the effect of air pollution on low birth weight. Professor Jordi Sunyer obtained a prestigious ERC grant (BREATHE) whose aim is to measure different grades of particulate air pollution both indoors and outdoors at schools, both continuously and on filter support for metal species. Air pollution levels in schools will be compared to performance at school and to brain function and structure. Finally, new joint initiatives with CRESIB have started to work on air pollution in developing countries.

The large TAPAS study has produced a number of important papers on the health impacts of active transportation, taking into account different transport mode scenarios, and resulting in a paper in BMJ.

PROGRAM SUMMARY

The ETEC project addressed some of the gaps in knowledge of the possible impacts of climate change on the Catalan population due to an increase in temperature. This study was a joint effort of CREAL and the Department of Health of the Catalan Government.

An important development in the air pollution program has been the incorporation of a GIS team, the use of satellite data for exposure assessment in green spaces, Saharan dust, temperature and UV, and the use of novel smartphone technology to improve exposure assessment. The software also allows the tracking and assessment of physical activity. The smartphone technology is now used in a number of projects, and CREAL is now a world leader in this field. This work also forms part of the new EC funded exposome projects EXPOsOMICs and HELIX (led by CREAL) and the people empowerment EC project, CITISENSE. Validation work is being conducted within the NIH funded CAVA project.

The new EC-funded exposome projects EXPOsOMICs and HELIX will also use OMICs technologies to identify new markers of air pollution and other exposures in biological samples. If successful, these markers could then be used in future epidemiological studies. The work is interdisciplinary with input from many groups.

The programme has incorporated new areas of research, including work on green spaces and health via the CREAL-led EC-funded PHENOTYPE project. Initial results have shown a reduction in air pollution in green areas, and the beneficial effects of green spaces on birth outcomes, neural development, obesity and asthma. Further work is ongoing in almost 20 European cohorts, in which green space indicators are assigned to subjects. Furthermore, 1,000 people are being interviewed in 4 cities in different countries. Research in this area has been internationally recognised in the form of Dr P Dadvand's 2012 award for Best Abstract by a Young Investigator for Surrounding Greenness and Pregnancy Outcomes. Dr Dadvand has also received the Rebecca James Baker Award for his research trajectory. Marie Pedersen received the 2013 Outstanding Abstracts by Young Investigators award for her paper, "Birth Weight, Head Circumference and Exposure to Ambient Air Pollution During Pregnancy: A European Cohort Study (ESCAPE)" and the Rebecca James Baker award for her overall work.

PROJECTS

ARIBA

TITLE: Air pollution and reproduction in Barcelona
PI: Mark Nieuwenhuijsen
PERIOD: 2009 - 2011
FUNDING SOURCE (and total amount):
FIS-ISCIII (119.790 €)

BACKGROUND AND AIMS

Ambient air pollution has been widely shown to have adverse health effects in a variety of ways both in the short and long term, mainly through respiratory and cardiovascular impacts. Studies have generally centred on morbidity and mortality in adults, and showing that the elderly are particularly susceptible. To date, the other end of the spectrum has mostly focused on childhood exposure and respiratory disease. The effects of exposure to ambient air pollution on the foetus is now appearing as a new research priority. Recent epidemiological studies have explored the relationship between air pollution and reproductive outcomes, such as low birth weight (LBW), very low birth weight (VLBW), intrauterine growth retardation (IUGR) or being small for gestational age (SGA), preterm birth, stillbirth, spontaneous abortion, congenital anomalies and infant death (Maisonet et al. 2004, Glinianaia et al. 2004a and b, Sram et al. 2005, Slama et al. 2008, Ritz et al. 2008). While the evidence for association is currently inconsistent and inconclusive, it suggests that air pollution may have weak adverse effects.

This study has examined the relationship between traffic-related air pollution and various reproductive outcomes, including pre-term delivery, low birth weight, being small for gestational age, foetal growth restriction and congenital anomalies, and incorporates sources of measurement error such as mobility of the pregnant women in any exposure response relationships.

As part of the work we have:

- monitored air pollution levels (PM2.5 and its elemental composition, NOx, PAHs) in Barcelona;
- modelled traffic-related air pollution levels in Barcelona using land use regression modelling (based on road network, traffic density and mix, population density, height and meteorological variables);
- integrated other sources of air quality data to produce more accurate and precise pollution maps and estimate prediction errors;
- conducted more detailed exposure assessment in a subset of women, including personal indoor and outdoor sampling of air pollutants;
- conducted source apportionment analyses;
- conducted analyses to evaluate and integrate information on measurement error;
- conducted statistical analyses to examine the relationship between modelled air pollution levels and pre-term delivery and foetal growth outcomes including low birth weight, being small for gestational age, foetal growth restriction and congenital anomalies after adjustment for known confounders.

METHODS

The study used an existing datasets of reproductive outcomes collected by the obstetrics department of Hospital Clinic, Barcelona, and a register of congenital anomalies in Barcelona. Modelled LUR air pollution exposure estimates for the home address were obtained under the ESCAPE programme. We focused on particulate matter (PM2.5) and its elemental composition, soot content and nitrogen oxides (NOx), and PAHs. We also recruited 60 pregnant mothers, 20 in each of the three predicted exposure tertiles from the ecological exposure assessment. We asked subjects to keep a 7-day diary of activities related to air pollution exposures, including mobility data. Simultaneous indoor, outdoor and personal air pollution monitoring was conducted for NOx and PM2.5. We used logistic regression to examine the relationship between the various air pollution estimates by trimester and the various reproductive outcomes, including pre-term delivery, low birth weight, being small for gestational age, foetal growth restriction and congenital anomalies. These analyses are adjusted for ethnic origin, maternal height, booking weight, smoking, education, employment, multiple pregnancies, gestational or pre-gestational diabetes, pre-eclampsia and congenital anomalies, where appropriate. In addition, we will account for estimates of measurement error using data from the personal monitoring study.

PROJECTS

ARIBA

MAIN FINDINGS

Three papers on personal exposure levels have been published, one describing the home-indoor, home-outdoor, and personal levels of PM2.5 and NOx, a second describing the sources of these PM2.5 levels using source apportionment techniques, and a third showing a reduction in personal, home-indoor, and home-outdoor PM2.5 levels associated with nearby green areas. Two more papers on the impacts of ambient temperature on pregnancy have been published, one showing a reduction in gestational age at delivery associated with maternal exposure to extreme heat conditions, and another demonstrating an increased risk of maternal infection during pregnancy associated with higher ambient temperatures. We also published a paper showing that Saharan dust has no harmful effects on a range of pregnancy outcomes and complications, and a paper showing that air pollution appears to have some effect on pre-eclampsia. Finally, following an earlier meta-analyses, we published a paper on the relationship between air pollution and congenital anomalies in Barcelona, which showed little effect with the exception of a small number of anomalies.

FUTURE AND TIME-LINE

We are currently developing maps of PM content (obtained from element analysis of PM samples) to evaluate their impacts on various pregnancy complications and outcomes. We are also planning to update our hospital dataset with more recent data.

CAVA

TITLE: Validating the CalFit Smartphone Sensor in two Epidemiological Investigations

PI: Mark Nieuwenhuijsen

PERIOD: 2011-2013

FUNDING SOURCE: NIH ($215,316), partner

BACKGROUND AND AIMS

Obtaining information on location and physical activity is important for health, and new tools such as smartphones have been proposed to be useful for this purpose. The aim of this study is to assess the validity, usability, and value of a novel cell phone-based personal exposure system, known as “CalFit”. The CalFit system runs on commercially available Android phones, and with its current configuration can be used to collect data on physical activity coupled with information on acceleration, geographic location through GPS, air pollution, and self-reported environments including mood and behaviour with ecological momentary assessment (EMA) through interactive text messaging. The system has already undergone numerous controlled validation studies and is ready for evaluation in real-world epidemiologic studies. An initial pilot study in Barcelona showed that the CalFit equipment is generally well accepted and can be used to assess physical activity levels and positioning.

CalFit Phone Showing (a) Basic Interface, (b) Calorie Counts by 30 second Epoch, and (c) Google Maps Display of Activity Levels in Different Locations

METHODS

200 people from the TAPAS travel survey were recruited for this study, field work been completed, and analyses are underway.

MAIN FINDINGS

Two papers based on data from a pilot study on 30 volunteers have been prepared. One describing the use of smartphone information on inhaled NO2 dose has been accepted (de Nazelle et al. 2013), and a second showing a good correlation between ActiGraph measures of physical activity and those from the Calfit system is under review (Donaire et al. 2013). Various other papers are in preparation.

PHENOTYPE

TITLE: Positive Health Effects of the Natural Outdoor Environment in Typical Populations in Different Regions in Europe

PI: Mark Nieuwenhuijsen

PERIOD: 2012-2015

FUNDING SOURCE: EU-FP7-Environment (985.189€), coordinator.

BACKGROUND

Indications exist that close contact with nature has benefits for human health and well-being. The proposed work will investigate interconnections between exposure to natural outdoor environments in both rural and urban settings and human health and well-being in the North West, South and East of Europe.

AIMS

The project explores the underlying mechanisms at work (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) and examines the health effects (general health and wellbeing, mental health/neural development, stress, cardiovascular, cancer and respiratory mortality and morbidity, birth outcomes and obesity) in different population groups (pregnant women and/or foetus, age groups, socioeconomic groups, ethnic minorities and patients). It uses conventional and innovative high tech methods to characterize the natural environment in terms of quality and quantity, and explores the preventive as well as therapeutic effects of contact with the natural environment. It addresses implications for land-use planning and green space management. The work will produce more robust evidence based on links between exposure to a natural outdoor environment and human health and wellbeing, and better integration of human health needs into land use planning and green space management in rural as well as urban areas.

MAIN FINDINGS

The project is in its third year and the main fieldwork has been completed and the results are analysed. Two papers showing the beneficial effects of green spaces on birth weight, and how they are modulated by socioeconomic status, have been published, and further papers showing the benefits of green spaces on neural development, obesity and asthma are in preparation.

PROJECTS

TAPAS

TITLE: Transportation, Air pollution and Physical ActivitieS; an integrated health risk assessment progamme of climate change and urban policies

PI: Audrey de Nazelle, Mark Nieuwenhuijsen

PERIOD: 2009 - 2012

FUNDING SOURCE: The Coca-Cola Foundation (1.656.000 €); AGAUR (Catalan funding agency), coordinator

BACKGROUND AND AIMS

International groups have recommended dramatic policy changes to control obesity, pollution, and climate change. Transportation and planning policies that promote walking and cycling can contribute to these goals, potentially yielding further co-benefits. However, unintended consequences could result from increasing traffic exposure for some individuals who shift to active travel modes. Little is known about the interconnection between the changes and policies being considered. The purpose of the TAPAS research programme is to help decision makers design urban policies that address climate change and to promote other health-related outcomes. In particular, we are interested in assessing conditions and policies that hinder or encourage active travel, and the resulting health impacts.

METHODS

We have developed a toolbox that allows policy makers to calculate and demonstrate the potential net health benefits of their policies, which they can use to encourage change. A quantitative assessment of the impacts of active travel policies will be developed for six case study cities: Barcelona, Basel, Copenhagen, Paris, Prague, and Warsaw. The modelling framework includes assessment of the determinants of active travel and the potential co-benefits and co-risks of modal shifts from motorized to non-motorized modes of travel. To populate variables and define relationships within the model, we use existing data from the literature and local data sources. Additionally, we have conducted two observational/experimental studies with primary data collection to address specific data gaps: exposure and intermediary health outcomes in travel environments in Barcelona, and determinants of active travel behaviour in Barcelona.

MAIN FINDINGS

A preliminary and evolving conceptual model was developed and debated during a workshop held in Barcelona on November 9th-11th 2009. Forty-five international experts from 29 institutes/research groups in 12 countries attended the meeting, reviewing current knowledge and discussing the strengths and limitations of evidence of different links between urban and transportation policies, exposures and public health, to determine the relevance and appropriateness of exposures, outcomes, and exposure-response functions to be included in a quantitative assessment of the health impacts of active travel policies.

There was general consensus among the workshop attendants about the importance of conducting a comprehensive assessment of the impacts of active travel policies. Participants agreed on the interest of all topics covered in the workshop in relation to active travel, and some suggested discussing other outcomes that were not explicitly reviewed (e.g. impacts of climate change, health effects of greenhouse gas pollutants, heat, congestion and time spent travelling). The complexity of conducting a formal quantitative integrative assessment was underlined and the choice of exposures and outcomes to be integrated as well as the choice of policy scenarios was debated. The conclusions have been written up as a paper (de Nazelle et al. 2011). Furthermore, results using the new tool for three health impacts have been published; one on the Barcelona Bicing system (Rojas-Rueda et al. 2011), a second on the various transport scenarios in Barcelona (Rojas-Rueda et al. 2012, Rojas-Rueda et al. 2013), and a third applying the tool to six cities in Europe is in preparation.

FUTURE AND TIME-LINE

5 papers on travel among more than 800 subjects in Barcelona, and 3 papers on the results of the TAPAS experimental study examining the short-term effects of physical activity and air pollution on cardiovascular and respiratory function are in preparation.

CITI-SENSE

TITLE: Development of sensor-based Citizens' Observatory Community for improving quality of life in cities

PI: Mark Nieuwenhuijsen

PERIOD: 2012-2016

FUNDING SOURCE: EU-FP7-Environment (457,560€), partner

BACKGROUND AND AIMS

CITI-SENSE will develop "citizens' observatories" to empower citizens to contribute to and participate in environmental governance, to enable them to support and influence community and societal priorities and associated decision-making. CITI-SENSE will develop, test, demonstrate and validate a community-based environmental monitoring and information system using innovative and novel Earth Observation applications. To achieve this, the project will: (i) raise environmental awareness in citizens, (ii) raise user participation in societal environmental decisions, and (iii) provide feedback on the impact citizens have in decisions. It will address the call's request for effective citizen participation in environmental stewardship, based on broad stakeholder and user involvement in support of both community and policy priorities. The project aims to learn from citizen experience and perception and enable citizenship co-participation in community decision-making and co-operative planning. The concept of CITI-SENSE rests on three pillars: technological platforms for distributed monitoring; information and communication technologies; and societal involvement. Three pilot case studies will focus on a range of services related to environmental issues of societal concern: combined environmental exposure and health associated with air quality; noise and development of public spaces; and indoor air quality in schools. Attention will be given to representativeness of citizen participation. The case studies will be designed in collaboration with citizens' groups and decision makers. They will be based on distributed data collection using innovative static, portable and personal devices (low-cost reliable microsensor packs) that communicate with data repositories through mobile phones or other devices. Participatory methods, data management strategies, and applications to facilitate exploitation of the data and information for policy and society will be developed.

MAIN FINDINGS

Citisense is in its second year and is currently performing pilot tests of the equipment.

PROJECTS

PASTA

TITLE: Physical Activity Through Sustainable Transport Approaches

PI: Audrey de Nazelle, Mark Nieuwenhuijsen

PERIOD: 2009 - 2012

FUNDING SOURCE: The Coca-Cola Foundation (1.656.000 €); AGAUR (Catalan funding agency), coordinator

BACKGROUND AND AIMS

PASTA focuses on the systematic promotion and facilitation of active mobility (AM, i.e. walking and cycling, including in combination with public transport) as an innovative approach to integrate physical activity (PA) in individuals' everyday lives. In contrast to sports or exercise, AM requires less time and motivation, since AM provides both the convenience of a mode of transport and a healthy lifestyle. As such, it has the potential to reach parts of the population that have not been receptive to appeals regarding the benefits of sports and exercise.

The objectives of the project are as follows:

- The project will review the literature on AM and identify innovative measures and systematic initiatives to promote AM as well as traffic safety interventions.
- A longitudinal study will be conducted to evaluate ongoing AM initiatives combined with traffic safety interventions to better understand correlates of AM and their effects on overall PA, injury risk and exposure to air pollution.
- An improved user-friendly tool for more comprehensive health impact assessment (HIA) of AM will be developed.
- The tool will be applied to AM behaviour observed in the case study cities and will allow the assessment of health and the economic impacts of the measures.
- The project will also produce a compendium of good practices for AM promotion by decision makers, implementing authorities, businesses, civil society organizations and end users.
- Findings and progress reports will be communicated to diverse target audiences, including policy makers, practitioners, researchers and end-users, through a number of media, i.e. reports, journals, brochures, web-content, workshops and presentations.

MAIN FINDINGS

PASTA is in its first year and the protocols are being drafted.

MED-PARTICLES

TITLE: Particles size and composition in Mediterranean countries: geographical ariability and short-term health effects

PI: Jordi Sunyer

PERIOD: 2011-2013

FUNDING SOURCE: Life+ (200.779€)

MED-Particles has characterized air pollution exposure and its relationship with health in 14 European Mediterranean cities. Short-term increases in PM concentrations were associated with increases in mortality and hospital admissions. For example, a 10 $\mu g/m^3$ increase in exposure to PM2.5 for two days was associated with a 0.55% (95%CI: 0.27%, 0.84%) increase in all-cause mortality, and a 0.51% (95%CI: 0.12, 0.90) increase in cardiovascular admissions. The composition of PM was analysed in five cities, and most PM elements tested were found to be associated with an increase in hospitalizations for cardiovascular and/or respiratory symptoms. The significantly associated elements were EC, SO_4^{2-}, $Si0_2$, Ca, Fe, Zn, Cu, Ti, Mn, V and Ni. The percentage increase in risk by one interquartile range (IQR) ranged from 0.69 to 3.29.

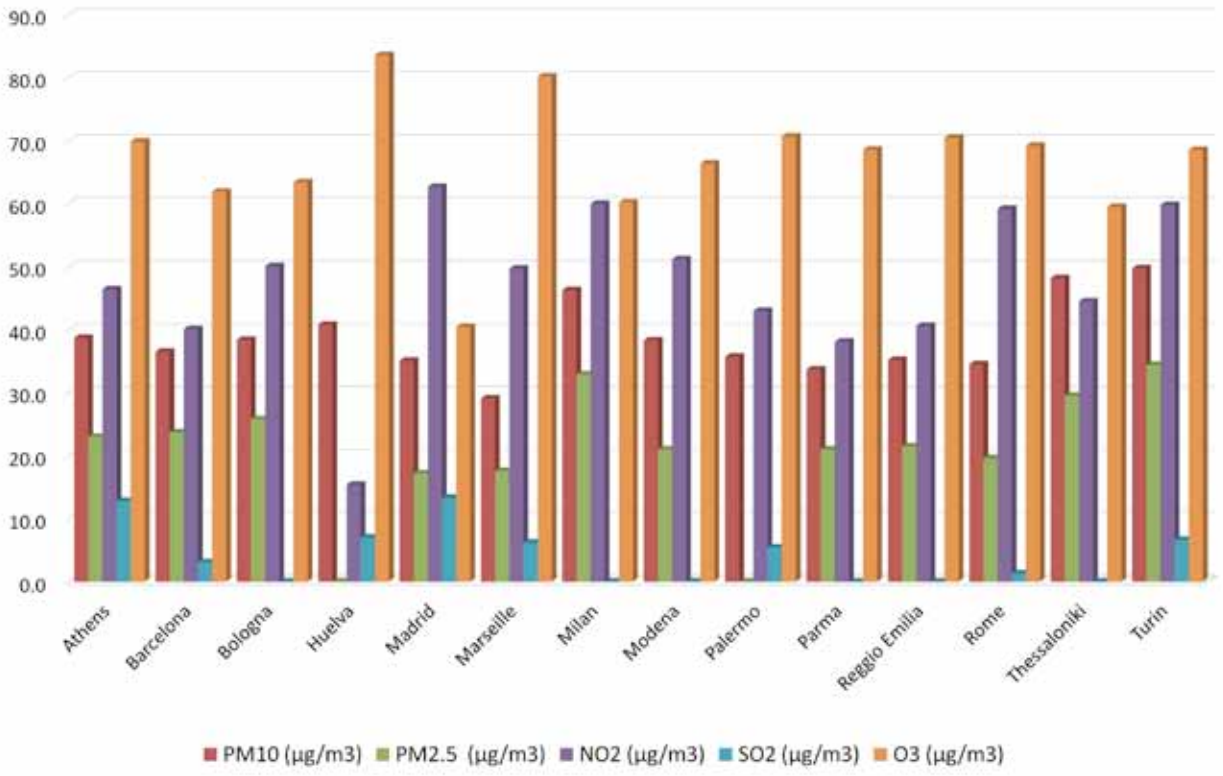

Fig. 1. *Air pollutant concentrations in 14 south-European cities.*

PROJECTS

ETEC

TITLE: Study of Extreme Temperature Effects in Catalonia
PI: Xavier Basagaña
PERIOD: 2009-2012
FUNDING SOURCE: without active funding.

The relationship between extreme heat and mortality has been recognized for many years, and is of increasing concern in the context of global warming. This project found that three consecutive hot days increased total daily mortality by 19% in Catalonia, and that 1.6% of all deaths during the warm months could be attributable to heat. The study was one of the first to quantify the effect of heat waves on infant mortality, which increased by 53% on extremely hot days for conditions originating in the perinatal period. Holding the population constant and only considering changes in temperature, the study predicted an increase of 720 attributable deaths in Catalonia by 2025 (5% of the warm season mortality) and an increase of 2,330 deaths by 2050 (8.8% of the warm season mortality). The project also mapped heat vulnerability in the Barcelona metropolitan area, and showed areas that have twice the risk of others.

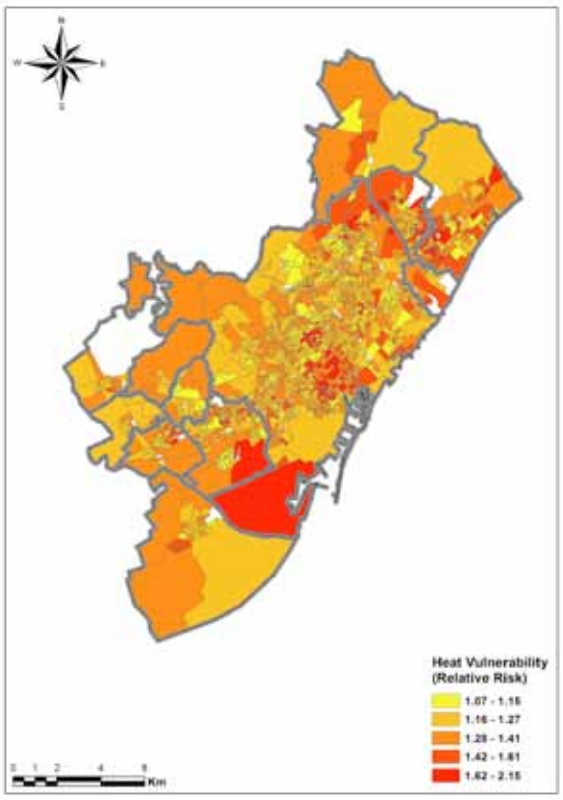

Fig. 2. *Heat vulnerability map for the Barcelona metropolitan area. Vulnerability is expressed as the relative risk of mortality after three consecutive hot days (as compared with non-hot days).*

APHEKOM

TITLE: Improving Knowledge and Communication for Decision Making on Air Pollution (http://www.aphekom.org/web/aphekom.org/home)
PI: Xavier Basagaña
PERIOD: 2008-2010
FUNDING SOURCE: EU-Public Health Programme-SANCO (164.592 €)

The Aphekom project is an international project involving 25 European cities in 12 countries whose aim is to close the gaps in understanding the impact of air pollution on health. Aphekom estimated that exceeding WHO Air Quality Guidelines on PM2.5 in 25 European cities with 39 million inhabitants results in 19,000 deaths and 31.5 billion euros in health-related costs annually. In addition, the project also estimated that living near busy roads could be responsible for some 15-30% of all new cases of asthma in children and of chronic obstructive pulmonary disease and coronary heart disease in adults over 65 years. The associated economic burden per

APHEKOM

year could be as much as 300 million euros. Aphekom also evaluated the effectiveness of air pollution reduction measures already in place. In 20 cities where sulphur in fuels was reduced by EU legislation, 2,200 premature deaths were prevented and some 192 million euros were saved.

REGICOR-AIR

TITLE: Life-style and environmental determinants of cardiovascular diseases in a Spanish cohort study (http://www.regicor.org/conttemp?idioma=angles)
PI: Xavier Basagaña
PERIOD: 2007-2012
FUNDING SOURCE: La Marató (Local funding agency; 150.022 €)

The REGICOR-AIR project aims to investigate the relationship between long-term exposure to traffic-related air pollution and noise and cardiovascular health. Data on long-term exposure to traffic-related air-pollution and noise were obtained through several measurement campaigns combined with geo-statistical modelling. The results show an association between high NO_2 concentrations and increased carotid intima media thickness, especially in men over 60 years of age, and among individuals with a higher educational level, for whom a 25µg/m3 increase in NO2 was associated with 4% thicker arteries. Residential levels of NO2 and traffic-related noise were independently associated with increased systolic blood pressure. In particular, systolic blood pressure increased by 1.23 mmHg (95%CI: 0.21, 2.25) following a 10 µg/m3 increase in NO2 levels, and by 0.72 mmHg (95%CI: 0.29, 1.15) for a 5dB(A) increase in noise levels.

MED-HISS

TITLE: Mediterranean Health Interview Surveys Studies: long term exposure to air pollution and health and surveillance
PI: Xavier Basagaña
PERIOD: 2013-2016
FUNDING SOURCE: Life+ (194.919 €)

Current understanding of the association between long-term exposure to air pollution and adverse health effects is based on cohort studies from the USA, Canada, Japan and China. Few studies have been conducted in Europe so far, with limitations regarding the age of the cohort recruited and the pollutant studied, and with poor geographical variability. MED-HISS aims to assess the feasibility of creating a surveillance system for the long-term effects of air pollution based on data already available. In particular, retrospective cohorts representing all populations and types of residential area (urban, rural, metropolitan) will be created on the basis of existing National Health Interview Surveys (NHIS). These cohorts will be followed-up for mortality and morbidity. Exposure to air pollution will be derived from national dispersions models.

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PUBLICATIONS

AIR POLLUTION PROGRAMME PUBLICATIONS 2012-2013

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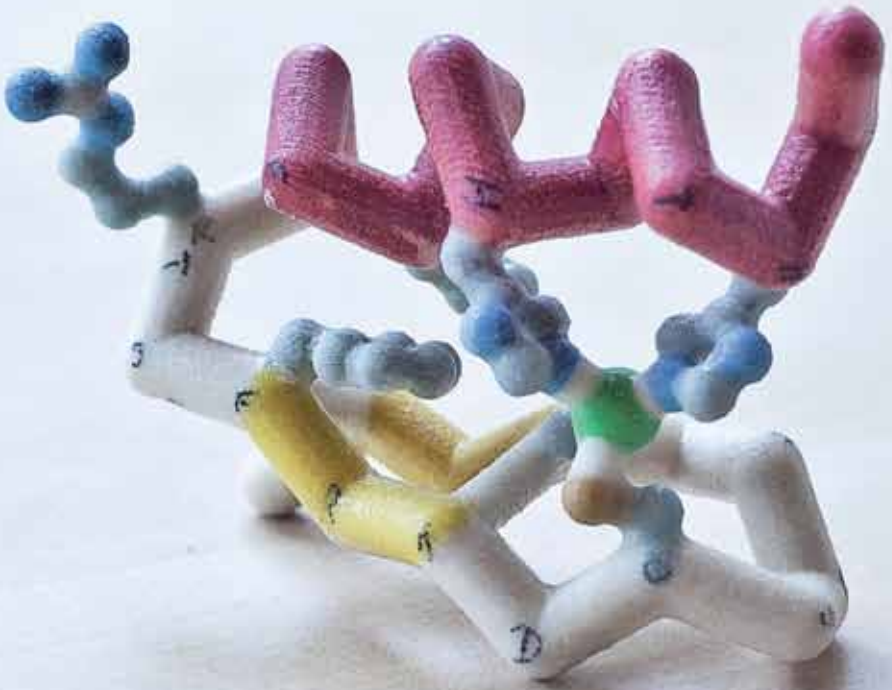
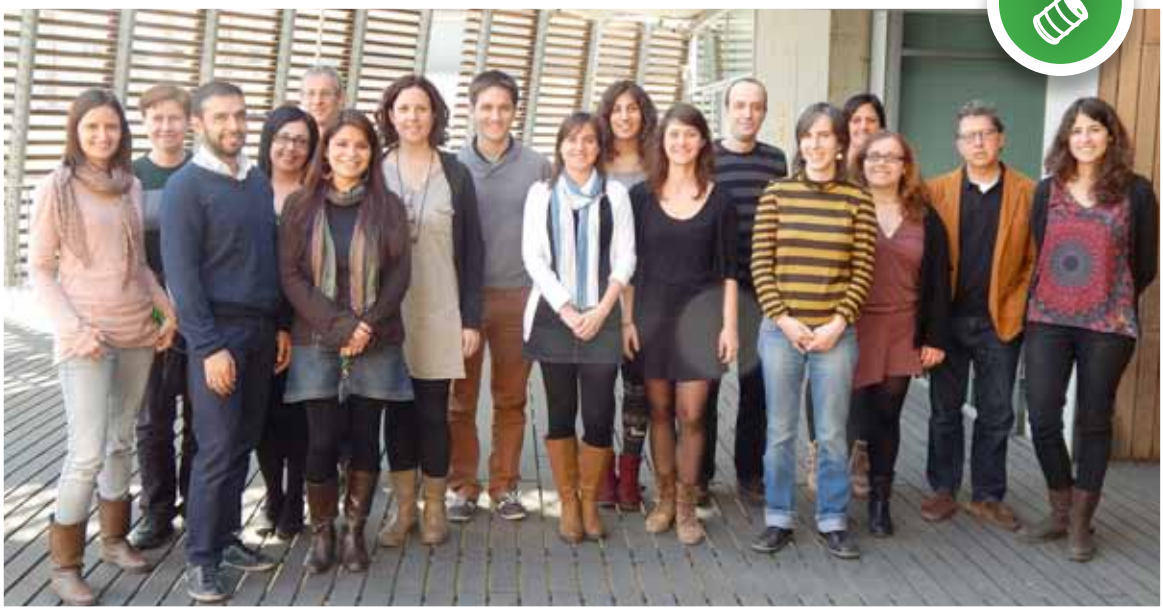


WATER POLLUTIO
PROGRAMME



PROGRAM SUMMARY

Safe drinking water is essential for human life. Water is a limited natural resource under pressure from population growth and climate change, and its quality may be compromised by the presence of microbes or chemicals. On a global scale, microbial contamination is the main stressor of drinking water quality, causing about one-tenth of the global burden of disease. Disinfection of drinking water to prevent water-borne infections represented a major improvement in public health, although undesired by-products are generated as a consequence of disinfection.

In the Water Programme at CREAL, we are particularly interested in disinfection by-products (DBPs), since all of us are exposed either by drinking tap water, showering, bathing or swimming in pools. Our research has shown that long-term exposure (over 40 years) increases risk of bladder cancer. However, exposure during pregnancy was not associated with reproductive outcomes. We are conducting further research to evaluate other chronic conditions (e.g. colorectal cancer), adverse effects in children and the molecular mechanisms of action.

Exposure to DBPs in swimming pools is also a main focus of our research, which has shown no association with respiratory effects, but suggested increased risk of eczema in children. Studies of short-term exposure in adults suggested an association with specific markers of genotoxicity, which is being re-evaluated in a new study of swimming pools.

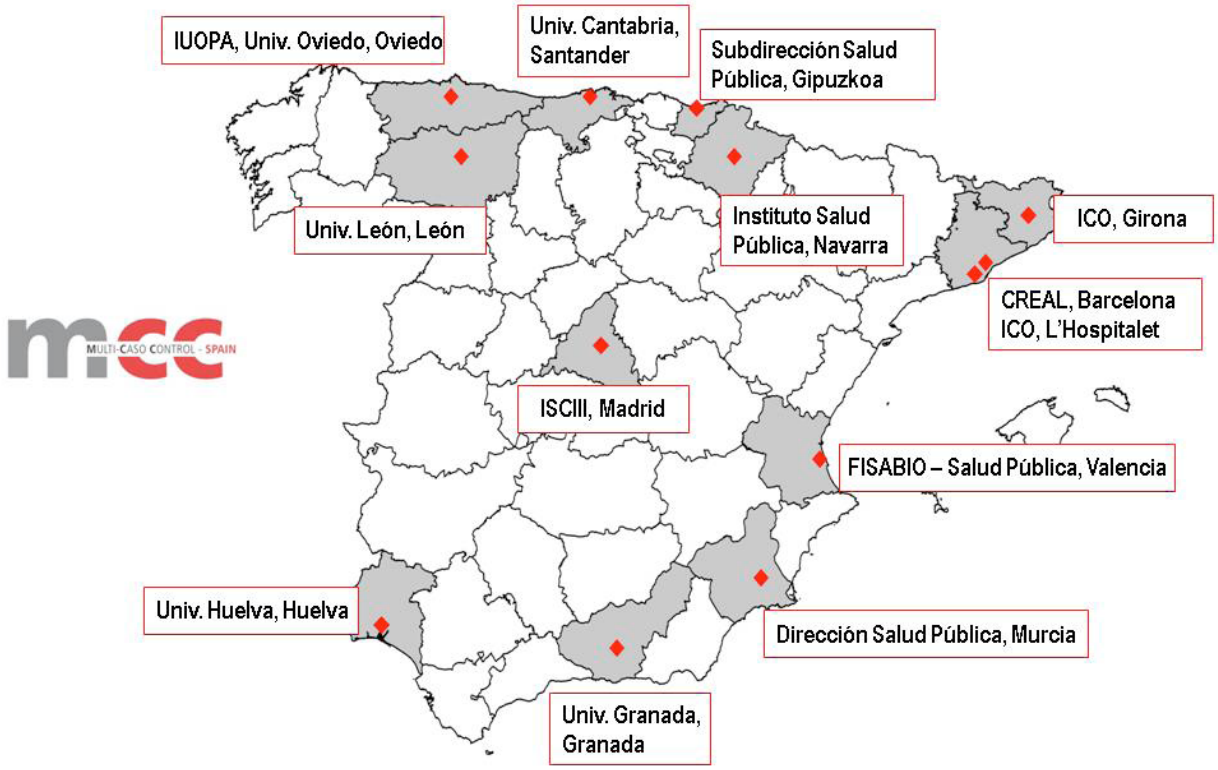
Apart from DBPs, we are interested in other chemicals such as nitrate, which accumulates in drinking water due to the use of fertilisers in agriculture and cattle rearing. We will evaluate whether chronic exposure through drinking water can increase risk of some cancers. In the future we will explore how climate parameters can affect the quality of drinking water.

PROJECTS

CÁNCER AGUA

TITLE: Riesgo de cáncer en España por carcinógenos en el agua de consumo
PI: Cristina Villanueva
PERIOD: 2012-2014
FUNDING SOURCE: FIS-ISCIII (69.642€)

This study aims to evaluate the role of chronic exposure to carcinogens in drinking water (specifically disinfection by-products and nitrate) in risk of colorectal, breast, and prostate cancer, and CLL, based on a robust exposure assessment. More than 10,000 subjects have been recruited in 11 Spanish provinces (Asturias, Barcelona, Cantabria, Gipuzkoa, Granada, Huelva, León, Madrid, Murcia, Navarra and Valencia), blood samples have been collected, and personal information has been ascertained through questionnaires. Biomarkers of exposure to disinfection by-products (urine trichloroacetic acid) and DNA methylation (Illumina 450K array) as a potential mechanism of action have been measured in a subset of controls (N~120). Lifetime exposure to disinfection by-products and nitrate has been accurately evaluated on the basis of environmental levels and personal behaviour. Preliminary results suggest a weak association between chronic exposure to disinfection by-products and colorectal cancer. Analyses are currently being conducted to evaluate risk of colorectal cancer following nitrate exposure. Future analysis will evaluate the association between disinfection by-products and nitrate and other cancer sites.



ENTERICOS

TITLE: Disinfection by-products and other environmental, genetic and molecular

PI: Cristina Villanueva

PERIOD: 2007-2010 (Hiwate), 2009-2011 (FIS-ISCIII)

FUNDING SOURCE: Funding source: FIS-ISCIII (244.420€), EC-FP6 (linked with the Hi-Wate project) (Note: this project financed the Barcelona part of the wider MCC-SP project, described in the cancer program)

This is a case-control study of colorectal cancer conducted in Barcelona to evaluate long-term exposure to disinfection by-products and its association with colorectal cancer. A total of 703 newly diagnosed cases and 995 controls were recruited. Data on potential risk factors for colorectal cancer, residential history and water uses including ingestion, showering, bathing, dishwashing and swimming in pools were obtained through a personal interview. Blood samples were collected to obtain DNA samples. Retrospective data on trihalomethane levels in the study areas have been ascertained from water companies and water samples have been collected to measure a range of DBPs. Preliminary results show that subjects who consumed bottled water (48% cases, 59% controls) had 34% less risk of colorectal cancer (OR=0.66, 95%CI=0.52-0.82) compared to subjects who consumed tap water (47% cases, 39% controls) at the longest residence (35 years on average). Levels of trihalomethanes at the residences were positively associated with risk of colorectal cancer. These results will be confirmed in a larger population in the MCC-Spain study.

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PUBLICATIONS

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RADIATION PROGRAMME

PROGRAM SUMMARY

FOCUS AND AIMS

The overall objective of the Radiation Programme is to better understand the potential risks associated exposure to all kinds of radiation across the frequency spectrum, encompassing electromagnetic fields (EMF) in the extremely low frequency, intermediate frequency and radio frequency bands, ultra violet light, and ionising radiation (resulting from internal and external exposures), in a wide range of exposure settings. Ultimately this aim serves the radiation protection of the general public, patients and those exposed in their work, and informing policy to achieve this goal. In addition, our research contributes to better understanding the processes by which radiation affects human physiology and human health.

PROJECTS AND RESEARCH STRATEGY

Broadly, the projects of the Radiation Programme can be divided into those focused on health effects of exposure to ionising radiation (IR) and those related to exposure to non-ionising radiation. Ionising radiation projects include those looking at both diagnostic and therapeutic medical exposures (EPI-CT, CH Interventional Cardiologists, ProCardio/Spain CCSS, Gene-Rad-Risk), occupational exposures (Alpha-Risk, CURE) and environmental accident-related exposures (INT-Thyr). Non-ionising radiation projects include those looking at various kinds of wireless communication (MOBI-Kids, EFHRAN) and occupational exposures to a wide range of frequencies of EMF (INTEROCC). The Radiation Programme has a key position in a number of networks of excellence and funding platforms such as DoReMi, OPERRA and MELODI.

TRANSLATIONAL ACTIVITIES

A number of translational activities are carried out by the Radiation Programme, including preparation of technical reports, reviews and advice to governmental and non-governmental organisations, membership of several advisory committees and working groups, and carrying out interviews with the press and television. In addition, the Radiation Programme has its own website with detailed information and news from projects and dedicated Twitter account @CREAL_Radiation, which is used to communicate and interact both with the broader public and other experts in the field.

PROGRAM SUMMARY

PERSONNEL

The group is led by Professor **Elisabeth Cardis**. Researchers working in the group include **Magda Bosch de Basea** (EPI-CT), **Chelsea Eastman Langer** (Mobi-KIDS, GERoNiMO), **James Grellier** (Alpha-Risk, INT-Thyr, GERoNiMO, CH Interventional Cardiologists), **Eileen Pernot** (INT-Thyr, ProCardio, Spain-CCSS, DoReMi, CH IC), **Michelle Turner** (INTEROCC, GERoNiMO, EPILYMPH), **Javier Vila** (INTEROCC, GERoNiMO) and **David Moriña** (CH-IC, EPI-CT, Mobi-Kids).

PROJECT ABSTRACTS

DoReMi

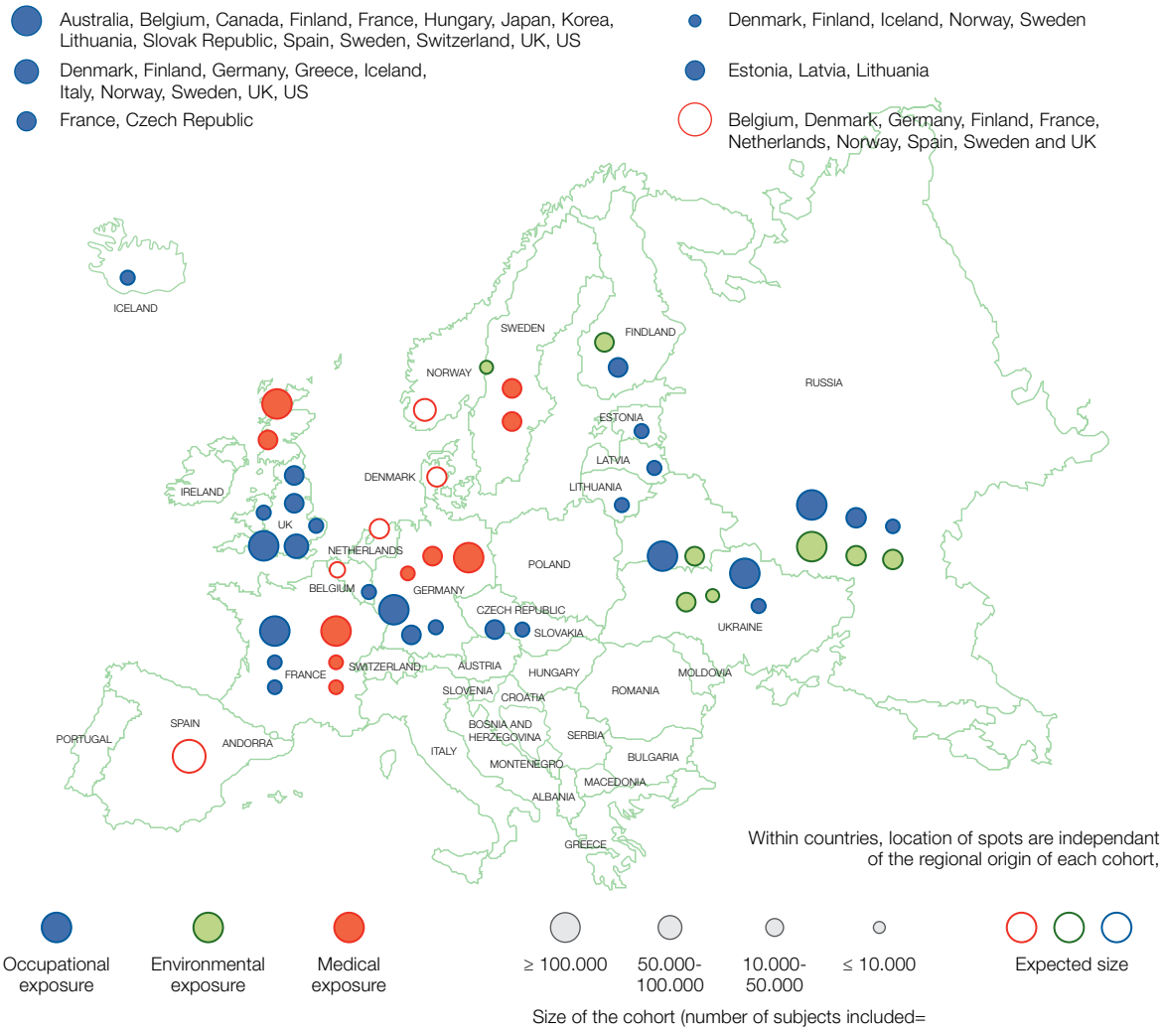
TITLE: Low Dose Research towards Multidisciplinary Integration

PI: Elisabeth Cardis

PERIOD: 2010-2016

FUNDING SOURCE: EU-FP7-EURATON (350.260€), partner and Member of the management Board.

In the 2012-2013 period we conducted a review of European epidemiological cohorts of populations exposed to low-dose IR in order to identify those most suitable for low dose radiation research. The review collected data about population, study design, follow-up, dosimetry and availability of biological samples for biomarker studies. We reviewed 53 cohorts of persons exposed occupationally, environmentally or medically to low doses of IR; those cohorts reflected public health concerns during the last century regarding consequences of technological progress: haemangioma treatment since the 20s, uranium mining, nuclear weaponry and Mayak nuclear facility releases during World War II and Cold War, development of nuclear power industry in the 60s, CT-scans in the 80s, etc. The cohorts most suitable to provide answers to current radiation protection questions have been identified and work is underway to include the information about these cohorts into the STORE radiation portal to facilitate future collaborations using these cohorts.



PROJECTS ABSTRACTS

INT-THYR // IONISING RADIATION

TITLE: Integrating radiation biomarker into epidemiology of post-Chernobyl thyroid cancer from Belarus
PI: Elisabeth Cardis
PERIOD: 2012-2014
FUNDING SOURCE: DoReMi Internal Call (70.000 €)

The increased incidence of thyroid cancer in young people following the Chernobyl accident is unique opportunity to study mechanisms of radiation-induced thyroid cancer. Two potential biomarkers of radiation-induced thyroid cancer—7q11 amplification and CLIP2 overexpression—have been identified among thyroid cancer cases in Ukraine. The objective of Int-THYR is to validate these biomarkers, assess their relationship with dose and evaluate whether their presence is affected by age at exposure, age at diagnosis and iodine deficiency. The ultimate aim is to evaluate their usefulness in molecular epidemiological studies designed to better understand molecular mechanisms of carcinogenesis after low dose irradiation. CREAL has been working primarily on collection of epidemiological with partner BelMAPO in Minsk and in reviewing dose reconstruction models.

CURE // IONISING RADIATION

TITLE: Concerted action for Uranium Research in Europe.
PI: Elisabeth Cardis
PERIOD: 2013-2015
FUNDING SOURCE: DoReMi Internal Call (9.150 €)

CURE is a concerted action to elaborate a collabo-rative research project on uranium contamination, integrating epidemiology, biology/toxicology and dosimetry. It aims to develop a common research protocol and to evaluate the feasibility of a molecular epidemiology approach to improve risk estimations. CREAL is involved in two working groups on biomarkers and on dosimetric uncertainties. A review of potential biomarkers has been conducted and a preliminary list prepared; a pilot study among Czech uranium miners is being planned. Within the working group on dosimetric uncertainty, CREAL has played a key role in sharing experiences in these issues within the Alpha-Risk project, and setting up a strategy for addressing similar issues within CURE.

EPI-CT // IONISING RADIATION

TITLE: Epidemiological study to quantify risks for paediatric computerized tomography and to optimise doses (http://epi-ct.iarc.fr/)
PI: Elisabeth Cardis
PERIOD: 2011-2016
FUNDING SOURCE: EU-FP7- Fission (393.884 €). Partner and member of the Steering Comittee. Consejo de Seguridad Nuclear (472 000€)

The growing use of CT scans in diagnostic radiology, especially in young people, is a radiation protection concern. A European cohort study, EPI-CT, is underway to evaluate potential health consequences and optimise imaging protocols. It is coordinated by the International Agency for Research on Cancer (IARC). CREAL leads the epidemiology work-package, the task on leukaemia analyses and the Spanish study, with approximately 140.000 paediatric and young adult CT scan patients from 24 hospitals (6 Spanish autonomous communities). Linkages with cancer, in-patient and mortality registries are underway. Analyses of socioeconomic characteristics of the patients, based on area of residence, suggest that less affluent groups tend to receive fewer CT scans then more affluent populations, unlike UK findings. Results are expected in 2015 (Spain) and 2016 (Europe).

GENE-RAD-RISK // IONISING RADIATION

TITLE: Gene-radiation interactions: effects on risk of breast cancer
PI: Elisabeth Cardis
PERIOD: 2008- ongoing
FUNDING SOURCE: Funding completed

The relative risks of breast cancer for women exposed to IR in childhood and adolescence and are among the highest known radiation-related risks for any cancer type. Several genes increase breast cancer susceptibility and are known to be involved in detection and repair of radiation-induced DNA damage. A European project, coordinated by the International Agency for Research on Cancer (IARC), was conducted to examine the joint roles of radiation exposure and genetic susceptibility in the aetiology of premenopausal breast cancer among survivors of childhood cancer and Hodgkin's disease and among BRCA1/2 mutation carriers. In the later, diagnostic exposure before age 30 increased the risk at dose levels considerably lower than those at which increases have been found in population based cohorts (Pijpe et al 2013).

CH-IC // IONISING RADIATION

TITLE: CH-IC (Swiss Interventional Cardiologists)
PI: Elisabeth Cardis
PERIOD: 2010-2011
FUNDING SOURCE: Funding completed

The Swiss Federal Office of Public Health (SFOPH) commissioned CREAL to investigate the possible health impacts of occupational exposures to ionising radiation received by interventional cardiologists. A systematic review of the epidemiological literature on dose-related risk of cataracts and brain tumours has been conducted. Based on this, and in collaboration with Swiss dosimetrists, the potential health impact of these exposures was assessed. The feasibility and statistical power of an epidemiologic study of cardiologists was judged insufficient and advice was provided to the SFOPH on the most appropriate strategy to address knowledge gaps in this area. A probabilistic tool to estimate doses to various organs (based on occupational and shielding history) and risk of cataracts and cancer has been developed and will be made available online.

PROJECTS ABSTRACTS

PROCARDIO // IONISING RADIATION

TITLE: Cardiovascular Risk from Exposure to Low-dose and Low-dose-rate Ionizing Radiation (http://www.procardio.eu/)
PI: Elisabeth Cardis
PERIOD: 2011-2014
FUNDING SOURCE: EU-FP7- Fission (218.800€), partner

ProCardio is a European study to assess the risk of cardiovascular diseases from radiotherapy received for the treatment of childhood cancer survivors. The first step in the process is the creation of a cohort of childhood cancer survivors. Following feasibility work, the cohort is being established in collaboration with large paediatric oncology departments. Collaboration is ongoing with Hospital Sant Joan de Deu (HSJD) in Barcelona, one of the largest paediatric oncology and paediatric haematology departments in Spain, and data collection on approximately 3000 patients is proceeding. Request for linkages to the national mortality registry and the hospital discharge registry was submitted.

OPERRA // IONISING RADIATION

TITLE: Concerted action for Uranium Research in Europe.
PI: Elisabeth Cardis
PERIOD: 2013-2015
FUNDING SOURCE: EU - 136.172,48€

OPERRA aims to support the MELODI (Multidiscipli-nary European Low Dose Initiative) Association in building an umbrella structure for the integration of radiation protection research in EUROPE and to create the necessary architecture for the facilitation of long-term European research programmes in radiation protection, taking advantage of the experience gathered through DOREMI. OPERRA will exploit the synergies of Euratom and other EC programmes for funding joint activities. It will strengthen links with national funding programs as well as with European education and training structures and take steps to promote the joint use of infrastructures in European countries. CREAL leads tasks to identify experiences and lessons learned from existing exposure situations for emergency preparedness and to integrate knowledge from non-radiation research.

INTERPHONE // IONISING RADIATION

TITLE: Medical exposures to ionising radiation and risk of brain tumours in INTERPHONE
PI: Elisabeth Cardis
PERIOD: 2008-2012
FUNDING SOURCE: Funding completed

The aim of this project is to estimate the magnitude of the association between radiation dose from medical procedures and the risk of glioma, meningioma and acoustic neurinoma by analysing data from participating INTERPHONE study countries (Canada, France, Israel, New Zealand, and Australia). An important preliminary step to the analyses was to estimate the doses of ionizing radiation received at the level of the brain before the diagnosis of brain tumour. We collected information on x-rays, CT-scans and fluoroscopy available in UNSCEAR reports and published reports since the 50s to create a dosimetry database that will be used for the analyses.

EPILYMPH // IONISING RADIATION

TITLE: Concerted action for Uranium Research in Europe.
PI: Elisabeth Cardis
PERIOD: 2011-2012
FUNDING SOURCE: Funding completed

Though IR exposure can induce a variety cancer types, the association with chronic lymphocytic leukaemia (CLL), lymphoma, and multiple myeloma (MM) remains unclear and few studies have considered radiation related risk of other lymphoma subtypes or exposure from diagnostic medical procedures. Epilymph, a multi-center case-control study conducted in 6 countries, is a unique source of data to fill this gap. A total of 2362 incident lymphoma cases and 2465 controls were recruited according to a common protocol. Data on self-reported number and type of diagnostic procedures was collected, together with age at first and last procedure. Radiation doses were estimated by combining questionnaire data and examination-specific dose levels obtained from the above mentioned review of dose information from UNSCEAR and other reports.

PROJECTS ABSTRACTS

MOBI-KIDS // NON-IONISING RADIATION

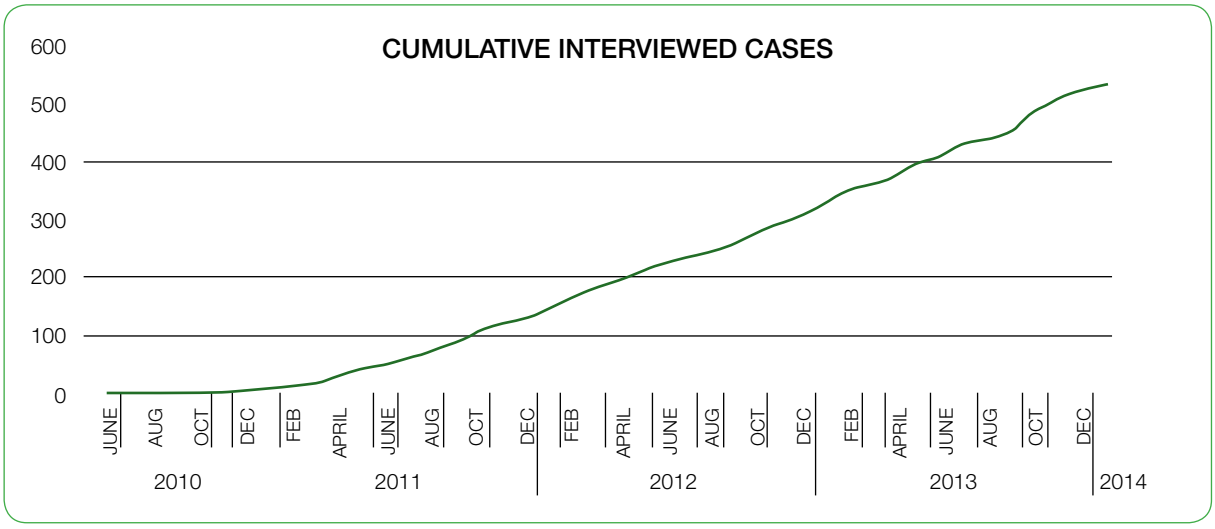
TITLE: Risk of brain cancer from exposure to radio-frequency fields in childhood and adolescence

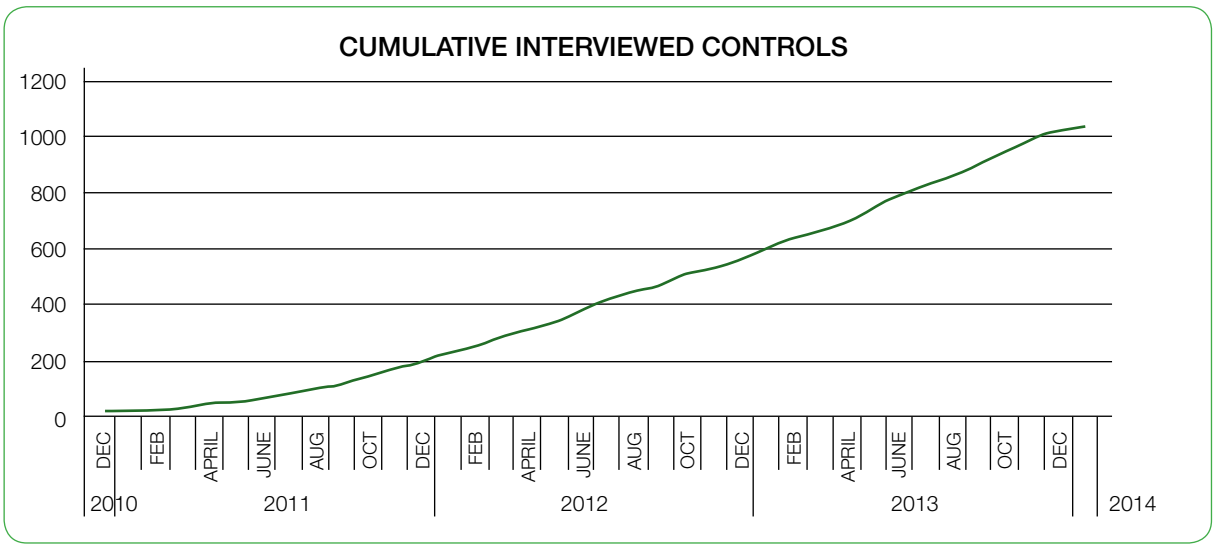
PI: Elisabeht Cardis

PERIOD: 2009-2016

FUNDING SOURCE: EUPF7 Environment (1.125M€) + 170.500€ MICINN + 198.440 ISCIII

Mobi-Kids, a multinational case-control project, studies potential effects of childhood and adolescent exposure to electromagnetic fields from mobile communications technology on brain tumour risk. By the end of 2013, 525 cases and 1021 controls had been interviewed (Figure) in 14 countries, with data collection still underway. Detailed information is collected on potential risk factors, including mobile phone use, other sources of EMF and residential, occupational, and medical history. To increase the validity of mobile phone exposure estimates and to characterise possible recall errors to be accounted for in the main analyses, self-reported phone use is compared to operator records and to a smartphone application recording use. Developing indices of exposure to RF and ELF from mobile phones and environmental and occupational sources is underway.





INTEROCC // NON-IONISING RADIATION

TITLE: INTEROCC (Occupational exposures and brain tumours)
PI: Elisabeth Cardis
PERIOD: 2008-2011
FUNDING SOURCE: NIH (467.878 USD)

INTERPHONE was a 13 country case-control study of mobile telephones and cancer risk, including 2,613 glioma and 2,343 meningioma cases and 7,557 controls. Within the CREAL-led INTEROCC project, occupational histories of subjects from 7 INTERPHONE countries were coded and improved Job-Exposure-Matrices applied to estimate exposure to chemicals and ELF, Analyses of brain tumour risk in relation to occupational exposure to ELF alone, and in combination with chemicals, were conducted. Papers examining associations between occupational solvents (McLean et al. 2014) and ELF (Turner et al. 2014) and brain tumour risk were recently published. A Source Exposure Matrix is being developed, based on a comprehensive database of measurements to allow a more detailed assessment of ELF, IF and RF exposures for o **TITLE:** INTEROCC (Occupational exposures and brain tumours)

EFHRAN // NON-IONISING RADIATION

TITLE: EFHRAN (European Health Risk Assessment Network on EMF exposure)
PI: Elisabeth Cardis
PERIOD: 2009-2012
FUNDING SOURCE: EU - DG Sanco - (75.339,98 €)

During this reporting period the EFHRAN project was completed, having fulfilled its remit to establish a network for performing health risk assessment of electromagnetic fields exposure across the non-ionising radiation frequency spectrum. EFHRAN generated a set of key reports detailing the state of the art in terms of risk characterisation, exposure data available within Europe, reviews of the evidence of associations and mechanisms from epidemiological and animal/in vitro studies, and a qualitative report detailing priorities of health risk management and communication on EMF exposure. CREAL played a key role in exceeding the specific objectives of the project, and published a quantitative assessment of exposures to extremely low frequency EMF and childhood leukaemia.

Work of the network will continue and research to fill gaps will be undertaken within GERoNiMO, a large European project coordinated by CREAL, starting in January 2014.

MEMBERS

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MANAGEMENT

Laura Argenté, Inma Cano

PUBLICATIONS

RESPIRATORY PROGRAMME PUBLICATIONS 2012-2013

- Kesminiene A, Evrard AS, Ivanov VK, Malakhova IV, Kurtinaitise J, Stengrevics A, Tekkel M, Chekin S, Drozdovitch V, Gavrilin Y, Golovanov I, Kryuchkov VP, Maceika E, Mirkhaidarov AK, Polyakov S, Tenet V, Tukov AR, Byrnes G, Cardis E. Risk of thyroid cancer among Chernobyl liquidator. Radiat Res 2012; 178(5): 425-36.

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- Van Tongeren M, Kincl L, Richardson L, Benke G, Figuerola J, Kauppinen T, Lakhani R, Lavoue J, McLean D, Plato N, Cardis E. Assessing occupational exposure to chemicals in an International Epidemiological study of brain tumours. Ann Occup Hyg 2013; 57(5): 610-26.

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MAIN RESEARCH COOPERATION

INTERNATIONAL ORGANIZATIONS

European Associated Laboratory with INSERM, Paris, France
International Agency for Research on Cancer, Lyon, France
WHO, Geneva, Switzerland

AUSTRIA
Institute of Environmental Health of Medical University, Vienna
University of Veterinary Medicine, Vienna

AUSTRALIA
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University of Sydney, Sydney

BELARUS
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Belarussian Centre for Medical Technologies, Information Computer System, Health Care Administration and Management, Minsk

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Istituto Superiore di Sanita, Rome

Lazio Region

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University of Pavia, Pavia

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Nagasaki University, Nagasaki

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Latvian Centre of Oncology, Riga

LITHUANIA

Lithuanian Cancer registry, Vilnius

Vytautas Magnus University, Kaunas

MEXICO

Instituto Nacional de Salud Pública

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University of Auckland, Auckland

THE NETHERLANDS

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Erasmus University, Rotterdam

Institute for Risk Assessment Sciences (IRAS), Utrecht

The Netherlands Cancer Institute, Amsterdam

University of Maastricht, Maastricht

Universiteit Utrecht, Utrecht

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Norwegian Radiation Protection Authority, Oslo

Norwegian Institute of Public Health

POLAND

Medical University of Lodz

RUSSIAN FEDERATION

Institute of Biophysics, Moscow

Medical Radiological Research Center RAMS, Obninsk

SPAIN

Center for Genomic Regulation, Barcelona

CRESIB, Barcelona Centre for International Health Research, Barcelona

Consejo de Seguridad Nuclear, Madrid

CSIC, Barcelona

Universitat Autonoma Barcelona, Department of Mathematics, Barcelona

Instituto Carlos III, Madrid

Universidad de Huelva, Huelva

Universidad de Valencia, Valencia

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Karolinska University Hospital, Stockholm

National Institute for Working Life, Umea

Scarab, Stockholm

Swedish Institute for Infectious Disease Control

University of Stockholm, Stockholm

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University of Basel, Basel

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London School of Hygiene and Tropical Medicine, London

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National Health Service,

NuKEM limited, Didcot

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University of Bristol, Bristol

University of Cambridge, Cambridge

University of London, London

University of New Castle, New Castle

Westlakes Research Institute, Cumbria

UKRAINE

Radiation Protection Institute, Kiev

Scientific Center for Radiation Medicine, Kiev

USA

Arizona Respiratory Center (Respiratory Sciences), University of Arizona, Tucson (F Martinez)

Environmental Protection Agency

Harvard. School of Public Health, Harvard

National Cancer Institute, Bethesda

National Institute for Occupational Safety and Health, Cincinnati

School of Public Health, University of North Carolina, Chapel Hill

University of Arizona, Tucson

University of Chicago, Chicago

University of South California, California

KNOWLEDGE TRANSFER ACTIVITIES

Translational activities and knowledge transfer are key to achieving CREAL's mission to "provide scientific knowledge relevant for public health actions". CREAL provides consulting and technical assistance to national and international public organizations and private entities.

EU CONFERENCES

Impact of early diagnosis and control of chronic respiratory diseases on Active and Healthy Ageing (Cyprus Presidency of the EU Council, 2012). A debate on the *Impact of early diagnosis and control of chronic respiratory diseases on Active and Healthy Ageing* was held at the European Union Parliament in November 2012. The debate was held under the auspices of the Cyprus Presidency of the European Union (2012) and represented a follow-up of the priorities of the Polish Presidency of the European Union (2011). It highlighted the importance of early life events in the occurrence of chronic respiratory diseases later in life and their impact on active and healthy ageing. Dr Josep M Antó presented the topic *Birth cohorts are essential to understand chronic diseases in adults and the elderly*. The presentation of epidemiological evidence was followed by a discussion of the actions that should be taken to prevent and manage chronic respiratory diseases in children. The debate ended with practical, feasible and achievable projects, demonstrating the strength of the political action in the field (Allergy, 2013; 68:555-61).

KNOWLEDGE TRANSFER ACTIVITIES

EXPERT CONSULTATIONS

Expert Consultation on Environment and Health Priorities for the European Region (World Health Organization - European Region and European Environment and Health Ministerial Board, 2012). Dr Josep M Antó has participated in *The World Health Organization Expert consultation on Environmental Health Priorities* organized by the European Environment and Health Ministerial Board (EHMB). The EHMB endorsed the proposal by the WHO secretariat to organize a consultative process involving experts from relevant national and international institutions with the aim of developing a concept of priorities in environment and health in the WHO European Region.

Evidence on health aspects of air pollution to review EU policies - REVIHAAP (World Health Organization - European Region, 2012). WHO/Europe is coordinating the international project 'Evidence on health aspects of air pollution to review EU policies' (REVIHAAP) whose aim is to provide the European Commission and its stakeholders with evidence-based advice on the health aspects of air pollution. This advice will be based on a review of the latest scientific evidence on the health effects of all pollutants regulated by Directives 2008/50/EC and 2004/107/EC. Project results will support the comprehensive revision of European Union air quality policies due in 2013. To effectively advise the revision of EU air quality policies, REVIHAAP is addressing a list of key questions on particulate matter (PM2.5 and PM10), ground level ozone, other pollutants and their mixtures, and epidemiology and health impact assessment. Dr Mark Nieuwenhuijsen participates in the expert group involved in the review of the evidence on health aspects of air pollution, with the aim of drafting an evaluation of the evidence, and answering key questions. Dr Josep M Antó and Dr Jordi Sunyer have participated as external reviewers, providing comments on the technical content and clarity of the document.

Swimming pools and asthma (Committee on the Medical Effects of Air Pollutants - COMEAP, 2012). Several studies conducted by CREAL researchers on respiratory health and attendance to swimming pools have been evaluated by the COMEAP, an Advisory Committee integrated by independent experts providing advice to UK government departments and agencies, for the statement "Asthma and exposure to chlorine and associated reaction products in swimming pools". The document includes a revision of the current literature and recommendations on the use of swimming pools in view of the current evidence.

Catalan Strategy for Adapting to Climate Change (Catalan Office for Climate Change, Government of Catalonia, 2012). Drs Josep M Antó and Xavier Basagaña have reviewed the report prepared by the Catalan Office for Climate Change to develop the Catalan Strategy for Adapting to Climate Change 2013-2020, which summarizes the goals and actions to be taken in order to adapt to new and/or current climate change conditions. The strategy was approved in November 13th, 2012. Besides, Dr Xavier Basagaña has been appointed as a member, together with other Catalan public representatives, in a working group organized by the Catalan Office for Climate Change.

KNOWLEDGE TRANSFER ACTIVITIES

REPORTS

Radiofrequencies and Health (ANSES - French Agency for Food, Environmental and Occupational Health & Safety, 2013). Dr Elisabeth Cardis has chaired the working group on Radiofrequency and health, convened by ANSES, tasked with regularly updating the collective expertise appraisal on the health effects potentially related to exposure to radiofrequencies; answering questions raised by the development of new technologies using radiofrequencies and responding to requests for the Agency to carry out collective expert appraisals on this subject; making annual recommendations for avenues of research; and informing stakeholders of the new results of research and thus contributing to the public debate on the topic of radiofrequencies. The updated report has been issued on October 2013

CHICOS- Strategy for European Birth Cohort Research (FP7-Health-2009). CHICOS is a coordination and support action launched in January 2010 funded through the EC 7th Framework Programme (HEALTH-FP7-2009-241604). The action, coordinated by Dr Martine Vrijheid of CREAL, finished in May 2013. This initiative has developed a joint European strategy for research using mother-child cohorts, focused on data harmonization, pooling and inventory. A valuable tool developed within the framework of this actions, continuing the effort of the previous action ENRIECO led by the CREAL researcher Dr Mark Nieuwenhuijsen, is the Birth Cohorts Inventory (http://www.birthcohorts.net/), whose aim is to facilitate the exchange of knowledge and collaboration between cohorts and researchers and to provide administrators, policy makers and other stakeholders with information on available cohort data on health and its determinants.

IARC Monographs (International Agency for Research on Cancer - World Health Organisation, 2012)

The IARC Monographs identify environmental factors that can increase risk of human cancer. These include chemicals, complex mixtures, occupational exposures, physical agents, biological agents, and lifestyle factors. National health agencies can use this information as scientific support for their actions to prevent exposure to potential carcinogens. The objective of the programme is to prepare, with the help of international Working Groups of experts, and to publish in the form of Monographs, critical reviews and evaluations of evidence on the carcinogenicity of a wide range of human exposures.

Dr Manolis Kogevinas and Dr Elisabeth Cardis from CREAL have coordinated two of these working groups:

Volume 100D: A review of human carcinogens - Part F: radiation (International Agency for Research on Cancer - World Health Organization, 2012). In 2012, the IARC published a monograph on chemical agents and related occupations. The publication represents the views and expert opinions of an IARC Working Group Evaluation of Carcinogenic Risks to Humans, which met in Lyon on June 2-9, 2009. The working group, which consisted of 20 scientists from nine countries, was chaired by Dr E Cardis from CREAL, Spain, together with Dr B Armstrong from the School of Public Health, University of Sydney, Australia. The aim of the working group was to re-assess the carcinogenicity of the types of radiation previously classified as “carcinogenic to humans” (Group 1) and to identify additional tumor sites and mechanisms of carcinogenesis.

Volume 100F: A review of human carcinogens - Part F: chemical agents and related occupations (International Agency for Research on Cancer - World Health Organization, 2012). In 2012, the IARC published a monograph on chemical agents and related occupations. The publication represents the views and expert opinions of an IARC Working Group Evaluation of Carcinogenic Risks to Humans, which met in Lyon on October 20-27, 2009. The working group, which consisted of 23 scientists from six countries, was chaired by Dr M Kogevinas from CREAL, Spain, together with Dr H Vainio from the Finnish Institute of Occupational Health, Finland and Dr CJ Portier from the Office of Risk Assessment Research, NIEHS, USA. The aim was to re-assess the carcinogenicity of a number of Chemicals compounds, complex mixtures and occupational exposures previously classified as carcinogenic to humans (Group 1) and to identify additional tumor sites and mechanisms of carcinogenesis.

GUIDELINES AND HEALTH PLANS

American Thoracic Society/European Respiratory Society (ATS/ERS) Statement on Pulmonary Rehabilitation (ATS/ERS, 2012) **American Thoracic Society/European Respiratory Society (ATS/ERS) Statement on Pulmonary Rehabilitation (ATS/ERS, 2012).** Dr Judith Garcia-Aymerich has participated as a member of a multidisciplinary committee of experts in the update of the guidelines for pulmonary rehabilitation of the ATS/ERS. Pulmonary rehabilitation is recognized as a core component of the management of individuals with chronic respiratory disease and since the last ATS/ERS Statement on Pulmonary Rehabilitation from 2006, there has been considerable growth in the knowledge of its effectiveness and scope. The update of the 2006 document includes a new definition of pulmonary rehabilitation and highlights key concepts and major advances in the field. The final content of this Statement has been published in the American Journal of Respiratory and Critical Care Medicine in October 2013.

Guidelines on Urban Settings and Health (Barcelona Municipality, 2012). The Barcelona Municipality, which encompasses all municipalities surrounding Barcelona, has prepared an online guideline on public health to be used as tool for public health technicians and services. Dr Mark Nieuwenhuijsen has coordinated the revision and validation of the health related issues of the guideline.

Clinical Practice Guideline for the Diagnosis and Treatment of Patients with Chronic Obstructive Pulmonary Disease (COPD) – Spanish Guideline for COPD (GesEPOC, 2012). The main aim of this guideline is to provide a tool for COPD physicians in the decision-making aspects of COPD management. Elena Gimeno, a PhD student at CREAL, has participated in preparing the pulmonary rehabilitation section of these guidelines.

WORKSHOPS

Health surveillance related to the handling of oil spills (University of Bergen, Norway, 2012). Dr Jan Paul Zock participated in health surveillance initiatives related to handling of oil spills, convened by the University of Bergen (Norway) in June 2012. The workshop brought together representatives from the Norwegian Coastal Administration and from the Petroleum Safety Authorities as well as from research institutions. During the workshop, strategies and methods for 1) Exposure assessments/measurements and 2) Health surveillance of clean-up workers, were presented and discussed. CREAL contributed with knowledge generated as a result of research on the Prestige oil spill.

KNOWLEDGE TRANSFER ACTIVITIES

COMMITTEES / OBSERVATORIES / WORKING GROUPS

European Advisory Committee on Health Research (World Health Organization - European Region, 2012-2014). Dr Josep M Antó has been appointed as a member of the EACHR-WHO for a 2-year period beginning May 2012. The EACHR, based in Copenhagen, is an advisory body with a consultative mandate to support the World Health Organization (Europe region) in the development of policies on health research addressing priority public health problems. This organism works in close cooperation with external institutions and with the scientific community. At the European level, the EACHR works to identify, harmonize and coordinate national and regional health research priorities, as well as to develop research potential and capability, both nationally and regionally.

Committees Starting before 2012:

- The Barcelona soy allergen surveillance system (Public-Private consortium, 1999-on-going)
- Committee for tracking the removal of sludge from the Flix reservoir in Delta del Ebro (Water Consortium of Tarragona, 2009- on-going)
- The Health and Environment Observatory of Tarragona (Tarragona Regional Office of the Department of Health, Generalitat de Catalunya, 2007- on-going)
- Plan for Improvement of Air Quality - Pla de Millora de la Qualitat de l'Aire (Departament de Territori i Sostenibilitat, Generalitat de Catalunya, 2011-2015).
- Health and Climate Change Observatory - Observatorio de Salud y Cambio Climático (Ministerio de Sanidad, Servicios Sociales e Igualdad, España, 2011).

INSTITUTIONAL COLLABORATIONS

INSTITUTIONAL COLLABORATIONS

Over the past two years CREAL has worked consistently within the framework of international collaboration, both under previously signed agreements, as well as new ones. These partnerships allow greater institutional projection of our research.

INTERNATIONAL LABORATORY FOR RESPIRATORY AND ENVIRONMENTAL EPIDEMIOLOGY INSERM-CREAL (LEA)

The agreement signed by INSERM and CREAL in July 2007 to establish the International Laboratory in Respiratory and Environmental Epidemiology was renewed in 2013. In recent years, LEA has developed into a remarkable scientific collaboration, principally in four areas:

1. **EXCHANGE OF RESEARCHERS.**
   - **1.1. Senior researchers** have made several short visits as well as longer stays to develop specific areas of research. Regarding the latter, important collaborations include: Dr N Le Moual's one-year sabbatical (2011-2012) to collaborate with Dr JP Zock on occupational exposures and asthma (this sabbatical was funded by the Spanish Ministry of Science and Innovation); the collaboration with Dr B Jacquemin (2011-2015) who is conducting research on air pollution at CREAL; and Dr F Kaufmann's sabbatical at CREAL (February - December, 2013).
   - **1.2. Postdoctoral researchers:** a tremendous effort has been made to promote the exchange of postdoctoral researchers, with four researchers having participated in the programme to date (B Jacquemin, R Varraso, who were recruited as INSERM researchers after their postdoctoral period; and M Pedersen and M Rava, who are currently doing their postdoctoral training at CREAL and INSERM, respectively).
   - **1.3.** Several **PhD students** have done or are doing their theses under the co-direction of researchers from both institutions (Estelle Rage from INSERM, co-supervised by Dr F Kaufmann and Dr J Sunyer; Orianne Dumas from INSERM in collaboration with Dr X Basagaña; and David Vizcaya from CREAL in collaboration with Dr N Le Moual).
2. **RESEARCH PROJECTS.**
   Under the LEA agreement, several collaborative projects have been funded by various agencies (ECRHS; EGEA; PAC-COPD; E3N). One of the main projects is The MeDALL Consortium, which is funded by FP7 and consists of 23 partners co-coordinated by INSERM and CREAL, and studies mechanisms of allergy development. In addition, Helix (FP7) is coordinated by Martine Vrijheid (CREAL) with Rémy Slama (INSERM) as a key partner; and Nicole Le Moual (INSERM) is co-PI and Jan-Paul Zock (CREAL) a consultant supported by a major NIOSH grant for work on the US Nurses' Health Study.
3. **Publications:** more than 32 joint articles have been published since the establishment of LEA.
4. **Joint seminars:** several seminars and meetings on topics of common interest have been organized.

INSTITUTIONAL COLLABORATIONS

INTERNATIONAL LABORATORY FOR RESPIRATORY AND ENVIRONMENTAL EPIDEMIOLOGY INSERM-CREAL (LEA)

In October 2013, a CREAL-INSERM workshop was held in Barcelona to evaluate the results and publications of common studies and activities carried out jointly by the two institutions. There was also an open discussion about future opportunities for the alliance.

After leading the project for the 6 years since its inception, Josep M Antó and Francine Kauffman passed the baton on to Judith Garcia-Aymerich (CREAL), Valérie Siroux (Grenoble-INSERM) and Raphaëlle Varraso (Villejuif-INSERM) in 2013.

ARIZONA RESPIRATORY CENTER (ARIZONA UNIVERSITY)

In 2012-13, outstanding research activity has continued under the agreement signed with the University of Arizona. Dr Stefano Guerra is directly involved in coordinating various studies that promote the synergy between the two institutions. Additional collaborations with the Arizona Respiratory Center are currently being developed in connection with the MeDALL project in the field of biomarkers of asthma and allergic diseases in childhood.

The main area of research is serum biomarkers. It is important to highlight the use of European cohorts (ERCHS) in replication studies following up on the identification of biomarkers in US cohorts (TESAOD). “Guerra S, Halonen M, Sherrill DL, *et al.* The relation of circulating YKL-40 to levels and decline of lung function in adult life. *Respir Med* 2013”.

Other areas of joint work include the participation of Prof Martinez, director of the Arizona Respiratory Center, in the European MeDALL project and a study of the effects of physical activity on lung function development in childhood and adolescents, with data from the Arizona Children’s Respiratory Study cohort, coordinated by Dr. Judith Garcia-Aymerich at CREAL and Dr. Debra Stern in Arizona.

HEALTH RESEARCH INSTITUTE – HOSPITAL DEL MAR (IIS-MAR)

On February 17 2014, the Secretary of State for Research, Development and Innovation from the Ministry for Economy and Competitiveness, Carmen Vela, signed an agreement to grant accreditation to the Health Research Institute of Hospital del Mar Medical Research Institute (IMIM) for a period of 5 years. CREAL has participated in two research groups, led by Drs. Manolis Kogevinas and Jordi Sunyer.

Highlighted cooperative projects with research groups at IIS-Mar

- **Pneumology unit**: Dr Sanjuás collaborates with Dr Zock and Dr Antó on asthma studies; Dr Balsells and Dr Rodríguez collaborate with Dr Garcia-Aymerich on COPD studies.
- **Research group on inflammatory dermatologic diseases**: Dr Giménez collaborates with Dr Zock and Dr Antó on hand eczema studies.
- **Research group on Molecular mechanisms of lung cancer predisposition**: Dr Barreiro collaborates with Dr Guerra and Dr Zock on studies of respiratory biomarkers; with Dr. Garcia-Aymerich and Dr Antó on mechanisms of oxidative stress related to the evolution of COPD; and with Dr. Villanueva on CC-16 blood analysis in relation to water pollution.
- **Research group on Myogenesis, inflammation and muscle function**: Dr. Gea and Dr Balcells collaborate with Dr. Garcia-Aymerich and Dr Antó on muscle capacity related to exercise, and the use of the public health system in COPD patients.
- **Research group on cardiovascular epidemiology and genetics**: Dr Elosua collaborates with Dr Basagaña in several projects including REGICOR-AIR, HERMES, TRI-TABS, and ESCAPE, studying the effects of noise and air pollution from traffic on cardiovascular disease. Dr Elosua and Dr Molina collaborate with Dr. Garcia-Aymerich on the validation of physical activity questionnaires. Dr Elosua collaborates with Dr Juan Ramon González in statistical methods for genetic association studies and analysis of genetic copy number variants.
- **Research Group on Bioanalysis**: Dr Ventura collaborates with Dr Vrijheid on Maternal phthalate metabolite measurements in urine and their effects on child health.
- **Maternity Unit**: Dr. Carreras and Dr Agramunt collaborate with Dr Kogevinas and Dr Pedersen on the study of biomarkers related to cancer and on diet in new borns.
- **Gynecology and Obstetrics Service**: Dr Checa, Dr Prat, Dr Robles, Dr Comadran and Dr Carreras collaborate with Dr Jacquemin, Dr Nieuwenhuijsen and Dr Cole-Hunter in a study of fertility.
- **Immunology Service**: Dr López Botet collaborates with Dr Stefano Guerra on a study of biomarkers of respiratory health.
- **Radiology Service**: This service collaborates with Dr Garcia-Aymerich and Dr Antó on the PAC-COPD project.
- **Urology Service**: Dr Lorente collaborates with Dr Kogevinas on the MCC-Spain study of common tumors.
- **Oncology Service**: Dr Tusquets collaborates with Dr Kogevinas on the MCC-Spain study of common tumors.
- **Gastroenterology Service**: Dr Andreu, Dr Bessa, Dr Bory and Dr Pera collaborate with Dr Kogevinas on the MCC-Spain study of common tumors.
- **Hematology Service**: Dr Abella and Dr Salar collaborate with Dr Kogevinas on the MCC-Spain study of common tumors.
- **Cardiology Unit**: Dr Cladellas collaborates with Dr Garcia-Aymerich on research into physical activity following cardiac surgery.
- **Department of Neurosurgery**: Dr Conesa and Dr Villalba collaborate with Dr Cardis on the Mobi-kids study.
- **Department of Epileptology**: Dr Rocamora and Dr Vivanco collaborate with Dr Cardis on the Mobi-kids study.
- **Department of General Surgery**: Dr. Grande collaborates with Dr Cardis on the Mobi-kids study.

INSTITUTIONAL COLLABORATIONS

JOINT RESEARCH NETWORK IN EPIDEMIOLOGY AND PUBLIC HEALTH (CIBERESP)

CREAL is part of CIBERESP (http://www.ciberesp.es/), the Spanish Network for Epidemiology and Public Health Research. Two CREAL research groups led by Dr. Jordi Sunyer and Dr. Manolis Kogevinas participate in CIBERESP. In addition, CREAL's director, Josep M Antó has been member of the Permanent Committee of CIBERESP from 2012 to 2013.

Through this partnership, CREAL has received funding seven research contracts. CIBERESP also contributes to the development of two important projects led by CREAL investigators: the INMA project and the MCC-Spain project.

Coordinated by Dr. Jordi Sunyer (CREAL), the **INMA • INfancia y Medio Ambiente [Environment and Childhood] Project** (www.proyectoinma.org) studies the role of environmental pollutants during pregnancy and the early stages of life and their effects on children's growth and development. The INMA Project includes seven mother-child cohorts (n=3,768) distributed throughout Spain (Ribera d'Ebre, Menorca, Granada, Valencia, Sabadell, Asturias, and Gipuzkoa) and involves more than 115 researchers. Thanks to the collaboration between these groups, 208 scientific articles were published between 2001 and 2013. The INMA Project participates in 13 European research projects, and has established 10 collaborations with national and international institutions in the past 2 years.

The **MCC-Spain project** (http://mccspain.org/), coordinated by Dr. Manolis Kogevinas (CREAL) and Dr. Marina Pollán (ISCIII), started in 2008 as an epidemiological case-control study of high incidence tumours in Spain, including breast, colorectal, stomach, and prostate cancers and Chronic Lymphocytic Leukemia (CLL). The project aims to evaluate environmental and genetic factors associated with cancer. Thanks to the efforts of more than 100 researchers, almost 6,100 cancer patients and more than 4,000 controls have been recruited to date at 23 hospitals throughout Spain.

MCC MULTI-CASO CONTROL - SPAIN

AGREEMENT BETWEEN CREAL AND THE MINISTRY OF HEALTH AND SOCIAL POLICY AND THE NUCLEAR SAFETY COUNCIL (CSN) TO STUDY MEDICAL DIAGNOSTIC EXPOSURE IN CHILDREN AND TEENAGERS.

This cooperative agreement, signed by the CSN and CREAL in October 2011, falls within the EU-Euratom-funded EPI-CT project (Epidemiological Study to Quantify Risks of Paediatric Computerized Tomography and to Optimize Doses), whose aim is study the potential direct health risks of exposure to low or moderate doses of diagnostic radiation in childhood and adolescents. The goal is to establish a cohort of approximately one million paediatric patients from all over Europe, 200,000 of which are to be recruited in Spain. One of the goals of the project is to disseminate the results of the EPI-CT project, which will have a significant impact on public health.

CATALAN INSTITUTE OF ONCOLOGY (ICO)

The agreement between CREAL and ICO regulates our collaboration in research on lymphoma and coordination between professionals from both institutions for the joint implementation of epidemiological tools in the analysis of lymphoma, as well as in the specific project, “Research on infection, cancer and the environment”. It also regulates the stay at CREAL of Dr Silvia Sanjosé, a renowned researcher in cancer epidemiology.

ISGLOBAL

BARCELONA CENTRE FOR INTERNATIONAL HEALTH RESEARCH (CRESIB) AND BARCELONA INSTITUTE FOR GLOBAL HEALTH (ISGLOBAL)

CREAL and CRESIB are research centres with complementary approaches to health challenges. Both centres have shown outstanding results since their establishment in 2005 and 2006, respectively, and despite being relatively new are both internationally recognized leaders in their fields. In addition, CRESIB and CREAL have developed an extensive network of collaborations and research platforms in Europe and the developing world. Research platforms such as the birth cohort networks coordinated by CREAL and the long-standing collaborations in Mozambique, Morocco and Bolivia established by CRESIB are unique assets for the development of research into Global Health.

In addition, the **Barcelona Institute for Global Health** (ISGlobal), a public-private partnership that builds on the existing research, training and health activities of CRESIB, extends the knowledge value chain of health research via three areas of activity: (i) a think tank that bridges the gap between research and public health policies through interdisciplinary analysis and debate; (ii) a training and education centre that provides high-quality programmes and trains future global health leaders; and (iii) a technical assistance unit that promotes equitable and effective health policies and programmes that are informed by scientific evidence and knowledge. Together with health research, these three areas of activity form a virtuous cycle that increases the impact of research on society.

While CREAL, CRESIB and ISGlobal have proven their capacity to compete with first-class centres, this increasingly competitive scenario calls for an increase in critical mass. The economic crisis also highlighted the need for a concentration and prioritization of the Catalan science and technology landscape. Moreover, achieving critical mass in Global Health strengthens Catalonia's capacity as a global leader in the health and biotechnology sectors. CREAL, CRESIB and ISGlobal have a unique opportunity to establish Barcelona as a world-class cluster for research, education and innovation in Global Health, and to become a leading player in this field.

Starting in 2011, CREAL, CRESIB and ISGlobal initiated the process of working towards an alliance. The proposed alliance is the first phase of a roadmap whose *ultimate goal is to establish a world-class research and translation centre in Global Health* with sufficient critical mass to play a leading role internationally in tackling global health problems, including infectious and non-communicable chronic diseases, with a strong focus on their environmental determinants. At the end of the two-year period covered by this proposal, the Boards of the three institutes will evaluate the opportunity and feasibility of a merger based on:

- The degree of accomplishment of the objectives set out in this proposal
- The availability of a common space to accommodate all of the staff and activities of the resulting institution

ISGLOBAL

ISGLOBAL ALLIANCE'S MAIN ACTIVITIES DURING 2012-2013

SUMA1 AND SUMA2 FUNDING CALLS

In April 2012, the CERCA institute, a Catalan organization that supports and encompasses major research centres in Catalonia, published the SUMA call for funding integration and merging, or alliance-partnership proposals among centres aiming to achieve a critical mass and increase the competitiveness of their research. The call was structured in two stages, the first requiring an initial proposal, and if approved, a second requiring a detailed executive project stating objectives, timeline and budget.

The ISGlobal Alliance project was approved, and has the following main objectives:

- Objective 1: Build a cohesive, efficient and sustainable coordination structure linking CREAL, CRESIB and ISGLOBAL.
- Objective 2: Develop a joint-research strategy with a portfolio that includes communicable diseases, non-communicable chronic diseases and their environmental determinants.
- Objective 3: Reinforce the translation of knowledge into innovative public health policies and interventions, and influence the Global Health agenda.
- Objective 4: Develop a high-quality postgraduate and continuing education strategy in Global and Environmental Health by coordinating current initiatives and developing new programmes.

In 2013, a second SUMA call was published and the ISGlobal Alliance was again funded with €200,000 to its work toward integration.

1ST CREAL-CRESIB-ISGLOBAL JOINT RETREAT, 3 OCTOBER 2012, CASA DEL MAR, BARCELONA.

Since the beginning of 2012, researchers and other professionals from the three centres have been carrying out the important joint task of identifying and defining main areas of common research interests, as well as management issues (in terms of research, administration, human resources, communication systems, etc.). This work was integrated in a joint retreat held on 3 October 2012. This retreat was divided into two parts, with a gathering in the morning of all research and management staff from the three research centres, in which they presented the different areas of research of each centre, and the objectives of the project submitted to the SUMA research funding call. In the afternoon, a meeting was held of working groups established on the basis of the objectives of the ISGlobal Alliance proposal, which, under the co-coordination of a representative from each centre, worked specifically on the definition of the activities to be undertaken during the following months and years.

INTERNAL PILOT PROJECTS

The goal of funding internal pilot projects is to promote collaborative research and enable investigators to seek external funding to pursue larger-scale collaborative projects in research areas of strategic relevance to ACCIS Global. Eight proposals were received and evaluated by external reviewers, and the following three projects were funded:

- C Menendez (CRESIB) - J Sunyer (CREAL). Assessment of exposure to air pollutants in pregnant women from southern Mozambique and its potential impact on respiratory health.
- A Picado (CRESIB) - M Nieuwenhuijsen (CREAL). Biosensors to quantify insecticide exposure in humans and insecticide concentration in treated materials.
- C Dobaño (CRESIB) - M Kogevinas (CREAL). The etiological role of infection with *Plasmodium falciparum*, Epstein Bar Virus, HIV and environmental exposures on endemic Burkitt's lymphoma.

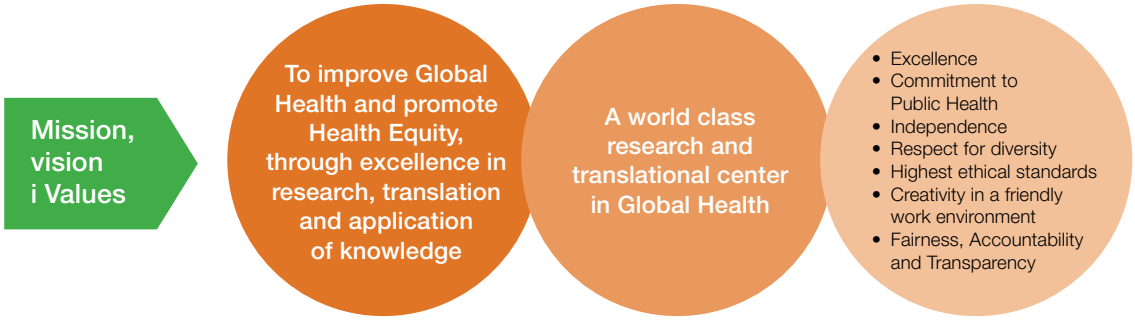
ISGLOBAL

ISGLOBAL ALLIANCE'S MAIN ACTIVITIES DURING 2012-2013

STRATEGIC PLAN

In October 2013 the development of a Strategic Plan was started, with the objective of laying the foundation for the future organization, with appreciation and integration of the different viewpoints, and addressing the cultural and human dimensions of the process.

Since then the plan has been developed and reviewed by the various actors of the centre as well as the presidents of the External Advisory Councils. This Plan will be submitted to the various Boards for approval during the last meeting of 2014.



ACCIS GLOBAL HEALTH LECTURES

Within the framework of the ACCIS Global Alliance, and within the joint research and translation program, the organisation of Conferences on Global Health is ongoing, with the aim of bringing together in Barcelona the world's leading researchers in global health to share their research with the ACCIS-Global community and with other researchers.

Preventing global non-communicable diseases through low carbon development
1st Global Health Conference
20 March 2013, PRBB Auditorium

Professor Neil Pearce, director of the "Centre for Global Non-communicable Disease, London School of Hygiene and Tropical Medicine, London, UK", gave a presentation entitled "Preventing global non-communicable diseases through low carbon development".

Genetics and Global Health
2nd Global Health Conference
8 May 2013, CEK Auditorium

Professor Dyann Wirth, co-director of the Infectious Disease Initiative at the Department of Immunology and Infectious Diseases, Harvard School of Public Health, and director of the Harvard Malaria Initiative at Harvard School of Public Health, gave a session on Genetics and Global Health.

THE CREAL PHD PROGRAM

THE CREAL PHD PROGRAM

Doctoral training is one of our main strategies for promoting a new generation of talented and innovative researchers in environmental epidemiology and the development of innovative research findings in ongoing large funded projects.

In January 2013, CREAL approved a formal policy regarding education and supervision of PhD students. The CREAL PhD Guidebook was developed with the participation of all PhD students, who reviewed and made contributions to the guidebook's structure and contents. The final document provides students with an overview of the organizational specifics of their pre-doctoral training at CREAL and informs them of their position, rights and obligations.

CREAL participates in the Public Health and Education in Health Sciences program of the PhD Program in Biomedicine organized by the Department of Experimental and Health Sciences of the University Pompeu Fabra, which has been verified by the Spanish Agency for the Evaluation, Quality and Accreditation (ANECA).

During 2012-2013, 24 PhD students have been developing their research at CREAL under the UPF PhD Program in Biomedicine; 8 of them were awarded a UPF PhD degree.

ADRIANA MARCELA RIVERA

Atherosclerosis and Air Pollution: understanding traffic-related exposure and its effects
Universitat Pompeu Fabra
Director: Nino Künzli / Codirector: Xavier Basagaña
Year: 2012

JOAN FORNS

Maternal and child mental development and mental health
Universitat Pompeu Fabra
Director: Jordi Sunyer
Year: 2012

TALITA DUARTE

Estimación de la exposición prenatal a contaminantes a través de la dieta y sus efectos sobre el desarrollo y la salud infantil
Universitat Pompeu Fabra
Director: Michelle Mendez /Codirector: Jordi Sunyer
Year: 2012

MARIA CONCEPCIÓN RUIZ CASTELL

Environmental contamination and infant development in a Bolivian mining city
Universitat Pompeu Fabra
Director: Jordi Sunyer
Year: 2012

TEACHING ACTIVITIES

THE CREAL PHD PROGRAM

LIDIA CASAS
Indoor pollution and childhood development
Universitat Pompeu Fabra
Director: Jordi Sunyer
Year: 2013

DAVID ROJAS
Transportion, air pollution and physical activities; an integrated health risk assessment progamme of climate change and urban policies
Universitat Pompeu Fabra
Director: Mark Nieuwenhuijsen
Year: 2013

ELENI PAPADOPOULOU
Maternal diet and occurrence of adverse reproductive outcomes in newborns (NewGeneris) including anogenital distance in the Rhea cohort
Universitat Pompeu Fabra
Director: Manolis Kogevinas
Year: 2013

MARIA FORASTER
Efectes a llarg termini de la contaminació atmosfèrica i del soroll sobre l'aterosclerosi
Universitat Pompeu Fabra
Director: Nino Künzli
Year: 2013

The CREAL PhD program also includes other national and international collaborations. CREAL researchers are thesis directors of PhDs conducted in other universities in Europe and United States.

EDUCATION AND TRAINING ACTIVITIES

EDUCATION AND TRAINING ACTIVITIES

Advanced education and training, both at undergraduate and postgraduate level, is a core activity at CREAL. The main activity is developed with the University Pompeu Fabra.

The most remarkable fact during the period has been the recognition of CREAL as a University of Pompeu Fabra (UPF) attached research university institute in April 2013, consolidating the historic relationship between both organizations. The agreement signed by CREAL and UPF establishes a collaboration framework that will allow CREAL to further develop the educational program at the centre.

Four CREAL researches are professors at the Department of Experimental and Health Sciences at Pompeu Fabra University. Josep M Antó and Jordi Sunyer are full professors and Judith Garcia-Aymerich and Martine Vrijheid are associate professors.

In addition, Josep M Antó is vice-director of the CEXS and a member of the Planning Council for Medical Studies at UPF and at the Autonomous University of Barcelona (UAB).

CREAL is deeply involved in the official Masters program in Public Health, and also participates in the Masters in Clinical Research - Respiratory Medicine Track (Interuniversity Masters' Degree co-directed by UPF and University of Barcelona) and the Masters Degree in Omics Analysis (Interuniversity Masters' Degree co-directed by UPF and University of Vic).

CREAL researchers also develop their educational activities in other universities. Cristina Villanueva and Juan R González are adjunct professors at the Autonomous University of Barcelona. We participate in several masters programs: Masters in Global Health, UB and IS-Global; Inter-university Masters Degree in Statistics and Operations Research, UPC and UB; Masters in Bioinformatics for Genomic and Drug Design, UAB; MPH Public Health, National School of Public Health, Athens, Greece.

OTHER NOTABLE INTERNATIONAL TRAINING INITIATIVES DURING **2012-2013** HAVE BEEN:

EEPE - EUROPEAN EDUCATIONAL PROGRAM IN EPIDEMIOLOGY FLORENCE (http://www.eepe.org/). The EEPE is a 5-day residential course under the patronage of the International Epidemiological Association, the WHO Centre for Environment and Health and the Italian Association of Epidemiology. The course provides intensive training of epidemiological topics. Several CREAL researchers participate and attendance at this course is part of the PhD and postdoctoral programs at CREAL.

ERACOL (http://www.erasmus-columbus.eu/about/). The Erasmus Columbus is a project for academic mobility scholarships in thematic fields related to Health and Public Health. ERACOL is an EU-funded joint initiative 6 of Latin American universities (Colombia, Panama and Costa Rica) and 5 European universities (The Netherlands, Sweden, Belgium, Italy and Spain), with several associated members, CREAL among them.

LIST OF SEMINARS

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LIST OF SEMINARS 2012

13/01/2012	**Dora Romaguera**	Imperial College London	Healthy lifestyle and cancer risk: results of the EPIC study
17/01/2012	**Prof. Neil Pearce**	London School of Hygiene and Tropical Medicine	Epidermiology in changing world
20/01/2012	**Juan Ramón González**	CREAL	Modelling count data in genetic and epidemiological studies
27/01/2012	**Jordi Julvez**	CREAL	Organochlorines, Thyroid Functions and Neurodevelopment
03/02/2012	**Alicia Borràs**	CREAL	Increased prevalence of respiratory symphtoms among children exposed to dampness and mould at scholl
10/02/2012	**Maria Antonia Ramon**	Hospital Vall d'Hebrón - CREAL	Effect of hospitalization on exercise capacity in patients with chronic obstructive pulmonary disease
17/02/2012	**Nicole Le Moual**	CREAL	Occupational exposure to cleaning products and asthma
24/02/2012	**Josep Maria Antó**	CREAL	MeDALL aproach to allergic disease
02/03/2012	**Anna Schembari**	CREAL	Air pollution and pregnant women
09/03/2012	**Xavi Querol**	ID/EA-CSIC	From ultrafine to coarse PM in Barcelona
16/03/2012	**Prof. Mauricio Barreto**	Institute of Collective Healh - Federal University of Bahia, Brazil	Understanding the high prevalence of asthma in Latin America
23/03/2012	**Audrey de Nazelle**	CREAL	A study of physical activity and air pollution exposure during travel using smart phone technology
28/03/2012	**Bruna Galobardes**	School of Social and Community Medicine, University of Bristol	Inequialities in height in high income countries: still existing today?
30/03/2012	**Chealsea Eastman**	CREAL	Respiratory health of workers on large-scale dairies in California
20/04/2012	**Oliver Robinson**	Dept. of Epidemiology and Biostatistics, School of Public Health, Imperial College London	Hirmi Valley Liver Disease: A novel disease associated with co-exposure to DDT and pyrrolizidine alkaloids in Nothern Ethipioa JOINT SEMINAR of CREAL and CRESIB
27/04/2014	**Ricard Marcos**	Universitat Auntònoma de Barcelona	Biomonitoring of human populations exposed to arsenic
02/05/2012	**Dr. Antonio Gasparrini**	Departament of Medical Statistics - London School of Hygiene and Tropical Medicine	Modeling of time dependencies in associations between health effects and protracted exposures
04/05/2012	**Delphine Casabonne**	Institut Català d'Oncologia	Infectious agents and monoclonal B-cell lymphocytosis (MBL) in healthy adults

LIST OF SEMINARS

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11/05/2012	**Orianne Dumas**	Centre de recherche en Epidémiologie et Santé des Populations, Inserm, Université Paris Sud	Quantification and control for healthy worker effect in asthma using marginal structural models: results from the EGEA study
18/05/2012	**Thomas Cole-Hunter**	CREAL	Effects of Air Pollution Exposure on Adult Bicycle Commuters: An Investigation of Perceptions, Symptoms and Risk Management
25/05/2012	**Patrick Levallois**	Département de médecine sociale et préventive, Faculté de médecine, Université Laval, Québec	Contribution of drinking water, house dust and paint to blood lead levels of young children in Montreal (Canada)
01/06/2012	**Elena Gimeno Santos**	CREAL	Preliminary validation of 2 PRO of physical activity in COPD patients (PROactive project)
05/06/2012	**James Grellier**	CREAL	Healyh Impact Assessment - ELF and chilhood leukemia in Europe
15/06/2012	**Lidia Casas**	CREAL	Early life exposures to home dampness, pet ownerships and farm animal contact, and neuropsychological development in 4 year old children: a prospective birth cohort study
22/06/2012	**Kyriaki Papantoniou**	CREAL	Night shift work, biomakers of circadian disruption and breast cancer risk
29/06/2012	**Maribel Casas - Dania Valvi**	CREAL	The BPA debate - first INMA results on exposure, predictors, and child health effects
17/07/2012	**Cristina O'Callaghan**	CRESIB	Epidemiology of viral respiratoty infections among paediatric patients in Manhiça, a rural area of Mozambique
14/09/2012	**Bruce Blumberg**	University of California, Irvine	Obesogens, Stem Cells and Maternal Programming of Obesity
21/09/2012	**Silvia Sanjosé**	Institut Català d'Oncologia - CREAL	Cervical cancer prevention: Recommendations and realities
28/09/2012	**Michael Friger**	Ben-Gurion University of the Negev, Beer-Sheva, Israel	Health Environmental Effects and Ways to Approach Them: Methodology and applications
05/10/2012	**Julian Marshall**	University of Minnesota	Air pollution kills! So what? Air quality Enginnering to Improve Public Health
19/10/2012	**Mariona Pinart**	CREAL	Co-occurence of IgE-mediated classical phenotypes in children: a MeDALL study
18/01/2013	**Washington Junger**	CREAL	Air pollution in Brazil: a very brief overview
01/02/2013	**Eva Morales**	CREAL	Epigenetics in birth cohort studies: looking for DNA clues on our responsibility towards future generations

LIST OF SEMINARS 2013

08/02/2013	**Jaime Mendiola**	Department of Health and Social Sciences. University of Murcia School of Medicine	Anogenital distance and reproductive characteristics in healthy young women and men
15/02/2013	**Marianella Farré**	Institut de Diagnosi Ambiental i Estudis de l'Aigua (IDAEA) - CSIC	Determination of glyphosate in groundwater in Catalunya
22/02/2013	**Jordi Julvez**	CREAL	Genetic predisposition to cognitive deficit at age 8 years associated with prenatal methymercury exposure
01/03/2013	**Alba Vilajeliu**	Servei de Medicina Preventiva i Epidemiologia de l'Hospital Clínic de Barcelona	Polio: the last 1%
08/03/2013	**Hernando del Portillo**	CRESIB	Plasmodium vivax malaria: from host-parasite interactions, to antigen discovery, to vaccine development
15/03/2013	**Maribel Casas / Mireia Gascon**	CREAL	Persistent organic pollutants and child health - two CHICOS initiatives
22/03/2013	**Javier Vila**	CREAL	Development of a job-exposure matrix (JEM) to describe pesticide exposure in Spanish workers (1996-2005)
14/04/2013	**Lucas Salas**	CREAL	LINE-1 methylation, lifetime trihalomethane exposure from drinking water and bladder cancer risk
19/04/2013	**Francesc Magrinyà**	UPC - Infraestructura Transport i Territori	Environmental health as a driver of change towards sustainable mobility
30/04/2013	**Tim**	Hasselt University, Centre for Environmental Sciences, Belgium	Population susceptibility towards air pollution
10/05/2013	**Jordi Vila**	CRESIB	Antimicrobial resistance: A global threat
17/05/2013	**Francine Kauffmann**	INSERM/CREAL	Genes x Occupational exposures Interactions in Asthma (IAGO)
25/05/2013	**Cathyrn**	London School of Hygiene and Tropical Medicine	Traffic related air pollution and health in London
31/05/2013	**Marcella Marinelli**	CREAL	Television viewing and sleep duration in children
07/06/2013	**Radim J. Sram**	Institute of Experimental Medicine AS CR, Prague, Czech Republic	The effects of air pollution on children health in Czech Republic
14/06/2013	**Mary Ann Pentz**	Institute for Health Promotion and Disease Prevention Research, Division of Healh Behavior, University of Southern California	Smart Growth as A Community Built Environment Intervention for Physical Activity and Obesity Prevention: The Healthy PLACES Trial

LIST OF SEMINARS

LIST OF SEMINARS 2013

21/06/2013	**Nadine Kubesch**	CREAL	TAPAS experimental study: Respiratory and inflammatory health effects of air pollution and physical activity
28/06/2013	**Benedicte Jacquemin**	CREAL	Impact of the geocoding technique on the associations between long-term exposure to urban air pollution and lung function
13/09/2013	**Noemie Travier i Antonio Agudo**	ICO	Participation, adherence and weight loss: results of a feasibility study involving a diet and physical activity intervention in breast cancer survivors
20/09/2013	**Malcom Sim**	Monash Centre for Occupational & Environmental Health (MonCOEH)	Occupational cohort studies - the Australian experience
27/09/2013	**Nadia Vilahur**	CREAL	Prenatal exposure to xenoestrogens, health effects in children and possible epigenetic mechanisms
04/10/2013	**Luis Pérez-Jurado**	Genetic Unit, Universitat Pompeu Fabra (UPF)	Human genome inversions, evolution and disease susceptibility
11/10/2013	**Quim Gascon**	CRESIB	Chagas: a negleted disease
18/10/2013	**Payam Dadvand**	CREAL	Residential Proximity to Major Roads and Term Low Birth Weight: A Bird's-eye View Over the Roles of Air Pollution, Heat, Noise, and Road-adjacent Trees
25/10/2013	**Benedicte Jacquemin & Xavier Basagaña**	CREAL	Short-term Effects of PM Constituents on health (MED-PARTICLES Project)
08/11/2013	**Jet Smit**	University Medical Center Utrecht	Early prediction of asthma in children: added value of the MeDALL birth cohorts?

COMMUNICATION AND PUBLIC DISSEMINATION

COMMUNICATION AND PUBLIC DISSEMINATION

PUBLIC COMMUNICATIONS AND OUTREACH

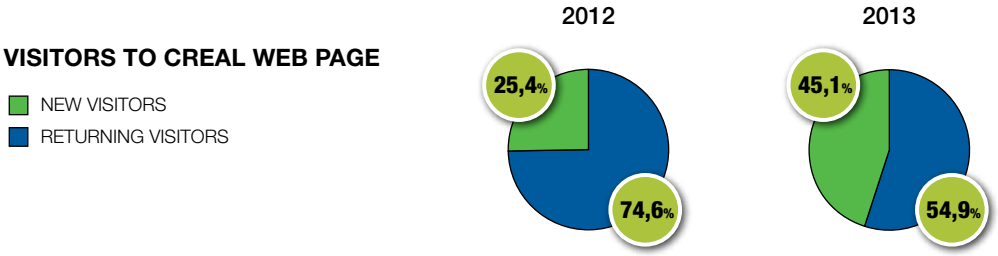
The CREAL Communications Department publicizes the conclusions of CREAL's scientific articles and research in general, not only to bring science closer to the citizens but also to enrich their knowledge and empowerment to improve their health according to public health aims.

MEDIA IMPACT

In 2012-2013 CREAL continued to receive important coverage in local, national and international media. During both years, our activities appeared more than 800 times in the form of news articles, interviews and in-depth reports. CREAL researchers also wrote feature articles about their research or were consulted as experts mostly in air pollution, cancer, respiratory illnesses, water pollution and radiation.

	2012	2013
Press Releases	7	7
Articles in the Press	60	47
Online News	417	153
Audio Pieces	10	14
Videos	15	20
TOTAL IMPACTS	510	231

VISITORS TO CREAL WEB PAGE



PRESS RELEASES PUBLISHED IN 2012

23/01: The MeDALL program to abate allergies on track after first year
08/03: Excessive cured meat consumption increases risk of hospital readmissions for COPD patients
02/05: CRG and CREAL identify genes involved in cranium size and childhood obesity
18/06: Respiratory problems among Prestige clean-up workers persist after 5 years
31/08: Green spaces surrounding maternal residence have beneficial impacts on foetal growth
23/10: Mothers with high dietary intake of acrylamide during pregnancy have babies with lower birth weight
20/11: Dioxins in pregnancy may affect the reproductive system of male infants

PRESS RELEASES PUBLISHED IN 2013

06/02: Maternal Exposure to Outdoor Air Pollution Associated with Low Birth Weights Worldwide
28/05: Supporting a collaborative European child cohort to benefit child health
10/07: European study finds that long-term exposure even to low levels of air pollution increases risk of lung cancer
05/09: CREAL participates in the 'Quit smoking with Barça' campaign
15/10: Large European study finds that exposure even to low levels of air pollution during pregnancy increases risk of lower birthweight babies
30/10: Cities with more green areas benefit the physical and mental health of the population
09/12: Air pollution kills well below European Union air quality limits

PRESS RELEASES PUBLISHED (2012-2013)

Tendències

La contaminació provoca càncer de pulmó

L'OMS demana reforçar les mesures contra la pol·lució

Trànsit lluny d'avis i nens

Nens de poble, nens de ciutat

Només un 19% dels infants catalans viuen en entorns rurals

Contaminats 'in utero'

TEMES DE DEBAT

Respirar (bé) a la ciutat

Contaminació i malalties

Barcelona, aire i salut

Study links air pollution and traffic with low birthweight

For every increase of 5 micrograms per cubic metre in exposure during pregnancy, risk of low birthweight rises by 18%

medi salud

LA VANGUARDIA

Cuando los pulmones se obstruyen

sociedad

Europa enferma por contaminación

COMMUNICATION AND PUBLIC DIFFUSION

OUTREACH ACTIVITIES

School Visits. CREAL organizes school visits for students to improve their knowledge of science and especially environmental epidemiology. We receive a visit per month approximately.

Participation in the PRBB Science Open Day. Every research centre in the PRBB is involved in this event, whose aim is to explain our research and the most important current scientific issues.

Participation in the Catalan Science Week.

Participation in 'Research in Live' Fair 2012 celebrated in La Pedrera and focused in informing young people about research carried out in Catalan research centres.

FUNDING EVOLUTION

FUNDING EVOLUTION

In 2013 the percentage of external funding was 68% while 32% was funded by CREAL's trustees. Regarding external funding, in 2012 and 2013, CREAL maintained its very successful track record in attracting competitive funding from the European Union (1.7m on 2012 and 2.5m on 2013), with 6 coordinated EU projects. EU funding accounts for 63% of CREALs external funding. At the national level, there was a decrease in funding in 2013. In the near future, we will have to be prepared for the gap in European funding between FP7 and H2020.

FUNDING								
	2006	2007	2008	2009	2010	2011	2012	2013
Generalitat	1,000,000.00	1,550,000.00	1,700,000.00	1,700,000.00	1,435,033.36	1,535,000.00	1.527.800	1.569.600
PS Mar	353,191.00	353,191.00	353,191.00	353,191.00	353,191.00	317,622.99	306.944	332.969,89
UPF	42,408.00	42,408.00	42,408.00	42,408.00	42,408.00	50,338.18	50.338	52.578
External	1,169.25	94,385.23	263,675.89	1,485,077.21	2,109,697.61	2,792,426.74	3.593.028	4.031.732
Total	1,396,768.25	2,039,984.23	2,359,274.89	3,580,676.21	3,940,329.97	4,695,387.91	5.478.110	5.986.880
	2006	2007	2008	2009	2010	2011	2012	2013
Trustees	1,395,599	1,945,599	2,095,599	2,095,599	1,830,632	1,902,961	1.885.082	1.955.048
External income	1,169	94,385	263,676	1,485,077	2,109,698	2,792,427	3.593.028	4.031.732
Total	1,396,768	2,039,984	2,359,275	3,580,676	3,940,330	4,695,388	5.478.110	5.986.880

EXTERNAL FUNDING					
	2009	2010	2011	2012	2013
FIS	214,878	308,094	467,234	736.367,58	612.164,25
MINECO	25,670	101,831	274,360	253.758,85	282.619,71
Pla Nacional	26,300	128,771	86,175	37.464,41	4.468,60
Marató TV3	19,010	93,625	128,602	79.438,98	45.590,31
AGAUR	-	-	60,521	32.695,39	54.355,41
Recercaixa	633,371	790,827	1,167,120	1.771.822,35	2.545.518,67
European Union	477,579	505,501	406,883	446.826,89	167.638,38
Out of European Union	88,270	181,048	201,531	234.653,40	319.377,06
Non competitives	1,485,077	2,109,698	2,792,427	3.593.027,85	4.031.732,39

EXTERNAL FUNDING					
	2009	2010	2011	2012	2013
National Projects	285,857	632,321	1,016,893	1.139.725,21	999.198,28
International Projects	1,110,960	1,296,329	1,574,003	2.218.649,24	2.713.157,05

centre for research
in environmental
epidemiology

CREAL
REPORT
2012-2013

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