EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

EUROCORES Programme
European Collaborative Research

Genomic research in Early life: Gene-environment Analyses in epidemiological cohorts (OMEGA)

DRAFT Call for Outline Proposals

What is EUROCORES?

The ESF European Collaborative Research (EUROCORES) Programmes offer a flexible framework for researchers in Europe to work on questions which are best addressed in large-scale collaborative research programmes.

The EUROCORES Programmes allow excellent researchers in the various participating countries to collaborate in research projects 'at the bench'. They also allow, when appropriate, colleagues in non-European countries, for example the US, to participate. The Programmes encourage and anticipate networking and collaboration between researchers in order to achieve synthesis of scientific results across the programme, to connect with related programmes, and to disseminate findings.

The EUROCORES Programmes allow national research funding organisations in Europe and beyond to support top-class research in and across all scientific areas, by matching their strategic priorities with the needs articulated by the scientific community.

Final funding decisions on the projects and the research funding remain with the national funding organisations, based on a single international peer review process operated by ESF. Financed by the participating national Funding Organisations, ESF also provides support for networking between the researchers and for the scientific synthesis of research results and their dissemination. In this way, the EUROCORES Scheme complements the EC Framework Programme and other collaborative funding schemes at European level.

For further information see:
http://www.esf.org/eurocores

Genomic research in Early life: Gene-environment Analyses in epidemiological cohorts (OMEGA)

Following agreement with XX funding organisations in *Country A, Country B, Country C, Country D, Country E, Country F, Country G, Country H, Country I, Country J, Country K, Country L, Country M, Country N, Country O and Country P* the European Science Foundation is launching a Call for Outline Proposals for Collaborative Research Projects (CRPs) to be undertaken within the EUROCORES Programme OMEGA. The Programme aims to support high quality multidisciplinary collaborative research in Europe, with involvement of leading scientists from outside Europe, when appropriate.

The research phase of OMEGA will run for three years [1] and includes national research funding as well as support for networking and dissemination activities. The research grants are provided directly to the eligible and successful Principal Investigators by their respective national funding organisations. The networking and dissemination support, also financed by the national organisations, is centrally managed by the ESF.

Outline Proposals are to be submitted by xth February 2011. It is expected that Full Proposals will be invited by xth March 2011 with xx May 2011 as expected deadline for submission.

A Programme-specific website can be consulted for the latest updates at **http://www.esf.org/omega**

Background and objectives

The past decade has seen major progress in the discovery of genes involved in common complex diseases and their determinants (e.g., diabetes, circulating lipid levels, blood pressure), which has provided important new insights in the aetiology and architecture of these complex traits. The EUROCORES Programme "Genomic research in Early life: Gene-environment Analyses in epidemiological cohorts (OMEGA)" is needed and timely for four reasons: 1) early life course outcome research has been neglected while these outcomes are major determinants of adult diseases (e.g., coronary heart disease, stroke, insulin resistance, type II diabetes, dyslipidemia, hypertension, obesity, neurological and mental illness); 2) identified variants explain only a small proportion of the heritability, thus requesting further research using new molecular approaches; 3) studies targeting early life are crucial to unravel the genetic origin of major disease determinants as they are unbiased by pathology and medication; and 4) the European long-term follow-up studies of pregnancy, birth and adolescence need to be used for further gene discovery and translational studies into clinical care and public health.

[1] The formal duration of EUROCORES programmes is three years; however, individual researchers will apply to the national or other funding organisations under their respective rules, which may allow for more than three years' funding. No networking and coordination support will be available outside the formal duration of the programme.

Scientific goals

The **general objectives** of the OMEGA EUROCORES Programme are to:

1) Facilitate and perform joint genomic studies on multiple phenotypes during fetal life, childhood and adolescence;
2) Facilitate and develop studies translating the findings into clinical care and public health.

The OMEGA **specific aims** are the following:

1) Perform cutting-edge genomic analyses to unravel the genetic architecture and mechanisms underlying various phenotypes in fetal life, childhood and adolescence through the application of new -omics technology including:
- biobanking DNA, RNA, cells and other tissue for current and future -omics research;
- enriching populations with state-of-the-art -omics technology;
- evaluating parent of origin effects for various outcomes in nuclear families;
- studying epigenetic effects including methylation, acetylation and phosphorylation and their relation to outcomes relevant to development, health and disease;
- discovering inherited and novel copy number variants and other structural variations and their relation to development, health and disease;
- examining gene-interactions in large and well characterized clinical and epidemiological studies;
- unravelling the function of genetic variants.

2) Translate findings of genomic studies into clinical practice and health care. This includes:
- evaluating the joint effects of genes identified in adult cohorts on phenotypes in fetal life, childhood and adolescence;
- examining the genes identified in early life on development and risks of disease late in life;
- studying the joint effect of genes, life events, environmental, social and economic factors on personal development, disease and health;
- translating the genomic findings (early/late) into clinical and psychosocial care and prevention.

OMEGA will apply innovative molecular genetic techniques in large European cohorts well characterized for diseases and outcomes related to health and personal development early or late in life, building up from current European projects (e.g., Biobanking and Biomolecular Resources Research Infrastructure, CHICOS, EAGLE, ENGAGE, CHARGE, EUROSPAN).

The **three-year milestones** of OMEGA are the following:
1) Identification of new genetic variants and their joint effect with other genetic, parental and environmental factors on a large number of phenotypes relevant for personal development, health, and the risk of future disease;
2) Identification of biological pathways relevant for personal development, health and disease in early and late life;
3) Determination of risk profiles determining development, health and risk of diseases in early and late life based on genetic, parental and environmental risk factors.

Scope

The scope of OMEGA goes beyond that of health and disease. The relation between socioeconomic status and health and disease has been long recognized. OMEGA aims to act as an inter-disciplinary **bridge between clinical research, epidemiology, sociology and economics**. There is increasing interest in the impact of early life events, nutrition, life style, family structure, divorce and economical factors on health and disease. Genes and biological pathways may determine these socio-economic outcomes. The influence of genetic and post-translational modifications on these outcomes has been neglected in the era of genomic research. Genetic factors and epigenetics may have (in) direct effects on socio-economical outcomes such as education, entrepreneurship, social mobility, substance abuse and crime through cognitive function, personality, anxiety, and behaviour. Genetics factors may further interact with major life events such as death of a parent or other relatives, child abuse, malnutrition, obesity and may to a large extent determine coping strategies of the individual to deal with these situations. Finally, life events such as child abuse, (parental) stress or substance abuse, food and emotional deprivation may determine epigenetics including methylation, acetylation and phosphorylation.

Research topics

OMEGA should be open to all outcomes in childhood with the following **main priorities** of research:
1) Early growth focussing on birth weight and height, gestational age, body mass index and puberty, both cross-sectional and longitudinal across childhood;
2) Cardiovascular risk factors including blood pressure, lipids and other relevant biomarkers;
3) Asthma and related respiratory outcomes, eczema and atopy;
4) Type 1 diabetes and other auto-immune disorders;
5) Behaviour, cognition and personality;
6) Brain development and febrile seizures;
7) Bone and body composition.
8) Personal social and economical development such as education, labour market performance, social mobility, family formation, divorce and crime.

To address the objectives outlined above OMEGA will focus on the following **topics**:

(i). Take the new -omics techniques to the next dimension by studying multiple outcomes in clinical and epidemiological studies.
(ii). Unravel the genetic origin of personal development, health and disease.
(iii). Improve the understanding of the determinants of personal development, health and disease in early life.
(iv). Determine profiles for development, health and disease in early or late life.

(i). Take the new -omics techniques to the next dimension by studying multiple outcomes in clinical and epidemiological studies.

Combining new high throughput genomic techniques in well characterized epidemiological cohorts has proven to be a very powerful, successful and efficient approach in genome wide association studies (time and money wise). In OMEGA, the view is to apply new -omics techniques in the same way in cohorts focussing on early life. To facilitate current and future -omics research, collecting and biobanking of additional DNA, RNA, cells, or other tissues in deeply phenotyped populations is part of the mission of OMEGA as well as the necessary preparations and work-up of raw material (blood and cell lines) for research, e.g., through the isolation of DNA and RNA. For discovery, OMEGA aims to enrich early life cohorts (parents and offspring) by additional genotyping of targeted regions or pathways or by whole genome approaches using array technology. Molecular, statistical and bioinformatical projects focusing on new -omics technology such as next generation sequencing of DNA and RNA are a further area of focus of OMEGA along with research of classical biomarkers and new technological -omics approaches such as lipidomics, metabolomics and proteomics.

(ii). Unravel the genetic origin of personal development, health and disease.

Despite the major progress in the past decades, our understanding of the genetic origin of diseases in early and late life is extremely limited. It will be crucial to improve the understanding of human physiology and the pathogenic processes underlying disease as well as other outcomes. The OMEGA cohorts offer the possibility to link state-of-the-art -omics research to multiple outcomes and determinants. Children have often been studied along with their parents, offering a unique opportunity for molecular and statistical research evaluating parent of origin effects. These effects may be of genetic origin but also environmental (e.g., diet, smoking, alcohol and medication use during pregnancy or early life) and socio-economical (e.g., related to education, social or economical status and psychological factors of parents). Family-based studies are also a powerful vehicle for molecular and statistical studies targeting inherited and novel rare variants and structural variations and relate these to various outcomes of interest. Embedding epigenetic studies in OMEGA will make it possible to examine the relation of structural variants and epigenetic effects to various health outcomes, environmental and socio-economic factors simultaneously.

(iii). Improve the understanding of the determinants of personal development, health and disease in early life.

This will be enabled by studying the joint effects of genes along with environmental and parental effects in large and well defined clinical and epidemiological cohorts. The availability of high-quality and detailed environmental and socio-enomical data is a limiting factor in the current studies of gene-interactions. Molecular, statistical and bioinformatical research projects on gene-interactions in well characterized clinical and epidemiological studies offer the opportunity of highly powerful multicenter studies. Enrichment of populations with data of molecular, environmental or socio-economical origin is part of the scope of OMEGA. Also within the scope of OMEGA are molecular, statistical and bioinformatics projects aiming to unravel the function of genetic variants and the encoded proteins from a molecular perspective (uncovering the biological and physiological function of genes, genetic variants and proteins) as well as a clinical perspective (uncovering the relation of genetic variants, RNA/protein regulation and epigenetic effects in relation to risks of various diseases).

(iv). Determine profiles for development, health and disease in early or late life.

The translation of -omics research to public health and clinical practice is one of the main challenges in the post-human genome era. One of the missions of OMEGA is to evaluate the joint effects of gene, environmental and socio-economical factors on risks of disease early and late in life. This is only possible in the EU through joint studies in large clinical and epidemiological cohorts which are well characterized for disease-related outcomes, environmental and socio-economic factors. A key question to be tackled is whether risks of disease in genetically determined high risk groups may be modified by intervention (pharmaceutical or life style). Finally, one of the missions of OMEGA is to use approaches developed in public health and clinical decision making to develop strategies for the translation of the genomic findings (early/late) into clinical care and early prevention.

Guidelines for applications

(Outline and Full Proposals)

This Call for Proposals is for Outline Proposals for Collaborative Research Projects (CRPs). Proposers should be individual scientists (or research groups represented by individual scientists) who are eligible for funding from a national funding organisation participating in the EUROCORES Programme OMEGA.

Scientists or groups not applying for or not eligible to apply for funding from such an organisation can be associated to a proposal when their scientific added value can be demonstrated. Participation of AssociateD Partners in a project must be fully self-supporting and will not be financially sponsored by the participating funding organisations.

Proposals are only eligible if they fulfil all of the following **criteria**:

- Proposals must involve, as a minimum, three eligible Principle Investigators (PIs) from **three different countries.**
- A maximum of 50% of the total number of Individual Projects (IPs) in a Collaborative Research Project (CRP) can come from one country.
- Proposals must involve more PIs than Associated Partners (APs).

Applications should envisage three years of research. Taking into account the two-stage proposal selection and approval process (described below), the successful projects are expected to begin their research phase activities during **March - June 2012**.

Online submission of applications

Outline and Full Proposals will be submitted online. Applicants should follow the proposal structure as indicated in the application template for Outline Proposals available on the Programme website at: **http://www.esf.org/omega**

Links to information on national funding eligibility and requirements as well as to a EUROCORES Glossary and Frequently Asked Questions (FAQs) are available on the Programme website.

Prior to submitting Outline Proposals, all applicants must contact their national funding organisations in order to verify eligibility and to ensure compliance with their national grant requirements and regulations. The list of participating organisations and their nominated contact persons is included on the last page of this document.

At the time of the online submission of the Outline Proposal, the Project Leader will be asked to confirm on behalf of the consortium that all the Principal Investigators in the CRP have consulted their national funding organisations and are eligible for funding from these organisations.

Outline Proposals

Outline Proposals are invited by xth February 2011.

Outline Proposals will be examined by the participating funding organisations for formal eligibility. Therefore, it is crucial that all applicants requesting funding contact their national funding organisation prior to submitting their proposals.
In compliance with the rules and regulations of the participating national funding organisations, the requested funds under the EUROCORES Programme OMEGA may include salaries for scientific and technical staff, equipment, travel costs and consumables within the project. The amounts requested from each funding organisation participating in the call must be clearly specified. National policies may also require the proposal to contain specific additional information. Applicants should be aware that the participating funding organisations can make adjustments to the requested funds in order to bring these in line with their normal grant regulations and standards.

As described below, applications will be reviewed according to specific assessment criteria in a two-stage procedure. The goal is to select scientifically excellent proposals which fit well within the scope of the programme and have significant potential to add value to its achievements.

At the outline stage, the Review Panel will select proposals based on the following criteria:

- Relevance to the Call for Proposals
- Novelty and originality
- European added value (scientific)
- Qualifications of the applicants

An Outline Proposal must comprise:

- A short description of the CRP (max. 1200 words, including objectives, milestones, methodologies (e.g., experiments and fieldwork);
  - Short description of how (and why) the partners contributing to the CRP will work together and how their contributions will be integrated;
- Short CVs of Project Leader (PL), all PIs and Associate Partners, including five most relevant publications (max. one page each);
- Estimated budget (consistent with the rules of relevant national funding organisation), tabulated according to a provided template.

Associated Partners (APs) are also considered part of a CRP and will be assessed as such at both the Outline and Full Proposal stage.

It will be assumed that arrangements for the handling of Intellectual Property Rights (IPR) will be in place within projects, following the applicable national legislation and national funding organisation's regulations. Applicants are strongly urged to have such arrangements in place, covering all research groups (including any associated groups) before the start of the projects. It is expected that the results obtained by the projects supported under this EUROCORES Programme will be placed in the public domain, through standard scientific dissemination activities.
It is also expected that compliance with all other relevant national or international regulations on research (for example ethics) will have been affirmed before funding is granted. It is the responsibility of applicants to clarify any such matters (if applicable) with their national contact points.

Full Proposals

Full Proposals will be invited following the recommendations of the Review Panel. The deadline for Full Proposals will be announced later, but is expected to be around xxth May, 2011.

Please note that only applicants who have submitted an Outline Proposal can submit a Full Proposal.

For the Full Collaborative Research Project (CRP) Proposals, the most important selection criterion is "scientific quality". Other criteria include interdisciplinarity (according to the scope of the call), qualifications of the applicants, level of integration and collaboration, feasibility and appropriateness of methodologies, European added value, relation to other projects (complementarities versus risk of overlaps and double-funding) and suitability of the requested budget.

The Full Proposals will be assessed by at least three independent external expert referees selected by the ESF. The expert referees are selected from a pool of scientists suggested by the participating funding organisations, the Review Panel and the ESF office. The names of all referees used in the international peer review of EUROCORES programmes, together with the names of those who have contributed to the peer review process in other ESF instruments, will be published on the ESF website once in a given year.
The referee reports will be made available (anonymously) to the applicants for their information and if necessary for their comments and clarifications. The Review Panel will rank all Full Proposals based on the assessment of the Full Proposal, the anonymous referee reports and the applicant's responses to these.
The Review Panel will create a rank-ordered list of the strongest Full Proposals and will subsequently make recommendations to the Management Committee for the funding of these proposals. The Management Committee assigned to each programme comprises representatives of all the participating funding organisations.

The actual granting of the funds to the Individual Projects will be based on the Review Panel's ranked list. The funding cut-off will be determined based on the total amount of funds available in each participating Funding Organisation and how the Individual Projects figure on the list. The use of funds in a project will be subject to the national requirements and regulations of each participating Funding Organisation.

Full proposals must include sound and well-argued scientific cases both at the level of the consortium's collective objectives and in terms of the expected contributions of each of the Individual Projects in the consortium. Full Proposals must also include a list of all participants and their contact information and shorts CVs, detailed tabulated budgets for the whole CRP and for each project within it. Full Proposals could include other necessary

supporting information. A coherent and common scientific case must be made throughout the proposal to demonstrate a collective and collaborative aim and for scientific synergy and integration of multinational expertise. In addition, the amount requested from each national funding organisation has to be clearly and separately specified. Detailed instructions on requirements and how to complete the application forms will be made available when inviting Full Proposals.

The **Project Leader** (PL) will be the main point of contact between the ESF and the CRP for the whole duration of the project. He/she will be responsible for the flow of information and communication between the ESF and all the participants in the CRP. The PL will represent the Collaborative Research Project in relation to its participation in programme activities and for the fulfilment of reporting requirements for the CRP as a whole and for the contributions of the individual Principal Investigators in the CRP.

In addition to their normal scientific and collaborative activities within the CRP, all **Principal Investigators** will be responsible for dealing with the requirements concerning the contributions of their national funding organisation, and for supporting the Project Leader in the overall progress of the CRP, including organising and participating in networking activities and in the fulfilment of reporting requirements.

Programme Structure and Management

Programme Structure

The overall responsibility for the governance of each individual EUROCORES programme lies with a *Management Committee*, whose members include one representative from each participating funding organisation in the programme (usually a senior science manager), together with an ESF representative.

Proposal assessment and selection are the responsibility of an international, independent *Review Panel*. The members of this panel are leading scientists, appointed by the ESF following suggestions from participating Funding Organisations. The membership of the Review Panel will be available on the Programme website for information. The Review Panel is also expected to monitor the overall scientific progress of the programme.

The Scientific Committee is formed by the Project Leaders of all funded CRPs and will be responsible for the overall scientific progress of the programme, including for the preparation of a work plan for the overall programme activities, including networking and dissemination. The Scientific Committee will also advise and support the EUROCORES Programme Coordinator in the coordination of the programme.

Programme Networking

Networking activities are designed to strengthen the scientific objectives of the EUROCORES Programme by promoting coherence and synergy in the activities of the scientific community involved. This will help to produce the European added value which is a main objective of all EUROCORES Programmes.

Networking and collaboration within EUROCORES Programmes take place at two levels:

1. Between the various Individual Projects within each Collaborative Research Project (CRP) (intra-CRP activities), and;
2. Between the funded CRPs in the programme (cross-CRP activities).

The intra-CRP activities must be supported through the individual research grants the participants receive from the national funding organisations in the given CRP.

The cross-CRP activities are centrally funded by the ESF through contributions from the participating organisations to the EUROCORES Programme.

The intra-CRP collaboration is motivated by the nature of the CRP's research objectives, i.e. by the scope and the complexity of the questions it deals with. In a CRP, the participating groups have the opportunity to gather the required critical mass to successfully address the objectives and challenges of their project.

The cross-CRP networking and collaboration is inspired by the aims and the nature of the EUROCORES Programme as a whole. The themes of EUROCORES Programmes are selected because they demonstrate a clear need for collaboration in the proposed field. The funded CRPs will collectively establish and streamline this new collaboration. To this end, the CRPs will

engage the programme participants and, when of clear benefit, colleagues from outside the programme in joint activities such as:

- Programme-wide meetings or conferences;
- Working group meetings for the exchange of information and results across the CRPs;
- Joint scientific meetings or summer schools;
- Short term visits;
- Development and delivery of joint training programmes;
- Seminars, workshops, symposia, invited sessions either stand-alone or as part of other larger events;
- Common web-facilities and publications.

Through active participation of scientists in the above mentioned activities, not only can existing collaborations be enhanced, but new and strategic partnership opportunities may also be identified.

Furthermore, these activities may provide opportunities to explore aspects of the programme which are not covered by the funded research projects.

The integrating activities between the CRPs should help to strengthen the field by building coherence within the existing and emerging research communities and will serve as platforms for the dissemination and outreach of the research conducted in the programme.

Project members are expected to participate annually in at least one cross-CRP activity.

When submitting your proposal, please note that the costs for networking within your CRP should be included in your proposal as part of the costs of meetings, travel and subsistence. Funds for networking between the CRPs will be centrally managed by the ESF through contributions from the participating funding organisations.

Programme evaluation

A mid-term evaluation involving the Review Panel will assess the overall progress of the Programme. The Review Panel may also comment on the CRPs' work plan in relation to the objectives of the overall Programme. A final evaluation at the end of the Programme will assess the overall achievements of the whole EUROCORES Programme.

Contacts in the participating organisations

As it is currently not known which Funding Organisations will support this programme, please contact your National Funding Organisation or Research Council to inquire about this programme.

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[1] The European Science Foundation (ESF) provides a platform for its Member Organisations to advance European research and explore new directions for research at the European level.
Established in 1974 as an independent non-governmental organisation, the ESF currently serves 79 Member Organisations across 30 countries.