



STIFTELSEN för  
STRATEGISK FORSKNING

## **Announcement**

### **The Swedish Foundation for Strategic Research (SSF)**

**announces a**

**call for proposals in the areas of**

***Design, development and validation of new predictive models and new biomarkers necessary for development of new drugs***

***Parasite resistant trees and crop plants***

***Epigenetic mechanisms in disease***

***New antimicrobial agents - the role of innate immunity***

The Swedish Foundation for Strategic Research announces a total of SEK 400 million (SEK 80 million per year during five years) in a national call for proposals for problem- or application-driven research projects of the highest international scientific standard with the aim of stimulating interdisciplinary research collaboration in the four above-mentioned areas of strategic relevance for the Swedish biopharmaceutical and forest/ plant breeding industry. The four areas are further defined and discussed below.

Selected research projects will be supported by framework grants ("rambidrag") in the range of SEK 4 - 7 million per year (incl. overhead and VAT) to be used for salaries, supplies etc. according to the needs of the projects over a period of five years. Funding during the two last years will be dependent upon a successful mid-term evaluation.

## **Design, development and validation of new predictive models and new biomarkers necessary for development of new drugs**

### *Background*

The greatest challenge in today's pharmaceutical research is the selection, with precision at an early stage in the developmental process, of new safe and efficient drug candidates acting on biological mechanisms central for disease. A solution would be to have truly predictive models for safety and efficacy evaluation, encompassing *in vivo* models (mouse, rat, higher vertebrates, lower model organisms), *in vitro* models (differentiated stem cells and advanced cell culture systems) and *in silico* models (computer-based models, including "knowledge management"). The predictive models must be based on extensive molecular knowledge concerning human diseases. This requires close collaboration between groups carrying out experimental studies on human tissue and groups generating and optimising the models.

Furthermore, the models must be validated with respect to their predictivity for safety and efficacy in humans in clinical practice. This requires development of analytical methods using different molecular biomarkers where effect in model and in humans can be compared. It is important that the models represent the specific parameter measured in the clinical trials and that the model be validated with respect to the expected clinical effect.

### *Aim*

This initiative aims to stimulate and strengthen interdisciplinary collaborative research with the ultimate objective of developing and validating new predictive methodology in model systems and in humans, or new biomarkers for safety or efficacy evaluation. The collaborative research projects should cover several aspects from *design* (such as human molecular pathology, pathophysiological mechanisms, experimental biology), through *development* (such as *in vivo*, *in vitro* or *in silico* models, computational biology, imaging, biochemistry, analytical methods) to *validation* (such as experimental and clinical pharmacology). Examples of important tools for the predictivity models are PET, MRI and optical imaging methods.

The projects should be based on a clinical problem and focused towards a demonstrator (diagnostics or therapy), and at least one of the applicants must have clinical expertise and experience.

### *Importance for industry and society*

Predictivity of safety and predictivity of efficacy have been identified as two principal research bottlenecks in the biopharmaceutical research and development process by Swedish pharmaceutical companies as well as by European pharmaceutical industry. The area is thus of strategic relevance for the pharmaceutical, biotech and medtech industry and the impacts of this research on industry and society at large are anticipated to be of great future value. Further, a large EU initiative, *Innovative Medicines Initiative Joint Undertaking (IMI JU: [www.imi-europa.eu](http://www.imi-europa.eu))*, has been launched with Calls for Proposals. The SSF programme might increase the chances that Swedish groups can participate in consortia applying for these grants.



## **Parasite resistant trees and crop plants**

### *Background*

Forest trees and crop plants represent large economic values to Swedish industry. Different parasites, both fungal, viral, bacterial as well as insects, pose a severe threat to crop yield and quality. Furthermore, changes in environmental conditions, e.g. a warmer climate and/or frequent storms, could lead to the parasites becoming more destructive than presently.

Most pesticides used for controlling different parasites are not compatible with sustainable tree or crop plant production. Thus, there is a need for increased knowledge of resistance/tolerance mechanisms and for new efficient control methods.

However, in order to find an efficient disease management strategy it is necessary to find out more about not only resistance/tolerance mechanisms in the host, but also the physiology and population dynamics of the parasite.

Resistance or tolerance to parasites in trees and crop plants involves many different types of mechanisms. Physiological traits, such as a thick cortex or different cell wall components, can constitute an effective first barrier to parasites. Different metabolic pathways, including production of defence-related molecules, constitute further barriers.

Forest tree breeding is traditionally based on quantitative genetics. For modern tree or crop plant breeding, molecular biology methods and DNA-based markers have become increasingly important. Therefore, successful breeding of stress-tolerant trees and crop plants must today involve a combination of classical genetics, molecular biology and plant physiology.

### *Aim*

This initiative aims to stimulate and strengthen interdisciplinary collaborative research leading to a better understanding of resistance/tolerance mechanisms in forest trees and crop plants. The ultimate objective is to apply the knowledge obtained in resistance breeding programs and to develop new and environmentally sustainable methods to control different parasites.

The collaborative research should consider both host and parasite aspects. Furthermore, the research should involve classical genetics as well as modern molecular biology and plant physiology.

### *Importance for industry and society*

Since trees and crop plants are of great importance for Swedish industry, it is vital to be able to control the different parasites that pose severe threats to yield and quality. A better understanding of resistance/tolerance mechanisms can lead to new and more environmentally friendly control methods, of benefit to public health.

Cultivation, use and processing of trees and different crop plants for purposes other than wood production or human consumption (e.g. for energy production) is already increasing in importance and will continue to do so in the future. It is anticipated that demand to find a more climate friendly lifestyle will exert further pressure on the development of stress-tolerant trees and crop plants in combination with suitable parasite control methods.



## **Epigenetic mechanisms in disease**

### *Background*

Epigenetics can be defined as studies of such hereditary changes in gene expression that are not caused by changes in the DNA sequence. Epigenetic changes can influence the regulation of gene activity in response to intracellular as well as extracellular signals such as hormones, diet or environmental factors.

Epigenetic mediators regulate cellular functions such as the stability of the genome, inactivation of the X-chromosome and gene imprinting. Hitherto identified mechanisms are DNA methylation, modification of histones, and changes in stability and translation of mRNA by modulation of polysome functions and chromatin structures through noncoding RNA (RNAi).

Epigenetic processes are important for a large number of biological phenomena including a number of diseases, such as cancer, lifestyle diseases and age-related diseases. Epigenetic impact in early human development (including before conception) can give rise to diseases later in life by permanently changing the body's metabolic programming and thereby increasing the risk of chronic diseases.

Epigenetic mechanisms may be as important for the manifestation of disease as mutations or other gene changes. Examples also exist of diseases (e.g. Rett's syndrome) which develop slowly as a combined effect of a mutation and epigenetic mechanisms.

### *Aim*

This initiative aims to stimulate and strengthen interdisciplinary collaborative research leading to a better understanding of how epigenetic mechanisms are involved in disease with the ultimate objective of predicting, preventing or treating diseases.

Projects with clinical or methodological links or a clear focus on applications in these areas will be given priority.

### *Importance for industry and society*

Epigenetics is a rapidly expanding research field with strategic relevance for the biopharmaceutical industry. The impacts of this research on industry and society at large are anticipated to be found in drug development and clinical diagnostics. The potential for drug development based on new knowledge in this field should be great.



## **New antimicrobial agents – the role of innate immunity**

### *Background*

Our defence against invading pathogens is the result of an intricate interaction between the innate and the adaptive immune system. In response to microbial products, several families of pattern-recognition receptors initiate intracellular signalling events, such as transmembrane receptors on the plasma membrane, in endosomal compartments or DNA/RNA sensing proteins in the cytoplasm. Such signalling ultimately leads to complex host immune responses designed to eliminate invading pathogens.

The innate immune system is the first line of defence and also has several functions in the orchestration of the immune system in inducing an adaptive response.

Increased efficiency of the innate immune system is desirable for fighting infections and cancer. In other diseases, such as autoimmune diseases, the innate immune system is in itself considered to have a role in pathogenesis, and here it should rather be desirable to limit the effects of innate immunity.

In both cases, an increased understanding of the innate immune system and its interaction with the adaptive system is important for an understanding of disease processes and how the innate immune system can be used actively in the treatment of disease.

### *Aim*

This initiative aims to stimulate and strengthen interdisciplinary collaborative research leading to a better understanding of how the innate immune system fights infectious diseases with the ultimate objective of preventing such diseases or treating them with new types of antimicrobial therapy focused on the innate immune system.

### *Importance for industry and society*

Multiresistant infections are a great economic problem in today's society. New types of antimicrobial therapy are urgently needed. Innate immunity is an emerging field of research with strategic relevance for the pharmaceutical industry. The impacts of this research on industry and society at large are expected to be great, since an understanding of the mechanisms of innate immunity has implications for the development of immunotherapies and vaccine adjuvants. The potential for drug development based on new knowledge in this field should thus be great.



### **Priorities according to strategic relevance**

The objective of the Foundation for Strategic Research is to support research in order to strengthen Sweden's future competitiveness. When the priority research areas supported by different research funding organisations are compared, the areas supported by the Foundation are positioned between those supported by the Swedish Research Council and those supported by VINNOVA, as shown in the diagram below. The Foundation interprets "strategic relevance" by giving a number of examples where research can be of use\*. The practical definition of strategic relevance, which will be used in the process of selection of applications, is that proposals should have a clear potential for exploitation in Sweden within a time span of 5 – 15 years after termination of the research project. Furthermore, applications assessed as being better able to contribute to Sweden's future competitiveness will be given higher priority.

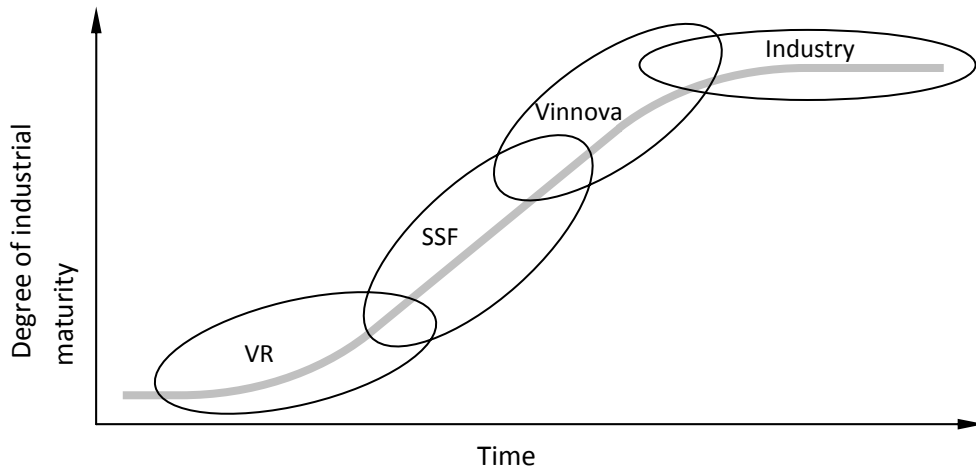


Fig 1. The areas of priority of Swedish research funding organisations

\* The Foundation's policy documents define use as consisting of:

- the ability of internationally high-class research settings to attract unique competence and international investment into the country
- people with graduate educations who through their broadened and enhanced research training are attractive for employment, primarily in industry and society but also in the universities and colleges
- research the results of which can serve as a basis for the development of existing enterprises or the founding of new ones
- improved quality of life through new job opportunities, better working conditions and better health
- research that is a focus for international cooperation, through which knowledge that is of interest to Swedish industry can be gathered.'

**Eligibility**

Applications should be submitted by the scientific coordinator of the proposed research project (the main applicant), who must be a prominent scientist prepared to assume scientific responsibility for the project for the duration of the grant period. The main applicant must be affiliated with either a university/university college or a public or private non-profit research institute. At least one of the applicants must work at a university/university college. Each scientist can submit only one application as a main applicant in this call.

All proposed projects should be based on reliable interdisciplinary collaboration between at least two, preferably three research groups with different types of relevant complementary scientific expertise, or proposed by one large interdisciplinary group which in itself contains the relevant complementary competence. Selected research projects will be supported by five-year framework grants in the range of SEK 2 - 3 million per year (incl. overhead and VAT) for each group in the project. The total grant amount for one project encompassing 2 - 3 collaborating research groups (or one interdisciplinary group) will be in the range of SEK 4 - 7 million per year. Funding during the two last years will be dependent upon a successful mid-term evaluation.

A maximum of 50% of the grant may be used for salary for the main applicant and/or the co-applicants, but only to cover up to a maximum of 50 % of the salary of each applicant.

The Foundation does not require any co-funding.

The following two paragraphs apply specifically to the area ***Design, development and validation of new predictive models and new biomarkers necessary for development of new drugs:***

The projects should be based on a clinical problem focused towards a demonstrator (diagnostics or therapy), and at least one of the applicants must have clinical expertise and experience.

Industrial representatives should preferably participate in the collaboration and contribute to fulfilment of the goals of the application which in turn should contribute to further development of the company. Furthermore, public authorities and organisations are preferably seen as collaborating partners. However, none of the collaborating partners mentioned here will be funded by the grant.

**Selection and decision procedure**

The applications will be reviewed using the following criteria:

- Scientific originality, strengths, weaknesses, interdisciplinarity, and feasibility of the research plan
  - Quality of the applicants' previous scientific accomplishments, international experience, and networks
  - Strategic relevance to Swedish industry and/or society and importance of the proposed research
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The application process takes place in a two-step procedure. One Evaluation Committee for each area, including scientific experts from academia and industry in the Nordic countries, will perform a first selection where pre-proposals are assessed with respect to what extent they are in line with the announcement, their strategic relevance and the choice of research problems. Applicants of selected pre-proposals will be invited to submit full proposals which will be evaluated by international scientific experts.

The results of the scientific evaluations and the assessments of the strategic value of the projects will be taken into account by the Evaluation Committees in arriving at a final recommendation to the Governing Board of the Foundation, which will make the final granting decision during 2009.

### ***Instructions for application and submission***

The pre-proposals must be written in English and submitted via the electronic application system of the Foundation at <http://apply.stratresearch.se> which will open on 12 October for this call. The applications must be submitted by no later than 4 **pm on 12 January 2009**. They should include a preliminary research plan, final objective, collaborating research groups and their scientific competence, the strategic relevance for Sweden of the project and a budget plan. Detailed instructions for the application will be available on the electronic portal.

The full proposals (probably requested to May-June 2009) will include:

- a description of the research project (including the expertise of the applicants, and a plan for how the suggested constellation will work in an effective way and who will be responsible for different parts of the project)
- a clear description of the strategic relevance for Sweden of the proposed project (including a preliminary plan for future exploitation, 10-15 years from now, of the research results)
- a budget plan (containing information about the actual work that the applicants intend to do in the project).

No additional material submitted after the deadline will be considered.

Please also note that the Foundation is subject to the principle of public access to official records (*Offentlighetsprincipen*). Avoid submitting information on details that could prevent patenting.

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