FreeNovation – A funding program of the Novartis Research Foundation

FreeNovation 2022: Can your project idea change biomedical research?

- Regulation of mitochondrial function
- Pre-symptomatic detection of metabolic diseases
- Immune memory of tissues

Submit your application by 16th April 2022!

Exploring New Avenues in Research Funding

Many scientific breakthroughs have occurred not because success was predictable, but thanks to the pioneering spirit of people who gave free rein to their creativity. But there is little room for free creativity and bold, untried ideas these days. This is why the Novartis Research Foundation *(Novartis Forschungsstiftung)* promotes offbeat project proposals with its FreeNovation program. It calls on researchers in Switzerland to submit proposals that are hard to fund by conventional programs.

This kind of research funding by a Swiss foundation is unique in the field of life sciences in Switzerland. With this program, the Novartis Research Foundation wants to encourage unconventional thinking and further enhance the attractiveness of Switzerland as a research location.

An opportunity for people and ideas

Researchers with a doctorate or equivalent that are engaged at a Swiss institute, university, university hospital, or university of applied sciences are eligible to apply. The projects will be selected by a top-class review panel under the leadership of Prof. em. Gerd Folkers, ETH Zürich, Chairman of the Board of the Novartis Research Foundation.

To ensure that both unusual ideas as well as younger scientists without a research track-record have a place in this funding program, the selection process is anonymized: What counts is the originality of the research approach and its potential to achieve something new. Ideas that involve interdisciplinary research are encouraged. Results from preliminary studies are not a prerequisite. Scientific risk-taking is encouraged.

The results of the funded projects shall be published and made available to the public without patent protection. FreeNovation is all about exploring new avenues, venturing into new dimensions, and further strengthening Switzerland's research landscape.

For the 2022 call for proposals, the Novartis Research Foundation is making available up to a total of CHF 2.7 million for a maximum of 15 projects. Each project can be funded with up to CHF 180,000. This will allow the researchers to pursue their objectives over a period of 18 months.

Guidelines for Applicants and the link to submit proposal are available on www.freenovation.ch

Regulation of mitochondrial function

Mitochondria generate most of the chemical energy needed to power the cell's biochemical reactions. The number of mitochondrial organelles in cell types correlates with the amount of energy required for the cells to function, e.g., muscle and liver cells have a high number of mitochondria whereas mature red blood cells have no mitochondria. In addition to the role of a powerhouse, mitochondria are also important for many ubiquitous cellular processes like signalling, differentiation, growth, and death. Mitochondria dysfunction can affect almost any part of the body and can contribute to a variety of diseases, such as ALS, heart failure and Parkinson's disease. How can we validate a role for mitochondria dysfunction in complex diseases and identify the molecular mechanisms involved?

Mitochondria activity can be measured in vitro, including production of ATP or of reactive oxygen species. How can we measure mitochondria function or dysfunction *in vivo* and in tissues? Can we exploit these readouts as biomarkers for diseases? Moreover, how can we gain a better understanding of the dynamic regulation of mitochondria's proteome and functionalities in specific cells and tissues?

Mitochondria interact with other organelles, including the endoplasmic reticulum. They undergo dynamic fusion and fission, and defective mitochondria are selectively degraded by mitophagy. Upon damage or stress, danger-associated molecular markers such as mitochondrial DNA may be released leading to sterile activation of innate immunity. Can we expand our understanding of these pathways to generate novel therapeutic opportunities?

Pre-symptomatic detection of metabolic diseases

Atherosclerosis, diabetes, kidney and liver failure: These and many other diseases occur as a result of metabolic disorders and have long been among the leading causes of death. Epidemiological studies indicate that genetic factors, diet and other lifestyle factors are significantly involved. But the interrelationships are exceedingly complex and the molecular processes only partially understood. Hormones, micro-RNAs, oxidative stress, epigenetic regulation, etc. are just a few keywords in this context. But how exactly does it work? What is a trigger and what is "just" a biomarker? And which measurable biomarkers allow reliable diagnoses and prognoses? How do metabolic diseases manifest themselves in children or in women and men as they get older?

"Omics" technologies of all kinds provide data on single cells, tissues and the whole organism. How can the data be integrated into an overall view? What new hypotheses can be generated? Can they be validated in the context of metabolic processes? Which controversial findings should be rigorously tested for once - and what would be the consequences if they were not correct?

An individual, pre-symptomatic diagnosis would allow personalized pharmacologic treatment or lifestyle modifications when it is most effective and complications can still be prevented. We would like to be warned before sugar levels are high and beta cells are already damaged. What research idea do you have that could lead to detecting a metabolic disease at an early stage, i.e. before clinical symptoms appear?

Immune memory of tissues

In addition to specialized immune cells, non-immune cells in tissues also contribute to protective responses against pathogens. Consequently, tissue cells may also play a role in the pathogenesis of inflammatory disorders. Immunological memory refers to the ability of our body to respond faster and effectively to previously encountered antigens. As a hallmark of adaptive immunity, immune memory was initially attributed to the rapid clonal expansion of T and B lymphocytes bearing genetically encoded antigen-specific receptors. However, it is now understood that memory responses may also rely on non-genetic mechanisms, not only to T and B cells. For example, the concept of trained immunity via epigenetic reprogramming of innate immune cells in response to infection or vaccination has recently been established. Tissues seem to have an immunological memory as well. This may explain why psoriatic skin lesions may reappear at the exact same site of a previous lesion after stopping effective therapies. Even brain cells can store immune-related information and influence peripheral immune responses remotely. What mechanisms, epigenetic, metabolic or other, underlie this phenomenon of immune memory? What role do tissue metabolites or environmental cues play? Does something like a “molecular scar” exist, i.e. a local signature of tissue memory? If so, how may it be encoded and in which cells? To understand this better, we need an integrated, system-level view of the interplay between immune and non-immune cells and the alterations that occur between acute and chronic stages of diseases. What original ideas do you have to get to the bottom of these questions?