How to address the high-risk / high-gain balance according to the funder's objectives – case ERC

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ERC objectives

Main aim is to advance research, beyond the scope of the project

In particular, the ERC encourages proposals of

- Proposals introducing unconventional, innovative approaches and scientific inventions (***Novelty***)
- Pioneering proposals addressing new and emerging fields of research (**New Horizons**)
- A **multi- or interdisciplinary nature** which crosses the boundaries between different fields of research

Novelty

- Novel approach such as:
  - Strategy
  - Methodology
- Novel idea such as:
  - Invention
  - Concept

Novel: new, inventive, recent, revised, adapted?

'…proposals introducing unconventional, innovative approaches and scientific inventions'.

Opening new horizons

- Academic impact: addressing a need in research community
- Beyond scope of the project proposal (containing a show case)
- New and emerging fields of research (long term impact)
  - New => ”unchartered” ?
  - Emerging => ”potential recognised” ?
- Be specific about what and how
- Bonus: impact beyond academic research (not all panels)

”... pioneering proposals addressing new and emerging fields of research” (New Horizons)

Multi- and interdiciplinary nature

‘ERC encourages proposals of a multi- or interdisciplinary nature which cross the boundaries between different fields of research’

‘Multidisciplinarity *draws on knowledge from different disciplines but stays within their boundaries.* ***Interdisciplinarity*** *analyzes, synthesizes and harmonizes links between disciplines into a coordinated and coherent whole.* ***Transdisciplinarity*** *integrates the natural, social and health sciences in a humanities context, and transcends their traditional boundaries’* (Pak and Choi: Clin Invest Med. 2006 Dec;29(6):351-64.)

On the level of knowledge, methodology, impact

Exercise

- Choose 1-2 of the abstracts in the handout to read
- Discuss in groups (15 mins)

1) Which one was funded?
2) Why was it better?
3) Mark where the succesfull meets the objectives

- Pioneering proposals addressing new and emerging fields of research or (**New Horizons**)
- Proposals introducing unconventional, innovative approaches and scientific inventions (***Novelty***)
- A multi- or interdisciplinary nature which cross the boundaries between different fields of research

CASE 1 VERSION 1: ACRONYM seeks to solve does ancestral exposure to various stressors transmit to offspring via epigenetic mechanisms. Thus far animal models have indicated that exposure to certain stressors can lead to phenotypic changes not only in the predisposed individuals, but also in the future generations, such that individuals can acquire phenotypes caused by exposures of their ancestors. Such effects do not involve new DNA mutations, but are transmitted to offspring via epigenetic mechanisms such as the transfer of non-coding RNA molecules in the semen. In humans, intergenerational transmission has been examined extremely little because a priori designed population-based studies across several generations are lacking. To close this gap ACRONYM will expand the well-characterized study to the parents and offspring of the original YFS participants. During the ERC funding period, we will perform field studies involving N~9000 individuals across 3 generations and test 3 key ancestral exposures with very high plausibility causing intergenerational effects on obesity-related phenotypes, cognitive function and psychological well-being. The studied exposures are 1) tobacco smoke, 2) persistent organic pollutants, and 3) accumulation of psychosocial adversities. We will collect serum, blood and semen samples for epigenetic marker analysis to provide understanding of the mechanisms of intergenerational transmission in humans. Specifically, we will seek proof for the hypothesis that paternal stressors can lead to phenotypic changes in the offspring via non-coding RNA molecules in the semen. Multigenerational epidemiologic data showing robust links between ancestral exposures and offspring phenotypes that operate with biologically plausible epigenetic mechanism would provide a conceptual change in the developmental biology in humans and have substantial ramifications on public health.

CASE 1 VERSION 2: ACRONYM seeks to solve does exposure of persistent organic pollutants (POPs) including pesticides and industrial chemicals. In humans, epidemiologic data indicate that chronic POPs exposure may play a role in the development of type 2 diabetes (T2D) and obesity, but causality remain uncertain. Thus far animal models have indicated that exposure to pollutants can lead to phenotypic changes not only in the predisposed individuals, but also their offspring, such that individuals can acquire phenotypes caused by exposures of their parents. There is particular concern that environmental exposures in childhood may have long-term health effects, as on a per-body-weight basis children are exposed to higher levels of POPs than adults.. At present, however, evidence linking childhood POPs exposure to these adverse adult outcomes is missing. The proposed study, ACRONYM, will address this gap by examining the role of early life POPs exposure in the development of T2D, obesity, and atherosclerosis in adulthood. To this end, ACRONYM will leverage blood specimens, historical and newly collected data in unique existing cohorts that have followed groups of well-phenotyped and genotyped individuals from childhood to mid-adulthood over three decades. Specifically, we will seek proof for the hypothesis that pollutants can lead to phenotypic changes in the offspring via non-coding RNA molecules. Generational epidemiologic data showing robust links between parental exposures and offspring phenotypes would be the first attempt to assess the independent role of childhood POPs exposures in the development of T2D, obesity, and related metabolic disturbances in adulthood. Therefore, the expected societal and scientific impacts may be substantial. If firm evidence supporting causal roles can be established, the study will have ground-breaking public health implications in the development and implementation of long-term international policies and programs aimed at reducing the levels of POPs.

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Case 1: *Novelty* – LS 7 Panel

- PI had the final idea already in first submission year
- Got more confidence from preliminary findings between the proposals
- First version was a small fraction of the idea without the *biologically plausible epigenetic mechanism*
- Version 1: “Overall the project is within the current state of the art, not beyond-in terms of hypotheses,design and methodology”.
- Version 2: ”The proposal is *ground-breaking and provides a singular opportunity to test the impact of intergenerational effects in health.”*

CASE 2 VERSION 1: Scientists have always been particularly intrigued by the extremes in nature and made significant efforts to study these; microscopes allow us to observe the smallest objects, while telescopes permit us to explore the largest objects and also those farthest away. The work proposed herein will provide new means and generate insights to phenomena occurring on the shortest timescales in nature. Past methods to probe ultrafast events – occurring on picosecond timescale or faster – have mostly relied on pump/probe scanning, yet these can only measure the dynamics of such processes if they are repetitive. Visualising all spatiotemporal aspects of ultrafast phenomena, however, requires experimental means to spatially, spectrally and temporally resolve them. Recently the PI invented a “coding” imaging concept called Frequency Recognition Algorithm for Multiple Exposures (FRAME) that can film at up to 5 trillion frames per second. To date, FRAME is the only videography method that can unify a femtosecond temporal resolution with spectroscopic compatibility, making it a powerful tool with high potential for visualising ultra-fast events. This project aims to (i) develop novel tools based on FRAME and (ii) apply FRAME videography to study ultrafast events, which could not be visualized in the past. Ultrafast science is a wide field, making the project highly interdisciplinary. The ensemble of work-packages proposed herein constitutes a significant step forward in the research area of ultrafast imaging and videography.

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Case 2 – New Horizons – PE4 panel

- New technique for coding images
  - FRAME: femtosecond videography for atomic and molecular dynamics: Femtosecond videography
  - *New knowledge* in ultraphast imaging and videography
  - Uncharted field (only single snapshots are possible with other techniques)
  - Principle technique published in September 2017 => not brand new
  - Enabling to study ultrafast events => new horizons
  - Application: lifetime of two fluorophores in paralllel: coherent state and decay
  - New avenues in physics, chemistry and biology

CASE 3 VERSION 1: Writing must rank among mankind's highest achievements. Yet the factors that enabled its invention independently in different parts of the world have never been subject to an analysis that encompasses both deciphered and undeciphered scripts. ACRONYM takes such an approach, combining a study of the world's first instances of writing, including the earliest in Europe, through the lens of archaeology and decipherment strategies. This methodology involves three strands of research. First, it will consider the original inventions, all of which are image-based, from Mesopotamia, Egypt, Mesoamerica and China, and other debated cases. The objective is to characterize their conception in terms of archaeological setting (what are the contextual preconditions, why does writing emerge when it does, and only four times in history?). Second, it will explore the earliest scripts in Europe from the second millennium BC Aegean, whose initial phase is highly iconic. The three undeciphered Aegean scripts (Cretan Hieroglyphic, Linear A and Cypro-Minoan) will be analyzed for the first time from a multistranded perspective that will shed unprecedented light on their creation and development. The objective is to analyze the relationship between these scripts and to apply a multi-stepped (and already successfully piloted) decipherment strategy. Third, ACRONYM proposes to go beyond the traditional standards applied to the corpora of inscriptions by producing the first complete digital corpus of all three Aegean undeciphered scripts, with 3D interactive models accompanied by a multidimensional interface tagging inscriptions, types of inscribed objects, provenance, archaeological contexts and functions.

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Case 3 – Multi- or interdisciplinary nature – SH5 panel

- New approach for deciphering scripts
  - *Three new scripts* – first words deciphered
  - *New decipherement strategy* piloting successful.
  - *New knowledge* visual cognition, archeological setting, application of use, language notation, new scripts
  - Comparing with deciphered European scripts
  - Through lens of archeology, anthropology, cultural evolution, cognitive studies and decipherment strategies
  - Deadline ERC 2017 call in February 2017 - > Grant awarded
  - Crossing boundaries on the level of scripts, disciplinary knowledge, methodologies, new multi-disciplinary research field
  - Enabling to decipher other scripts => New horizons

Panel differences in general

- High gain / high risk balance
- Gap of knowledge versus burning questions / issues
- PI expertise and capacity

Gap of knowledge => feasibility based on PI

Burning questions => feasibility based on PI and preliminary data

How to tackle these issues with your ERC candidates?

- Analyse what is the most obvious panel(s)
- Analyse what kind of research is funded by the primary panel
- Analyse whether the project idea fits the ERC objectives
- Check whether the PI ”profile” matches the ERC objectives
- Check whether the PI profile matches the (core of the) project idea