National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

NC3Rs strategic award: Non-mammalian model systems for asthma research

Call Handbook

Background

Non-mammalian model systems, for example *C. elegans, D. melanogaster,* zebrafish and *Dictyostelium*, offer powerful tools to better understand molecular mechanisms of human health and disease. These models have been employed widely in diverse disease areas including oncology, neurodegenerative disease and ageing. They offer many advantages over more complex vertebrate systems, including genetic amenability, low cost and culture conditions compatible with large scale screens – allowing high-throughput screening in a physiological context.

Despite these advantages, non-mammalian model systems have not, with the exception of a handful of groups, been adopted by the asthma research community. The lack of lungs and adaptive immune systems (*C. elegans* and *D. melanogaster*) are the most commonly cited reasons for overlooking these model organisms for respiratory disease research. However, numerous biological processes and genes are conserved between these model systems and humans. This includes asthma susceptibility genes involved in innate immunity, making these model systems attractive options for studying innate immune responses in isolation of an adaptive immune system. The genetic tractability of these organisms, together with the rapidly increasing number of transgenesis tools available, make them ideal models for understanding the role of individual genes, or gene clusters in a disease pathway, identifying putative candidate genes for further downstream functional analysis in other model systems.

The NC3Rs is supporting the asthma research community through the development of a toolkit of alternative approaches to reduce the use of mammalian model systems. This includes *in vitro* models of asthmatic airways, exploring opportunities for the wider uptake of human tissue, and providing opportunities for asthma researchers to link with mathematicians in applying mathematics to asthma research questions. The current funding call complements this ongoing work and aims to provide the asthma research community with additional innovative tools with which to conduct their research.

The NC3Rs held an initial workshop in collaboration with the British Thoracic Society Difficult Asthma Network in November 2013 to connect experts in non-mammalian model development and asthma researchers from academia and industry, to promote interaction between the two disciplines and cross-fertilisation of novel research ideas. The aim was to build new partnerships and raise awareness of the challenges of asthma research and the power of these alternative model organisms.

Strategic award overview

The present Strategic Award call was launched to support research and development ideas coming from the workshop

This call aims to fund high-quality research proposals, to address genuine asthma research questions through the development and application of non-mammalian model systems, with the aim of:

- Providing more scientifically relevant disease pathways information to better understand the molecular mechanisms of human asthma
- Reducing reliance on mammalian model systems.

Applications focusing on human tissue-based approaches or mathematical *in silico* modelling approaches are outside of the scope of the current call. Applications can include a component of this, but must be focused on developing and applying non-mammalian organisms as models for asthma research.

The NC3Rs Strategic Award Scheme provides funding opportunities in specific research areas identified as being strategically important to the Centre's goal of using the 3Rs to support science, innovation and animal welfare in the biosciences. The Scheme enables the NC3Rs to invest in:

- Research identified as priority areas, either because there are particular concerns about the number or suffering of animals used or a belief that new thinking may reinvigorate 3Rs efforts.
- Technologies that may advance the 3Rs.

Budget

A total budget of £500k is available for this Strategic Award call. Awards will be administered as Pilot Study grants to allow researchers to generate the data necessary to support a larger research application to either the NC3Rs or other funders.

Up to five £100k pilot studies will be awarded for projects up to 12 months in duration.

Application Process

Before completing the proposal form on Je-S , all applicants must submit an outline form to the NC3Rs Office to ensure the project is suitable for the scheme and that the application fits the 3Rs remit (strategicawards@nc3rs.org.uk).

All applications must be submitted via the RCUK joint electronic submission system (Je-S).

More information on the application process and guidance on completing the proposal form on Je-S can be found in the NC3Rs Applicant and Grant Holder Handbook.

Eligibility

- Applications **must** include expertise in both asthma and non-mammalian model development.

- A clear scientific rationale for the proposed work and a description of how it will impact on the 3Rs is essential.

- The scheme is open to any UK research establishment, including Higher Education Institutions, Hospital/NHS trusts, Research Council establishments, Charity laboratories and Industry.

- Applicants must be UK-based researchers who can demonstrate that they will direct the proposed research.

The NC3Rs current research portfolio, detailing all awards including abstracts, is available on the NC3Rs website at www.nc3rs.co.uk/our-science

Timelines

Launch call	30 April 2014
Expression of interest deadline	4 June 2014
Deadline for applications	2 July 2014
Panel meeting	November 2014