WHRF WILLIAM HARVEY RESEARCH FOUNDATION

Research Proposals

Examples of specific projects that need your support.

Funding opportunities!

The William Harvey Research Foundation (WHRF) is a UK registered charity that seed-funds high-risk, early stage research that advances our knowledge of human diseases.

Developing new treatments

In particular drug discovery, to address unmet medical need for people suffering from:

- Heart failure
- Heart disease
- Strokes
- High blood-pressure
- Multiple-organ failure
- Trauma
- Kidney disease
- Vascular dementia
- Arthritis
- Diabetes
- Blindness

These are just a few of the conditions in which we research.

The Foundation supports and conducts this work through its world leading pharmacological research centre, William Harvey Research (WHR), based in the heart of the City of London.

Our approach is exceptional as we invest 100% of all donations to seed-fund this vital new research. In this way, our investment exclusively kick-starts pioneering work from innovative researchers.

Through our work on innovative therapeutic approaches that target urgent, unmet medical needs, WHR is in the vanguard of global medical research.

So, what does all this mean? People often ask us, 'what do you want money *for*, exactly?' Well, here are some examples of specific projects that need your support!

Obesity in Down syndrome

Dr Li Chan, Centre for Endocrinology

The unmet medical need

Down syndrome (DS) is the most common genetic condition: an estimated 220,000 DS babies are born every year worldwide, and in the UK there are around 60,000 people with DS. One of its problematic features is excessive weight gain: 48% of children with DS are obese (compared with 12% of the general population), which leads to severe breathing problems, and increased risk of diabetes, cardiovascular disease, cancer and arthritis. If DS-related obesity could be controlled, the quality of life in DS would be dramatically improved.

WHR's discoveries

DS (also known as trisomy 21) occurs because there is an extra copy of genetic material in one chromosome, number 21. Chan and colleagues at WHRI discovered a gene in a critical region of this chromosome, called MRAP, which increases the amount of cortisol circulating in the blood – and it is known that excess cortisol promotes obesity. A drug which inhibits the actions of MRAP has recently been discovered at WHRI; this could lead to a potential treatment for DS-related obesity.

Next steps – WHR's strategy for therapeutic innovation

- Confirm that the additional copy of MRAP in DS causes obesity.
- Optimise the MRAP antagonist discovered at WHR for use in experimental models.
- Demonstrate that the MRAP antagonist is safe to use.
- Design and initiate clinical trials of the MRAP antagonist in DS.

The ask

£300K to support two scientists, one to work on DS pathology, the other to work on the early stages of drug development. Later stages of drug development will be conducted in partnership with a commercial company.

Help us raise £300K to support this project

A novel therapy to promote longer, healthier life for the ageing

Dr Sian Henson, Centre for Translational Medicine and Therapeutics

The unmet medical need

Ageing is often thought to be inevitable, but some aspects can be reversed, and this could lead to a longer lifespan and a healthier life. As we age, more cells become "senescent": this means they no longer behave like healthy young cells, and these senescent cells can adversely affect the immune system and cause inflammation. Many older people who outwardly appear healthy have damaging levels of inflammation, poor infection control, and lower protection from vaccinations. Such effects, over time, can be profound, resulting in increased hospital admissions and healthcare costs, and a lower quality of life. With the numbers of older people in the population increasing disproportionately, this will put extra strains on the NHS. Because inflammation plays an important role in many age-related diseases (including rheumatoid arthritis and cancer), there is an urgent need to identify novel therapeutics that can counteract this.

WHR discoveries, funded by WHRF

In senescent immune systems, T lymphocytes (a type of white blood cell) contribute significantly to inflammation. We recently identified a new type of senescent T lymphocyte in elderly people which is highly inflammatory and can cause a lot of damage in susceptible organs. With a grant from the WHRF, we showed that senescent T lymphocytes have a unique protein, which changes the "internal wiring" of the cells, making them pro-inflammatory. WHRF then supported further research in which we identified a novel molecule (TAB1β) that targets this protein in senescent lymphocytes. This could form the basis of a new therapeutic approach.

Next steps – WHR's strategy

The Centre for Translational Medicine and Therapeutics has a "bedside to bench and back again" approach to science and drug discovery. With access to state-of-the-art scientific equipment and a clinical trials unit, together with capability for commercialisation, WHR is well placed to explore the therapeutic potential of TAB1β. If successful, this research could help restore function in senescent T lymphocytes.

The ask

£100,000 over three years to fund a PhD studentship, with the following aims.

- Quantify senescent T lymphocytes in the ageing population, including patients with diabetes or cardiovascular disease.
- Compare the invasive potential of normal and senescent T lymphocytes, and assess the inflammatory damage they cause.
- Study the effects of TAB1β blockade on inflammation caused by senescent T lymphocytes.

This programme, if successful, would allow WHR to seek a partner to collaborate in the later stages of drug development.

Help us raise
£100K
to support this research project

A new treatment for common causes of blindness

Dr James Whiteford, Centre for Microvascular Research

The unmet medical need

Two of the commonest causes of blindness are wet age-related macular degeneration (AMD) and diabetic retinopathy, which affect over two million people in the UK alone. In both conditions, excessive blood vessels form in the eye; this affects the function of the retina and leads to blindness. No current treatments are satisfactory: they are all difficult to administer, and/or expensive, and/or of limited effectiveness.

WHRF grants feed into WHR's world-leading therapeutic innovation programme

Thanks to a £10,000 award from WHRF to pump-prime our research into a protein called syndecan-2 (SD2), present on most cells in the body, we were the first to discover that parts can shear off and bind to another protein (CD148) on the surface of blood vessels; this sends a signal that stops the blood vessel growing.

In experimental models, we then showed that administering SD2 could block new blood vessel formation in the eye, and with collaborators at Moorfields Eye Hospital we are now planning the first clinical trial of SD2 in AMD and diabetic retinopathy.

These discoveries are exciting: they have the potential to produce better, cheaper and more easily administered therapies, thus revolutionising the treatment of devastating conditions.

Next steps: WHR's strategy

There is much work to be done:

- we need to understand precisely how SD2 and CD148 work;
- next, we must investigate the therapeutic effects of SD2 (and fragments of it) in detail;
- with that information, it should be possible to optimise a drug molecule for extensive clinical testing, which will establish its safety and efficacy.

The main focus of WHR is on therapeutic innovation: this programme of research into the mechanism of action of SD2, studying its effects in experimental models, and planning early clinical trials to develop a new drug, exemplifies what WHR does best.

The ask

£300k, funding two researchers for three years, should allow us to make the necessary progress to be in a position to seek a partner for the later work needed to bring this programme to a successful conclusion.

How do I donate to WHRF?

Simply contact Development Manager, Kuki Taylor at **development@whrf.org.uk**

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