Inaugural winners of the Lord Alliance Prize

Exploring the secrets of our immune system.

Prof. Werner Muller
The University of Manchester

Werner is a Geneticist and Immunologist and leads a worldwide research group studying Inflammatory Bowel Disease.

Prof. Steffen Jung
Weizmann Institute of Science

Steffen is an expert in the function of our immune cells.

This partnership has demonstrated excellent results and is the worthy winner of the Lord Alliance Prize. A scientific paper published in spring 2014 by a top journal was strengthened hugely by the results of the experiments funded by the Get Connected Grant. In the paper, Steffen and Werner describe how their experiments shed light on how the cells which live in our gut respond to foreign parasites such as worms and how these cells may trigger diseases such as Inflammatory Bowel Disease (IBD).

This work concentrates on the action of a particular immune cell, the macrophage. Macrophages play a vital role in our health by ingesting foreign cells such as bacteria or parasites and by killing our own cells when necessary, such as in cancer. Macrophages are also known to be important in the development of IBD although little is known about how their action is controlled. Using Werner's expertise in modelling inflammatory diseases in mice and Steffen's knowledge of the actions and control of immune cells, this research has now shown that IL-10 (a messenger protein) is a key controller of macrophage activity and as such this offers a potential new avenue for treatment of inflammatory gut diseases such as IBD as well as parasitic infections. Current treatments for IBD are mainly limited to treating the symptoms rather than the cause of the disease – this research hopes to change that, in the hope that by influencing the route of the problem we will achieve a long term solution for those who suffer from conditions caused by gut inflammation.

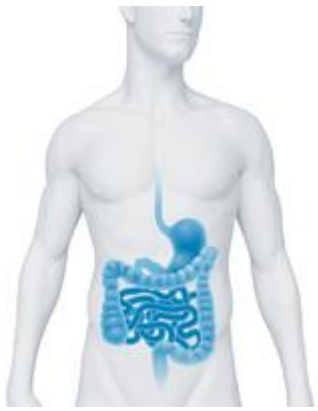
IBD affects 5 million people worldwide with most developing the disease before the age of 35

IBD is incurable and 50% patients will require surgery during their lifetime

Incidence of IBD is increasingly rapidly in the developing world

Werner was delighted to hear that he and Steffen have won the inaugural Lord Alliance Prize;

"I have known Steffen and his research for many years but we have never had the opportunity to join forces on a collaborative project. I knew that if we got the chance to bring our laboratories together that we would both learn so much and make real progress. The prize now gives us the opportunity to build on our early results which show so much scientific promise."



Steffen was similarly appreciative of the opportunity to continue working with Werner;

"The immune system is responsible for our overall health, in so many cases it is a protective barrier but in some cases (such as IBD or rheumatoid arthritis) it is the route of the problem. Only by understanding the complex ways in which our immune cells act and communicate can we hope to design treatments which may boost or suppress the immune system, as required."

The Lord Alliance Prize will allow Steffen and Werner to deepen and extend their joint research, looking at further messenger proteins which are implicated in inflammation of the brain as well as the gut. Given the remarkable progress which has been made by this partnership since 2012, there is a great deal of confidence in both Manchester and Rehovot that this collaboration will produce great things as a result of their well-deserved Lord Alliance Prize.

Progress of other Get Connected Grant holders;

Following the blueprint; exploring the mechanisms which allow our nerves to join together correctly

Dr Andreas Prokop
The University of Manchester

Andreas's lab carries out research into the development of neurones in the brain.

Prof. Alexander Bershadsky
Weizmann Institute of Science

Alexander is an expert in how cells move and attach to each other and their surroundings.

Axons are slender nerve cell extensions, up to a metre long, that form the essential cables that wire the brain into an information network. When axons grow and join together in the developing brain, they follow a specific blueprint for how connections between cells are to be made. If mistakes occur in this wiring process then the result is likely to be mental impairment or even fatal. As axons grow, they receive chemical messages from the tissues they are growing within, these messages help guide the nerve to the correct areas within the tissue and to make a connection. Currently, we know very little about how the process of axon growth, maintenance and repair operates and thus our ability to treat disorders where axon damage occurs (spinal injuries, coma, neuro-degeneration) is limited.

One big barrier to the research of axon growth is that it is very hard to replicate the external cell environment in a laboratory. Previously, axons were grown on glass but this did not offer a true representation of what happened in the body. Andreas' skills in cell biology combined with Alexander's knowledge of biomechanics have allowed the pair to produce a new hydrogel using their Get Connected Grant. This clever material acts as a suitable substrate on which axons will grow in a way which is much more analogous to that which would occur in body tissue.

Following the remarkable early success of this work, a PhD student has recently started in Andreas' lab to pursue this research and create further alliances between the disciplines of cell biology and biomechanics. They are aiming to secure funding for a joint research grant in the future; as well as offering scientists around the world the opportunity to address biomedical issues which arise from axon death and improper development.

The worldwide economic burden of dementia is estimated at $604bn

No effective treatments exist for dementia illnesses

By 2050, the number of dementia patients will have tripled to 135million

How do our neurones send signals which represent our sense of touch?

Prof Ehud Ahissar
Weizmann Institute of Science

Ehud's lab conducts experiments into our sense of touch

Dr Rasmus Petersen
The University of Manchester

Rasmus researches the sense of touch and has particular expertise in mathematical modelling.

Our sense of touch is controlled by a huge network of nerve endings and touch receptors in the skin which are vital and integral to our everyday experiences of the world around us. These sensors and nerves send signals to the brain which interpret the information as our sense of touch. Despite the importance of our sense of touch, relatively little is known about how our neurones encode stimuli from our immediate environment - Rasmus and Ehud are experts in complementary fields in this area. Rasmus is an expert in mathematical modelling whilst Ehud's laboratory has a great deal of experience in designing experiments to study sensory systems in mammals. Having met previously at a number of conferences, the two researchers have seized this opportunity to combine their skills and knowledge to shed light on this relatively unknown area.

The importance of this research to the world was demonstrated on the biggest stage possible in the summer of 2014. The opening ceremony of the Brazil World Cup featured a person who has lost use of his legs scoring a goal using a so-called 'neuroprosthetic' leg! This is an artificial limb controlled by a computer connected to the brain. The key to this technology – which is still in its infancy – is to understand the relationship between events in the physical environment and the electrical language of neuronal activity. Essentially, Rasmus and Ehud's work is about building a 'dictionary' to do this translation. With a good dictionary, we can then seek to build 'neuroprosthetics' devices that will restore the sense of touch to people with nerve damage.

Applying Rasmus's mathematical models to Ehud's experimental data has proved successful and enlightening, with both researchers having published the results of this work in top scientific journals. This research has helped to open new avenues of research for both individuals and to govern the future direction of research in their respective laboratories. They have exchanged not only data but also personnel as a PhD student from Ehud's lab is now employed as a research scientist with Rasmus in Manchester – further deepening the relationship between the laboratories.

Life and death for our cells – what makes the difference in cancer?

Prof. Atan Gross
Weizmann Institute of Science

Atan's lab investigates the mechanisms of cell life and death

Dr Andrew Gilmore
The University of Manchester

Andrew is a Senior Lecturer within the Wellcome Trust Centre for Cell Matrix Research

Every second, around one million cells in our bodies kill themselves because they have become damaged or are surplus to requirements. This process is known as apoptosis and is vital for the normal functioning of our organs. When regulation of this system goes wrong it is likely to result in extremely serious health conditions such as cancer, where damaged cells proliferate instead of dying, and neurodegenerative diseases like Alzheimer's. Apoptosis is controlled by mitochondria, the part of a cell that produces energy. Specifically, it is proteins on the mitochondria surface which act as messengers and therefore control the fate of the cell. The method by which these proteins interact and are themselves regulated is currently unknown. With cell survival being such a vital aspect of so many diseases, discovering how apoptosis pathways function may give crucial clues as to new treatments for a variety of diseases.

Andrew and Atan have been combining their unique expertise to investigate the action of these all-important messenger proteins. Using their Get Connected Grant they have created a protein reporter which helps them to visualise the movement of these proteins in healthy and unhealthy cells. This has allowed them to highlight a particular protein which may be vital in the apoptosis pathway, MTCH2. Following Andrew's trip to Rehovot in spring 2014, they have created a joint research programme to investigate the action of this protein, amongst others, in the coming months. Atan and Andrew are confident that this research programme will provide the foundation on which they can apply for joint funding in the near future to gain further understanding of how we might overcome the cancer cells ability to survive.

Worldwide, there are eight million cancer related deaths each year

The number of new cases of cancer is set to increase by 70% in the coming two decades

Survival rates for some cancers remain unchanged from those of 1960

What helps our immune cells to cross from the bloodstream to the tissue in order to fight infection?

Prof. Ronen Alon
Weizmann Institute of Science

Ronen is a world expert in the adhesion of immune cells

Dr Mark Travis
The University of Manchester

Mark is a researcher with the Manchester Collaborative Centre for Inflammation Research

Dr Christoph Ballestrem
The University of Manchester

Christoph is part of the Wellcome Trust Centre for Cell Matrix Research

The ability of T cells to fight infection makes them a vital aspect of our immune system. T cells circulate in the blood stream and once activated, they are transported into the body tissue via a complex process called extravasation. The extravasation process is controlled by a number of proteins at the membrane of the T-cell which facilitate binding to molecules on the inside of our blood vessels. This research aims to find out how one such protein, vinculin, may play an important role in co-ordinating the process when fighting inflammation and infection. If vinculin is found to be a vital element in the ability of T-cells to stick to vessel walls then it may be a target for drug intervention to prevent inflammatory conditions such as Crohn's disease, allergies and rheumatoid arthritis.

The members of this exciting group are all experts in highly complementary fields, offering a rare opportunity to study the extravasation process from its molecular level (Christoph), to its local level in the blood vessels (Ronen), up to its effect on a whole animal (Mark). Until summer 2014, work has been focussed on breeding the animal models that lack the genes which code for the production of vinculin, a time consuming process. The breeding process is now complete and the animal models have successfully been verified as lacking the necessary vinculin gene. The role of vinculin in helping the T-cells to leave the bloodstream will be tested in the coming months – a potentially vital first step in validating new targets for drugs to fight chronic inflammatory diseases.

The rise in prevalence of allergic diseases has continued for the last 50 years

14% of the worlds children experience asthma symptoms

Rheumatoid arthritis affects 21 million people around the world

Producing more resilient crops through understanding what governs cell death in plants

Dr Patrick Gallois
The University of Manchester

Patrick studies how plants activate cell death in a bid to survive environmental stresses

Prof. Robert Fluhr
Weizmann Institute of Science

Robert is the former head of the Department of Plant Sciences and is an expert in plant responses to environmental stresses

Just as life is a planned series of developmental steps, so can be the process of death. For example, when a parasitic organism infects a plant, the infected parts of the plant can elect to undergo programmed cell death in order to trap and isolate the disease. This kind of defence strategy has also evolved to protect the plant in times of drought or stress when enzymes within the plant cell, called proteases, act like molecular bulldozers – dismantling the cell structure from within to cause cell death. Patrick's laboratory has expertise in the actions of these proteases whilst Robert's lab study protease inhibitors, molecules which act to keep the proteases in check.

Since receiving their Get Connected Grant, Patrick and Robert have visited each other's laboratories to discuss their research and to share samples of enzymes and enzyme inhibitors which each has developed. Together, they have discovered a link between the pathways which control disease resistance and the pathways which control tolerance to drought. This work has been presented to other top research groups around the world and will shortly be published more widely in a scientific journal. This important research finding will be used by Patrick and Robert as they develop strains of crop which are more tolerant to changes in their local environment (such as drought or disease). Developing these strains of crops will require the involvement of industrial partners, something which Robert and Patrick are currently working towards. With food security an ever growing concern due to our warming climate and an expanding global population, the importance of this area of research cannot be overstated.

An estimated 900million people in the world are hungry

Crop productivity in developing countries will need to double by 2050

Climate change poses a huge threat to our ability to grow enough food

Investigating the actions of immune cells - how do they move to fight infection in the gut in inflammatory bowel disease?

Dr Guy Shakhar
Weizmann Institute of Science

Dr Sheena Cruickshank
The University of Manchester

Guy's lab studies cellular communication between immune cells.

Sheena is a researcher within the immunology and molecular biology group at Manchester.

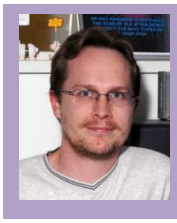
The human gut is populated by a substantial population of immune cells which have a key role in protecting us from infection. In addition to seeking and killing dangerous organisms, these cells are required to permit the existence of "friendly" bacteria which allow a healthy digestive system to operate. Inappropriate responses to these helpful bacteria can result in serious chronic illnesses such as inflammatory bowel disease (IBD). Sheena and Guy are investigating how our immune cells travel through the gut to the site of infection, the mechanisms of which are currently unknown.

Both Sheena and Guy are experts in a particular type of immune cell called a dendritic cell (DC). DCs are hugely important in our immune response; their role is to recognise foreign pathogens and to switch on the body's immune response to them. Whilst they are vital for our well being, they are capable of responding inappropriately, as they do in IBD, causing chronic illness. Guy and Sheena's research has shown that when presented with an infection, DCs travel to the walls of the gut where they play their role in defending against the threat which has been presented. This work will progress to look at how receptors in the wall of the gut and on the DCs affect this process. By understanding the relationships between immune cells, the gut and pathogens it is hoped to gained greater knowledge of how inflammation is managed and therefore how diseases like IBD may be better treated or managed.

Why do some wounds heal faster than others?

Dr Valery Krizhanovsky
Weizmann Institute of Science

Valery is an expert in tissue damage response, based within the Department of Molecular Cell Biology



Dr Mat Hardman
The University of Manchester

Mat is an expert on wound healing, based within the Manchester Healing Foundation Centre

In order to prevent the advance of diseases like cancer, our cells are able to stop dividing; this process is known as cellular senescence. Whilst senescent (ageing) cells are a naturally occurring aspect of healthy tissue, the accumulation of such cells can lead to age related degenerative changes within tissues, including the skin. The effect of the accumulation of senescent cells on the body's ability to heal wounds is currently not understood but is believed to be of great importance. Delayed wound healing is often seen in elderly or diabetic patients and frequently results in infection and ulcers, potentially even amputation; the treatment of chronic wounds in the UK is estimated to cost over £4bn per year. Mat and Valery's Get Connected Grant has allowed them to bring their research expertise together to reveal the importance of cellular senescence in the healing of wounded skin in young, old and diabetic animal models.

The Get Connect Grant allowed Mat and Valery to perfect a biological test which detects senescent cells in tissue samples. This test was shown to demonstrate the increased proportion of senescent cells in aged tissue compared to young tissue but also, for the first time, that diabetic tissue demonstrated higher levels of senescent cells than non-diabetic tissue. More recently, this work has progressed to monitor wound healing in animals which are genetically incapable of inducing senescence, this work has been carried out in Israel by a Post-doctoral researcher from Mat's Manchester laboratory.

Patients with diabetes are 25 times more likely to require an amputation

85% of diabetic amputations are caused by foot ulcers

Global wound care expenditure is estimated at £15bn

This fruitful scientific partnership has flourished thanks to the complementary skills of each laboratory, with Mat an expert in wound healing and Valery a leading figure in senescence and the breeding of animal models. Mat and Valery are exploring the option of deepening their collaboration through the co-supervision of a PhD student between the two laboratories which would help to further explain the mechanisms behind wound healing and address the unmet clinical need of chronic wounds.