



MEDIA RELEASE
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Australian scientists unravel Leukaemia link

Scientists have unravelled the structure of a cell signalling receptor in the blood control system which when damaged is responsible for diseases such as leukaemia. Their discovery helps to explain, for the first time, how this receptor is activated and will form the springboard for the development of new treatments.

The findings, published on 8 August in the prestigious science journal, *Cell*, are the result of an interstate collaboration between a team of scientists led by Professor Michael Parker, St Vincent's Institute (SVI), Melbourne and Professor Angel Lopez, Hanson Institute at the Institute of Medical and Veterinary Science, Adelaide.

Using leading edge technology that allows scientists to view minute parts of cells, the scientists have developed the first 3D image of the receptor's structure and will use the unique knowledge it provides to find drugs to modify its action and control diseases such as Leukaemia and asthma.

Professor Lopez said: "Leukaemia is a type of cancer where an excessive number of malfunctioning white blood cells are produced. We have established the structure of a receptor that controls the actions of a blood-forming regulator called GM-CSF."

He continued: "GM-CSF has been of interest to researchers and clinicians for many years now because its 'controller' or 'receptor', found on the surface of blood cells, is critical in regulating their many functions. In leukaemia some of the signals coming from the "receptor" are abnormal causing the blood cells to grow uncontrollably, malfunction or dangerously persist past their use-by-date."

Professor Parker said: "Because our discovery shows precisely what the receptor looks like and also how it works, we can now begin to design new drugs to rein in the deadly abnormal blood cells. At the moment many leukaemias are treated with chemotherapy that destroys the diseased blood cells and bone marrow as well as normal cells. We hope that this discovery will lead to targeted therapies, more specific to the malfunctioning cells seen in diseases such as leukaemia."

"To maximise the drug development opportunities of this discovery both Institutes have recently signed an agreement with biopharmaceutical company CSL Limited. Under the agreement the Institutes will work with CSL to discover and develop new therapeutic antibodies". he continued.

Professor Andrew Roberts from the Walter and Eliza Hall Institute and Royal Melbourne Hospital said: "This is a major step forward. Abnormal GM-CSF signalling is pivotal to a variety of serious and difficult-to-treat diseases. With this discovery, rational design of targeted therapies can now be accelerated greatly."

SVI Director, Professor Tom Kay, said: "SVI's Australian Cancer Research Foundation Rational Drug Discovery Facility, Michael Parker and his collaborators are world leaders in their field. In the past ten years the Unit has discovered the structure of more than 30 disease-causing proteins, forming the basis for ongoing research into potential therapies. This latest discovery is very exciting."

Director, SA Pathology and Hanson Institute, Professor Ruth Salom said: “We are delighted with the resounding success of the collaboration between Professor Lopez and Professor Parker. Professor Lopez and his team lead the way in understanding how growth factor receptors signal. This is a wonderful recognition of the importance of the research and its implications for the development of new drugs.”

Co-first authors of the *Cell* report are Dr Guido Hansen from SVI and Dr Tim Hercus from the Hanson Institute. Senior and corresponding authors are Professors Michael Parker and Angel Lopez. Additional co-authors are: Barbara J. McClure, Frank C. Stomski, Mara Dottore, Jason Powell, Hayley Ramshaw, Joanna M. Woodcock, Yibin Xu, Mark Guthridge and William J. McKinstry. The study was supported by grants from: Australian Research Council, Australian Synchrotron Research Program, National Health and Medical Research Council of Australia and National Institutes of Health (U.S.). Michael Parker is an Australian Research Council Federation Fellow and a National Health and Medical Research Council Honorary Fellow.

See page 3 for illustrated explanation of the discovery

About SVI

St Vincent’s Institute is an independent medical research institute which conducts laboratory research into the cause, prevention and treatment of high-impact diseases such as cancer, diabetes, obesity, bone diseases, Alzheimer’s, cardiovascular disease and infectious diseases. SVI is affiliated with St. Vincent’s Hospital and the University of Melbourne.

About The Hanson Institute

The Hanson Institute is the research arm of the Institute of Medical & Veterinary Science and Royal Adelaide Hospital and is dedicated to excellence in basic and clinical research. Its innovative research ranges from the investigation of basic cell and molecular biology of cancer and the immune system to new therapies for their treatment.

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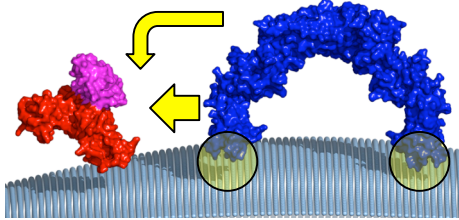
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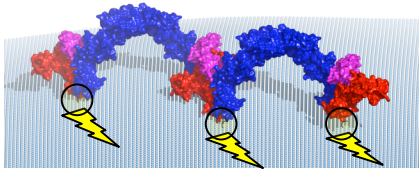
GM-CSF Receptor Structure Discovery

The GM-CSF hormone controls the production of blood cells and is sent by the body to give the signal for more blood cell production if, for example, more white blood cells are required.



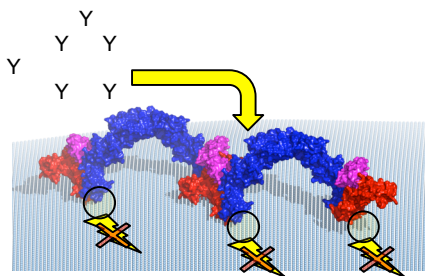
The GM-CSF hormone (purple) binds to the receptor which consists of two chains (red & blue) on the cell surface.

St Vincent's Institute and Hanson Institute scientists have discovered the structure of the GM-CSF receptor bound to the hormone for the first time and have created a computerised 3D model to visualise it.



The binding process happens several times, creating a chain of bound receptors until a signal is generated and sent into the cell.

Abnormal receptor signaling causes the over-production of cells, the production of malfunctioning cells or cells that persist too long, resulting in diseases such as leukaemia.



The next stage is to find drug compounds that will block the abnormal GM-CSF receptor signaling.