



VPTN

Victorian Platform Technologies Network

Platform technologies solve plasminogen puzzle

The immunology and coagulation team at Monash University recently made a discovery that could lead to new treatments for clotting and bleeding disorders.

The team, led by structural biologist Professor James Whisstock, has been able to determine the structure of Plasminogen, a protein that is responsible for dissolving blood clots.

Blood clots cause heart attack and strokes and represent one of the leading causes of long term disability. The discovery will help scientists understand how this enzyme functions to dissolve blood clots.

When Plasminogen is activated, it is converted to plasmin, which dissolves the fibres around the blood cells in a blood clot (a process called fibrinolysis). In treating heart attack and stroke patients, clinicians currently use an enzyme called tissue plasminogen activator (TPA) to convert the inactive protein plasminogen into the active plasmin, to dissolve blood clots and clear away other damaged tissue.

"Now we can see the atomic details of the plasminogen we can finally get a detailed picture of how the whole system works and how plasmin is produced," Whisstock says.

"But we're still not entirely sure of the molecular details of how plasminogen is activated in the body," says Whisstock. "More data is needed before we can commit to translational studies and to developing potential therapeutics that can activate plasminogen on demand".

Collecting that data will involve many more hours of research.

Cross disciplinary research

"Challenging projects like this require different approaches and cross disciplinary research in an open collaborative approach.

"Our research has been guided by the expertise found in many research Platforms and we've had the good fortune to use of some of Victoria's very expensive state of the art technology.

"In Australia I think we are doing it far better than in other parts of the world where equipment is not shared and is often sequestered away in people's labs.

"Each of the Platforms is world class and has a group of leading scientists closely allied with the state of the art technology. This ensures the platform genuinely delivers on what it is supposed to. This is what gives us the competitive edge internationally. We rely on our experiments being reproducible, quality controlled and state of the art.

Expertise in technology

"Victoria's Platform scientists are often experts in their field, not just service providers – they make intellectual contributions to the projects and have direct input into publications. Indeed, in certain cases they are lead authors on some of our publications.

"We use the Protein Production Unit at Monash for making proteins for drug discovery, the Macromolecular Crystallisation Facility to grow crystals of protein for structural and the Biomedical Proteomics Facility to look at protein modification. We also use the expertise and the crystallography beam lines at the Australian Synchrotron.

"Open collaboration through Victoria's Platform Technologies Network – has not only enabled us access to very expensive equipment, it inspires cross disciplinary research.

"For example, using the platforms, I have successfully been able to make mouse knockouts in order to take our structural studies further with respect to biology. From a structural biology perspective it is fantastic to have access to this capability," Whisstock says.

For more information

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