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New target in treatment of heart attack and stroke

Melbourne researcher wins national award

A Melbourne researcher working on a new therapeutic treatment for coronary heart disease and stroke is the winner of this years prestigious Amgen Medical Research Award.

Associate Professor Shaun Jackson, of the Australian Centre for Blood Diseases at Monash University, has lead a team in the discovery and development of a new class of anti-clotting drugs. His internationally-recognised research was recently published in the Journal Nature Medicine.

The discovery focuses on PI 3-kinase inhibitors. Associate Professor Jackson said "PI 3-kinase p110β was not previously known to play an important role in platelet function or in thrombus development. We have now identified specific inhibitors of this enzyme which inhibit the formation of the 'sticky' contacts between the platelets and prevent thrombus formation, An added advantage of these inhibitors is that these compounds are well-tolerated and do not cause bleeding side-effects.

The new anti-thrombotic compounds have been patented world-wide and have been extensively tested in preclinical toxicology programs and Phase I human trials. Further clinical and commercial development of the compounds is currently being undertaken."

With an estimated 48,700 coronary heart disease events and 40,000 – 48,000 stroke events in Australia each year[1] and direct costs (including hospital, pharmaceuticals and residential care) for these conditions close to $3 billion in 2004[2] Associate Professor Jackson's research highlights the enormous potential for the treatment and reduced financial burden of the disease.

Kaylene O'Shea, Director of Scientific Affairs at Amgen Australia, will present the Amgen Medical Research Award to Associate Professor Jackson at a luncheon in Sydney today.

Ms O'Shea said " Amgen is committed to bringing the benefits of science to patients. We can all be proud of the world-leading contributions made by Dr Jackson, which clearly have the potential to improve health outcomes patients through out the world. Amgen Australia is delighted to be able to recognise Associate Professor Jackson with this award."

The award was judged by an independent panel of experts.

Contact: Dr Sarah Meachem on 0412 640 774 or Catherine West on 0415 928 211 for interviews.

[1] Heart, Stroke and Vascular Disease, Australian Facts 2004 – Australian Institute of Health and Welfare / National Heart Foundation of Australia

[2] The Shifting Burden of Cardiovascular Disease in Australia (2005) report prepared for the National Heart Foundation of Australia by Access Economics.

APPLICATION – Brief Description:

Acute myocardial infarction and ischemic stroke are Australia's leading health problems. These diseases cause more morbidity and mortality in Australia and the western world than any other medical conditions. Over 200 million people world-wide suffer from such diseases and the economic and health impact is enormous. Acute myocardial infarction and ischemic stroke are typically caused by the development of an occlusive arterial thrombus at sites of atherosclerotic plaque rupture, leading to ischemic end-organ damage in the heart or brain. As a result, antithrombotic agents are first line therapies in these diseases with aspirin remaining the preferred treatment. However, the major limitation of aspirin is its relatively weak antithrombotic action, resulting in a ~25% reduction in ischemic complications and only a ~16% reduction in vascular death. Thus, a great deal of effort has gone into developing more potent and effective antithrombotic agents. To date, the only anti-platelet agents that have shown to be beneficial over aspirin in selected patient groups is clopidogrel and the GPIIb-IIIa inhibitors, with the former only marginally better and the latter restricted to inpatient hospital use. However, extensive clinical trialling has demonstrated that the major limitation with more potent antithrombotic approaches is a corresponding increase in bleeding complications, occasionally with fatal consequences. For over 30 years the pharmaceutical industry has been searching for a class of drugs that preferentially inhibit pathological arterial thrombosis without significantly undermining haemostasis. Despite intense investigation such drugs have never been discovered or developed.

In a major breakthrough recently published in Nature Medicine, our research team has developed for the first time a class of antithrombotic agents that are more effective than aspirin at preventing arterial thrombosis without increasing bleeding risk. In fact, these drugs can be administered concurrently with other antithrombotic agents, including anticoagulants such as heparin, without prolonging the bleeding time. The unique ability of these drugs to differentiate between pathological thrombosis and haemostasis is based on their ability to inhibit a specific enzyme that is required for shear-activation of platelets, necessary for arterial thrombus formation. This enzyme PI 3-kinase p110β was not previously known to play an important role in platelet function, nor was it appreciated to be involved in thrombus development. Our studies have uncovered the molecular basis by which PI 3-kinase p110β regulates platelet adhesive function and have demonstrated that inhibition of this enzyme provides a complimentary antithrombotic approach to all existing antiplatelet agents. Our new antithrombotic compounds have been patented world-wide and have been extensively tested in preclinical toxicology programs and Phase I human trials. The results to date have been extremely encouraging as these compounds are well tolerated and do not cause bleeding side-effects. The further clinical and commercial development of these compounds is currently being undertaken by the Melbourne-based biotechnology company, Cerylid Biosciences Pty Ltd.

The discovery of a central role for PI 3-kinase p110β in promoting shear-activation of platelets and arterial thrombosis represents the culmination of over 8 years work in our laboratory. Central to this discovery was the establishment of a state-of-the-art haemorheology laboratory which has provided us with fundamental new insights into the processes which regulate platelet activation and thrombus formation. Many of these studies have been published in leading international scientific journals.