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ASIA EDITION

Singapore develops oral-anti-diabetic drug

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Singapore: Singapore has completed phase I clinical trial of an oral-anti-diabetic drug developed by Department of Pharmacology of the NUS Yong Loo Lin School of medicine (NUS Medicine) together with Singapore Clinical Research Institute and National University Health System (NUHS).

In normal individuals, insulin that is released from the pancreas after a meal binds to insulin-sensitive cells and activates insulin pathway. This insulin pathway is connected to a glucose transporter, and when activated by inslun the pathway brings the glucose transporter from the inside of the cell to its surface. At the surface, the glucose transporter is then able to transport glucose from the bood into the cell for energy usage or storage.

In diabetes, this pathway is faulty and becomes resistant to insulin (i.e. the cell develops insulin resistance or does not response to insulin). There are switches in the insulin pathway connecting insulin to the glucose transporter that malfunction in diabetes. The result is that insulin loses its ability to initiate uptake of glucose into the cell.

DAA-I rectifies all the four switches found to be malfunctioning in diabetes, said Associate Professor Sim Meng Kwoon, retired faculty member of the Department of Pharmacology at NUS Medicine and one of the lead investigators who carried out the study.

"Chronic inflammation in diabetes damages the endothelial lining of blood vessels, leading to vascular and organ damage, e.g. cardiovascular diseases, damage of retina leading to blindness, damage of the nephrons leading to kidney failure, damage of nerves leading to neuropathy. Thus, the importance of reducing chronic inflammation in diabetic individual is critical," he added.

"The drug molecule, des-aspartate-angiotensin I (DAA-I), is an endogenous angiotensin peptide, which acts on the angiotensin AT1 receptor and produces biological responses that improve the action of insulin (i.e. attenuation of insulin

resistance) leading to increased uptake of glucose into insulin-sensitive cells. Concurrently, DAA-I also reduces the damaging chronic inflammation that accompanies diabetes and attenuates pancreatic beta cell death."

Clinical studies

The single-dose Phase I trial, involved 18 healthy individuals, aged 24 years old to 47 years old, and was carried out from end September to December 2015 at the NUHS Investigational Medicine Unit together with SCRI, which provided project management and supported trial monitoring. The trial was led by Clinical Principal Investigator, Professor Lee Kok Onn from NUS Medicine's Division of Endocrinology.

Said Prof Lee, who is also a Senior Consultant at the National University Hospital's Division of Endocrinology, "The current anti-diabetic drugs target mainly the lowering of the blood glucose in diabetes, and generally lack the specificity of improving the action of insulin and reducing chronic inflammation in peripheral tissues."

The clinical trial successfully established that DAA-I was well tolerated by human subjects and this paves the way for further clinical trials on DAA-I, which the SCRI will continue to partner the NUHS and NUS Medicine.

"We are privileged to collaborate with both A/Prof Sim and Prof Lee on this landmark clinical trial which showcases the capabilities of Singapore in the drug development field. This study demonstrated the strong partnership between Singaporean research organisations in developing new drugs to treat common chronic diseases like diabetes mellitus, which affects about 11 percent of our adult population aged 18 to 69, said Associate Professor Teoh Yee Leong, CEO, SCRI.