Development of pan-Nox inhibitor as the first-in-class agent against diabetic kidney disease

Hunjoo Ha

The Graduate School of Pharmaceutical Sciences, College of Pharmacy

Ewha Womans University

Oxidative stress plays a critical role in the development and progression of diabetic kidney disease, and NADPH oxidases significantly contribute to intra-renal reactive oxygen species (ROS) generation. Nox4 has been identified as the key source of renal ROS generation, but other catalytic subunits of NADPH oxidase are expressed in the kidney. While the downstream effectors of Nox remains to be established, a considerable effort has been devoted to develop Nox inhibitors. GKT137831-a novel, orally active, dual Nox1/Nox4 inhibitor from the pyrazolopyridine chemical series- effectively attenuates kidney injury (albuminuria, glomerular hypertrophy, inflammation, and fibrosis) in both type 1 and type 2 diabetic animals, but reduction in albuminuria was not achieved in type 2 diabetes with albuminuria treated with GKT137831 for 12 weeks. Our progress is now being made on development of the better pyrazole derivative Nox inhibitors for the treatment of diabetic kidney disease. In this seminar, I will present our ongoing studies on the development of pan-Nox inhibitor as the first-in-class drug against diabetic kidney disease.