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Proteomic analysis of the effects of farnesyltransferase inhibitor on vascular disease in experimental model of chronic renal failure

Igor G Nikolov

University St Cyril and Methodius, Republic of Macedonia

The mevalonate pathway plays an important role in both dyslipidemia and inflammation because of its implication in cholesterol synthesis, and in the activation of several key cellular proteins such as the GTPases and Ras. An increase of plasma mevalonate concentration has been documented in chronic kidney disease (CKD) patients. The importance of mevalonate products in CKD has been demonstrated indirectly by the beneficial effects of statins. The specific inhibition of protein prenylation, by a farnesyltransferase inhibitor (FTI), offers the possibility to test the hypothesis of a direct role of isoprenoids in CKD-associated vascular lesions.

In our studies we have explored the role of the specific inhibition of protein prenylation on the vascular calcification process and atherosclerosis in a well-defined apolipoprotein E null (apoE^{-/-}) mouse model with CKD. Proteomic analysis and profiling by MALDI-TOF-MS to identify the relevant peptides and then nano LC-MSMS to sequence were used. It was observed that an inhibitory action of FTI on systemic inflammation and oxidative stress in CKD mice which was suggested by the observed changes in apolipoprotein AIV, α globin, and fetuin A. Moreover, by using immunohistochemistry, we observed reduced vascular nitrotyrosine expression as a marker for oxidative stress.

In conclusion, it will be shown in the presentation that the FTI is effective in slowing the accelerated progression of atherosclerosis and vascular calcification in apoE^{-/-}-mouse model with CKD. The talk will also show that the inhibition of protein prenylation leads to a decrease in oxidative stress, inflammation, atherogenesis, and vascular calcification, via both systemic and direct local effects on the vessel wall.

Biography

Igor G Nikolov has completed his PhD thesis at the age of 34 years at the University Pierre and Marie Curie, Paris 6, and received scholarship from the French Society of Nephrology. He was a fellow of Internal medicine at the Faculty of Medicine in Skopje. In 2012 he was elected for an Associated Professor of Internal Medicine at the Faculty of Medicine in Skopje. His main field of interest is atherosclerosis and vascular calcifications in patients with chronic kidney disease. He serves as a National Focal Point for the SEEHN working on organ transplantation in the country. He has published more than 20 papers in reputed journals.

nikolov_igor@yahoo.com