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Role of Serum and Glucocorticoid induced kinase-1 (SGK1) in cardiac angiogenesis

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The Serum and glucocorticoid inducible kinase (SGK1) lies downstream of insulin and growth factor signaling pathway. SGK1 is highly homologous to the AKT kinase, but unlike AKT the role of this enzyme in the heart has not been well established. In this study we used a knockout mice model in which the activity of SGK1 is abolished. These animals has been first generated in 129/SV background and bred to C57BL/6 background. Our previous study showed when these animals were back crossed in C57BL6 background for more than 5 generation; they die at embryonic day 10.5-11.5 due to severe angiogenic defect. However the mixed 129/SV-C57BL/6 animals are viable, fertile and do not have a drastic phenotype a part from their smaller body and heart size compare to their WT littermate. The cardiac function measured by echocardiography showed similar EF and FS among the two groups of animals. When studied downstream signaling pathway of SGK1, we found that phosphorylation of "N-Myc downstream regulated gene-1 (NDRG1)", a specific SGK1 target, was drastically decreased in the heart of SGK1 KO animals. On the other hand the expression level of VEGFa was increased in SGK1 KO hearts. Furthermore, the primary isolated endothelial cells from the heart of SGK1 KO mice showed similar decrease in NDRG1 phosphorylation compare to the WT endothelial cells. The tube formation capacity of endothelial cells on Matrigel was also decreased in isolated endothelial cells from SGK1 KO animals. Together these results suggest that SGK1 may play an important role in angiogenesis and vessel remodelling through phosphorylation of NDRG1.

Biography

Dr. Elham Zarrinpashneh is a postdoctoral research associate working at Imperial College London, National Heart and Lung Institute. She graduated with a Master degree in Pharmacy from Tehran University of Medical Sciences. She obtained her PhD in Biomedical Sciences from Catholic University of Louvain, (Belgium).