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고포도당으로 자극한 족세포에서 시간에 따른 유전자 발현의 차이

연세대학교 내과학교실[1], 의과학사업단[2], 암전이연구소[3]

한승혁[1] · 정동섭[2] · 곽승재[2] · 이금희[2] · 박제현[2] · 이순하[2]
이정은[1] · 김동기[1] · 문성진[1] · 한대석[1] · 강신욱[3] · 양상화[1]

Time-Dependent Gene Expression Profile in High Glucose-Stimulated Podocytes

Seung Hyeok Han[1], Dong Sub Jung[2], Seung Jae Kwak[2], Jin Ji Li[2], Jehyun Park[2], Sun Ha Lee[2]
Jung Eun Lee[1], Dong Ki Kim[1], Sung Jin Moon[1], Dae Suk Han[1], Shin-Wook Kang[3], Sang Hwa Yang[1]

Department of[1] Internal Medicine Yonsei University College of Medicine, Brain Korea 21[2], Cancer Metastasis Research Center[3]

Background : Recent studies have shown that podocyte injury plays a role in the pathogenesis of various glomerular diseases, including diabetic nephropathy, but the molecular and cellular mechanisms responsible for these are not fully understood. Although the role of some genes was described and a few gene-profiling studies were reported in diabetic nephropathy, global gene expression pattern specific to podocyte has not been explored so far. In this study, we investigated the time-dependent gene expression profile in cultured podocytes exposed to high glucose medium.

Methods : Differentiated conditionally immortalized mouse podocytes were exposed to medium containing 5.6 mM glucose (NG), NG+24.4 mM mannitol (NG+M), and 30 mM glucose (HG). RNAs were extracted after 2, 6, 24, and 48 hours, and cDNA microarray was conducted on mouse cDNA 38K chip in triplicate at each time point. The results obtained by direct comparative analysis between NG and HG cells were further confirmed by real-time PCR and Western blot. In addition, immunohistochemistry with renal tissues from 6- and 12-weeks streptozotocin-induced diabetic (DM) and control rats was performed to verify the in vitro results.

Results : Microarray analysis identified 3,256 differentially expressed genes with at least a 1.5-fold difference at one time point in expression levels and concordant log ratios between NG and HG cells, and they were classified into 11 clusters. Three of them consisted of persistently up-regulated genes, including thrombospondin-1 (TSP-1), thrombomodulin, vascular endothelial growth factor (VEGF), and heme oxygenase-1 (HO-1). On the other hand, three clusters were groups with persistently down-regulated genes, including angiotensin-converting enzyme-2 (ACE2) and peroxisomal proliferator activator-gamma (PPAR-γ). Real-time PCR and Western blot also revealed that mRNA and protein expression of TSP-1, thrombomodulin, VEGF, and HO-1 were significantly increased, whereas those of ACE2 and PPAR-γ were significantly decreased in HG-stimulated podocytes compared to LG cells. These results were further verified in DM glomeruli by immunohistochemistry.

Conclusion : Microarray analysis provides valuable information on the molecular mechanisms of high glucose-induced podocyte injury. Further investigation is needed to ascertain the specific role of the identified genes in the present study.