

Oral Communication Abstract

Presentation No. **OC4-02** (Abstract Submission No. 2357)

Oral Communications 4 Sep. 2 (Thu), 16:40-17:40

The role of STAT3 against fibrosis injury in human podocyte and tubular epithelial cell through proteomic profiling

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Objectives: One of the pleiotropic function of transcription factor, signal transducer and activator of transcription 3 (STAT3) in the kidney is its involvement in the interstitial fibrosis process. We aimed to elucidate the role of STAT3 in kidney fibrosis at the cellular level through the proteomic analysis.

Methods: Primary cultured human podocyte and human tubular epithelial cell (hTEC) were treated with rTGF- β 2 ng/mL alone, rTGF- β and Stattic 1 μ M (inhibitor of the STAT3 SH2 domain regardless of the STAT3 phosphorylation), and the untreated control group, respectively. Label-free quantitative proteomic analysis based on liquid chromatography-tandem mass spectrometry was performed for podocyte and hTEC.

Results: After hierarchical clustering, in podocyte, we found that 135 differentially expressed proteins (DEPs) increased after Stattic treatment. There were calcium-regulated heat stable protein 1 (CARHSP1), DNA damage-binding protein 1 (DDB1), and glutathione S-transferase Mu 3 (GSTM3), and it has been reported that they have the effect of antioxidant, antiinflammation, and cell stabilization. In hTEC, 58 DEPs were identified that the level was decreased after Stattic treatment. Among them, procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 (PLOD1), junction plakoglobin (JUP), and protein disulfide-isomerase (P4HB) have the function of extracellular matrix maturation, cell-cell junction, and tumorigenesis.

We discovered biomarkers through analysis of proteins showing common changes after Stattic treatment in both cell types. Ornithine aminotransferase (OAT), involved in the catabolism of L-ornithine, mitochondrial survival, and collagen deposition, decreased after Stattic treatment. The level of perilipin-2 (PLIN2), insulin-like growth factor 2 mRNA-binding protein 3 (IGF2BP3), and glucose-6-phosphate dehydrogenase (G6PD) was increased after Stattic treatment. These proteins are related to adipose differentiation, oncogenesis, and glucose metabolism, respectively.

Conclusions: This results can suggest the antifibrotic and antiapoptotic function of STAT3 axis control by the discovery of biomarkers through proteomic profiling in cellular level.

Figure 1. Hierarchical clustering in podocyte and hTEC

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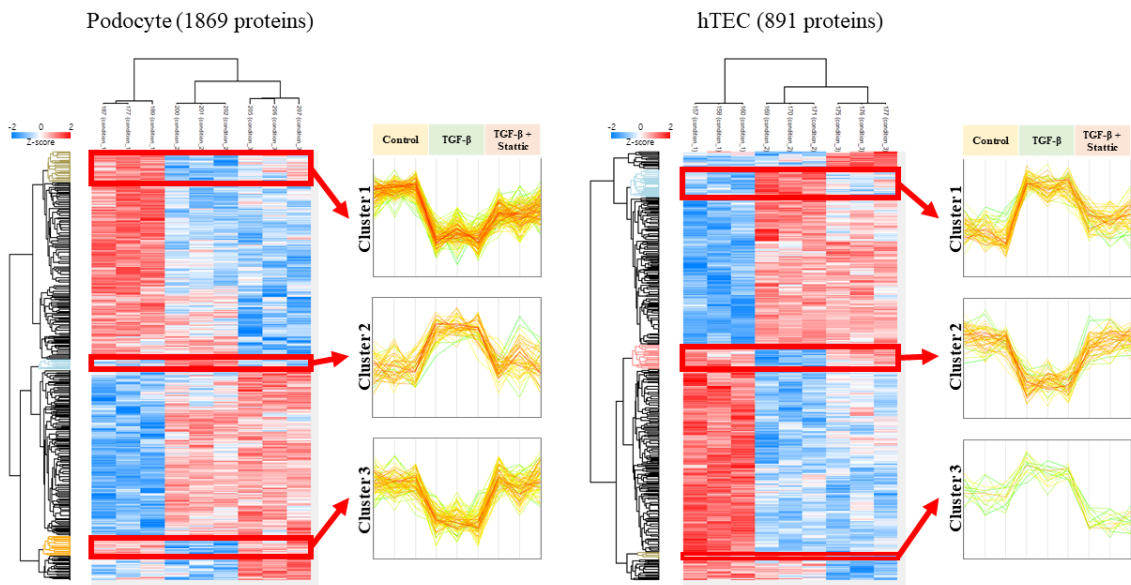


Figure 2. Common expression pattern in podocyte and hTEC

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