Elucidation of Metabolic Syndrome-Related Paracrine System by Co-Culturing Renal Tubular Epithelial Cells and Adipocytes

Introduction and Objective: Epidemiologically, a strong association is observed between kidney stone disease and metabolic syndrome (MetS). Under MetS conditions, adipocytokines, such as adiponectin, play an important role in MetS-induced atherosclerosis formation. In this study, we established an experimental system to co-cultivate renal tubular epithelial cells and adipocytes to investigate kidney stone formation mechanism under MetS environment, and hypothesized the interaction between these cells morphologically and genetically.
Materials and Methods: Mouse renal tubular epithelial cells (M-1) and mouse adipocytes (3T3-L1) were used. Dexamethasone, isobutylmethylxanthine, and PPARγ agonist were administered for the differentiation of 3T3-L1 preadipocytes to mature adipocytes. The cell culture was divided into 3 groups: control (CON), where the cells were cultured individually; replacement (RP), where 24h culture media from each cell type was added to the other cell type; and transwell (TW), where the cells were cultured in 2-layer co-culture dishes. We collected M-1 and 3T3-L1 cells and their supernatants at 6, 12, 24, and 48h. Total RNA was extracted and assayed for the expression of kidney stone-atherosclerosis-related genes: secreted phosphoprotein 1 (*Spp1*), adiponectin (*Adipoq*), C-C chemokine ligand 2 (*Ccl2*), transforming growth factor-β1 (*Tgfb1*), Tumor Necrosis Factor α (*Tnf-α*), interleukin 6 (*Il6*), superoxide dismutase 2 (*Sod2*), intracellular adhesion molecule 1(*Icam1*).
Results: In the RP group, M-1 showed significant upregulation of *Adipoq* and downregulation of *Tnf-α* and *Icam1,* and 3T3-L1 showed significant upregulation of *Ccl2* and downregulation of *Adipoq* as compared to the CON group. In the TW group, M-1 showed significant upregulation of *Spp1*, and 3T3-L1 showed significant upregulation of *Spp1*, *Tgfβ1*, *Icam1*, and *Ccl2* as compared to the CON group.
Conclusions: The renal tubular epithelial cells and adipocytes showed characteristic expression patterns of kidney stone-related genes in the coculture. These phenomena might be due to MetS environment-induced paracrine system between renal tubular epithelial cells and adipocytes, and suggests that MetS environment may lead to kidney stone formation.