Podocyte, Slit Diaphragm, Proteinuria

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The visceral glomerular epithelial cell, also called the podocyte, is a highly specialized, terminally differentiated cell that lines the outer aspect of the glomerular basement membrane (GBM). Podocytes possess interdigitating cell extensions, called foot processes, which are bridged by the slit diaphragm (SD). Since the neighboring foot processes were derived from the different cell bodies of the podocytes, the SD is a highly developed variant of the cell to cell junction. The recent discovery of several novel components of the SD (nephrin, Neph1, P-cadherin, etc.) and their physical and functional interactions with intracellular adaptor proteins (ZO-1, CD2AP, podocin, etc.) revealed the region of the SD as the major filtration barrier. However, the molecular composition of the SD is not well understood yet. Another important question how the mechanism for the formation and for the maintenance of the SD is remains quite uncertain.

Our group has been investigating the mechanism of proteinuria resulted from podocyte dysfunction. We have reported that nephrin and podocin are functional molecules of the SD and that the altered expression of these molecules contributes to the development of proteinuria[1, 2]. We also showed that the expression of these molecules is regulated by interferon inducible protein 10 (IP-10)[3, 4]. Since it is conceivable that the molecules whose expression decreased before the onset of proteinuria may have been involved in the initiation events of proteinuria, we intended to purify the molecules whose expressions were downregulated at 24 hr of puromycin aminonucleoside nephropathy, an experimental model of minimal change type nephrotic syndrome, using cDNA subtractive hybridization techniques. We identified 28 genes downregulated, and 8 molecules of them were confirmed to be expressed in glomeruli and cultured podocyte. Among them, we focused on synaptic vesicle protein 2B (SV2B). SV2B is known to play a role in vesicle trafficking by binding to other cell surface proteins. We observed that SV2B is expressed at the SD and play a role in the trafficking of the SD associated molecules.

In my presentation at the meeting, I will introduce our group's recent works on IP-10 and SV2B. In addition, I will talk our strategy for the future studies.

References

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