특별 강연 II

Understanding Nephrotic Syndromes Through Advances in Podocyte Biology

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The glomerulus is the elemental unit of kidney filtration. The glomerular filtration barrier consists of two monolayers of cells, endothelial cells on the circulatory side and podocytes on the urinary side, separated by a specialised basement membrane. The exact role of each component in barrier function remains a subject of great debate, and discoveries in recent years have focussed attention on the podocyte as the central component. This is because proteins expressed solely in the podocyte within the glomerulus are found to be mutated in the congenital or familial nephrotic syndromes, implying an essential functional role for these molecules in intact filtration.

These proteins include nephrin, podocin, α-actinin-4, TRPC6 and INF2. The unifying factor amongst these is that they are expressed at the podocyte slit diaphragm (the specialised cell-cell junction), and/or in the foot processes, and are intimately linked to the cytoskeleton. The cytoskeleton is thought to be key to podocyte function because it is responsible for maintaining cellular architecture, and disruption leads to foot process effacement, a cardinal histological feature of nephrotic syndromes. The elucidation of TRPC6 as an important player is intriguing, as it is a cation channel, suggesting a role for calcium mediated signalling events in maintaining podocyte health. A challenge for the future is to link this with function of the known slit diaphragm proteins. Finally there is a growing appreciation of proteins in the basement membrane, that interact with the base of the podocyte foot process, as part of the specialised mechanism of the filtration barrier. For example mutations in laminin-β-2 cause childhood NS and ocular anomalies, in Pierson syndrome.

For the clinician, it is important to have a knowledge of nephrotic diseases that may be due to genetic mutations, and direct treatment and counselling appropriately.

Therefore, overall we have learned much in recent years about the critical components of the filtration barrier, and are starting to put together the pieces of the jigsaw to gain a more complete picture of the physiology of glomerular filtration. The exciting prospect is that this can be applied to the mechanisms of glomerular pathology, and lead to novel targeted therapies.