

Beyond immunosuppression, a new role for cyclosporine

Corticosteroids were initially introduced in the 1950s for use in patients diagnosed with nephrotic syndrome (NS) and FSGS. For patients diagnosed with steroid resistant or steroid dependent forms of the disease combination therapy with other drugs has been suggested and used in clinical practice¹.

Cyclosporine A (CsA) was introduced as a treatment for idiopathic NS over 20 years ago, particularly effective for those patients with steroid-responsive NS who suffer from multiple relapses as well as for patients with steroid resistant forms of the disease. CsA is an immunosuppressive drug used in the treatment of these conditions because of its ability to reduce proteinuria, the leakage of protein into the urine, as seen in these kidney diseases².

It was previously believed that the effect of CsA was a result of its immunosuppressive action, by which it inhibits signaling in cells of the immune system. However, a study by Dr. Faul and colleagues has recently found that the effects of CsA on proteinuria may be independent of inhibition of immune cells. Rather, Dr. Faul suggests that CsA has a direct effect on the podocytes, specialized cells involved in filtration within the kidneys. The effect of CsA on cells is caused by the inhibition of the enzyme calcineurin, present in both immune cells and podocytes³.

This study sheds light on the function of CsA and calcineurin allowing researchers to better understand their involvement in the cause and progression of NS. This may eventually allow researchers to find a drug that can be more effective in the treatment of NS while at the same time reduce the well-documented side effects and the potential for nephrotoxicity found with long term use of CsA.

1. Gipson D, Gibson K, Gipson P, Watkins S, Moxey-Mims M. Therapeutic approach to FSGS in children. *Pediatr Nephrol.* 2007; 22:28-36.



2. Cattran DC, Appel GB, Hebert LA, Hunsicker LG, Pohl MA, Hoy WE, Maxwell DR, Kunis CL. A randomized trial of cyclosporine in patients with steroid-resistant focal segmental glomerulosclerosis. North America Nephrotic Syndrome Study Group. *Kidney Int.* 1999; 56:2220-2226.
3. Faul C et al. The actin cytoskeleton of kidney podocytes is a direct target of the antiproteinuric effect of Cyclosporine A. *Nat Med.* 2009, Feb; 15(2):133.

