• Communiqué de presse •

A new therapeutic approach for rare and serious kidney diseases.

In an article published in the journal *JANS* on 22 May last, a team at the Paris Cardiovascular Research Centre (PARCC) (Paris Descartes University / Inserm / AP-HP) proposes a new approach for the treatment of serious kidney diseases. Under the leadership of Pierre-Louis Tharaux, this team focused on the ability of kidney cells to react to inflammation.

The kidney is an essential organ of the body. Its function is to filter the blood and eliminate wastes collected by the urine. This filtering function is mainly performed by specialised cells, the podocytes, located in structures known as glomeruli. In some people, an abnormal inflammatory process is triggered and results in lesions in the kidney and in these glomeruli, leading to serious kidney failure, constituting a genuine diagnostic and therapeutic emergency.

To date, the only treatment for these diseases, known as glomerulonephritis, involves targeting the immune system in order to reduce the inflammation causing this condition. Unfortunately, these therapies are only partly effective, and expose the patients being treated to a high risk of infection. For this reason, the team led by Pierre-Louis Tharaux at the Paris Cardiovascular Research Centre (PARCC) chose a different approach: they studied the possibility of stopping renal destruction by influencing the manner in which the kidney cells (the podocytes) react to inflammation.

In people without disease, a receptor known as PPARγ (peroxisome proliferator-activated receptor-gamma) is present in the kidney podocytes. While studying this molecule, the researchers discovered that it partly disappeared from the glomerular cells in a mouse model of the disease. Similarly, this reduction was also observed in the kidneys of affected patients, suggesting an important role for this receptor in the development of glomerulonephritis. To confirm their hypothesis, the scientists completely deleted PPARγ from the podocytes of mice. They then observed a clear aggravation in the severity of the kidney damage in these mice, thereby corroborating the requirement for PPARγ to protect the kidney.

For therapeutic purposes, the team then had the idea of administering a PPARγ activator, pioglitazone, to these mice. Clinically developed to treat some kinds of type 2 diabetes, it was known for its beneficial anti-inflammatory effect. Surprisingly, its administration to mice, up to 4 days after onset of the disease, considerably reduced renal inflammation, and enabled the structure and function of the kidney to be maintained. This efficacy was lost when the PPARγ gene was absent from the podocytes, indicating that the core effect of the drug comes from its action on these cells rather than from a general anti-inflammatory effect, as had been thought.

“These results suggest a new indication for this class of drugs activating the PPARγ pathway, which could turn out to be of benefit in cases of glomerulonephritis by preventing serious kidney failure, which still affects many patients,” says Pierre-Louis Tharaux.

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Source :

Nuclear Factor Erythroid 2-Related Factor 2 Drives Podocyte-Specific Expression of Peroxisome Proliferator-Activated Receptor γ Essential for Resistance to Crescentic GN.

Henique C, Bollee G, Lenoir O, Dhaun N, Camus M, Chipont A, Flosseau K, Mandet C, Yamamoto M, Karras A, Thervet E, Bruneval P, Nochy D, Mesnard L, Tharaux PL.

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