Be cautious when measuring renin

Renin levels may vary between blood plasma and kidneys, says Bibi van Thiel. This has implications for the diagnosis of hypertension.

SHURAILA STOPPEL

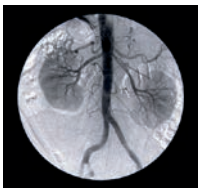
'My research focuses on the renin-angiotensin system (RAS) in the elderly," says Bibi van Thiel, PhD student at the Erasmus MC. RAS is a hormonal signalling system that regulates blood pressure and fluid balance in the body, Van Thiel explains. Dysregulation of the system may cause cardiovascular and renal disorders. "My project involves important fundamental research", she says. "The goal is to understand RAS regulation in elderly people. To investigate this I make use of a well-established mouse model for premature ageing."

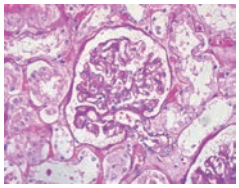
Doctors traditionally measure renin in patient plasma, for instance as part of the diagnosis and treatment of hypertension. Van Thiel: "However, I showed that renin levels in the kidneys of 'elderly' mice are much higher than the levels in their plasma."

AGEING

The underestimation of renin levels by focusing on plasma may have implications for medical intervention in elderly patients, she points out. Patients with high blood pressure, for example, are usually treated with RAS-blocking drugs. Unfortunately, these do not seem to work very well in some older patients. "Based on my results you could conclude that alternative drugs can be a better choice in some patients."

One of the characteristics of the RAS is its complexity. Not only kidneys play a role in its regulation, but also the brain, lungs, blood vessels and liver. This





'Some patients may benefit from alternative drugs'

complexity is well reflected in the collaboration between the three Rotterdam departments where Van Thiel works: Genetics, where the mouse model was designed, Vascular Surgery and Pharmacology.

Van Thiel's mouse model ages prematurely due to a mutation in a DNA damage repair gene. These mutant mice already show signs of ageing at six weeks of age. Pathology demonstrated that their kidneys show the same features as those of elderly people – and the mice have no general ageing illnesses that affect renal health.

"This is a good model to study ageing", explains Van Thiel, "because it can take years before regular mice become naturally old. In addition, we can study the ageing process without the interference of other diseases that could influence the results of the renin experiments."

In the premature ageing mice, a fluorescent probe that is activated by renin was applied *in vivo* to allow non-invasive imaging of renin activity. Van Thiel explains: "This probe is injected. With a molecular imaging technique called Fluorescence Molecular Tomography the activity of renin that is secreted by the kidneys can be visualized and measured. We validated the specificity of the probe by demonstrating increased plasma renin concentrations and intrarenal RAS activity after treatment with the angiotensin II receptor antagonist losartan, which increases renin due to removal of the angiotensin II feedback."

Ideally, these results could be translated to a more personalised medical treatment, says Van Thiel. "Patients with, for instance, chronic kidney failure may not benefit from medication that causes RAS-blockade. We would like to be able to prescribe more effective medication and avoid drugs that cause unwanted side effects." |

Bibi van Thiel is participating in the PhD Student Competition at the FIGON Dutch Medicines Days. See also page 19.