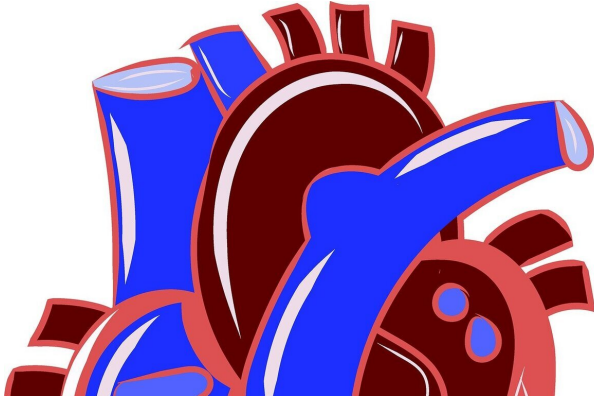


# Researchers identify biomarker for cardiovascular diseases

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The role of the enzyme dipeptidyl peptidase 3 in the blood pressure-regulating renin-angiotensin system was investigated in the inter-university cooperation project BioTechMed-Graz. The results could pave the way for new therapies for cardiovascular diseases.

The renin-angiotensin system (RAS) becomes active at [low blood pressure](#) and forms angiotensin II, a hormone that causes [blood vessels](#) to constrict, causing [blood](#) pressure to rise again. The enzyme dipeptidyl peptidase 3 (DPP3) is significantly involved in the metabolism of angiotensin II.

The head of the Institute of Biochemistry at Graz University of Technology, Peter Macheroux, and his team are [world leaders](#) in DPP3 research: "For example, we now know that people who suffer a [heart attack](#), blood poisoning or acute kidney injury have elevated levels of DPP3 in their bloodstream. This increase correlates with increased mortality." However, little is known about the physiological function of DPP3. For this reason, the working group led by Macheroux, together with researchers from the University of Graz and Med Uni Graz,

investigated how DPP3 affects the RAS. The results were published in the *Journal of Biological Chemistry*.

## Effects of DPP3 deficiency

The DPP3 gene was specifically switched off in a mouse model at the University of Graz (knock-out [mouse model](#)). Using mass spectroscopic analyses, the researchers discovered that DPP3 regulates RAS processes and the water balance by breaking down angiotensin peptides. The DPP3 deficiency led to increased fluid and food intake. Nevertheless, the knock-out mice had a lower body weight and less fat mass than the mice of the control group (wild type mice). Furthermore, the concentration of angiotensin II was significantly higher in knock-out mice. This increased angiotensin II level caused oxidative stress and reduced metabolism. "The exact effects of these changes are still unclear, however, and will have to be examined in more detail in follow-up studies. For example, the [blood pressure](#) did not change measurably," said Macheroux.

## Gender-specific differences

For the first time it was also possible to prove that there are gender-specific differences. While major changes in RAS were found in male mice, female mice were hardly affected by DPP3 knock-out. "This documents a [direct connection](#) between the hormone system and the physiological role of DPP3. Estrogen in particular is likely to inhibit the production of [angiotensin II](#)," say the two first authors Shalinee Jha and Ulrike Taschler from the Institute of Biochemistry at TU Graz and the Institute of Molecular Biosciences at the University of Graz.

## Development of an inhibitor

The characterization of DPP3 in this study shows that DPP3 can modulate metabolic and cellular

processes in RAS. This property could be of great benefit in the treatment of various cardiovascular diseases in the future.

Macheroux: "In a next step, we would like to advance the development of an enzyme-inhibiting substance (inhibitor) for DPP3. Work on this has already begun at the Institutes of Biochemistry and Organic Chemistry at TU Graz."

**More information:** Shalinee Jha et al. Dipeptidyl peptidase 3 modulates the renin–angiotensin system in mice, *Journal of Biological Chemistry* (2020). DOI: [10.1074/jbc.RA120.014183](https://doi.org/10.1074/jbc.RA120.014183)

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