8 Summary

The Renin Angiotensin Aldosterone System and the NO system are two important components of the blood pressure regulation that are closely intertwined. It is hypothesized that the AT₁ receptor is influenced by the AT₂ receptor in participation with NO. To test this hypothesis, complex physiological investigations of the heart and kidney were performed on AT₂ receptor-deficient mice.

In this animal model, the AT₁ receptor is upregulated and provides the opportunity to examine the function of the AT₁ receptor without concomittant effects of the AT₂ receptor. Additionally, the NO system was suppressed by L-NAME and stimulated with DOCA salt respectively. For a better understanding of systemic processes, the physiological results were taken into consideration with both gene expression analyses and histological findings.

Both L-NAME and DOCA had strong effects on kidney function. The influence on heart function was much weaker. These findings underline the dominat role of the kidney in long-term blood pressure regulation.

L-Name hypertension is mainly caused by AT₁ receptor effects. Both the NO blockade and the knockout of the AT₂ receptor were strong stimuli for alterations in kidney function. The stronger renal effects, as well as the more pronounced left ventricular hypertrophy in AT₂⁻/⁻, underline the antagonistic effects of the AT₂ receptor on the AT₁ receptor. The gene expression analysis of the AT₁ receptor does not support the view, that the AT₁ receptor is influenced by the AT₂ receptor acting on NO.

The blood pressure increase in DOCA-salt treated mice is also caused by an increase in total peripheral resistance, that is not primarily determined by the AT₁ receptor. It has been shown that both DOCA-salt and the knockout of the AT₂ receptor are strong stimuli for the renal iNO synthesis. The pharmacological blockade of iNOS showed no hemodynamical relevance.

The analysis of kidney and heart function, together with gene expression analyses and histological investigations, showed no effect on the AT₁ receptor by the AT₂ receptor via NO. The initial hypothesis was rejected.