8 Summary

The Renin Angiotensin Aldosteron System and the NO system are two important components of the blood pressure regulation that are closely intertwined. It is hypothesized that the AT_1 receptor is influenced by the AT_2 receptor in participation with NO.To test this hypothesis, complex physiological investigations of the heart and kidney were performed on AT_2 receptor-deficient mice.

In this animal model, the AT_1 receptor is upregulated and provides the opportunity to examine the function of the AT_1 receptor without concomittant effects of the AT_2 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 AT_1 receptor effects. Both the NO blockade and the knockout of the AT_2 receptor were strong stimuli for alterations in kidney function. The stronger renal effects, as well as the more pronounced left ventricular hypertrophy in AT_2-/y, underline the antagonistic effects of the AT_2 receptor on the AT_1 receptor. The gene expression analysis of the AT_1 receptor does not support the view, that the AT_1 receptor is influenced by the AT_2 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 AT_1 receptor. It has been shown that both DOCA-salt and the knockout of the AT_2 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 AT_1 receptor by the AT_2 receptor via NO. The initial hypothesis was rejected.