The history of the renin-angiotensin system (RAS) dates back to the 19th century. Angiotensin II (ANG II) is still considered the most potent component of the RAS. This octapeptide plays an important role in the control of body fluid volume, regulation of blood pressure, and cardiovascular remodeling through its direct effects on protein synthesis, cell growth and differentiation, induction of growth-promoting genes, and modulation of the synthesis of oxygen radicals, prostanoids, and cytokines.

The main objective of this dissertation was to investigate the role of the interaction between systemic and intrarenal RAS in the development of hypertension.

We based our work on the following hypothesis: in transgenic rats, during the development of hypertension, there is an accelerated intrarenal production of ANG II that is not followed by a corresponding downregulation of AT1 receptor expression in the renal vasculature and tubular system of the kidneys. The combination of these two factors is responsible for increased renal vascular resistance, enhanced tubular sodium reabsorption, and an overall deterioration of the pressure-natriuresis mechanism in the kidneys, ultimately leading to the development of hypertension.

The entire dissertation is divided into several chapters. The first part focuses on the classical RAS, its known and newly discovered key components, and the various local tissue-specific RAS systems. The main topic of the second part is animal models of hypertension. Four experimental models of hypertension used in our laboratory are described.

The final and largest part consists of original research studies.
The aim of the first study was to determine the concentrations of ANG II in plasma and kidney tissue in anesthetized, surgically stressed animals compared to conscious animals. Until now, the effect of anesthesia had not been studied in ANG II-dependent models of hypertension, nor had a detailed comparison of plasma and renal concentrations of ANG II been performed between ANG II-dependent hypertensive models and normotensive control rats.