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Regulation of blood vessel diameter by the renin-angiotensin system and the vanilloid receptors

Our clinical investigations focused on the association of the genetic polymorphisms (ACE I/D; AGT M235T; AT1R A1166C) of the renin-angiotensin system (RAS) with the in-stent restenosis (ISR) of coronary vessels. Our aim was to determine whether these polymorphisms are predictive markers of ISR. We set up the procedures to determine the genotypes of the patients and we improved the published PCR-RFLP based genotyping of AGT M235T polymorphism (by designing a new primer and application of a new restriction enzyme). As a matter of the association of the genetic background of the patients with ISR, our data did not support a significant role of the determined polymorphisms in the development of ISR.

Our basic research efforts were directed to the vascular functions of the vanilloid receptor (TRPV1), which is a non-specific cation-channel, characterized mainly in primary sensory neurons. Surprisingly, TRPV1 stimulation with capsaicin caused a vasoconstriction, which was inhibited by the specific antagonist capsazepine in isolated, perfused arterioles (vessel diameter 132-223 μm at 80 mmHg) of rat skeletal muscle (m. gracilis). RT-PCR experiments and immunohistochemistry confirmed TRPV1 expression in the smooth muscle cells of blood vessels, which observation provides an explanation for the constriction. Next, effects of the endogenous TRPV1 agonist anandamide were studied. Anandamide caused a phosphorylation-dependent desensitization of TRPV1 in skeletal muscle arterioles and in TRPV1 overexpressing CHO cells. This suggests that anandamide may be an endogenous desensitizer of TRPV1 instead of being an agonist on this receptor. Finally, we demonstrated that TRPV1 can function as a phosphorylation-gated (metabotrop) receptor in the continuous presence of anandamide.