New paradigms in RAS



Classical and New Paradigms of The Evolving Renin-Angiotensin System

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- Tigerstedt and Bergman discovered renin more than 115 years ago.
- Since then, our understanding evolved from the recognition of Renin/ACE/ANGII/AT1 and AT2 receptors as the exclusive pathway within the RAS for regulating BP and blood volume to the recognition of 3 new pathways (2,3,4 on the pic)
- ANG II can be hydrolyzed by various angiotensinases, ACE2 and neprilysin, to generate ANG (1-7), ANG III and ANG IV.
- * appropriate concentrations of ANG (1-7), ANG III and ANG IV may activate their respective Mas receptors, AT2 receptors or AT4 receptors to oppose the known effects of ANG II.
- Conversely, high concentrations of ANG (1-7), ANG III and ANG IV may activate AT1 receptors to induce the effect of ANG II.
- the renin/ prorenin receptor PRR not only generates ANG II but also induces intracellular responses independent of ANG II (3)
- Finally, the RAS is no longer considered to act as an endocrine system but also as a paracrine, autocrine and intracrine system. It is likely that ANG II and its smaller peptides may both act as an endocrine, paracrine and intracrine peptides stimulating cell surface, cytoplasmatic and nuclear receptors to exert biological, physiological and nuclear effects.