Animal Model

TGR(hKLK1) Transgenic rats as a Tool to Study the Kallikrein-Kinin System

Reference Number 03-00189

Abstract
The Challenge
Blood pressure and circadian rhythmicity of cardiovascular parameters underlly many different molecular regulation mechanisms. One system playing a crucial role in the regulation of these mechanisms besides the well known renin-angiotensin system (RAS) is the kallikrein-kinin system (KKS). While RAS exerts its regulatory function in leading to an increase in blood pressure, KKS is known to have a hypotensive effect. The correct interplay of both systems is essential to ensure proper regulation of blood pressure as well as its circadian rhythmicity. Dysfunction of the interplay can lead to a multitude of damages of cardiovascular organs such as hypertrophy and fibrosis. The physiological and pathophysiological mechanisms of the KKS in general are still poorly pharmacological target. There is a strong demand for an animal model to investigate this system in detail.

The Technology
A transgenic rat line, harbouring the human tissue kallikrein gene, has been generated resulting in kallikrein overproduction in all organs. These animals show reduced blood pressure and further investigations on this model already proved that kinins have a protective effect on cardiovascular hypertrophy and fibrosis. With this knowledge TGR(hKLK1) provides an ideal system for further investigation of kinin's potential protective function in cardiovascular diseases. Furthermore, it opens new avenues to shed light on the physiological role of the KKS.

Commercial Opportunity
Breeding pairs of TGR(hKLK1) are available under Tangible Property Licence Agreement.

Further Reading

- Silva et al., 2000, FASEB J, 14, 1858-1860.
- Pinto et al., 2000, FASEB J, 14, 1861-1863.
- Schanstra et al., J Clin Invest 2002; 110:371-379.
- Thongboonkerd et al., J Biol Chem 2002; 277:34708--34716.
- Tschöpe et al., 2004, FASEB J, 18:828-835.