

Regulation der GH/IGF-1 Achse im Nagermodell

Regulation of the GH/IGF system in rodents

The growth hormone (GH)/Insulin-like growth factor (IGF)-system is highly conserved throughout species and of utmost importance for postnatal growth. In addition, both GH and IGF-I exert independent effects, e.g. on lipid and glucose metabolism or on bone formation.

Growth hormone (GH) is secreted from the hypophysis under the control of GH releasing or inhibiting factors. Some of these factors (e.g. GHRH, somatostatin) are well documented in literature, whereas others are still under debate. GH can either stimulate growth directly or via the IGF-system, by stimulating hepatic IGF-I release. Results from the past years have given more and more evidence that also locally, extra-hepatic secretion of IGF-I impacts on body and organ growth. The IGF-system is composed of soluble peptide hormones (IGF-I and -II), IGF-receptors and IGF-binding proteins (IGFBPs). The IGFs can also bind to six IGFBPs, which have higher affinities to the IGFs than the IGF-receptors. Thus, the IGFBPs are competitive inhibitors of the IGFs but also show IGF-independent effects.

In humans, growth hormone (GH) administration increases IGF-I secretion already a few hours after application. IGF-I is therefore the most important pharmacodynamic marker for diagnosis as well as for follow-up controls of diseases involving the GH/IGF-axis (e.g. acromegaly, dwarfism). Mice overexpressing GH or administration of GH to hypophysectomized/dwarf rodents have been shown to affect body- and organ weights. Simultaneously, an increase in serum IGF-I levels can be detected.

Surprisingly, little is known about the adequacy of IGF-I as a pharmacodynamic marker of GH action in generic, "wild-type" mice. In various rodent studies, an increase in serum IGF-I is often simply assumed to occur after GH administration, but never analyzed.

To understand GH action and regulation of the GH/IGF system in rodents, we have subdivided this project into three main research areas:

- Analysis of short term effects of growth hormone administration on body and organ growth, as well as to investigate if IGF-I is a suitable pharmacodynamic marker of GH action in rodents
- Nutritive regulation of the GH/IGF system in rats
- Effects of the GH/IGF system on bone turnover and osteoblastogenesis