

311 -

Respiration/Hypoxia

Subcellular localization and differential expression of two novel Anti-Hif-1 α variantsForster H.¹, Tug S. ¹, Callau D. ¹, Simon P. ¹¹Faculty of Social Science, Media and Sports, Department of Sports Medicine, Mainz

The Hypoxia inducible factor-1 (HIF-1) is known as an important transcription factor in the context of cellular response to hypoxia. Although the structure of HIF-1 α and its mechanisms are well known, numerous aspects concerning its regulation are still unexplored. One assumed reaction is the RNA-Interference of antisense variants of HIF-1 α (aHIF-1 α), which may enforce degradation in the nucleus or alternative splicing of HIF-1 α .

Therefore we aimed to explore expression and localization of two so far unknown aHIF-1 α -variants under defined conditions *in vitro* and *in vivo* to enlarge the state of knowledge about the posttranscriptional regulation of HIF-1 α . In *in vitro* experiments we succeeded to detect two novel aHIF-1 α variants, terminating in exon 2 (aHIF-1 α Ex2) and exon 14 (aHIF-1 α Ex14) in different cell lines. We verified them as spliced antisense variants of the HIF1 α -gene locus through sequencing and *in silico* analysis. The comparison of GAPDH and 7sk as housekeeping genes allowed us to identify aHIF-1 α Ex2 as nuclear and aHIF-1 α Ex14 as cytoplasmatic variant. *In vitro* trials revealed that both variants are differentially expressed after induced hypoxia (CoCl₂) and that aHIF-1 α Ex14 correlates significantly with HIF-1 α mRNA with and without exon 14 (0,953 and 0,949). Exercise induced hypoxia *in vivo* (half marathon) showed no effect on expression manner of the two antisense RNAs.

Due to specific sub-cellular localization, ubiquitous and differential expression we suggest here that these aHIF-1 α -variants are presumably associated with the regulation of HIF1 α .