

## **PROJECT REVIEW**

### ***"Fc-based fusion proteins in sports drug testing: Detecting GDF15/Fc and the myostatin inhibitor ActRIIB-Fc by proteomic approaches"***

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Fc-fusion based drugs are an emerging class of pharmaceuticals which already found their way into competitive sports: EPO-Fc is an erythropoiesis-stimulating agent where the attachment of two immunoglobulin Fc domains to the protein results in a prolonged therapeutic activity due to an increased plasma half-life and enables administration via inhalation. While EPO-Fc can be simultaneously detected with other recombinant erythropoietins by routine doping control assays, there are currently no tests for other doping-relevant Fc-fusion proteins such as the myostatin inhibitor ActRIIB-Fc (ACE031) or the cytokine GDF15/Fc, which is a member of the transforming growth factor beta (TGF $\beta$ ) superfamily.

The TGF $\beta$  superfamily includes several growth factors which are promising therapeutic targets for metabolic disorders and muscular dystrophies. Both TGF- $\beta$  inhibitors and the cytokines themselves have been pursued as drug candidates. Within this study, a proteomics-based detection assay for emerging Fc-fusion proteins relevant as performance-enhancing agents in sports will be developed. ActRIIB-Fc (ACE-031), a fusion protein composed of the extracellular domain of the human activin receptor type IIB (ActRIIB) and the Fc domain of human immunoglobulin G (IgG), which was found to significantly increase muscle mass and function by inhibition of myostatin and other ligands of ActRIIB, will be used as model compound in addition to GDF15/Fc, a fusion protein of the TGF $\beta$  cytokine growth/differentiation factor 15 (GDF15) and the immunoglobulin Fc fragment. Different peptides, mutants and constructs of GDF15 are currently tested as pharmaceuticals for the treatment of different age-related and metabolic disorders.

The proactive development detection assays for therapeutic Fc-fusion proteins, TGF $\beta$  cytokines and TGF $\beta$  inhibitors is of great interest as several drugs of these categories are already available on the black market as well as for research purposes.