

"Phase-II metabolites as target biomarkers in doping analysis – part 2: Biotechnological generation of sulfoconjugate reference material by fission yeast technology"

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Project overview

In the fight against doping the laboratories are confronted with an increasing number of substances to screen on. Thus, a comprehensive screening for different classes of substances using dilute-and-inject methods in anti-doping screening is desirable. As lots of xenobiotics are excreted as conjugates a detection of the intact conjugates is performed by this approach. While chemical synthesis of sulfoconjugates works efficiently for compounds having only one potential conjugation site, several analogous compounds could not be chemically synthesized effectively, due to their more complex chemical structure. For the synthesis of the phase-II metabolites (glucuronides and sulfates) of these compounds a biotechnological production will be implemented.

In part 1 of the project fission yeast strains, that enable the biotechnological production of glucuronides and sulfates that cannot be synthesized efficiently via classical chemical synthesis were generated. In part 2 they will be used to produce the relevant human conjugates of prohibited substances. It is planned to address the sulfoconjugation of some challenging compounds such as salbutamol-sulfate, salbutamol-glucuronide, fenoterol-sulfate and 4-hydroxy-DHEA-sulfate within the project.

The produced reference material can be used for method set-up for direct detection. If laboratories still rely on hydrolysis of the conjugates, these reference compounds may serve as control for hydrolysis efficiency and quality assurance. Furthermore, artifact generation during conjugate cleavage can be evaluated by the help of this newly generated reference compounds. The relevance of the generated reference substances in doping control analysis will be demonstrated by comparison with authentic samples from doping control analysis.