

PROJECT REVIEW

“Phase-II metabolites as target biomarkers in doping analysis: generation of reference materials and methods optimization”

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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 phase-II metabolites 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. Fission yeast strains, that enable the biotechnological production of glucuronides and sulfates that cannot be synthesised efficiently via classical chemical synthesis will be generated and used to produce the relevant human conjugates. 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.

As proof of concept the use of the generated fission yeast strains will be demonstrated by generation of salbutamol-sulfate, salbutamol-glucuronide, fenoterol-sulfate and 4-hydroxy-DHEA-sulfate within the project.