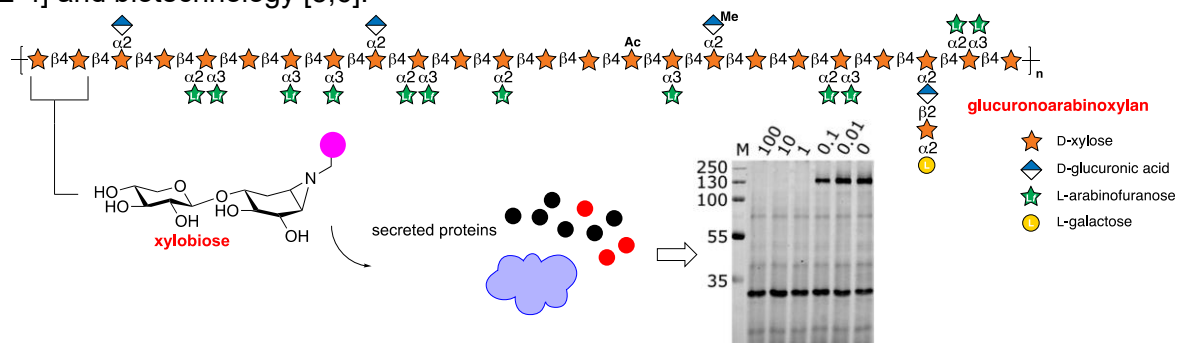


ACTIVITY-BASED GLYCOSIDASE PROFILING

Herman Overkleeft

Leiden Institute of Chemistry, Leiden University, The Netherlands
h.s.overkleeft@lic.leidenuniv.nl

Activity-based protein profiling (ABPP) is a rapidly emerging field in chemical biology research. Enzymes that employ a mechanism in processing their substrate that involves formation of a covalent enzyme-intermediate adduct can be blocked by mechanism-based suicide inhibitors: compounds that react within the enzyme active site to form a covalent and irreversible adduct. Introduction of a reporter moiety (the purple bulb in the below picture) yields an activity-based probe (ABP) through which enzyme activities are discovered (comparative ABPP) and the efficacy of enzyme inhibitors analysed (competitive ABPP). Our work on ABPP development focuses on retaining glycosidases: hydrolytic enzymes able to cleave interglycosidic linkages and that do so through the formation of covalent enzyme-substrate intermediates [1]. Configurational and functional analogues of the natural product and mechanism-based retaining beta-glucosidase inhibitor, cyclophellitol, prove to be highly versatile tools to study retaining glycosidases of various nature and origin in relation to human health and disease [2-4] and biotechnology [5,6].



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