

## Drug Metabolites

### Production of human and non-mammalian metabolites

**We provide a range of services for our clients using our expertise in microbial chemistry**

- Mimic mammalian phase I (CYP & non-CYP) & phase II metabolism to produce material for Met ID, use as quantitation standards, for stability studies or larger amounts for DMPK/ADME/TOX.
- Lipophilic rescue through creation of more polar metabolites.
- Creation of analogues for lead diversification and optimisation studies, and to protect/widen IP.

#### Reactions possible

Alkyl and phenolic hydroxylation  
N-oxidation ✓

N- + O-dealkylation/  
hydrogenation/  
dehydrogenation ✓

N-, O- and acyl glucuronidation  
(+ other conjugation such as glycosidation) ✓

Sulfation ✓

It is well known that metabolites of drug compounds may have different efficacy and side effects to that of the parent compound. Investigation and production of these metabolites is critical for exploration and understanding of SAR, and to ensure thorough patent coverage. Metabolites can also be sourced to create antibodies used in development of assays for therapeutic drug monitoring.

Hypha's has the ability to create both mammalian and microbial metabolites of drug candi-

dates at scale, in order to permit characterization and assessment towards full SAR and patent coverage.

All of the main human metabolites of Cyclosporin A were observed through biocatalysis using Hypha's microbial panel, which results in selective hydroxylation as illustrated below. Additionally we are able to form novel microbial-derived metabolites.

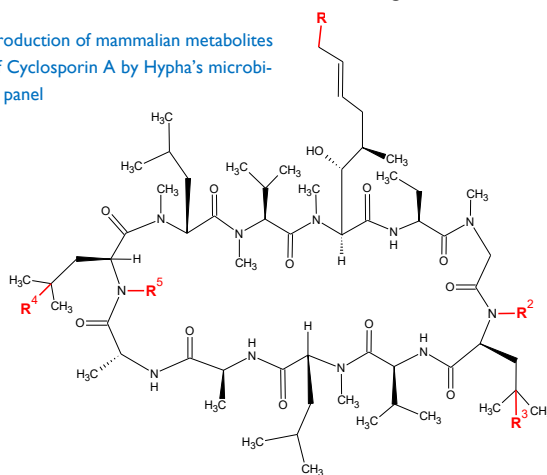
We can produce both phase I and phase II metabolites, including N-, O- and acyl glucu-

ronides and other conjugates such as sulfates.

*"We contacted Hypha Discovery to generate specific phase I and phase II metabolite standards in sufficient quantities and purity to allow structural confirmation and quantitation. Hypha exceeded expectations, providing 60mg of a phase I metabolite and over 100mg of a phase II metabolite at high purity. Hypha's team was a pleasure to work with and communicative and responsive throughout the process. We will undoubtedly be working with Hypha Discovery in the future."*

**Jason Boer, Senior Principal Investigator, Incyte Corporation, USA**

Production of mammalian metabolites of Cyclosporin A by Hypha's microbial panel



Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	R <sup>5</sup>
Cyclosporin A	H	CH <sub>3</sub>	H	H	CH <sub>3</sub>
AM1	OH	CH <sub>3</sub>	H	H	CH <sub>3</sub>
AM19	OH	CH <sub>3</sub>	H	OH	CH <sub>3</sub>
AM19N	OH	CH <sub>3</sub>	H	H	H
AM4	H	CH <sub>3</sub>	OH	H	CH <sub>3</sub>
AM4N	H	H	H	H	CH <sub>3</sub>
AM49	H	CH <sub>3</sub>	OH	OH	CH <sub>3</sub>
AM4N9	H	H	H	OH	CH <sub>3</sub>
AM9	H	CH <sub>3</sub>	H	OH	CH <sub>3</sub>
AM9N	H	CH <sub>3</sub>	H	H	H

### Why work with us?

**High success rates.** A high % of compounds have been derivatised by our strains. The process is applicable to broad structural types and provides a method for capturing multiple metabolites in a single screen.

**Scalable and reproducible process.** We have an excellent

reproducibility rate where target molecules can be scaled up to produce mg to gram quantities.

**Defined timelines and costs.** Metabolites are produced on a simple-fee-for-service basis, i.e. no downstream terms. The process is

stage-gated so the client has control throughout.



**We work with 8 out of 10 of the top pharma companies and 4 out of 6 of the top agrochemical companies worldwide. Some of our clients include:**



### ABOUT HYPHA DISCOVERY

Hypha Discovery Ltd is a UK-based microbial biotechnology company providing solutions to pharmaceutical and agrochemical R&D partners worldwide through the production of mammalian and microbial metabolites, as well as specialising in microbially-derived chemicals.