

## Drug Metabolites

### Production of mammalian and non-mammalian metabolites

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**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 (UGTs and SULTs).
- Metabolites produced 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., both mammalian and non-mammalian.
- Creation of analogues for lead diversification and optimisation studies, and to protect/widen IP.

#### Reactions possible

- Alkyl and aryl / heteroaryl Hydroxylation ✓
- Selective N-oxidation ✓
- N- + O-dealkylation/ hydrogenation/ dehydrogenation ✓
- N-, O- and acyl glucuronidation (+ other conjugations such as glycosidation) ✓
- Sulfation ✓

Hypha has the ability to create both mammalian and non-mammalian metabolites of drug candidates at scale. Such metabolites may have different potency, selectivity and DMPK characteristics to those of the parent compound. Production and investigation of these metabolites is therefore critical for exploration and understanding of metabolite-derived toxicity, SAR and to ensure thorough patent coverage.

In the example below, the major human metabolites of Cy-

closporin A were observed from application of Hypha's microbial panel, which resulted in selective alkyl hydroxylation and N-demethylation, as illustrated below.

Furthermore, our process generates microbial-derived metabolites for prodrug formation, ADC tethering or creating handles for fluorination aimed at metabolism blocking or PET ligand formation.

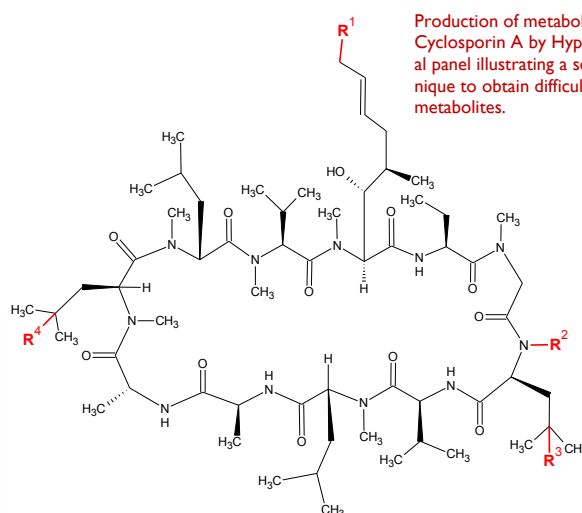
In addition to phase I metabo-

lites, we can also produce phase II metabolites at scale, including N-, O- and acyl glucuronides.

*"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 metabolites of Cyclosporin A by Hypha's microbial panel illustrating a scalable technique to obtain difficult-to-access metabolites.



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

#### 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 g 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.



Some of our partners and clients include:



#### ABOUT HYPHA DISCOVERY

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