www.hyphadiscovery.co.uk

HYPHA DISCOVERY

Metabolites and molecules for tomorrow's drugs

We provide a range of services for our clients using microbial chemistry, mammalian tissue and enzymology expertise to produce:

Mammalian Phase I (CYP & non-CYP) and Phase II metabolites:

- *For DMPK / ADME / TOX*
- *For Met ID*
- *As standards for quantitation*
- *For bioactivity testing*
- *For stability studies*

Analogues for lead diversification and optimization:

- *Obtain novel derivatives*
- *Improve activity / selectivity*
- *Improve ligand lipophilicity efficiency*
- *Protect / widen IP coverage*

Reactions	
Aliphatic and aromatic hydroxylation Selective *N*-oxidation	✓
N- + *O*-dealkylation/ hydrogenation/ dehydrogenation	✓
N-, *O*- *and acyl* glucuronidation (+ other glycosidation)	✓
Glutathione conjugation	✓
Sulfation	✓

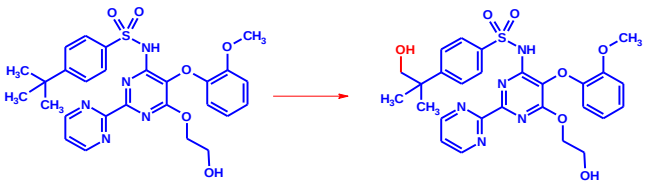
New flexible options for Met ID

Our pharma and agchem clients make use of Hypha's new parent-to-product **"one step synthesis" process**, to generate 50-500µgs of >90% pure metabolites.

Coupled with this, we can now offer definitive structural identification of metabolites using state of the art NMR technology. We are able to provide **rapid, unambiguous identification** of metabolites, such as specific sites of hydroxylation, sulfation, glucuronidation and thiol conjugation, in contrast to LC-MS/MS which provides only regional assessment. The access to a 700MHz NMR equipped with a 1.7mm Micro-cryoprobe means that only low µg amounts of metabolites are required for full data sets to be acquired. Data analysis can be performed by our NMR experts or by clients.

In addition to our microbial strains, which can be **scaled to produce gram amounts** of metabolites, we also offer the option of using recombinant enzymes and multiple species liver preparations, according to individual client needs.

2D COSY & HMQC correlations on 4.5µg material were consistent with the expected hydroxylation of bosentan.



"We commissioned Hypha to produce 50-200 µg of an oxidative metabolite where structural details were ambiguous. They provided 1mg of highly pure metabolite enabling full structure elucidation."

Manfred Birkel, Head of DMPK, Phenex Pharmaceuticals AG

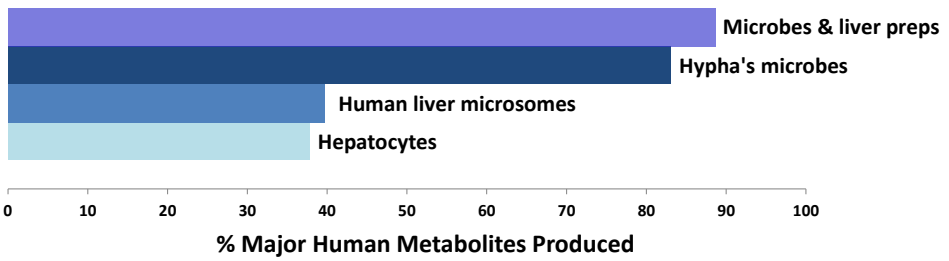
Industry-proven metabolite generation

The results of an independent evaluation* presented at the latest ISSX meeting in Florida describing the formation of metabolites from 16 commercial drugs, showed that **83% of the major *in vivo* human metabolites were accessible** using Hypha's biotransformation platform, while human liver microsomes and hepatocytes were only able to generate approximately 40% of these. In addition, Hypha were consistently better at generating **secondary and tertiary metabolites**. Furthermore, the microbial system was also able to generate many of the **phase II metabolites** (specifically glucuronides), without additional cofactors.

*Katyayan et al., 2015. Poster, ISSX, Orlando, FL

***For more information about our services, contact us at* mail@hyphadiscovery.co.uk**

Hypha uses both microbial and liver preps providing nearly 90% coverage of human metabolites



We work with 7 out of 10 of the top pharma companies and 4 out of 6 of the top agrochemical companies worldwide. Some of our partners and clients include:

DuPont, Gilead, Lundbeck, Syngenta, Selcia, Glactone Pharma, University of Bristol, Phenex Pharmaceuticals AG, Incyte, evotec, ferrer, Scynexis

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.