www.hyphadiscovery.co.uk

HYPHA DISCOVERY

Metabolites and molecules for tomorrow's drugs

We produce and scale-up mammalian Phase I and II metabolites using microbial chemistry, S9 fractions and pure enzymes:

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

Proven Reactions

Methyl hydroxylation
Methylene hydroxylation
Methine hydroxylation
Aromatic hydroxylation
N-oxidation
N-demethylation
O-demethylation
Carbonyl reduction
Heterocycle oxidation (AO)
Aromatic *O*-glucuronidation
Aromatic *N*-glucuronidation
Non-aromatic *O*-glucuronidation
Non-aromatic *N*-glucuronidation
Acyl-glucuronidation
N-sulfation
O-sulfation
Glycosidation
Thiol conjugation (GSH/NAC)
Sequential reactions e.g. hydroxylation & glucuronidation
N-acetylation
Transamination

Scale-up of human metabolites from mixed metabolism of epacadostat

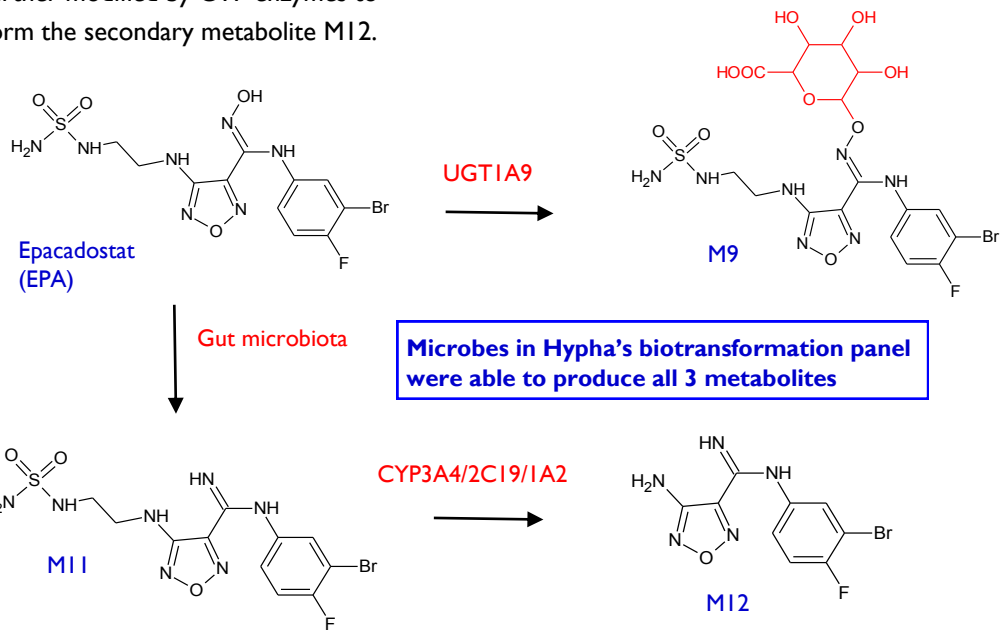
Supply of a glucuronide, gut metabolite and secondary CYP metabolite to support clinical development

Formation and scale-up of human metabolites formed through **mixed metabolic pathways** is possible using Hypha's microbial biocatalysis system.

In vivo human metabolism of Incyte's IND epacadostat (EPA) forms 3 major circulating metabolites, from both primary and secondary pathways. Glucuronidation of EPA forms M9, the dominant metabolic pathway, in conjunction with formation of an amidine M11 and an *N*-dealkylated metabolite, M12. Boer *et al.* showed reductive metabolism by gut microbiota results in M11, which is absorbed and further modified by CYP enzymes to form the secondary metabolite M12.

Hypha's microbial panels provided a route to achieve formation of **all three human metabolites**, with several strains shown able to effectively biotransform EPA. Different strains and dosing regimes were found to be optimal for production of each metabolite. Although M12 was produced by the microbes, it was more easily synthesised.

Scale-up of the most productive biotransforming strains for M9 and M11 enabled the supply of 112mg of the glucuronide and 69mg of the gut metabolite at 95% purity to Incyte Corporation.



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

Ref: Roles of UGT, P450 and Gut Microbiota in the Metabolism of Epacadostat in Humans. Boer *et al.*, 2016. DMD 44(10), 1668-1674.

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.