An Exploration of Interdisciplinary Insights: Unravelling CYP2C9 Inhibition via Metabolomics

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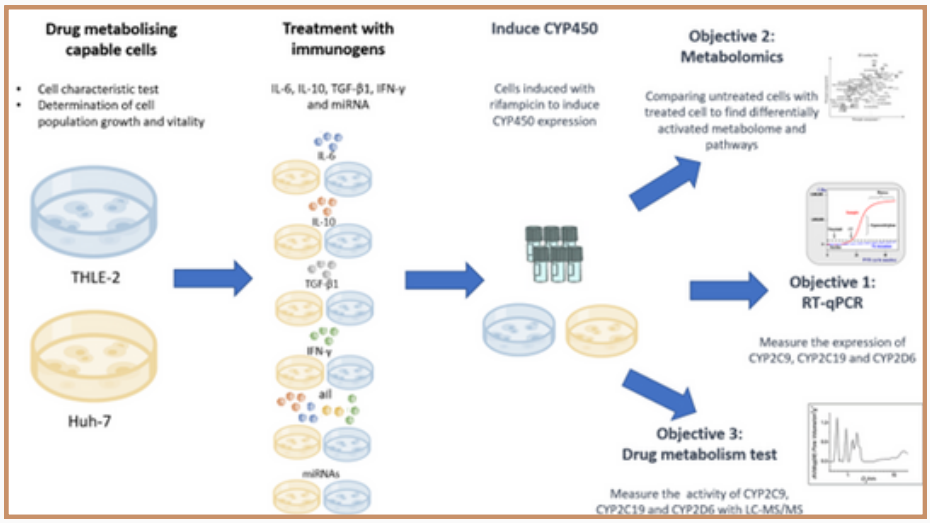
The cytochrome P450 (CYP450) enzymes play a crucial role in drug metabolism, detoxification, and synthesis of endogenous compounds. They are expressed primarily in the liver, involved in the biotransformation of a wide range of drugs and xenobiotics. The activity of CYP450 enzymes can be modulated by a variety of factors including genetic polymorphisms, drug-drug interactions, and the environment. Several studies have demonstrated that exposure to immunogens can significantly affect the expression and activity of CYP450 enzymes. For example, cytokines such as interleukin-6 (IL-6), transforming growth factor beta (TGF-β) and interferon-gamma (IFN-γ) have been shown to influence the expression of various CYP450 isoforms, including CYP2C9, CYP2D6, and CYP2C19.

Other cytokines such as interleukin-10 (IL-10) have been shown to downregulate the expression of certain CYP450 isoforms. microRNA-130 (miRNA-130), a small non-coding RNA that plays a key role in post-transcriptional gene regulation, is involved in mediating the immunogens on CYP450 expression. We have previously found that CYP2C9 activities are significantly lowered in Turkish patients with Behcet's disease, compared to healthy Turkish subjects. The gap in the knowledge is that the effects of these molecules on the expression and metabolic activity of CYP450 enzymes have not been fully characterized.

We aim to specifically identify the mechanisms and pathways mediated by the exposures to the immunogens using human liver model. Metabolite expression data will show the differentially activated pathways between the treated cell lines and the non-treated. Precursor drugs will be used to test the metabolism activity of the cells after treatment. Validation of CYP450 enzyme expression will be done using RT-qPCR. Understanding the interplay between immunogens and CYP450 expression is of clinical importance, with direct implications on drug efficacy and toxicity. This study will provide detailed illustration on the impact of these immunogens, enabling precision medicine, in magnitude of orders including identification of biomarkers, therapeutic target discovery, diagnostics and therapeutic monitoring.

Our interdisciplinary approach bridges immunology, pharmacology, and metabolomics. By unravelling the intricate web of CYP2C9 inhibition in Behçet's disease, we hope to enhance drug safety and personalized medicine. As we embark on this scientific journey, let curiosity guide us toward novel therapeutic avenues.

Research Directions



1. Sample: Drug metabolism capable hepatocytes cells, treated with immunogens in contrast to untreated.
2. CYP2C9 Expression: Assess CYP450 levels in cells using HPLC and qPCR.
3. Metabolite Profiling: Employ mass spectrometry or nuclear magnetic resonance (NMR) to identify metabolites.
4. Drug metabolism assessment: The drug metabolism activity of each cell group will be measured using HPLC and qPCR.
5. Pathway Analysis: Map altered metabolites to relevant pathways (e.g., arachidonic acid metabolism).

Correlation Studies: Investigate associations between metabolite levels and CYP450 activity.

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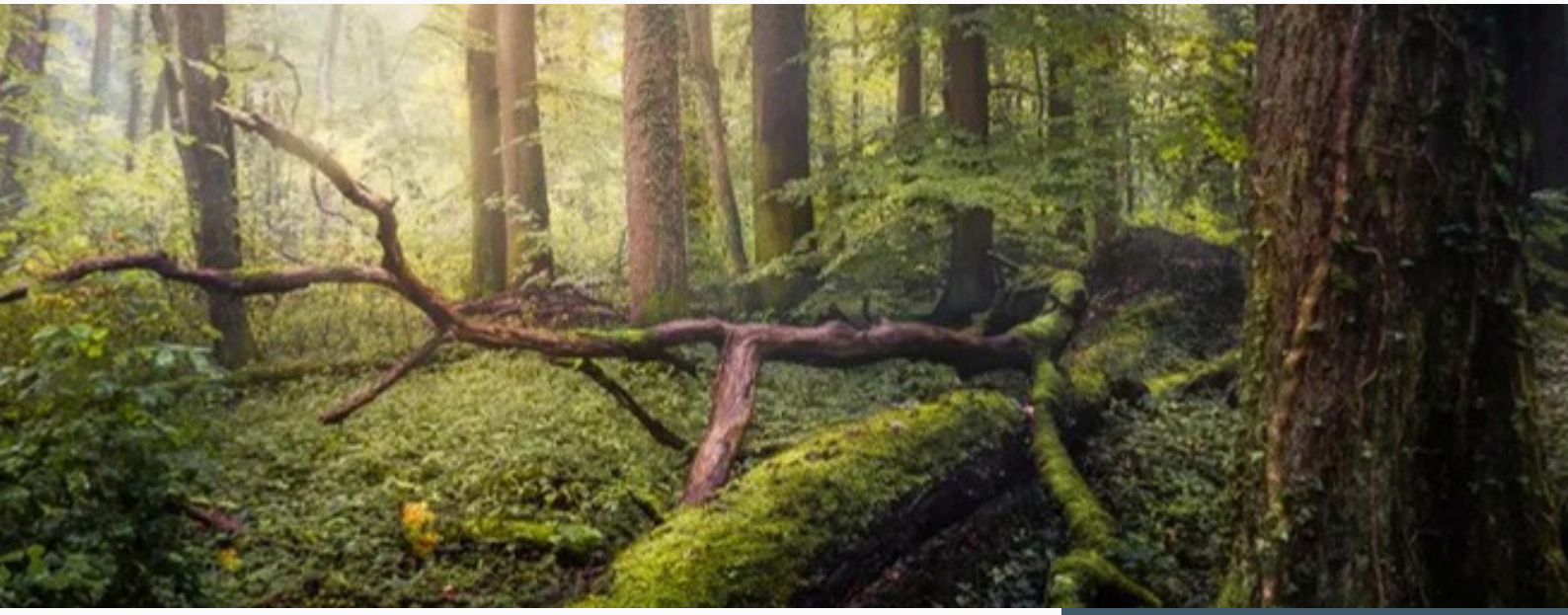

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