Accepted Manuscript

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PII: S1931-5244(16)30159-1

DOI: 10.1016/j.trsl.2016.08.002

Reference: TRSL 1090

To appear in: *Translational Research*

Received Date: 31 May 2016

Revised Date: 21 July 2016

Accepted Date: 5 August 2016

Please cite this article as: Wilson ID, Nicholson JK, Gut Microbiome Interactions with Drug Metabolism, Efficacy and Toxicity, *Translational Research* (2016), doi: 10.1016/j.trsl.2016.08.002.

Gut Microbiome Interactions with Drug Metabolism, Efficacy and Toxicity

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Keywords. Microbiome, Deconjugation, drug metabolism, prodrug activation, toxicity, efficacy.

Abstract

The gut microbiota have both direct and indirect effects on drug and xenobiotic metabolism and this can have consequences for both efficacy and toxicity. Indeed microbiome-driven drug metabolism is essential for the activation of certain prodrugs such as e.g., azo drugs such as prontosil and neoprontosil resulting in the release of sulphanilamide. In addition to providing a major source of reductive metabolizing capability the gut microbiota provide a suite of additional reactions including acetylation/deacylation decarboxylation, dehydroxylation, demethylation, dehalogenation and importantly, in the context of certain types of drug-related toxicity, conjugate hydrolysis reactions. In addition to direct effects the gut microbiota can affect drug metabolism and toxicity indirectly via e.g., the modulation of host drug metabolism and disposition and competition of bacterial-derived metabolites for xenobiotic metabolism pathways. And, of course, the therapeutic drugs themselves can have effects, both intended and unwanted, which can impact on the health and composition of the gut microbiota with unforeseen consequences.

Introduction:

To state the obvious, the aim of very many studies in drug metabolism and toxicity is ultimately to understand the factors that cause compounds to be ineffective therapeutically or cause toxicity in patients and, by using this knowledge to design better compounds, provide safe and effective treatments to patients. Whilst the