"Making the most of your model - PK and Met ID in the mouse"

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The development of genetically modified, humanized and “chimeric” mouse models that enable pharmacokinetics and metabolism questions to be asked and, possibly, answered prior to administration to man represent a real opportunity. However, these models come with a number of potential limitations including cost, transportability and limited availability. One part of the solution to some of these problems is the development of high sensitivity analytical methods based on UHPLC-MS and advances in miniaturisation. Examples will be provided of humanized chimeric mice where metabolism studies and PK have been performed in animals where the mouse hepatocytes have been largely replaced with human-derived hepatocytes. In addition studies on mice where hepatic P450’s have been effectively neutralised (the so called HRN, or hepatic reductase Null, mouse), or alternatively specific CYPs have been replaced with the human equivalent.

The utility, limitations and associated problems, of these animal models for the study of pharmacokinetics and metabolism will be discussed.

References


