THE INTESTINAL METABOLISM IN HUMANS AND MONKEYS—DOES MONKEY PREDICT HUMAN PK?
OR JUST EVOLVED—
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Have you ever found the curiosity about bioavailability in cynomolgus monkeys? That is, this primate gives us a critical problem on the decision process for selecting candidate compound. Probably people are thinking that cynomolgus monkeys must be a practical animal to simulate characteristics in human based on the Darwin’s theory of evolution. However DMPK scientists don’t say “Yes”, because they know that cynomolgus monkeys show different pharmacokinetics, especially bioavailability.

One question we tried to answer was “Does the clinical candidate with low F in monkey show low F in human as well?” For this, we performed monkey PK studies using commercially available drugs with reported human PK parameters such as F, fraction absorbed multiplied by intestinal availability (FaFg), and hepatic availability (Fh). Then, we compared the human parameters to what we found in monkeys.

As a result, the majority of clinically available drugs metabolized by CYP enzymes showed markedly reduced F (<15%) in monkeys. The species difference in F correlated with those in FaFg (1). These results highlighted the importance of the intestine as a metabolic organ for explaining differences in F observed between human and monkeys.

On the table, I introduce some of the approaches used in Astellas to assess the intestinal metabolism and would like to discuss how to interpret the monkeys PK data in drug discovery.

References:

Biography
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