Drug-related hepatopathology in animals and man

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Although drug-related hepatic injury is a common occurrence in preclinical, animal, studies it is a relatively rare, if serious, side effect of drugs in man once they have entered the clinic. This presentation will concentrate on a description of the known forms of hepatopathology commonly seen in laboratory animals as a result of drug exposure such as necrosis, fatty change and phospholipidosis, and where current histopathology is insensitive, such as in cases of intra-hepatic cholestasis. It will describe species specific differences in the responses to known hepatotoxic drugs, compare these with of drug-induced hepatotoxicity seen in man and will outline the reasons why current preclinical studies may be failing to detect subsequent adverse liver effects in man. The role of predictable versus idiosyncratic adverse drug reactions will also be discussed together with current thinking in terms of how, and if, preclinical animal studies can be altered to address these particular problems. The seminar will also describe where gaps exist in the sensitivity and specificity of current preclinical testing for liver specific pathology, and how improvements to the procedures, such as enhanced pathology, and the introduction of in silico, in vitro, and genomic and proteomic technologies, should help avoid costly, and potentially dangerous, hepatic pathology occurring in the clinic.

技術紹介:
毒性試験領域における組織マイクロアレイ法の利用
(株式会社組織科学研究所 病理診断部・横浦進一郎, 橋爪昌美)
組織マイクロアレイ法は現在まで国内の毒性試験領域で積極的に用いられていない。当研究所技術グループで実施した実例を提示して、毒性試験における組織マイクロアレイ応用の有用性について紹介する。