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3-D cell based Pk/Pd assays in hollow fiber bioreactors

Many drug effects are dependent upon not just concentration, but also time. Cell based assays and in vitro testing methods are a useful, time and cost effective tools for drug discovery. However, it is generally accepted that many of the available assays are not effective for examining the effects of both time and concentration, and do not closely mimic physiologic kinetics or the complex environment required for virus or parasite testing. Static cell based assays in plates, flasks or other formats do not readily permit changes in drug concentration as would be seen in human Pk/Pd. Animal models generally do not provide the same drug kinetics as would be found in humans and can be difficult to quantitate. Hollow fiber (HF) bioreactors can mimic complex, 3-D and multi-cellular structures and environments required for virus and parasite culture in vitro. HF cartridges have continuous medium circulation supporting dynamic control of drug concentration over time and resulting in the mimicking of dynamic tissue drug concentrations. A high surface-area-to-volume ratio permits extremely rapid exchange of metabolites and pharmacoactive molecules between the central reservoir and cells growing in the relatively small ECS of the cartridge. Furthermore, the volume of this central reservoir can be easily adjusted to permit rapid and reproducible changes in drug concentration. Simulation of the kinetics of multiple drugs can also be accomplished so drug/drug interactions and combination therapies can readily be modeled. The system is compact enough that multiple cartridges can be conveniently manipulated in a relatively small space, providing multiplexed or parallel and higher throughput type assays. Such systems can be configured for cell based assays employing either a single-cell type or multi-cell in co-cultivation. These assays can generate data that is not available in any other manner, and bridge an important gap between animal studies and phase I clinical trials. Large number of cells can be assayed over a pharmacologically relevant period of time. Drug concentrations can be controlled in a dynamic fashion and both adsorption and elimination curves can be modeled. Multiple tests can be performed on the same cell population. Three dimensional cultures of multiple cell types can model complex processes such as virus infections in tissues, parasite infections, hematopoiesis, cancer cell propagation, cancer cell metastasis, and the blood brain barrier.

Biography

John J S Cadwell has received his Degree in Pharmacology from the University of Miami in 1981. He spent additional time studying at the University of Nottingham and the National Institute of Medical Research at Mill Hill, UK. In 2000, he founded Fiber Cell Systems Inc., a company specializing in the research and supply of hollow fiber bioreactors. He has over 10 publications in the field and three patents relating to hollow fiber systems and is considered a world expert in the field.

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