**317c A Cell Culture Analog for Multidrug Resistant Cancer Chemotherapy Screening**

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The success of chemotherapy treatment on cancer is often limited due to the development of multidrug resistance. Several proteins have been associated with this phenotype, and for the last three decades chemical modulators that block these proteins have been sought to supplement treatment with chemotherapeutic drugs. At present there are several of these modulators under clinical evaluation, though none have been very successful due to an almost unavoidable increase in toxicity levels in normal tissue. Often these toxicities cannot be discovered along the drug development pipeline until well into animal trials or clinical trials. We propose the use of a cell culture analog as an intermediate system for use in evaluating candidate compounds prior to animal and clinical trials. A cell culture analog is a series of animal cell bioreactors interconnected with a network of recirculating culture medium. This in vitro system of bioreactors and fluid is scaled in size and flow rate to replicate corresponding tissues and blood flows in vivo. The described device is fabricated in silicon and contains four cell types to represent different tissues. A cell line of tumor origin and a multidrug resistant variant are used in the system to assess efficacy of the chemotherapeutic and modulator mixture. Additionally we include a hepatocyte cell line to model liver metabolism of compounds, and a cell type of bone marrow origin to serve as an indicator of systemic toxicity. In this talk, we will present some findings utilizing this system in a study with a classical drug mixture, doxorubicin and verapamil.