



PRINCIPE FELIPE

CENTRO DE INVESTIGACION

Seminario CIPF

Liver 'organ on a chip'

Speaker: Alan Wells, MD, DMSc

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Abstract: The liver plays critical roles in both homeostasis and pathology. It is the major site of drug metabolism in the body and, as such, a common target for drug-induced toxicity and is susceptible to a wide range of diseases. In contrast to other solid organs, the liver possesses the unique ability to regenerate. The physiological importance and plasticity of this organ make it a crucial system of study to better understand human physiology, disease, and response to exogenous compounds. At the lecture I will discuss biologically engineered organoids and micro physiological systems which have impelled many to develop liver tissue systems for study in isolation outside the body. In addition I will show you how we have adapted an all-human 3D ex vivo hepatic microphysiological system (MPS) (a.k.a. liver-on-a-chip) to investigate human micro metastasis regulation and development.

Alan Wells, MD, DMSc, is the Executive Vice-Chairman of the Section of Laboratory Medicine (encompassing Clinical Chemistry, Clinical Microbiology, Hematopathology, Immunopathology, Transfusion Medicine, and Clinical Pathology throughout the UPMC Health System). He also serves as the Medical Director for the UPMC Clinical Laboratories (the largest integrated academically-based clinical laboratory enterprise in the US). His clinical expertise resides in clinical laboratory medical management and how that impacts quality care. As the Thomas Gill III Professor of Pathology, Wells directs a large research endeavor investigation how cells interact with and respond to their microenvironment during cancer dissemination and wound healing, with an eye towards biologically engineered and stem cell therapeutics in these arenas.

His Laboratory research program, in close collaboration with its research partners, aims to understand cell migration in terms of how motility processes are regulated, and understand how this regulation of migration plays a role in physiologic and pathologic situations. He is integrating the knowledge gained from our biochemical and biophysical mechanistic studies into our investigations concerning conditions of dysregulated (tumor invasion) and orchestrated (wound healing and organogenesis) cell motility. As part of understanding the motility response, he is investigating both how this particular integrated cell response is selected from among others and the metabolic consequences of motility. This integrative approach provides reinforcing insights and novel avenues for exploration into the basic signaling pathways as well as functioning of whole organism. As a model system, we explore motility signaling from the epidermal growth factor receptor (EGFR) in adherent cells. EGFR plays a central role in the functioning in a wide variety of both stromal and epithelial tissues, and is the prototype for other receptors with intrinsic tyrosine kinase activity. Thus, these studies should have widespread implications.

The two central foci are tumor progression and wound repair. In tumor progression, we examine breast and prostate carcinoma invasion and metastases in terms of molecular signals and the special micro-environments. For this, the laboratory uses human tissues, animal models, and a unique 4-dimensional liver microtissue. In wound repair, the current



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model system is skin wound healing, in which the communications between the epidermis, dermis, and blood vessels is parsed at the molecular levels. The role of stem cells in the natural repair process and as a rationale therapeutic is also being investigated. These two areas are re-inforcing as many of the key molecules and cellular processes are part of the generalizable onco-fetal-wound program.