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Session Fr2D: 1:00pm -2:30pm, Friday, February 1, 2013 (Room 005)
Engineering Extracellular Matrices
Session Organizer: Nancy W. Karuri, Illinois Institute of Technology
Session Chair: Nancy W. Karuri, Illinois Institute of Technology

1:00pm **Optimal Control for Dosage Prediction in Superovulation Stage of IVF**
Kirti M. Yenkie and Urmila Diwekar, University of Illinois at Chicago, Vibha Bhalerao, Jijamata Hospital, Nanded, India
In vitro fertilization (IVF) is one of the most highly pursued assisted reproductive technology worldwide. The IVF procedure is divided into four stages: Superovulation, Egg-retrieval, Insemination/Fertilization, Embryo transfer. Superovulation is the most crucial stage in IVF, since it involves external injection of hormones to stimulate development and maturation of multiple oocytes. The maximum amount of effort and money for IVF procedure goes into superovulation. Although numerous advancements have been made in IVF procedures, medication quality, etc little attention has been given to modifying the protocols based on a predictive model. A model for the follicle growth dynamics and number as a function of the injected hormones and patient characteristics has been developed. The modeling basics were adapted from batch crystallization moment model, since moments are representatives of specific properties like number, shape and size of the particles under consideration. Based on this model, the dosage of the hormones to stimulate multiple ovulation or follicle growth is predicted by using the theory of optimal control. The objective of successful superovulation is to obtain maximum number of mature oocytes/follicles within a particular size range. Using the mathematical model involving follicle growth dynamics and the optimal control theory, optimal dose and frequency of medication is predicted for obtaining the desired result. The model will be modified to consider the sources of uncertainty due to patient's age, previous medical history, suitability of medicine and protocol used. The optimal drug delivery regime predicted in the presence of uncertainty will be compared to the current dosage regime predicted. Thus, a phenomenon currently based on trial and error will get a supportive basis to start with. This will aid as a predictive tool for medical professionals and provide them with a specific dosage strategy for a patient. This will bring down the probability of failure, decrease cost of complex monitoring and excess medication. Thus, it will decrease the overall cost of IVF treatment for the patient as well as the physician.

1:30pm **The Proteolytic Stability and Activity of Fibronectin-polyethylene Glycol Composites**
Nancy W. Karuri, Chen Zhang, Sogol Hekmatfar, Anand Ramanathan, Illinois Institute of Technology
Delayed wound healing in many chronic wounds has been linked to the degradation of fibronectin (FN) by abnormally high protease levels. We sought to develop a proteolytically stable and functionally active form of FN. For this purpose, we conjugated 3.35 kDa polyethylene glycol diacrylate (PEGDA) to human plasma fibronectin (HPFN). Conjugation of PEGDA to HPFN or HPFN PEGylation was characterized by an increase of approximately 16 kDa in the average molecular weight of PEGylated HPFN compared to native HPFN in SDS-PAGE gels. PEGylated HPFN was more resistant to α chymotrypsin or neutrophil elastase digestion than native HPFN: after 30 minutes incubation with α chymotrypsin, 56% and 90% of native and PEGylated HPFN respectively remained intact. PEGylated HPFN and native HPFN supported NIH 3T3 mouse fibroblast adhesion and spreading, migration and focal adhesion formation in a similar manner. Fluorescence microscopy showed that both native and PEGylated HPFN in the culture media were assembled into extracellular matrix fibrils. Interestingly, when coated on surfaces, native but not PEGylated HPFN was assembled into the extracellular matrix of fibroblasts. The proteolytically stable PEGylated HPFN developed herein could be used to replenish FN levels in the chronic wound bed and promote tissue repair.

2:00pm **Three-dimensional Dynamic Transcription Factor Profiling of Cancer Cells in Model Microenvironments**
Juan Sánchez-Cortés and Lonnie Shea, Northwestern University
The cellular niche refers to the immediate microenvironment around a cell, and has been instrumental supporting a range of biological processes. Reconstituting this niche in vitro can provide mechanistic insight into biological systems and may be key for developing novel therapies. Several microenvironment cues affect cellular function by imparting changes in signaling pathways within the cell. These chemical factors, wherever soluble or embedded within the matrix, are presented in vivo within a three-- dimensional environment. Though the potential of in vitro three-- dimensional cell niches to recapitulate biological effects has been recognized, these technologies suffer from the shortcoming of being impractical to use with standard molecular analysis used to scrutinize signaling pathways. In this talk, I will introduce a novel technique that combines the analysis of signaling pathways with model three-- dimensional niches that support relevant cellular function. This method relies on the dynamic measurement of transcription factor (TF) activity based on the bioluminescence

of TF-luciferase constructs. This method employs large scale delivery of TF reporter constructs combined with bioluminescence imaging, to capture the activity of numerous TFs, which can identify synergistic or counteracting signaling pathways. The first part of the talk will describe the system: its opportunities and challenges. Further, two examples of the application of this method will be presented: the changes in TF activity as a result of changes in ErbB2 signaling in cancer cells, and also the effect of cell surface receptor binding and matrix degradation in cancer cell TF activity. Taken together, this technology will prove useful to study changes in TF activity as a result of microenvironmental cues in normal and disease states.