"A New Spin on Wound Healing Scaffolds: Optimization Through Molecular and Physical Design"
Amardeep Greewal, Detroit Country Day School, Beverly Hills, MI and Ran (Ron) Li, Valley Stream Central High school, Valley Stream, NY – 2005-06 National Team Finalists
Abstract: A novel hydrogel matrix, composed of fibronectin functional domains (FNfds) and hyaluronan (HA), has recently been shown to offer great promise in promoting wound repair. However, in order to further accentuate wound healing, especially in a chronic wound setting, the hydrogel matrix must closely mimic the native extracellular matrix (ECM) both biologically and structurally while remaining stable for long periods of time. In this study, we demonstrate that these FNfd hydrogel matrices are able to bind Platelet Derived Growth Factor (PDGF) and produce a synergistic effect on fibroblast migration, a crucial step in granulation tissue induction. Such binding would enhance the bio-mimetic properties of the hydrogels by allowing enough PDGF to be presented at high local concentrations for tissue repair without the need for additional growth factors to be added exogenously. Furthermore, we produced and characterized a three-dimensional (3-D) anhydrous, nano-porous electrospun derivative of the FNfd hydrogel matrices that mimics the porous and fibrous native ECM, supports fibroblast attachment and invasion, and resists hydrolytic degradation. Together, these studies both biologically and structurally optimize engineered acelluar hydrogel wound healing matrices.

"A Novel Action of Follicle Stimulating Hormone (FSH) on Bone Explains the Genesis of Post Menopausal Osteoporosis" *(Cell Biology)*
Samir Zaid, Hackley School, Tarrytown, NY – 2004-05 National Individual Finalist
Abstract: Osteoporosis after the menopause has traditionally been thought to arise from failing ovaries and reduced estrogen levels. However, ovarian failure also increases follicle stimulating hormone (FSH) production from the anterior pituitary gland. Whether these elevated FSH levels contribute to bone loss has never been tested. The objective of the study was to examine any direct effects of FSH on the osteoclast, the cell that resorbs bone. First, FSH receptors were identified on the osteoclast by reverse transcriptase polymerase chain reaction (mRNA) and immunolabeling (protein). Second, FSH directly stimulated the differentiation of osteoclast precursors into mature bone-resorbing cells. Finally, estrogen inhibited FSH receptor expression in promoter-reporter assays, suggesting that estrogen could potentially regulate not only FSH release, but also expression of its receptor. We have therefore identified a novel stimulatory action of an "old" hormone, FSH, on bone. Our in vitro studies are supported by recent genetic evidence from the laboratory that bone is conserved when FSH is low in FSH$^{+/-}$ mice. We thus speculate that elevated FSH levels after the menopause contribute to the bone loss that was attributed solely to declining estrogen levels. Therapeutic implications may eventually arise from these studies.

"From Micro- to Nano- Patterning: Organizing the Extracellular Matrix and Directing Cell Adhesion"

Jessica Fields, Jericho High School, Jericho, New York and Taylor Bernheim, Ramaz Upper School, New York, New York – 2004-05 National Team Finalists

Abstract: The control of extracellular matrix (ECM) organization and cell adhesion are critical to future advances in tissue engineering, where precise placement of cells is needed. While it has been established that fibronectin, one component of the ECM, can be organized through contact with charged polymers, the present study demonstrates that we can induce ECM self-assembly from cells to provide a more natural re-creation of *in vivo* conditions. Micro-patterning directs ECM and cell organization, but it is also critical to investigate nano-patterning since cells have nano-meter sized receptors that may be targeted for more precise cell adhesion. A new, cost-effective methodology for nano-patterning was devised, by harnessing the dewetting process, to optimize cell organization and adhesion on the nano-scale. Further, micro-patterning techniques provided a comparison of normal cells and their emergent ECM to cancer cells and their emergent ECM to elucidate protein and cell abnormalities, leading to an enhanced understanding of cancer. Differences in cancer cell versus normal cell adhesion to the ECM may provide a potential diagnostic for identifying malignancies at the single-cellular level. Atomic force and confocal microscopy were employed. This research improves our overall understanding of cellular physiology, with implications for medical technology, tissue engineering, and understanding cancer.

"Control of Fibronectin Organization by Micro- and Nano- Patterning and the Impact on Cell Morphology"

Madelyn Ho, William P. Clements High School, Sugar Land, TX and Lenny Slutsky, Ward Melville High School, East Setauket, NY – 2002-03 National Team Finalists

Abstract: Effective repair or replacement of tissues requires precisely defined cellular architecture. The organization and composition of the extracellular matrix (ECM), which contains proteins, have been shown to have a drastic effect on cell behavior, thus critical to the development of tissues. Fibronectin (Fn) is a prominent adhesive protein for cells and has been shown to undergo spontaneous fibrillogenesis under the influence of SPS 28% polymer coated on silicon substrate.

Using gold/silicon patterning on the micro- and nanoscale, we show that the morphology of the Fn formed on the patterned surfaces was directly related to the pattern dimensions and to the underlying nature of the substrate, demonstrating that proteins do not adsorb onto metal substrates. Cells were shown to be sensitive to the structure of the protein. Therefore, we were able to control the precise spatial development of the cells, which is essential to future advances in tissue engineering.

Mentors: John Jerome and Dr. Miriam Rafailovich

"Sontaneous Fibrillogenesis on Charged Polymer Surfaces"

(Cell Biology)

Michelle Simpser and Rikki Frenkel, Stella K. Abraham High School for Girls, Hewlett Bay Park – 2002-03 National Team Finalists

Abstract: Recently, Pernodet et al have demonstrated that spontaneous fibrillogenesis can be induced without cells by using Sulfonated Polystyrene (PSS) coated surfaces. Furthermore, fibrillogenesis was found to occur only when the surface charge resembled that of the cell membrane.

We showed that fibrillogenesis observed using purified Fn was indeed the physiological form that could be produced spontaneously by actual cells on charged surfaces. Since serum is a mixture of different proteins (such as Elastin and collagen) and minerals (such as Fe and Ca), we studied the effects of other proteins found in the extra cellular matrix (ECM) on the nature of the fibrillar lattice. We found that substances that bind to Fn, such as trivalent ions and heparin, prevent growth of the lattice. We hypothesized that this may be a mechanism through which toxic substances affect cell adhesion and growth. We propose to use these substances to modify the tip of an atomic force microscope and thereby detect Fn produced in vitro by living cells.

Mentors: Rebecca Isseroff, Dr. Nadine Pernadet, Dr. Miriam Rafailovich.