**Improving on "Disease-in-a-dish" with Engineered Niche**

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After nearly a decade of recognition that extracellular matrix (ECM) properties can influence cell behavior to similar degree as growth factors, in particular ECM composition, topography, porosity, and elastic modulus (i.e. stiffness), biologists have come to recognize its importance. However matrix is highly dynamic, changing how much of it is secreted and assembled during development and disease. Most synthetic ECM mimics made initially to study this phenomenon were static but there is growing interest in making matrices that have tunable properties with time. Using several material systems in 2D and 3D, I will highlight how we have used matrix dynamics to study the mechanics of heart development and to induce disease phenotypes in the differentiated cardiac progeny of induced pluripotent stem cells (iPSCs). The patient-derived iPSCs on which I will focus carry several categories of genomic variants that predispose them to higher risk for coronary artery disease and myocardial infarction. While mechanisms in protein-coding loci are obvious, variants in non-coding loci are difficult to determine, and so I will use our materials-based approach to highlight methods that can induce disease-in-a-dish in order to study its mechanisms. Based on these exciting results, I will advocate that any *in vitro* culture system should employ dynamic materials that change as the niche does *in vivo*.