BDRC SEMINAR SERIES: Structural adaptation in response to load guides stem cell differentiation
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Abstract: Bone marrow mesenchymal stem cells (MSC) exist in a multipotential state, where osteogenic and adipogenic genomes are silenced in heterochromatin at the inner nuclear leaflet. During loading/exercise, MSC experience mechanical force through their cytoskeletal attachments to substrate, inducing signaling that alters gene expression to regulate output of osteogenic and adipogenic cells.

Although both dynamic and static mechanical force activate RhoA to control formation of the actin cytoskeleton, the nature of these forces appear to have widely variant effects on gene expression – dynamic force inhibits adipogenesis and promotes multipotentiality, while static force is associated with osteogenesis. Dynamic versus static applications may affect gene expression through generating different forces on the nucleus, affecting nuclear structure and nuclear translocation of the mechanoresponders, Yap and βcatenin.

Furthermore, intranuclear actin structure is affected by force distributed through the cytoplasmic cytoskeleton. Our work suggests that changes in intranuclear actin can have profound regulatory control over gene expression potentially through altering chromatin to allow access to transcription machinery.

Narrative Biosketch:
Janet Rubin, MD is Professor and Vice Chair for Research in the Department of Medicine at the University of North Carolina. Dr Rubin's career has explored signal transduction regulating bone remodeling. Most recently, her laboratory has made significant contributions toward understanding how exercise and exercise-generated signals regulate mesenchymal stem cell lineage selection. This has led to novel understanding of how the actin cytoskeleton contributes to signal reception, signal density and regulation of gene expression. She has served on multiple NIH study sections including as Chair, and at the American Society of Bone and Mineral Research as Councilor. In 2016 she was elected to the American Clinical and Climatological Society. At UNC she devotes time to junior faculty development, and sees endocrinology patients with a specific interest in metabolic bone disease.