

## Role of Discoidin Domain Receptors in Bone Remodeling

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### ABSTRACT

Collagen type 1 is the major component of bone. Processes regulating collagen deposition and structure are bound to impact bone remodeling. Our work focuses on the role of non-integrin collagen receptors, discoidin domain receptors (DDR1 and DDR2) in bone remodeling. DDRs are widely expressed receptor tyrosine kinases also found in osteoblasts, osteoclasts and macrophages. We demonstrate how the extracellular domain (ECD) of DDRs inhibits fibrillogenesis of collagen type 1 in both in-vitro and cell-based assays. The expression of DDR1 or DDR2 ECDs in preosteoblasts reduced the rate and quantity of collagen deposition, disrupted the native banded structure of collagen fibers and altered the mechanical properties of collagen fibers. To understand how DDRs impact bone remodeling in-vivo, we examined the collagen fibril structure, micro-architecture, and mechanical properties of femurs from wild-type and DDR1 knockout mice in an age-dependent manner. Our results indicate that thicker collagen fibrils were present in DDR1 KO mice which affected osteocyte morphology. DDR1 KO bones were weaker but with increased cortical thickening and trabecular growth in older mice. Osteoclastogenesis was impaired in DDR1 KO cells. Our results thus provide novel insights into how DDRs may serve as diagnostic markers and/or therapeutic target(s) for age-related bone diseases.

### ABOUT THE SPEAKER

Dr. Gunjan Agarwal is a Professor in the Department of Mechanical and Aerospace Engineering at the Ohio State University. She received her PhD in Biophysics from the Tata Institute of Fundamental Research in Mumbai, India and came to the US for her post-doctoral training at the Albert Einstein College of Medicine (Bronx, NY) and at Procter and Gamble Pharmaceuticals (Cincinnati OH). After a brief period as a scientist at the Wright Patterson Air Force Base, she joined the Ohio State University in 2003.

Prof. Agarwal's research interests lie "outside the cell" on extracellular matrix remodeling, with a particular focus on the collagen receptors discoidin domain receptors (DDR1 and DDR2). Like integrins DDRs are ubiquitously expressed and are understood to be important for several diseases such as cancers and fibrosis. Dr. Agarwal has been a pioneer in the field of DDRs and her laboratory has yielded seminal work on collagen fibrillogenesis and cell-matrix interactions. Her ongoing research is directed to unravel the causes and consequences of an altered collagen fibril structure with a particular emphasis in age related vascular and bone diseases. In another line of research, she is investigating magnetic behavior of nanoparticles at the microscale level.

Prof Agarwal extensively employs atomic force microscopy (AFM) and other microscopy approaches for her research. She directs a multiuser AFM core facility and is the co-director of the interdisciplinary Biophysics graduate program at the Ohio State University. She has published 4 book chapters and over 60 journal articles in well-reputed journals like Acta Biomaterialia, J. Mol. Biol, Small etc. Her research has been continuously funded by the NSF, NIH and the American Heart Association. Dr. Agarwal has also been recognized for her efforts in diversity and inclusion.



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