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Evaluating epigenetic regulatory pathways of collagen 2 α 1 expression using Alginate encapsulated chondrocytes

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Osteoarthritis (OA) is a degenerative joint disease of the articular cartilage (AC) characterized by disrupted balance between cartilage-type extracellular matrices (ECM) synthesis and breakdown. Collagen 2 α 1, is one of the major AC constituents which is downregulated with OA progression. Here we propose to explore the epigenetic mechanism involved in collagen 2 α 1 expression, with regards to healthy and degenerative cartilage. To coax tissue differentiation, isolated human chondrocytes were encapsulated in 3D alginate hydrogel microbeads (3D). 3D chondrocyte cultures were systematically compared to their equivalent monolayer (2D, passage 2) cultures, to assess epigenetic diversity in collagen 2 α 1 expression. 3D-cultured human chondrocytes possessed augmented expression of collagen 2 α 1 and other cartilage anabolic ECM genes, as compared to monolayer cultures (2D). As well, 3D cultured chondrocytes display increased protein levels and activity of the histone deacetylase SirT1, which is known to promote collagen 2 α 1 expression. Chromatin immunoprecipitation (ChIP) analyses for the promoter of collagen 2 α 1 exhibited enrichment for SirT1 and the histone methyl transferase SET7/9 in 3D cultured chondrocytes as compared to 2D cultures. Consistently, collagen 2 α 1 promoter of 3D-cultured chondrocytes also displayed enriched levels of trimethylation on histone 3 lysine 4 (3MeH3K4), which is a necessary histone hallmark of gene transactivation. Overall, 3D/2D experimental platforms provide a valuable tool for deciphering epigenetic mechanisms of gene regulation towards a better understanding of processes leading to tissue degeneration and disease. Elucidating these mechanisms could lead to developing novel targets for the treatment of OA and the early diagnosis of susceptible individuals.

Biography

Mona received here PhD in BioMedical Engineering in 2006 and completed her post-doctoral studies at NIAMS, NIH in 2009. She is currently a Lecturer at the Faculty of Dental Medicine, and heads the Laboratory of Cartilage Biology at the Hebrew University of Jerusalem, Israel. She is an expert in tissue engineering and biomaterials, and also specializes in the field of epigenetic regulation. Her Scientific achievements and publications won her numerous awards such as the New Investigator Recognition Award (NIRA) of the Orthopedic Research Society and the Kreitman Foundation Fellowship award. Mona has published her work in top tier peer-reviewed scientific journals within the field of Tissue engineering and Rheumatology.