

Interdisciplinary Colloquium Regenerative Medicine I

Tuesday, 28th Nov. 2017 at 12:30 – 1:30 pm,
Kleiner Hörsaal OST,
University Hospital Zurich

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Why location matters in arthritis

Rheumatoid arthritis is a chronic inflammatory autoimmune disease, which results in severe joint inflammation and joint destruction. Rheumatoid arthritis characteristically affects joints in specific anatomical locations, most prominently the small distal joints of hands and feet. We suggest that three, probably interconnected, mechanisms underlie the joint-specific development of arthritis, including site-specific local cell types that drive disease; systemic triggers that affect local cell types; and site-specific exogenous factors, such as focal mechanical stress, that activate cells locally. We focus on studying the role of site-specific local stromal cells, specifically synovial fibroblasts, in setting the joint-specific patterns of arthritis. Synovial fibroblasts are the major stromal cells in the joint synovium and have a key role in inflammation and joint destruction in rheumatoid arthritis. We show that synovial fibroblasts from distinct joint locations differ in transcriptional programs, epigenetic landscapes, and functional properties such as proliferative, chemotactic and, adhesive activity. In particular, the expression of genes that are involved in the embryonic development of the respective joint regions (e.g. *HOX* genes) differs highly between synovial fibroblasts from different joints. We hypothesize that the joint-specific phenotypes shaped during embryonic development and maintained during adult life, contribute significantly to the pathognomic patterns of joint affection in rheumatoid arthritis. Thus, we investigate the joint-specific composition of synovial tissues in health and disease, and study the functions of key regulators of joint-specific gene expression (e.g. long non-coding RNA, transcription factors). We explore the joint-specific effects of genetic risk loci in rheumatoid arthritis and analyse the joint-specific differences in response to inflammatory stimuli and therapy.

Organiser: Prof. Dr. Dr. Simon P. Hoerstrup

Execution/Chair: Dr. Steffen M. Zeisberger

IREM & Wyss Zurich, Univ. of Zurich and ETH Zurich