Give and Take
Evidence for Transfer of Mitochondria Via Nanotubes in Fibroblast-like Synoviocytes

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Background: The synovial membrane of diarthrodial joints is primarily composed of fibroblast-like synoviocytes (FLS) that form a complex tissue via discrete cell-to-cell connections with wide intercellular matrix spaces. The distinct synovial tissue function that is crucial to joint homeostasis depends upon integrated activity of individual FLS. Using a in-vitro synovial organ culture system, we explore mechanisms of FLS cellular cooperation with special interest in the cell-to-cell transfer of mitochondria via interconnecting membrane nanotubes.

Methods: Human FLS were prepared from synovial tissues obtained as discarded specimens following joint arthroplasty. Cells were cultured in spherical matrigel micromasses with an average size of 2 mm Ø. Data was acquired by confocal live cell imaging. Analysis of the resulting 4D movies was done with Imaris® software.

Results: To examine whether or not FLS transfer cytoplasmic cargo, we labeled 50% of FLS with red cell tracker dye and loaded the other 50 % with green non-degradable microspheres. In a time series (8 days), we found that microspheres appear in red labeled cells. First evidence was found on Day 1 and over the course of the following days microspheres accumulated in red labeled cells with a transfer rate of 10 % of newly affected cells/day.

With special interest in the transfer of mitochondria, we repeated similar experiments with labeled mitochondria. We found that the transfer rate for these organelles is similar to the one for microspheres. Additionally, we were able to capture evidence that FLS indeed use their nanotube connections for transfer of mitochondria.

Conclusions: Our experiments suggest transfer of cytoplasmic cargo, including organelles such as mitochondria, between FLS. These studies may provide insight into how synoviocytes orchestrate their activity. Further studies will demonstrate the significance of directed cargo exchange for cellular cooperation and the function of the normal as well as the diseased synovium.