



Title	Quantitative characterization of mesenchymal cell aggregation process
Author(s)	HU, J; Sham, MH; Huang, W
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Theme 3: Development & stem cells

Poster
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Sequential expression of Lgr5 and Col22a1 in developing synovial joints marks the progressive differentiation of progenitor cells to articular chondrocytes

Feng Chen (HKU)

(Supervisor: Professor Danny Chan, HKU)

Healthy articular cartilage in synovial joints provides a smooth, wear-resistant structure that reduces friction and absorbs impact forces. They are enclosed in joint capsules, containing a fibrous connective outer layer and a synovial inner layer, and stabilized by ligaments and tendons. Degenerative joint diseases involve destruction of the articular cartilage. Damaged articular cartilage is difficult to heal due to their poor regenerative capacity, leading to widespread suffering from arthritis and joint injuries. A clear understanding of how a synovial joint develops and the progenitor cells that contribute to its formation and maintenance is essential for the development of therapeutic strategies for degenerative joint diseases. We identified a stem cell marker, Lgr5, expressed specifically in interzone cells at the earliest stage of joint formation. We showed that Lgr5-expressing (Lgr5+) interzone cells are progenitors that contribute to the formation of the supporting tissues such as the ligaments and synovial membrane, and more importantly to specific regions of the articular cartilage surfaces. We further identified that cells co-expressing Lgr5+ and an extracellular matrix gene, Col22a1 (Lgr5+/Col22a1+ double-positive cells) are progenitors committed to becoming articular chondrocytes. Available mice with molecular tags for Lgr5 and Col22a1 expression will allow the isolation of these specific cell pools in a developing joint to gain an understanding of the molecular signature and the signals that regulate this lineage progression and the maintenance of the interzone cells.

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Quantitative characterization of mesenchymal cell aggregation process

Hu Jianjiang (HKU)

(Supervisor: Professor MH Sham and Dr. Wei Huang, HKU)

Mesenchymal cell aggregation (or named 'condensation' in developmental biology) is a fundamental phenomenon in a wide variety of physiological and pathological processes. Although the mechanisms of mesenchymal cell condensation in kidney, vertebrate and limb bud development are still not clear yet, scientists have found ways to create the mesenchymal cell aggregates in vitro for tissue engineering applications. Mesenchymal cell aggregation with proper size and timing is key to the efficiency of subsequent differentiation and generation of functional cells. Nevertheless, there is still little knowledge on the general principles controlling the aggregate formation and the determination of their size and time. The research aim of this study is to quantitatively characterize mesenchymal cell aggregation process in order to identify its governing principles. By combining mathematical analysis and modelling tools with image analysis tools, several quantitative analysis methods have been established. Based on these methods, we identified a unique aggregation principle, and developed approaches to tune the aggregation process based on this principle. Further research will be focused on the correlations of mesenchymal stem cell differentiation efficiency and tuning of the aggregation process.