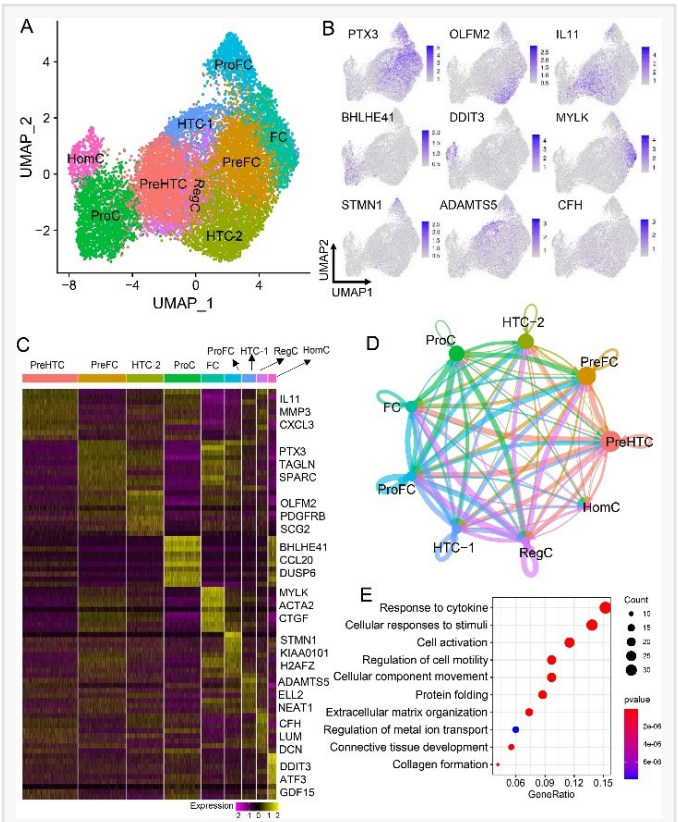
Single-Cell Transcriptomic Atlas of Chondrocytes Sheds New Light on Osteoarthritis (OA) Mechanisms

Mapping Chondrocyte Diversity in Healthy and Osteoarthritic Cartilage to Uncover New Therapeutic Targets

CHONGQING, CHINA, February 25, 2025 /EINPresswire.com/ -- Chondrocytes are specialised cells that are essential for cartilage maintenance and repair, and their dysfunction is central to the development of joint diseases like osteoarthritis (OA). However, the cell heterogeneity of chondrocytes in human articular cartilage is still not well defined, which hinders understanding of the pathogenesis of OA.



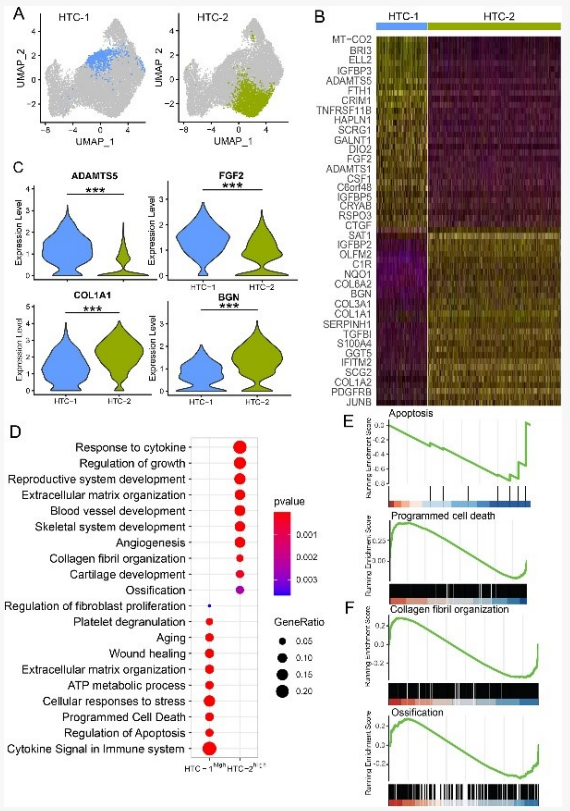
(A) UMAP visualization of the 13,363 chondrocytes from healthy human cartilage. Color represents the chondrocyte subset. (B) UMAP visualization of the expression of representative marker genes for each chondrocyte subset. (C) The heatmap of chondrocyte su

This research, published in the Genes & Diseases journal by a team from the Harbin Institute of Technology, Southern University of Science and Technology, Shenzhen University, Guangxi University of Chinese Medicine, Guangdong Medical University, and the University of Chinese Academy of Sciences, employs Single-cell RNA sequencing (scRNA-seq) to uncover distinct subpopulations of human tissue chondrocytes (HTC).

The researchers used scRNA-seq to construct a single-cell transcriptomic atlas of chondrocytes in healthy human cartilage, identifying two HTC subpopulations, namely HTC-1 and HTC-2. HTC-1, the novel THC subset, specifically expressed genes associated with cell apoptosis and programmed cell death and was found to be expressed more in the cartilage of OA patients compared with healthy individuals. This finding indicates that an increased presence of HTC-1 and decreased chondrocyte apoptosis play pivotal roles in the pathogenesis of OA.

In addition to HTC-1, the researchers also identified a significant expansion of population size in proliferate fibrochondrocytes (ProFC), especially a newly discovered subset, namely ProFC-2, in OA cartilage. Different from ProFC, ProFC-2 showed a heightened inflammatory response, and increased cytokine signalling and cellular responses to stimuli. Thus, ProFC-2 is an OA cartilage-specific subpopulation and may contribute to the development of OA via inflammation.

This study also highlights homeostatic chondrocytes (HomC), a subpopulation known for its pronounced expression of human circadian clock rhythm genes and protective effects against cartilage degeneration. Interestingly, the researchers found that HomC expression was significantly lower in OA cartilage compared to healthy cartilage, providing new insights into the molecular mechanisms of OA.



(A) Highlighting of the two HTC subpopulations on the UMAP plot of chondrocytes. (B) The heatmap of the expression level of differentially expressed genes (DEGs) between HTC-1 and HTC-2. (C) The violin plots showing the expression levels of representative

The key findings of this study include the identification of HTC-1, a subpopulation involved in apoptosis, and the discovery of an OA-specific ProFC-2, linked to inflammatory processes. A comparison of chondrocyte subsets between healthy cartilage and OA cartilage showed that ProFC and HTC-1 populations expanded in OA patients, whereas the HomC population decreased. This study deepens our understanding of chondrocyte heterogeneity in articular cartilage and thereby provides valuable clues about the cellular mechanisms driving the development and progression of OA. In conclusion, the researchers highlight that these insights could pave the way for future therapeutic approaches aimed at modulating chondrocyte populations and preventing cartilage degeneration in OA.

Reference

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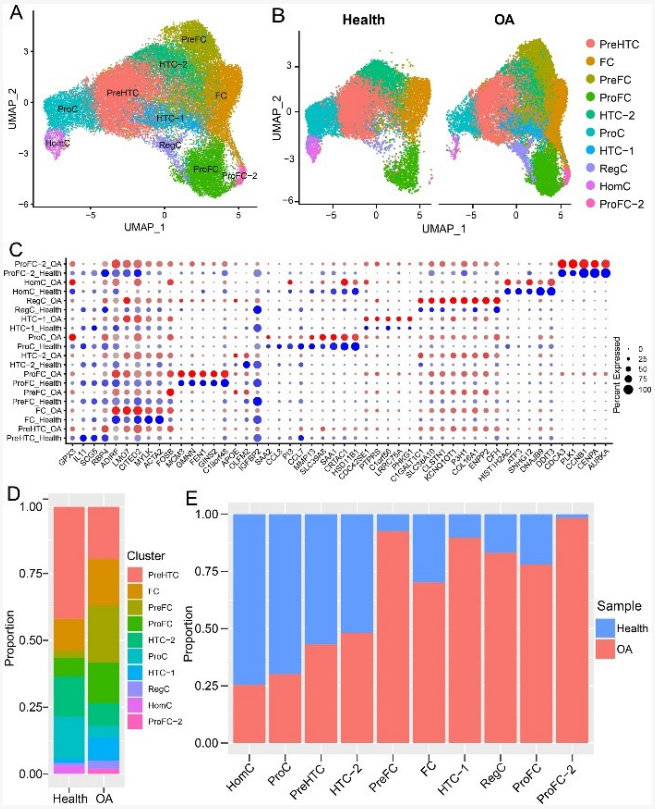

(A) UMAP visualization of 34,941 chondrocytes in healthy and OA cartilage. (B) UMAP visualization of chondrocytes in healthy cartilage (left) and OA cartilage (right). (C) Comparison of the expression of chondrocyte subset-specific genes between healthy c

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