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OSTEOARTHRITIS

Epigenetic clues into the molecular basis of OA

"Epigenetics has a key role in the onset and progression of common diseases, providing a link between genetic and environmental risk factors," says Dr Michael Rushton (Newcastle University, UK). Previous studies indicate that altered DNA methylation in chondrocytes might result in altered gene expression and shift cartilage homeostasis towards degradation but, "No study has yet provided a comprehensive genome-wide analysis of the epigenetic alterations that occur in OA cartilage," continues Rushton. In their *Arthritis & Rheumatology* paper Rushton *et al.* now address this issue.

The researchers used the Illumina Infinium HumanMethylation450 BeadChip array—the highest density array available—to compare the DNA methylome of OA hip chondrocytes and healthy chondrocytes, and also of hip OA and knee OA chondrocytes. Genome-wide methylation was analysed in chondrocyte DNA from cartilage samples obtained from 23 patients with hip OA and 73 patients with knee OA, plus 21 healthy hip controls. "The 450k array allowed us to measure methylation at a total of 454,167 CpG sites throughout the whole genome, including within genomic features such as promoters," explains Rushton. This allowed for a more comprehensive analysis than a previous study using a 27k array (Fernandez-Tajes, J. *et al.*).

The authors confirmed that OA hip and healthy hip controls have unique chondrocyte methylation profiles, with 5,322 differentially methylated loci (DMLs) identified. Some DMLs were in genes encoding proteins known to be associated with OA pathogenesis, but others were in genes involved in cartilage homeostasis that have not before been linked to OA.

5,547 DMLs were also identified between the hip OA and knee OA groups, again including some in genes associated with OA pathogenesis or cartilage development. Interestingly, a large number of DMLs did not overlap between the knee and the hip, suggesting that despite similar pathologies different pathways of pathogenesis occur in the two sites. As Rushton says, "The DNA methylome is able to distinguish OA by joint type."

Finally, the authors confirmed previous findings that knee OA samples cluster into two groups, and also for the first time showed that the same is true for hip OA. "Between the two hip OA clusters, DMLs were enriched in genes involved in inflammation and immunity, suggesting at least for a subgroup of patients, that inflammation may have a more integral role in OA than previously assumed," Rushton concludes.

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Original article Rushton, M. D. *et al.* Characterization of the cartilage DNA methylome in knee and hip osteoarthritis. *Arthritis Rheum.* doi: 10.1002/art.38713