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OSTEOARTHRITIS

Circulating miRNAs—early osteoarthritis biomarkers?

"We are the first to identify a specific miRNA signature that predicts the development of severe osteoarthritis of the hip and knee joint," says Christian Beyer, the corresponding author of a multicentre European collaborative study published in *Annals of the Rheumatic Diseases*.

Current methods of detecting osteoarthritis (OA), such as MRI, are not sensitive enough to detect the very early stages of disease, limiting their usefulness for early intervention. Beyer's data identify the microRNA (miRNA) let-7e as a potential biomarker for early detection of severe OA. He says of his new data, "the lower the let-7e levels, the higher the likelihood of more than one joint replacement surgery."

Currently, validated biomarkers for the early detection of severe OA do not exist. MiRNA signatures in OA cartilage have been associated with severity of disease but joint miRNAs are not necessarily representative of the miRNAs found in the blood. Beyer's team used the Bruneck cohort, a close representation of Western populations, which has previously been used to assess miRNA profiles associated with diabetes and cardiovascular disease, to analyse serum miRNAs as candidate biomarkers that could easily be detected by high throughput screening of blood.

> "...let-7e inversely correlated with the likelihood of study participants having OA-related arthroplasty..."

Serum miRNAs were measured at the beginning of the study (baseline). During the following 15 years, 67 of the 816 Bruneck cohort participants had ≥1 total joint replacement for knee OA ($n = 28$) or hip OA ($n = 41$). Pooled serum samples ($n = 13$) were screened by microarray and 12 differentially expressed miRNAs were further examined by conventional PCR. Standardization and a lack of statistical significance excluded some candidate biomarkers, but the serum concentration of let-7e inversely correlated with the likelihood of study participants having OA-related knee or hip arthroplasty.

Beyer says that let-7e still needs to be validated "in additional cohorts with other disease subtypes and ethnicities," and he wants to link the data with imaging results, but so-far let-7e seems to be a suitable biomarker for severe OA. Whether or not let-7e is also involved in the pathogenesis of OA is unknown, but he points out that let-7e has been shown to "target MMP-9 in the context of adipose-derived stem cell development," hinting at a potential link with cartilage degeneration. "Future studies," he predicts "might change the status of let-7e from 'OA marker' to 'important player' in OA."

Nicholas J. Bernard

Original article Beyer, C. *et al.* Signature of circulating microRNAs in osteoarthritis. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2013-204698