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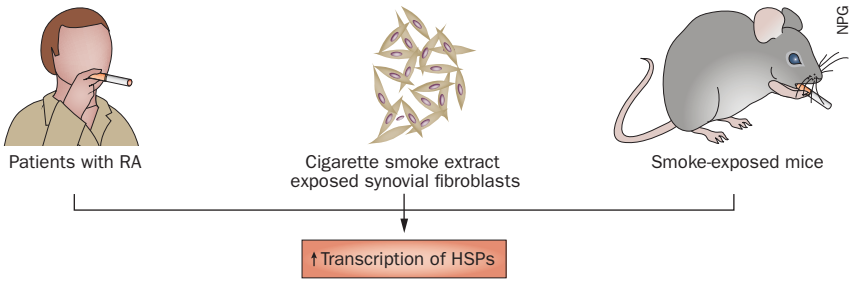
RHEUMATOID ARTHRITIS

Where there's smoke, there's altered transcription

"Smoking affects gene expression of synovial cells in the joints," reports Caroline Ospelt, lead author of a Swiss study to understand previous findings "that smoking is one of the major risk factors for developing RA." Ospelt's new data suggest that rheumatoid arthritis (RA) could be regulated by cigarette smoke-induced alterations to the transcriptional regulation of heat shock proteins (HSPs) in the joints. She says her team began work on the project because "there are few studies to clarify how smoking confers this risk."

HSPs are ubiquitous and have various cellular functions, ranging from acting as molecular chaperones and mediating molecular folding to affecting the stress response.

The researchers assessed the effect of smoke *in vitro* and *in vivo*, in mice and humans. RA synovial fibroblasts were exposed to 5% cigarette smoke extract and microarray analysis showed that various HSPs, including *HspB8*, *Hsp70* and *Hsp40* family members, were among the most 'smoke-inducible' genes. Real-time PCR of synovial tissue also showed greater transcription of these genes in smoking than nonsmoking patients with RA. The human data were supported by a model in which mice 'smoked' for 6 hours a day, 5 days per week. Transcription of *HspB8* or *Hsp70* in the ankle joints of mice was not altered by cigarette smoke, but levels of Hsp40 family member transcripts, *DnaJB4* and *DnaJC6*, were more than doubled by smoking. Consistent with human smokers, erythropoiesis was also increased in these mice, compared with nonsmokers.



Ospelt says "not a lot is known about the DnaJ proteins," and, when asked how she plans to continue this work, she concludes that "it will be interesting to see how they contribute to joint disease."

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Original article Ospelt, C. *et al.* Smoking induces transcription of the heat shock protein system in the joints. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2013-204486