Nature Reviews Rheumatology | Published online 22 Sep 2016; doi:10.1038/nrrheum.2016.160

RHEUMATOID ARTHRITIS

Smoking influences autoimmunity to vimentin

> cigarette smoke induces different humoral and cellular responses to vimentin in … HLA transgenic mice

A new study using humanized mouse models of rheumatoid arthritis (RA) suggests that cigarette smoke induces different humoral and cellular responses to vimentin in arthritis-susceptible and arthritis-resistant HLA transgenic mice. "The observations imply that a differential response to vimentin in the context of host genotype may influence immunity and ultimately determine inflammation and tissue injury in RA," says Veena Taneja, corresponding author of the study.

Epidemiological and clinical evidence has clearly demonstrated that cigarette smoking is a predisposing factor for the development of seropositive RA, and smokers have increased levels of antibodies against citrullinated self-proteins such as vimentin. However, the mechanisms underlying RA-related autoimmunity are not well established. In previous work, the investigators found that although exposure to cigarette smoke did not enhance arthritis severity in transgenic mice expressing the *HLA-DRB1*0401* allele (which is associated with RA susceptibility), immune response to vimentin was increased. "That led us to ask, what would be the impact of smoking on the adaptive immunity to vimentin and on arthritis in genetically resistant individuals?" explains Robert Vassallo, one of the authors of the study.

The investigators have now found that exposure to cigarette smoke induces distinct T-cell responses to vimentin in transgenic mice expressing the *HLA-DRB1*0401* allele and in mice expressing the RA-resistance-associated *HLA-DRB1*0401* allele. In arthritis-susceptible vimentin-immunized mice, exposure to cigarette smoke led to a trend towards increased levels of IFNγ and reduced production of IL-10 in splenocytes. By contrast, exposure to cigarette smoke increased the number of $CD4^+CD25^+FOXP3^+$ T regulatory cells in the arthritis-resistant vimentin-immunized mice. The investigators also found that exposure to cigarette smoke increased the levels of autoantibodies against native and citrullinated vimentin in naive mice of both strains.

The researchers plan to further investigate smoking-induced autoimmunity in the onset of RA. "We are performing studies to determine how smoking affects the lung microbial profile that may contribute to the pathogenesis of RA," comments Taneja. "We plan to conduct studies that will characterize metagenomic and metabolomic profiles following cigarette smoke exposure and define pathways relevant to understanding the mechanism of disease induction in RA."

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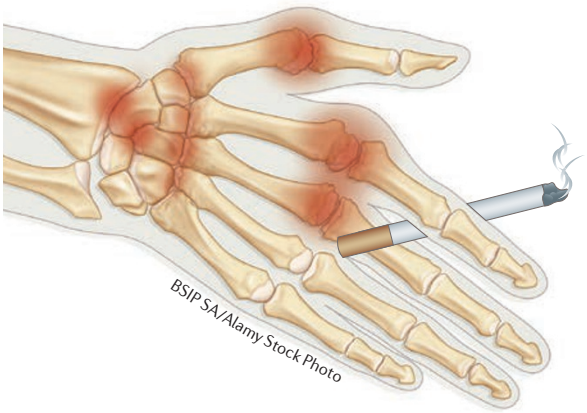

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ORIGINAL ARTICLE Bidkar, M. *et al.* Cigarette smoke induces immune responses to vimentin in both, arthritis-susceptible and -resistant humanized mice. *PLoS ONE* **11**, e0162341 (2016)