REFERENCES

1. Fanny Arnoux, Charlotte Mariot*, Elisa Peen*, Nathalie Lambert, Nathalie Balandraud, Jean Roudier, Isabelle Auger. Peptidyl arginine deiminase immunisation induces anti-citrullinated protein antibodies in mice with particular MHC types. *PNAS* 2017.
2. Nathalie Balandraud, Christophe Picard, Denis Revirion, Cyril Landais, Eric Tousseiro, Nathalie Lambert, Emmanuel Telle, Caroline Charpin, Daniel Wendling, Etienne Pardoux, Isabelle Auger, Jean Roudier. HLA DR and the risk of developing RA. *Plos One* 2013.

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0023

RARE SERONEGATIVE DESTRUCTIVE RA: IDENTIFICATION OF SOMATIC MUTATIONS IN THE EXPANDED CD8+ LYMPHOCYTES

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Introduction Clonally expanded CD8 +lymphocytes harbour somatic mutations in RA patients.¹ Seronegative RA, that often displays milder symptoms and slower disease progression, does not share the genetic linkage to the MHC II locus. Thus, we hypothesise that somatic mutations in the clonal CD8 +lymphocytes could modulate inflammation in these patients.

Objectives Our aim was to validate the concept of somatic mutations as regulators of chronic inflammation.

Methods We collected blood samples from seronegative RA patients (n=8) who displayed unusually aggressive, progressive disease that was refractory to treatment and had led to severe joint erosions.² Flow cytometry was used to screen lymphocyte clonality in both CD4 and CD8 lymphocytes and to enrich the mutated clone. TCR-repertoire analysis was performed by TCRB-deep sequencing. Somatic variants were called from deep sequencing data (panel of 1000 immunological genes and exome sequencing) and the data was confirmed by capillary sequencing.

Results Similarly as in our earlier work, there were more suggestive clonal expansions in CD8 +lymphocytes than in CD4 +lymphocytes. The overall clonality of CD8 +cells did not statistically differ between our seronegative destructive RA cohort and age-matched healthy controls (n=19), seropositive (n=53) or seronegative diagnostic phase patients (n=12).

Sequencing of one of the seronegative RA patients' CD4 and CD8 T cells with the targeted gene panel, revealed novel somatic mutations in the CD8 +cell pool. The expanded T cell clone was enriched using flow cytometry and from this clone, 22 mutations were identified in genes that are expressed in healthy CD8 +cells. Eight of these mutations were selected and confirmed using capillary sequencing. Based on computational prediction algorithms, we hypothesise that the identified mutations (in *PIK3CG*, *KPNA1*, *PLCG2*, *ITGAE*, *NKAP* genes) may regulate the clonal properties, immunological phenotype and even contribute to the regulation of chronic inflammation.

Conclusions We identified somatic mutations in the clonally expanded CD8 lymphocytes from a patient with unusual, aggressive seronegative RA. More work is warranted to elucidate the biological and clinical consequences of the identified mutations.

REFERENCES

1. Savola P, et al. Somatic mutations in clonally expanded cytotoxic T lymphocytes in patients with newly diagnosed rheumatoid arthritis. *Nature Communications* 2017;**8**:15869.
2. Nikiphorou E, et al. Long-term outcomes of destructive seronegative (rheumatoid) arthritis: Description of four clinical cases. *BMC Musculoskelet Disord* 2016;**17**:246.

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0024

HUMAN MEMORY TH17 CELL POPULATIONS CHANGE INTO ANTI-INFLAMMATORY CELLS WITH REGULATORY CAPACITY UPON EXPOSURE TO ACTIVE VITAMIN D

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Introduction In autoimmune diseases such as rheumatoid arthritis (RA), an important therapeutic goal is to normalise the imbalance between pro- and anti-inflammatory cells. This imbalance is illustrated by elevated levels and activity of memory CCR6 +Th17 cell populations, such as Th17 and Th17.1 cells, in RA patients compared to healthy controls. Therefore, modulating these cells to become anti-inflammatory could contribute to restoring the immunological balance.

Objectives The active vitamin D metabolite 1,25(OH)₂D₃ is known to inhibit pro-inflammatory cytokine production by CCR6 +Th memory cells. Therefore, we investigated whether 1,25(OH)₂D₃ can induce an anti-inflammatory phenotype in these memory T cells.

Methods CCR6 +Th memory cells, excluding Tregs, were sorted from treatment-naïve early RA patients or healthy controls and cultured with or without 1,25(OH)₂D₃. Effects were analysed using microarray, RT-PCR, ELISA or flow cytometry. Functional properties were assessed via suppression and chemotaxis assays.

Results 1,25(OH)₂D₃ inhibits pro-inflammatory cytokines such as IL-17A, IL-17F and IL-22 in CCR6 +Th memory cells from both healthy controls and RA patients. This is accompanied by induction of anti-inflammatory factors, including IL-10 and CTLA4. Interestingly, these formerly pathogenic cells suppress proliferation of autologous CD3 +T cells, similar to classical Tregs. Importantly, the modulated memory cells still migrate towards the site of inflammation, modelled by synovial fluid, and retain their suppressive capacity in this environment.

Conclusions Committed pro-inflammatory IL-17A-producing CCR6 +Th memory cells can become anti-inflammatory cells with functional regulatory capacities upon exposure to active vitamin D. This process can contribute to restoring the immunological balance and inhibiting synovial inflammation in RA.

Disclosure of interest None declared

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UNOPPOSED INTERLEUKIN 18 SIGNALLING LEADS TO SEVERE TOLL LIKE RECEPTOR 9-INDUCED MACROPHAGE ACTIVATION SYNDROME IN MICE

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