

## IN BRIEF

## VASCULITIS

## Nasal dysbiosis linked to GPA

Using deep sequencing methods, researchers have identified differences in the nasal microbial composition of patients with granulomatosis with polyangiitis (GPA) compared with that in healthy individuals, including a decreased relative abundance of *Propionibacterium acnes* and *Staphylococcus epidermidis*. In patients with GPA, the use of non-glucocorticoid immunosuppressive therapy was associated with a healthy nasal bacterial composition, whereas disease activity was associated with an altered nasal microbiota, including a decreased relative abundance of the order *Malasseziales* in patients with active disease compared with patients in remission.

**ORIGINAL ARTICLE** Rhee, R. L. et al. Characterisation of the nasal microbiota in granulomatosis with polyangiitis. *Ann. Rheum. Dis.* <https://doi.org/10.1136/annrheumdis-2018-213645> (2018)

## CLINICAL TRIALS

## Safety concerns of rivaroxaban use in APS

In a randomized, open-label, phase III study comparing the efficacy and safety of rivaroxaban and warfarin in patients with antiphospholipid syndrome (APS), rivaroxaban use was associated with an increased rate of adverse events. 120 patients with APS at high risk of thromboembolic recurrence were randomly assigned to receive either rivaroxaban (n = 59) or warfarin (n = 61), but the trial had to be stopped prematurely owing to safety concerns. In the rivaroxaban treatment group, adverse events occurred in 19% of patients (compared with 3% in the warfarin group), which included thromboembolic events (12% of patients) and major bleeding (7% of patients).

**ORIGINAL ARTICLE** Pengo, V. et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. *Blood* <https://doi.org/10.1182/blood-2018-04-848333> (2018)

## SPONDYLOARTHRITIS

## Testing the ABILITY to withdraw adalimumab

Continued therapy with adalimumab in patients with nonradiographic axial spondyloarthritis was associated with better maintenance of remission than withdrawing adalimumab in the ABILITY-3 study. Of the 305 enrolled patients who achieved sustained remission after 28 weeks of open-label adalimumab treatment (40 mg subcutaneously every other week), 152 were randomly assigned to continue adalimumab treatment and 153 received placebo instead. At the end of the 40-week double-blind period, more patients in the placebo group had experienced a flare than in the adalimumab group (70% versus 47%).

**ORIGINAL ARTICLE** Landewé, R. et al. Efficacy and safety of continuing versus withdrawing adalimumab therapy in maintaining remission in patients with non-radiographic axial spondyloarthritis (ABILITY-3): a multicentre, randomised, double-blind study. *Lancet* **392**, 134–144 (2018)

## OSTEOARTHRITIS

## New recommendations for physical activity

A EULAR task force has put forward evidence-based recommendations concerning physical activity in individuals with inflammatory arthritis or osteoarthritis, advocating physical activity as an integral part of standard care. The task force, consisting of a multidisciplinary team of 22 experts in physical activity (including three rheumatologists) from 16 countries, agreed upon four overarching principles and 10 recommendations, as well as related research and education agendas.

**ORIGINAL ARTICLE** Rausch Osthoff, A. et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann. Rheum. Dis.* <https://doi.org/10.1136/annrheumdis-2018-213585> (2018)

## CONNECTIVE TISSUE DISEASES

## Prematurely aged stem cells in pSS

Over the past 25 years, theories around the cause of salivary gland hypofunction, a major clinical manifestation of primary Sjögren syndrome (pSS), have steadily moved away from inflammation towards other possible factors, including salivary gland stem cells. Now, in the first study of its kind, salivary gland stem cells from patients with pSS have been isolated and characterized, revealing a prematurely aged, senescent phenotype.

“Salivary gland stem cells are epithelial populations of adult stem cells,” explains corresponding author Sarah Pringle. “They reside in the ducts of the salivary gland and are responsible for maintaining salivary gland homeostasis.”

“Prior to this work, nothing at all was known about salivary gland stem cells in pSS,” says co-author Frans Kroese. “We investigated the regenerative potential of salivary gland stem cells in pSS to attempt to understand the basis for long-term hyposalivation.”

Using a salivary gland stem cell 3D organoid culture system pioneered in the lab of Rob Coppes at University Medical Center Groningen, Pringle and colleagues isolated and cultured stem cells from the parotid glands of healthy individuals, patients with pSS and patients with so-called ‘incomplete’ pSS, who have hallmarks of the disease but minimal lymphocytic infiltrates in the salivary glands.

Overall, patients with pSS had fewer stem cells in their biopsy-obtained parotid gland tissue samples than did healthy individuals. In vitro, the few stem cells isolated from patients with pSS had a lower capacity to self-renew and proliferate than those from healthy individuals, and also had a diminished ability to form mature organoids, suggestive of reduced regenerative potential. “These results may explain why new, saliva-producing acinar cells are inadequately generated by salivary



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gland stem cells in pSS, and why saliva production remains low,” states Pringle.

Differences in the proliferative capacity of salivary gland stem cells from patients with pSS and from those with incomplete pSS led the researchers to theorize that stem cells might be stimulated to divide early in the disease process and to subsequently become senescent. Telomere length analysis revealed shorter telomeres in stem cells from patients with pSS than in those from healthy individuals, suggesting that stem cells from patients with pSS had replicated extensively.

Additional studies showed that healthy salivary gland stem cells stimulated in vitro with the pro-inflammatory cytokines TNF, IL-6 and IFN $\alpha$  underwent increased proliferation. “Interestingly, these cytokines also seemed to induce differentiation of salivary gland stem cells into a subset of cells considered to be regeneratively inferior,” says Pringle.

“The results of this study suggest that after successful treatment of the glandular tissue to minimize lymphoid infiltration, the salivary gland will still not, or very poorly at best, undergo regeneration,” explains Kroese. “Looking to the future, we are aiming to provide a solution for patients with pSS whose salivary gland stem cells are senescent by generating fresh salivary gland stem cells from induced pluripotent cells.”

Joanna Collison

**ORIGINAL ARTICLE** Pringle, S. et al. Salivary gland stem cells age prematurely in primary Sjögren's syndrome. *Arthritis Rheumatol.* <https://doi.org/10.1002/art.40659> (2018)