

IN BRIEF

SYSTEMIC LUPUS ERYTHEMATOSUS

Pregnancy outcomes in SLE are improving

In the USA, in-hospital maternal mortality and overall outcomes improved considerably from 1998 to 2015, especially in pregnant women with systemic lupus erythematosus (SLE), according to a retrospective cohort study. Of the 93,820 hospitalizations of pregnant women with SLE recorded in the National Inpatient Sample database over the 18 year-period, the rate of in-hospital maternal deaths declined from 442 per 100,000 admissions (for 1998 to 2000) to <50 per 100,000 admissions (for 2013 to 2015), which was a greater decline than that reported for pregnant women without SLE.

ORIGINAL ARTICLE Mehta, B. et al. Trends in maternal and fetal outcomes among pregnant women with systemic lupus erythematosus in the United States: a cross-sectional analysis. *Ann. Intern. Med.* <https://doi.org/10.7326/M19-0120> (2019)

GOUT

Genetic loci associated with progression to gout

Researchers have identified two genetic loci (in *CNTN5* and *MIR302F*) and one potential locus (in *ZNF724*) associated with progression from hyperuricaemia to gout. The first-of-its-kind genome-wide association study (GWAS) compared patients with gout to individuals with asymptomatic hyperuricaemia, rather than patients with gout to normouricaemic individuals (as has been done in previous GWAS), to identify loci that influence the transition from hyperuricaemia to gout. Comparisons with results from previous GWAS suggested the existence of distinct mechanisms during the normouricaemia-to-hyperuricaemia and hyperuricaemia-to-gout transitions.

ORIGINAL ARTICLE Kawamura, Y. et al. Genome-wide association study revealed novel loci which aggravate asymptomatic hyperuricaemia into gout. *Ann. Rheum. Dis.* <https://doi.org/10.1136/annrheumdis-2019-215521> (2019)

RHEUMATOID ARTHRITIS

Mass cytometry markers for stratification of RA?

An exploratory mass cytometry analysis identified candidate markers for distinguishing between patients with newly-diagnosed rheumatoid arthritis (RA) and healthy individuals. A panel of 13 phenotyping and 10 functional markers were used to characterize TNF-mediated signalling patterns in peripheral blood mononuclear cells from patients with RA or healthy individuals, leading to the identification of a small set of RA-specific markers. A combined model of these markers could correctly classify 18 out of 20 patients with RA and 17 out of 20 healthy individuals. These markers could potentially be used for the diagnosis and stratification of RA in the future.

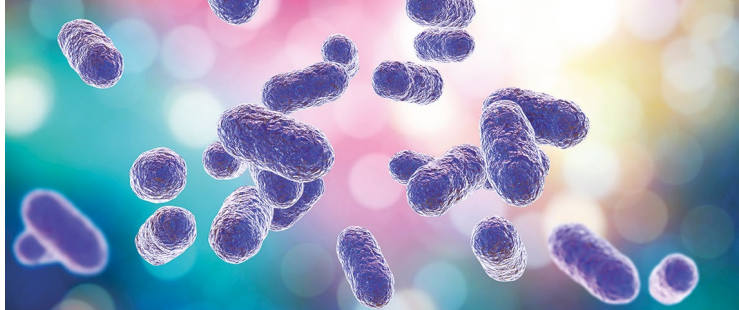
ORIGINAL ARTICLE Bader, L. et al. Candidate markers for stratification and classification in rheumatoid arthritis. *Front. Immunol.* <https://doi.org/10.3389/fimmu.2019.01488> (2019)

AUTOIMMUNITY

NET formation differs in SLE and vasculitis

Sera from patients with either systemic lupus erythematosus (SLE) or anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) induce distinct forms of neutrophil extracellular trap (NET) formation, according to a new study. In an ex vivo comparison, the NET formation differed in morphology, kinetics, triggers and pathways and resembled lytic and non-lytic mechanisms for AAV sera and SLE sera, respectively. Furthermore, the NETs produced had different compositions and immunogenic properties.

ORIGINAL ARTICLE van Dam, L. S. et al. Neutrophil extracellular trap formation is intrinsically distinct in ANCA-associated vasculitis and systemic lupus erythematosus. *Arthritis Rheumatol.* <https://doi.org/10.1002/art.41047> (2019)



Credit: Dr. Microbe/ iStock/Getty Images Plus

INFLAMMATION

P. gingivalis exacerbates arthritis via gut barrier dysfunction

Porphyromonas gingivalis has frequently been implicated in the pathogenesis of rheumatoid arthritis (RA), but little is known about the mechanisms linking this oral pathobiont to joint inflammation. New findings suggest that, during arthritis, disruption of intestinal resolution pathways impairs gut barrier function, which facilitates pathogenic barrier breach by *P. gingivalis*.

The researchers showed that intestinal lipid mediator profiles were altered in mice with K/BxN serum transfer-induced arthritis in comparison with naive (non-arthritic) mice, with arthritic mice having reduced concentrations of several specialized proresolving mediators (SPMs), including the gut-protective n-3 docosapentaenoic acid (n-3 DPA)-derived resolvin RvD5_{n-3 DPA}. These alterations were linked with reduced expression of genes involved in epithelial barrier function and *Il10* in gut tissue, as well as a reduction in the number of mucus-producing goblet cells. Expression of IL-10 and IL-10 receptor (IL-10R) was also downregulated in lamina propria macrophages.

Further experiments revealed that inactivation of RvD5_{n-3 DPA} during inflammatory arthritis was promoted by upregulation of the SPM-inactivating enzyme 15-prostaglandin dehydrogenase (15-PGDH) and increased metabolism of RvD5_{n-3 DPA} to its inactive metabolite 17-oxo-RvD5_{n-3 DPA}. Notably, incubation with immune complexes upregulated 15-PGDH expression in bone marrow-derived macrophages.

Mice with K/BxN serum transfer-induced arthritis had impaired gut barrier function in comparison with naive mice, marked by downregulation of *Tjp1* and *Lyz1* (encoding a tight junction molecule

and an antimicrobial protein, respectively) as well as increased plasma endotoxin concentrations. Inoculation of arthritic mice with *P. gingivalis* exacerbated these changes and led to an increased bacterial load in the lamina propria and the colonic inner mucus layer in comparison with non-inoculated arthritic mice. This breach of bacteria across the gut barrier was not observed in non-arthritic mice inoculated with *P. gingivalis*.

Administration of RvD5_{n-3 DPA} restored gut barrier function in *P. gingivalis*-inoculated arthritic mice; bacterial levels in mesenteric lymph nodes were reduced and the lamina propria and colonic inner mucus layer of RvD5_{n-3 DPA}-treated mice were free of bacteria. RvD5_{n-3 DPA} administration also restored expression of *Tjp1*, *Lyz1* and *Il10* in the intestinal epithelium. The rescue of gut barrier function following RvD5_{n-3 DPA} administration was associated with reduced joint inflammation and swelling.

The research could have implications for the management of RA, particularly in patients with periodontal disease. “Our findings suggest that there could be scope for the stratification of patients with RA based on the presence of increased levels of *P. gingivalis* and/or periodontal disease, to devise personalised therapeutic strategies,” says corresponding author Magdalena Flak. “In addition, our findings suggest that new therapeutics modelled around RvD5_{n-3 DPA} might also be useful drug candidates in RA, since they regulate both the gut barrier and joint inflammation.”

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ORIGINAL ARTICLE Flak, M. B. et al. Inflammatory arthritis disrupts gut resolution mechanisms, promoting barrier breakdown by *Porphyromonas gingivalis*. *JCI Insight* 4, e125191 (2019)