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Dr. Hajishengallis earned a D.D.S. from the University of Athens (1989) and a Ph.D. in Microbiology/Immunology from the University of Alabama at Birmingham (1994). He is currently the Thomas W. Evans Centennial Professor at the University of Pennsylvania, School of Dental Medicine. His field of interest lies at the host-microbe interface where his work has illuminated novel mechanisms of microbial dysbiosis and inflammation as well as inflammation resolution and tissue regeneration. A current focus of his laboratory involves the immunometabolic regulation of trained myelopoiesis and its effects on health and disease. He combines basic and translational research leading to innovative approaches to clinical problems, such as exemplified by periodontitis, where his preclinical work has recently led to a successful complement-targeted phase 2a clinical trial in patients with periodontal inflammation. He published over 210 papers (with over 27,000 citations), including in Cell, Nature Immunology, Science Translational Medicine, J. Clin. Invest., Cell Host Microbe, PNAS, N. Engl. J. Med., and Nature Reviews Immunology. He received the IADR Distinguished Scientist Award in Oral Biology in 2012 and the NIH/NIDCR MERIT Award in 2016. He was named Highly Cited Researcher (Clarivate/Web-of-Science) in 2018, 2020 and 2021.

Inflammatory memory, periodontal disease and comorbidities

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Periodontal disease can cause systemic inflammation and is epidemiologically associated with systemic comorbidities, such as cardiovascular disease and rheumatoid arthritis. Although periodontitis increases the risk of systemic inflammatory comorbidities and vice versa, a bidirectional causal mechanism of how periodontitis affects and is affected by comorbidities was not documented before. Many chronic inflammatory diseases are in large part driven by the action of inflammatory myeloid cells. We thus hypothesized that inflammation-driven epigenetic alterations in their hematopoietic progenitors in the bone marrow, *i.e.*, the development of innate immune inflammatory memory ('trained immunity'), could influence the initiation and/or the progression of distinct inflammatory disorders that emerge as comorbidities. Specifically, we investigated whether maladaptive inflammatory memory underlies the comorbid connection between periodontitis and arthritis, as modelled by ligature-induced periodontitis (LIP) and collagen antibody-induced arthritis (CAIA) in mice. We demonstrated that LIP-associated systemic inflammation induces long-lasting qualitative adaptations, including a sustained myeloid-differentiation bias, in hematopoietic stem and progenitor cells (HSPCs). Following resolution of periodontitis, this myeloid-differentiation bias in HSPCs was retained predominantly at the epigenetic level, indicating prolonged readiness for induction of myelopoiesis upon future challenges. Indeed, this adaptation resulted in sustained increase in the production of myeloid cells, which additionally displayed enhanced inflammatory responsiveness to recall stimulation. The LIP-induced inflammatory memory was transmissible by bone marrow transplantation to naive recipients, which exhibited increased inflammatory responsiveness and arthritis severity when subjected to CAIA. IL-1 signaling in HSPCs was essential for the induction of inflammatory memory by LIP-associated systemic inflammation. Conversely, and in line with the bidirectional association of periodontitis and rheumatoid arthritis, CAIA induced alterations to HSPCs towards a maladaptive inflammatory phenotype, which exacerbated periodontitis in transplanted mice. Our findings establish the principle that maladaptive innate immune training of myelopoiesis underlies the bidirectional association of inflammatory comorbidities, paving the way for their treatment in a holistic manner.