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The emerging role of innate chemokines in inflammatory disease and atherosclerosis

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Inflammatory processes such as those promoting atherosclerotic lesion formation are pivotely driven components of the Innate and adaptive immune axis. Chemokines and their receptors are a particularly prominent part of the innate immune arm. While the role of classical chemokines, i.e. belonging to the CC or CXC families, is increasingly well understood, it also has become clear that the underlying ligand/receptor system is characterized by a previously unanticipated complexity of cross-reactivities and homo- and heteromerization events. Moreover, an emerging family of chemokine-like inflammatory mediators termed 'innate chemokines', CLF chemokines or micro-chemokines, which additionally structurally and functionally overlaps with the mediator class of alarmins has been identified to modulate inflammatory reactions in the atherogenic arterial wall but also numerous other inflamed tissues. Innate or CLF chemokines share functional homology with classical chemokines and signal through classical chemokine receptors, whereas they do not exhibit conserved structural features such as N-terminal tandem cysteine residues or the chemokine fold. This lecture will address the molecular basis of target cell activity and the pathophysiological role of several 'innate chemokines'. Examples will encompass high mobility group binding protein-1 (HMGB1), macrophage migration inhibitory factor (MIF), and certain β -defensins. Receptor usage, signaling, innate immune cell regulation, and involvement in various inflammatory conditions, including atherosclerosis will be discussed. Finally, the lecture will outline potential strategies to specifically and therapeutically target such mediators either in conjunction or explicit exclusion of the co-targeting of classical chemokines.

Biography

Jurgen Bernhagen studied Biochemistry and Immunology at the University of Tübingen, Germany, and at Queen Mary College, London, UK. He performed a sandwich PhD thesis at the University of Tübingen and at the Picower Institute for Medical Research, Manhasset, NY, USA, and was trained as a postdoc at the Picower. Professor Bernhagen currently is a Full Professor of Biochemistry and Molecular Cell Biology at RWTH Aachen University, Germany, and is the Chair and Director of the homonymous institute. His main research interest has been on cytokines, chemokines and their role in inflammation, with a focus on MIF and the biochemical and structural features and mechanisms of such inflammatory mediators. He also studies the COP9 signalosome. Studied disease models encompass rodent model of atherosclerosis, sepsis, liver and kidney disease as well as colitis and colorectal cancer. Professor Bernhagen has authored more than 120 peer-reviewed papers in these areas, several of them published in leading journals such as Nature, Nature Medicine, or PNAS. He has serves on the editorial board of several journals and serves on several review committees for extramural funding and various fellowship organizations.

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