Resolution of inflammation: a game of Lipid networks

Specific Seminar – Curriculum 4

2024, May 10, 3:00 p.m.

Speaker:

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Abstract:

Resolution of inflammation is the physiological process that in the aftermath of the acute immune event confines the inflammatory surge to avoid chronic inflammation and irreversible tissue damage that uncontrolled inflammation might trigger. This process is promoted and arranged by a class of bioactive lipids, altogether referred to as specialized pro-resolving mediators (SPM), which are produced by immune cells starting from essential polyunsaturated fatty acids such as arachidonic, docosahexaenoic, docosa pentaenoic and eicosapentaenoic acid (AA, DHA, DPA and EPA, respectively). These mediators, which include D- and E-series resolvins, protectins, maresins and lipoxins, act on all immune cells involved in inflammation, by hindering neutrophil recruitment, deactivating lymphocyte and macrophage pro-inflammatory phenotypes while inducing pro-resolving ones, antagonizing the effect and production of pro-inflammatory cytokines and other lipid mediators (e.g., AA-derived eicosanoids), promoting clearance of tissue debris and dead cells (i.e., efferocytosis) and altogether avoiding fibrosis while promoting tissue regeneration. SPMs have always been considered the main orchestrators of resolution, and to date their impaired production or defective metabolism and signalling, have been involved in the pathogenesis of many – if not virtually all – pathologies that feature inflammation either as a primum movens or a concomitant element derived from tissue damage. On the other hand, other lipids have been reported in the past that display immunomodulatory and, as a matter of fact, pro-resolving-like features, including endocannabinoids (eCB) (i.e., the endogenous lipids that bind the same receptors engaged by the psychoactive products of Cannanbis sativa and indica); incidentally, even cannabidiol (CBD), one of the two most prominent phytocannabinoids have recently been reported to induce production of SPMs in human macrophages. This suggests an interplay between SPM and cannabinoid signalling, in which these lipid genres might participate together during resolution. This is further supported by the well-known fact that N-arachidonoylethanolamide (AEA, or anandamide) – one of the two main eCBs – shows affinity for both its main receptor targets – i.e., cannabinoid receptor type 1 and 2 (CB1 and CB2) – and for GPR18, a prominent SPM receptor. Nonetheless, the biochemistry of resolution in respect to the study of a bigger picture that includes the role of other bioactive lipids, other than bona fide SPMs, has been barely investigated to date. In the past 2 years our group has even produced data showing that AEA is not only able to enhance pro-resolving properties such as efferocytosis in human primary monocyte-derived macrophages (MoDM) in a CB2- and GPR18-dependent manner, but that this eCB can also induce the production of a vast array of SPM lipids when given at nanomolar concentrations to these cells. It is becoming gradually clear that tissue homeostasis might represent a significantly-more complex process than previously thought, in which many endogenous lipid compounds participate together to adjuvate the effect of SPMs to avoid inflammatory pathophysiological processes leading to tissue loss of function.

Short Bio:

Alessandro Leuti is assistant professor of Biochemistry at Campus Bio-Medico University of Rome (UCBM), where he also teaches Biochemistry at the Medicine and Surgery and Medicine and Surgery 'MedTech' master degrees. He is group leader of the Biochemistry and Molecular biology Research Unit at UCBM. To date he has authored 29 papers (Total citations: 1578; h Index: 18). His main field of research is the study of endogenous immunomodulatory lipids such as specialized pro-resolving mediators (SPM) and endocannabinoids, and their role – as well as that of their interaction – in resolution of inflammation in cell and animal models of inflammation and neuroinflammation.

Online attendance:

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