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Functional lipid mediator profiling in dissecting disease pathophysiology

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Uncontrolled inflammation form an important component of many chronic diseases such as arthritis, asthma, periodontal disease, cardiovascular diseases and neurodegenerative diseases. Using a systems approach with self-limited sterile and infectious inflammatory exudates we mapped tissue events, cell trafficking and protein mediators and identified novel mediators from 3 families of n-3 essential fatty acid (EPA, DPA, DHA), termed resolvins, protectins and maresins. These potent mediators are coined specialized pro-resolving mediators (SPM). Complete structural elucidation and total organic synthesis of SPM demonstrated their functions *in vivo* in the resolution of acute inflammation in many animal models. Each SPM is structurally and functionally distinct and expedite the duration and magnitude of acute inflammatory response with actions in pico-nanogram concentration range *in vivo*. Using LC-MS-MS-based lipid mediator-metabololipidomics we also found that the production of these novel molecules is temporally separated from that of the classic eicosanoids in mammalian tissues. In addition, SPM were identified in a number of human tissues including lymphoid organs and milk. We also found that acute supplementation with n-3 and acetylsalicylic acid increases peripheral blood SPM levels and phagocytosis of *Escherichia coli* by blood leukocytes. SPM are subject to further local conversion by leukocytes, which may lead to their inactivation. We recently identified two novel maresin 1 further metabolites in the context of infection and conducted their structure elucidation. Together these findings indicate that endogenous resolution pathways may underlie prevalent diseases associated with uncontrolled inflammation and provide novel opportunities for patient stratifying using functional profiling and resolution-based pharmacology.

Biography

Romain A Colas has completed his PhD from University of Lyon (France) and Post-doctoral studies at Brigham and Women's Hospital and Harvard Institutes of Medicine (USA) with Prof. Charles N Serhan. His work describing SPM regulation and their actions in various disease settings has lead to several publications in the field of Resolution. He is currently a Post-doctoral fellow at the recently established Lipid Mediator Unit at the William Harvey Research Institute, Queen Mary University of London (UK). His research efforts are focused on the structural elucidation of n-3 polyunsaturated fatty acid-derived bioactive lipid mediators, assessing their cellular targets and the molecular mechanisms through which they exert their actions in the resolution of inflammation.

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