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The immunoresolvents regulate the host response to sterile and infectious inflammation

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Inflammation is a coordinated host response that when self-limited is protective. Many cell types upon activation produce mediators that regulate the physiological function of inflammation. Arachidonic acid derived mediators that include the leukotrienes, prostaglandins and thromboxane orchestrate the initiation of the inflammatory response. Termination or resolution of inflammation is also appreciated to be an active response coordinated by a novel genus of lipid mediators coined as specialized pro-resolving mediators (SPM). These mediators actively control leukocyte responses counter-regulating the production pro-inflammatory signals, promote leukocyte phenotype switch from inflammatory to protective and

orchestrate tissue cellular trafficking. Using mass spectrometry-based structure elucidation we recently identified four new mediator families that regulate the progression of inflammation as well as fine tune the host response to clear the invading pathogens, repair and regenerate damaged tissues in tissues during ongoing infectious-inflammation. These include the thirteen series resolvins (RvT) and the protectin conjugates in tissue regeneration (PCTR). Failure to engage these protective pro-resolving pathways is implicated in the etiopathogenesis of many inflammatory diseases including infections, cardiovascular disease and neurological disease. We recently found that lipid mediator profiles from both experimental systems and humans provide an insight into the body's inflammation-resolution status. Thus, these results indicate that resolution-based personalized medicines may be useful in both preventing and treating diseases with an inflammatory component.

The most relevant publications:

1. Frigerio F, Pasqualini G, Craparotta I, Marchini S, van Vliet E, Foerch P, Vandenplas C, Leclercq K, Aronica E, Porcu L, Pistorius K, Colas RA, Hansen TV, Perretti M, Kaminski R*, **Dalli J*** and Vezzani A* *Dynamics of active proresolving mechanisms against neuroinflammation during epileptogenesis: therapeutic potential of the lipid mediator* $PD1_{n\text{-}3\ DPA}$. Brain. *2018 Nov 1;141(11):3130-3143. doi: 10.1093/brain/awy247.*

2. Pistorius K, Souza PR, De Matteis R, Austin-Williams S, Primdahl KG, Vik A, Mazzacuva F, Colas RA, Marques RM, Hansen TV, **Dalli J**. $PD_{n\text{-}3\ DPA}$ *Pathway Regulates Human Monocyte Differentiation and Macrophage Function*. Cell Chem Biol. 2018 Jun 21;25(6):749-760.e9.

3. Colas RA, Souza PR, Walker ME, Burton M, Marques RM, Zasłona Z, Curtis AM, **Dalli J**. *Impaired Production and Diurnal Regulation of Vascular RvDn-3 DPA Increases Systemic Inflammation and Cardiovascular Disease*. Circ Res. 2018 Feb 5. pii: CIRCRESAHA.117.312472. PMID: 29437834.

4. **Dalli J**, Colas RA, Arnardottir HH, and Serhan CN *Group-3 Innate lymphoid cells and PCTR1 govern phagocyte response and infectious resolution via neuronal control*. Immunity 2017 Jan 17;46(1):92-105.

5. **Dalli J,** Vlasakov I, Riley IR, Rodriguez AR, Spur BW, Petasis NA, Chiang N, Serhan CN. Maresin conjugates in tissue regeneration biosynthesis enzymes in human macrophages. Proc Natl Acad Sci U S A. 2016 Oct 25;113(43):12232-12237.

6. **Dalli J**, Chiang N, Serhan CN. *Elucidation of novel 13-series resolvins that increase with atorvastatin and clear infections.* Nat Med. 2015 Sep;21(9):1071-5.
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8. **Dalli J,** Chiang N, Serhan CN. *Identification of 14-Series Sulfido-Conjugated Mediators That Promote Resolution of Infection and Organ Protection.* Proc Natl Acad Sci U S A. 2014 Nov 4;111(44):E4753-61