Resolution Pharmacology: Exploiting pro-resolving GPCRs for therapeutic innovation

M. Perretti

Queen Mary University of London

The process of acute inflammation relies on the active engagement of a series of pro-resolving mediators which assure temporal and spatial containment of the host reaction: a pro-inflammatory phase is followed by an anti-inflammatory and pro-resolving phase in line with 'the beginning programmes the end' concept (Cash et al., 2014). Within the network of pro-resolving mediators is emerging a pattern of biological properties, shared by a variety of players, rendering specific actions paradigmatic (e.g. promotion of efferocytosis). Harnessing endogenous homeostatic pathways can lead to innovative anti-inflammatory therapeutics with beneficial applications for chronic inflammatory pathologies.

Within this area of investigation, Lipoxin A_4 and Annexin A1 are two players able to halt leukocyte migration and promote macrophage phagocytosis of infective agents as well as apoptotic leukocytes. These effects are mediated by a specific receptor, the formyl peptide receptor type 2 (the acronym FPR2/ALX is currently used to identify the human receptor) (Trentin et al., 2015, Gallo et al., 2014). Generation of a colony of mice deficient in the mouse orthologues of FPR2/ALX is helping elucidate the patho-physiological impact of this receptor (and its agonists) in acute inflammation providing, at the same time, proof-of-concept data for its exploitation in drug discovery programmes.

Supported by the Wellcome Trust (programme 086867/Z/08)

References

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