Professor Charles N. Serhan is the Director of the Center for Experimental Therapeutics and Reperfusion Injury (CETRI) in the Department of Anesthesiology, Perioperative and Pain Medicine at BWH and Harvard Medical School, Boston. In his current research he leads a multidisciplinary team of experts whose goal is to reveal the mechanisms of resolution of acute inflammation and tissue injury in the body.

**Lipid mediators put an end to inflammation**

Inflammation is an essential part of our defence against infections, cancer and other attacks to our body’s normal function. Ideally, any inflammatory process should be self-limiting so that the body returns to its previous healthy state. But how does this happen? Prof. Serhan’s research aims to elucidate the mechanisms underlying the resolution of inflammation with a view to drug development.

**WHAT HAPPENS AFTER THE STORM?**

Historically, a lot of focus of immunological research has been on the build-up of an inflammatory reaction and its effects on the body or harmful intruders like bacteria. Little emphasis had been given to the events afterwards. What happens when all the action is no longer needed? It is important to understand how immune reactions resolve in order to develop effective treatments for diseases with aberrant ongoing inflammation such as Alzheimer’s disease, cardiovascular disease or arthritis.

For a long time, there was only a vague idea about the passive mechanisms that stop the inflammatory response. This has changed in recent years thanks to researchers like Prof. Serhan who have taken a closer look. As it turns out, the resolution of inflammation is an active process that involves much more than merely antagonising inflammatory mechanisms.

**ACTIVE RESOLUTION MEDIATORS**

Prof. Serhan’s research has discovered potent anti-inflammatory and pro-resolving compounds made by the body that he calls specialised pro-resolving mediators (SPM). One group of SPM comes from the lipids that we eat - namely from essential omega-3 fatty acids. Within this group, we can distinguish between resolvins, protectins and maresins. SPMs have been measured at bioactive levels in body fluids like human tears and blood, as well as tissues like the brain, lymph nodes, spleen and fat. Interestingly, aspirin can enhance the formation of specific SPM: aspirin-triggered resolvins and protectins have been described. This is a further detail for understanding the mechanism of action for this widely-used drug and may indicate possible new uses.

Prof. Serhan’s research has unveiled an unexpected complexity to the resolution phase of the inflammatory response, making clear that we need much more clinical research into this niche of immunology.
Biochemistry

Cardinal signs of inflammation: Rubor, calor, tumor and dolor
- Vasodilation: TAs and CGs
- Vasodilation: PGD2, PGE2, PGI2
- Vascular permeability: CGs
- Chemotaxis, adhesion: LTB4

Acute inflammatory response
Resolvins
Lipoxygenase
Maresins
Chronic inflammation:
PIG
Leukotrienes
Organ Fibrosis
Wound healing

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A main function of SPM is stimulating the uptake and clearance of dying immune cells and microbes by cells with the capability to engulf, i.e., phagocytes (neutrophils and macrophages). Resolvins and protectins improve survival and regulate both the intensity and duration of inflammation in animal models.

Often, we cannot predict whether a serious inflammatory condition will resolve or become chronic and elicit pathologies such as inflammatory bowel disease, sepsis or multi-organ failure. It is tempting to speculate that measurements of SPM levels could be used as indicators of the bias of the immune system needs to be manipulated to improve inflammatory regulation is an even bigger question.

Enhanced SPM levels achieved by additional omega-3 fatty acid consumption can indeed improve inflammatory regulation is an even bigger question.

Why has research into the resolution of inflammation only come into focus recently?
I am not sure – maybe no one thought it was going to be interesting.

What initially interested you in this field of immunology?
The functions of white blood cells, phagocytes in host defence mechanisms and in human diseases.

Are pharmaceutical companies interested in specialised pre-resolving mediators (SPM)?
Yes, they are interested.

What are the advantages of SPM-based therapies over immunosuppressants?
The SPM stimulate natural mechanisms in resolution and control pain. They are not immunosuppressive and hence do not disable the body’s defense mechanisms against microbes.

Will chronic inflammatory diseases be completely preventable one day?
Won’t that be a great world to live in!

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