LABORATORY OF AUTOIMMUNITY AND INFLAMMATION
Medical School-University of Crete
Head: DIMITRIOS T. BOUMPAS, MD, FACP

BACKGROUND

Inflammation - a type of a non-specific immune response - is the biologic process by which the body reacts to infection, irritation or other injury. When inflammation involves primarily the musculoskeletal system, the result is diseases collectively called "inflammatory rheumatic diseases". As a group, inflammatory rheumatic diseases are not uncommon affecting approximately 1-2% of the population. Some of the best known inflammatory rheumatic diseases include: a) the chronic inflammatory arthritides (rheumatoid arthritis and spondyloarthropathies); b) the collagen vascular diseases (systemic lupus erythematosus or SLE, systemic sclerosis, myositis); c) the systemic vasculitides; and d) the familial Mediterranean fever (FMF). People of both sexes and across all ages may be affected. In general women tend to be affected more commonly than men; some autoimmune rheumatic diseases such as SLE, have a very strong predilection for young women of the reproductive age.

Inflammatory rheumatic diseases are characterized by acute and chronic inflammation. Inflammation is provoked either by an immune response directed against self-constituents (autoimmunity) or-in the case of FMF- by yet unidentified non-self, non-pathogen targets (auto-inflammation). Research has thus far revealed the important role of cells (B and T cells, monocytes and neutrophils), co-stimulatory or inhibitory molecules such as CTLA4 and PD-1, and cytokines such as tumor necrosis factor (TNF), interferon-gamma (IFNγ) and the interleukins in mediating tissue injury. De-regulation of cytokine production or cytokine networks have also been implicated in their pathogenesis. In the case of FMF neutrophils seem to be the key effector cells.

RESEARCH

The laboratoty is interested in medical inflammation, in the context of autoimmune inflammatory rheumatic diseases, and explores mechanisms for both tissue injury and repair with the ultimate goal of developing novel therapies. This represents a multidisciplinary effort of molecular/ structural biologists and medical geneticists working together with experts on autoimmune rheumatic diseases.

To this end, we use a combined approach that involves animal models of systemic lupus erythematosus and rheumatoid arthritis together with the investigation of tissues obtained from humans (blood, bone marrow, skin, synovium and kidney). Emphasis is placed on inflammatory pathways involved in both innate and adaptive immune responses under the general theme of the "homeostatic regulation of the inflammatory response". More specifically:

1. We are developing the idea that effector mechanisms in autoimmune inflammation involve components of both the adaptive and the innate immune responses. The pathways under investigation include:

- Extracellular immune receptors such as toll like receptors (TLRs) and receptors that transduce signals via the adaptor molecules FcRγc and DAP12 (eg FcγR, OSCAR, TREM-1 and -2 and CD200 receptors).
- Intracellular immune receptors such as NOD-LRRs (NLRs such as the NOD and the NALP family group) that participate in the formation of the inflammasome.
- Cytokines (such as IFNs, IL-10 and IL-21).

2. We also explore novel cellular mechanisms to induce antigen specific immune tolerance in the periphery by the use of regulatory T cells.

3. At the translational level, we use novel biologic therapies targeting specific components of the immune response to characterize their overall importance in the disease as well as in selected aspects of the disease.

4. Based on preliminary clinical and laboratory information, we are promoting the notion that quantitative and qualitative characteristics of the response of tissues to the inflammatory attack (kidneys, joints) may contribute to the disease phenotype.

5. In collaborative studies with the laboratory of Hematology, we investigate the biology of bone marrow mesenchymal stem cells and their ability to repair injury.

Sections and Units (leaders)

A. Cytokines and immune receptor signaling (I. O. Tassiulas)
B. Immune tolerance (P. Verginis)
C. Systemic lupus erythematosus (D.T. Boumpas)
D. Rheumatoid arthritis (P. I. Sidiropoulos)
E. Clinical research unit (H. Kritikos)

***Affiliated Section* (*Division of Internal Medicine*)**
Familial Mediterranean Fever (G. N. Goulielmos)

Laboratory Manager-Research Assistant
Christiana Choulaki, PhD

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Contact

Dimitrios T. BOUMPAS, MD, FACP
Professor of Medicine
Director, Internal Medicine/Rheumatology, Clinical Immunology and Allergy
University of Crete, Medical School, 1 Voutes str., 710 03, Heraklion, Greece
Tel: +30(281)0392024 (Hosp); +30(281)0394770 (Univ);+30(281)0394635 (Office)
Fax: +30(281)0392806 (Hosp);+30(281)0394796 (Univ)
E-mail: boumpasd@med.uoc.gr