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Biomedical Sciences Research Center

PRESS RELEASE

Mesenchymal cell replacement as future therapy for chronic inflammatory joint and intestinal diseases?

Researchers discover common cellular targets of Tumor Necrosis Factor, a key molecule involved in the pathogenesis of various arthritic and inflammatory bowel diseases.

Vari - Athens, Greece - 11 February 2008. Chronic inflammatory diseases, such as spondyloarthritis, rheumatoid arthritis and Crohn's disease, often coincide in the same patient, suggesting that they may share common features in their pathogenic development. Therapies that aim to shut off the function of a key signaling molecule, the Tumor Necrosis Factor (TNF), have yielded exciting results for the treatment of these diseases. Our understanding of how TNF acts, however, remains limited, thus hindering further efforts for specific, efficient and safe drug development. Researchers at the BSRC Fleming in Vari - Athens, have now discovered the target cells that mediate the function of TNF in murine models of human inflammatory diseases. They report in *The Journal of Experimental Medicine*, that mesenchymal cells (cells that form the structural framework of tissues) are sufficient responders of pathogenic TNF signals. Their discovery opens the way to novel, more efficient therapeutic approaches against chronic inflammatory diseases.

Dr. George Kollias and his group at BSRC Fleming, have long been using genetically engineered mice to model human diseases. They have shown that transgenic mice that produce excessive amounts of TNF, develop both chronic inflammatory polyarthritis as well as a Crohn's-like disease, with clinical manifestations very similar to human spondyloarthropathies (the combination of gut and joint chronic inflammatory diseases). These earlier studies contributed to the development by industry of today's successful anti-rheumatic drugs such as Infliximab, Enbrel and Humira.

Current hypotheses suggest that TNF activates very early, innate immune responses, by signaling through a variety of cell types. Using an elaborate combination of transplantation experiments and genetic engineering in mouse models of spondyloarthropathies (chronic polyarthritis and Crohn's-like disease), Kollias and colleagues have now shown that pathogenic TNF signals received by specific tissue stromal cells (joint and gut fibroblasts) through TNF receptor I (TNFRI) are sufficient to drive development of full joint and gut pathology in their mouse model.

Researchers can now specifically target these cells and modulate their TNF/TNFR1 signaling, for example through mesenchymal cell replacement, as a future therapeutic approach for joint and gut diseases. Pinpointing TNF's target cells opens the way for better mechanistic understanding of its functions in the pathogenesis of chronic inflammation, as well as more rational and efficient design of treatments for rheumatoid and other arthritides, Crohn's inflammatory bowel disease and spondyloarthropathies.

Source article

M. Armaka, M. Apostolaki, P. Jacques, D. L. Kontoyiannis, D. Elewaut, and G. Kollias. Mesenchymal cell targeting by TNF as a common pathogenic principle in chronic inflammatory joint and intestinal diseases. *The Journal of Experimental Medicine*, 4 February 2008
(<http://www.jem.org/cgi/content/full/205/2/331>)

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About BSRC Fleming

The Biomedical Sciences Research Center "Alexander Fleming" is a Greek, governmental, non-profit research institution that was established in 1998 and is today actively involved in cutting-edge research in the areas of immunology, molecular biology and genetics, and molecular oncology. Researchers at BSRC Fleming have achieved international acclaim for their contributions to disease modeling via transgenesis, cellular immunology, regulation of gene expression, cell signaling and functional genomics. Because of its commitment to outstanding research and strategic prioritization, the Center obtains a large proportion of its funding from competitive national, European Commission, and international sources, as well as from the local and international industry. BSRC Fleming is also committed to offering top quality training to scientists of all levels, as well as state-of-the-art services and facilities.

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