"ALEXANDER FLEMING"
Biomedical Sciences Research Center

PRESS RELEASE

Blocking β7 integrin as future therapy for Crohn's disease?

Using a unique animal model for human Crohn's disease Fleming researchers identify key molecules that control T lymphocyte migration to the small intestine in inflammation and are essential for Crohn's disease pathogenesis.

Vari - Athens, Greece - 5 May 2008. Crohn's disease is a chronic inflammatory disorder that primarily affects the terminal ileum of the small intestine. A key feature of disease is the persistent recruitment of immune cells into the gut. The entry of immune cells from the blood to the tissues is controlled by an elaborate system of adhesion molecules, chemokines, and their receptors. This had led to the generation of a novel class of therapies aiming to prevent cells from migrating to the inflamed tissue, through interference with these molecules. Currently such drugs are being developed or tested in the clinic for the treatment of Crohn's disease. However our understanding of mechanisms that control intestinal homing under inflammatory conditions remains limited, thus hindering further efforts for specific, efficient, and safe drug development. Researchers at the BSRC Fleming in Vari - Athens, have now identified molecules that control lymphocyte migration in a murine model of human Crohn's disease. They report in *Gastroenterology*, that β7 integrin is critical for T lymphocyte migration into the small intestine and the development of small intestinal inflammation. Their discovery brings into focus the use of novel, more efficient therapeutic approaches against Crohn's disease.

The research group at BSRC Fleming has long been using genetically engineered mice to model human diseases. They have shown that transgenic mice that produce excessive amounts of Tumor Necrosis Factor (TNF) develop Crohn's-like inflammatory bowel disease, with clinical manifestations very similar to human disease. The relevance of these mice to the human disease is evident as therapies that aim to shut off the function of TNF have proven beneficial for the treatment of Crohn's disease. Thus they represent a unique tool for identifying additional mechanisms that are important for disease pathogenesis, such as those involved in T lymphocyte migration into the small intestine under inflammatory conditions, and lead to the identification of novel targets for the treatment of Crohn's disease.

Source article

Apostolaki M, Manoloukos M, Roulis M, Wurbel MA, Müller W, Papadakis KA, Kontoyiannis DL, Malissen B, Kollias G. Role of beta7 Integrin and the Chemokine/Chemokine Receptor Pair CCL25/CCR9 in Modeled TNF-Dependent Crohn's Disease. *Gastroenterology* (2008) doi:10.1053/j.gastro.2008.02.085. (Gastroenterology. 2008 Mar 5 [Epub ahead of print])

Contact
Dr. George Kollias, BSRC Fleming, Vari, Greece.
kollias@fleming.gr– www.fleming.gr

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.

Funding
This work was supported by the European Commission Network of Excellence (NoE) Project MUGEN (LSHG-CT-2005–005203) under the Sixth Research Framework Programme of the European Commission.

www.mugen-noe.org