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EDITORIAL

Adipose-derived Stromal Cells: The Good Side of Fat?

Inflammatory bowel diseases (IBDs) are a group of chronic inflammatory conditions of the gastrointestinal tract triggered by inappropriate immune responses to commensal microorganisms, environmental factors, and genetic susceptibility. The molecular pathomechanisms of IBD remain largely elusive. Further understanding of both pathogenic and protective factors for IBD is critical for the development of innovative treatment modalities.

Although adipose tissue has been well-recognized as a lipid storage compartment, there is growing evidence that adipose tissue also mediates endocrine organ functions, with multiple roles in regulating metabolism, inflammation, and immunity.[1] Obesity has been documented to have a negative effect on disease activity and progression to surgery in patients with Crohn's disease.[2] In contrast, adipose-derived stromal or stem cells have been shown to exhibit regenerative and anti-inflammatory function by modulating cellular immunity and secretion of cytokines, chemokines, and growth factors.[3] The safety and therapeutic potential of mesenteric adipose-derived stromal cells (ADSCs) have been studied in various diseases, including multiple sclerosis, liver failure, diabetes mellitus, and orthopedic disorders.[3] In the context of IBD, systemic infusion of ADSCs has been shown to inhibit inflammation in experimental colitis.[4] Moreover, ADSCs have been shown to induce immunomodulatory macrophages that possess therapeutic potential in experimental colitis.[5] Although ADSCs might be attractive for cell-based therapies in IBD, the key soluble factor(s) responsible for controlling the intensity and complexity of anti-inflammatory effects have not yet been identified.

In this issue, Hoffman et al[6] reported an immunoregulatory potential of ADSCs from Crohn's disease patients. They examined the mRNA expression profile of ADSCs from patients with Crohn's disease and assessed the paracrine effects of ADSC-derived extracellular mediators on intestinal epithelial cell gene expression, signaling, and proliferation. The authors demonstrated that ADSCs from Crohn's disease and control patients exhibit differential gene expression profiles. Treatment with conditioned medium from Crohn's disease patient–derived ADSCs enhanced proliferation and altered inflammatory gene expression in human colonocyte cell lines. Moreover, they report that intracolonic injection of conditioned medium from Crohn's disease patient–derived ADSCs attenuated the disease in a chemically induced murine model of colitis. The amelioration of disease was accompanied by decreased expression of proinflammatory cytokines in colonic tissue. On the basis of these studies the authors concluded that disease-dependent alterations in mesenteric adipose tissue occur during Crohn's disease and that extracellular mediators of ADSCs might have a protective role in the pathophysiology of Crohn's disease. Most interestingly, as a potential mechanistic link for the ADSC-mediated protective effects, they identified the antimicrobial peptide lactoferrin by subprofiling of microarray data from patient-derived ADSCs and documented functional relevance of this extracellular candidate in a colitis mouse model. Therapeutic potential of lactoferrin has been previously suggested in experimental colitis and was associated with the modulation of imbalances of proinflammatory and anti-inflammatory cytokine responses.[7,8] Hoffman et al[6] report that human ADSC-derived lactoferrin has protective effects in experimental colitis, thus highlighting lactoferrin as a potential therapeutic agent for IBD. Future studies are required to elucidate the role of human ADSC-secreted lactoferrin in modulating intestinal inflammation and to define other ADSC-regulated networks and paracrine factors altering mucosal homeostasis in a disease-dependent fashion.

Taken together, the published study provides evidence for a beneficial role of ADSCs during intestinal inflammation and new insights in the biology of adipose tissue–derived lactoferrin.

DANIEL KOTLARZ, MD, PhD
Dr. von Hauner Children's Hospital
Department of Pediatrics
University Hospital LMU Munich
Munich, Germany

AMLAN BISWAS, PhD
Division of Gastroenterology, Hepatology and Nutrition
Boston Children's Hospital
Department of Pediatrics
Harvard Medical School
Boston, Massachusetts

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Conflicts of interest
The authors disclose no conflicts.

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