Bone marrow stem cells may help control inflammatory bowel disease

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Massachusetts General Hospital (MGH) investigators have found that infusions of a particular bone marrow stem cell appeared to protect gastrointestinal tissue from autoimmune attack in a mouse model. In their report published in the journal *Stem Cells*, the team from the MGH Center for Engineering in Medicine report that mesenchymal stem cells (MSCs), known to control several immune system activities, allowed the regeneration of the gastrointestinal lining in mice with a genetic mutation leading to multiorgan autoimmune disease.

"Our findings suggest that MSC therapy could become a useful treatment for inflammatory bowel disease," says Biju Parekkadan, PhD, of the Center for Engineering in Medicine, the paper's lead author. "Several previous studies have observed these cells' ability to inhibit specific subsets of T cells and relieve symptoms in particular autoimmune disorders. But this is the first demonstration of their ability to suppress a broad-based autoimmune reaction and protect gastrointestinal tissue."

Autoimmune disease occurs when the immune system loses control over lymphocytes (white blood cells) that attack an individual's own tissues. Treatments for these diseases – more than 80 conditions, ranging from type 1 diabetes to rheumatoid arthritis to gastrointestinal disorders like Crohn's disease – are primarily directed against symptoms; and even those that target the immune system do not completely suppress the out-of-control response. Found in the bone marrow, MSCs give rise to tissues supporting blood cell development and secrete factors that can

modulate several immune system activities. Their use has recently received FDA approval to treat severe graft-versus-host disease in children.

The current study was designed to investigate MSCs' therapeutic potential in a model of multiorgan autoimmune disease. The researchers used a strain of mice in which a genetic mutation leads to deficiency in regulatory T cells, which suppress the activity of self-reactive immune cells, resulting in overwhelming autoimmune disease. The mice were treated with infusions of either MSCs or regulatory T cells, and a week later the researchers examined the effects on tissues from the pancreas, the liver and the distal ileum – the lower end of the small intestine – which are usually attacked by autoimmune reactions.

While little improvement was seen in the pancreatic or liver tissue, in four of the six MSC-treated mice, intestinal tissues appeared almost identical to those of normal mice. Structural defects seen in the intestinal lining of untreated autoimmune mice had disappeared in the MSC-treated mice, an improvement seen in only one of six mice treated with regulatory T cells.

Analysis of the animal's lymph nodes revealed that MSC treatment produced a significant reduction in inflammation. Surprisingly, cell-tracking studies indicated that the MSCs – which were administered by infusion into the peritoneum, the membrane lining the abdominal cavity – moved into abdominal lymph nodes rather than to the intestine itself. The presence of MSCs was associated with a reduction of activated T cells and changes in other indicators of immune system activity, indicating suppression of the out-of-control immune reaction.

"The intestine may be an ideal site for MSC therapy, given its rapid ability to regrow tissue and its extensive local supply of lymph nodes; and the route by which the cells were administered may have ensured a

greater amount of engraftment in gut-associated lymph nodes," explains Martin Yarmush, MD, PhD, director of the MGH Center for Engineering in Medicine and senior author of the study. "Before we can think about testing this approach in patients, we need to know more about long-term effects of MSC infusion – including immunosuppressive effects – and gain more understanding of how MSCs modulate immune cell activity in more realistic models of inflammatory bowel disease."

Source: Massachusetts General Hospital