
Dear Reader,

Crohn’s disease is a chronic inflammatory enteropathy that manifests through three phenotypes: inflammatory, stricturing and penetrating. Rather than being three separate behaviours, these phenotypes actually represent the natural progression of bowel damage, with epithelial-to-mesenchymal transition being a leading mechanism. Arguably, the stricturing phenotype is burdened by a high rate of hospitalization and surgical procedures due to a progressive fibrosis of the gut wall leading to lumen obstruction. The number of resections may ultimately lead to functional impairment and short bowel syndrome, largely affecting patients’ quality of life.

Despite the fact that the advent of biological therapies has dramatically changed the outcome of these patients, the benefit in terms of reduction of surgery rate is still limited. Therefore, there is a growing need for a better therapeutic approach, and mesenchymal stromal cells (MSCs) seem to be the best candidate in fulfilling this need. Up to now, either systemic or local administration of MSCs has been applied in both experimental models of colitis and clinical trials recruiting patients suffering from treatment-resistant inflammatory or fistulizing Crohn’s disease with promising results; however, no evidence on the putative ability of MSCs in limiting fibrosis has been collected so far. In this context, the study by Lian and coworkers, who investigated the preventive and therapeutic effects of MSCs in an experimental model of colonic fibrosis, carries novel information on both scientific and clinical grounds.

Briefly, intestinal fibrosis was induced by treating Balb/c mice with increasing doses of 2,4,6-trinitrobenzene sulfonic acid enema over a period of seven weeks, and allogeneic bone marrow-derived MSCs were intravenously infused before or during the induction of colitis to test both their preventive and therapeutic efficacy. Notably, the prophylactic MSC treatment inhibited not only colon shortening, but also the accumulation of fibrotic tissue, the expression of fibrotic proteins and the epithelial-to-mesenchymal transition. On the other hand, the therapeutic use of MSCs reversed intestinal fibrosis and reduced the epithelial-to-mesenchymal transition. In addition, the study of the molecular and signaling pathways involved, showed a down-regulation of secretion of the fibrogenic factors transforming growth factor-β, interleukin (IL)-1b, IL-6 and IL-13 and an up-regulation of IL-10, an anti-fibrogenic and immunomodulant factor. In parallel, the phosphorylation of Smad2 and Smad3 was strongly reduced upon MSC administration, thus critically hampering the epithelial-to-mesenchymal transition.

In addition to the contribution to scientific knowledge, this work paves the way for a phase I-II clinical studies aimed at inhibiting/reverting intestinal fibrosis, hence blocking the progression of tissue damage and the natural history of this debilitating condition. Should the results confirm the anti-fibrogenic action of MSCs against CD-associated fibrosis, the chance of safely and efficaciously treating this dreadful condition becomes a real prospect. Patients will have the opportunity to enjoy a safer and possibly more efficacious treatment, ultimately ameliorating their outcome and quality of life.

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