Investigating the Protective Effects of Interleukin 22 on Intestinal Epithelium: Potential Graft-versus-Host Disease Treatment

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Gastrointestinal graft-versus-host disease (GVHD) is a severe complication of allogeneic hematopoietic stem cell transplantation in which donor T cells attack host tissues. Immunosuppressants are utilized as a primary therapy for GVHD, however their side effects often inhibit patient recovery. As a result, alternative GVHD treatments are critical. While interleukin 22 (IL-22) deficiency has been linked to worsened GVHD in a murine model, the protective mechanism of IL-22 in the intestine remain unclear. Thus, we aimed to elucidate the effects of IL-22 on intestinal epithelium to determine if IL-22 treatment can improve tissue recovery in GVHD. Three-dimensional murine organoids that mimic intestinal crypt structure in vivo were cultured and treated with recombinant murine IL-22. Subsequently, a novel quantitation technique was used to assess organoid growth. We found that IL-22 increased small intestinal ($p<0.0001$) and large intestinal ($p<0.05$) organoid size, indicating increased proliferation and potential protection from GVHD. Additionally, new crypt formation in organoids ($p<0.05$) and percentages of intestinal stem cells (ISCs; $p<0.05$) were increased by IL-22. This increased growth was associated with activation of the IL-22 receptor pathway preferentially in intestinal stem cells (ISCs), suggesting direct effects of IL-22 on ISCs. These findings are the first to indicate that IL-22 promotes intestinal regeneration by functioning as an ISC growth factor. Treatment of murine organoids with recombinant human IL-22 also resulted in increased proliferation of intestinal cells ($p<0.05$), suggesting human IL-22 may be a promising candidate for tissue regeneration therapies for patients with intestinal pathology.

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