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Titel des Beitrags: RIG-I/MAVS and STING signaling promote gut integrity during irradiation- and immune-mediated tissue injury.

Abstract: The molecular pathways that regulate the tissue repair function of type I interferon (IFN-I) during acute tissue damage are poorly understood. We describe a protective role for IFN-I and the RIG-I/MAVS signaling pathway during acute tissue damage in mice. Mice lacking mitochondrial antiviral-signaling protein (MAVS) were more sensitive to total body irradiation- and chemotherapy-induced intestinal barrier damage. These mice developed worse graft-versus-host disease (GVHD) in a preclinical model of allogeneic hematopoietic stem cell transplantation (allo-HSCT) than did wild-type mice. This phenotype was not associated with changes in the intestinal microbiota but was associated with reduced gut epithelial integrity. Conversely, targeted activation of the RIG-I pathway during tissue injury promoted gut barrier integrity and reduced GVHD. Recombinant IFN-I or IFN-I expression induced by RIG-I promoted growth of intestinal organoids in vitro.
and production of the antimicrobial peptide regenerating islet-derived protein 3 α (RegIIIα). Our findings were not confined to RIG-I/MAVS signaling because targeted engagement of the STING (stimulator of interferon genes) pathway also protected gut barrier function and reduced GVHD. Consistent with this, STING-deficient mice suffered worse GVHD after allo-HSCT than did wild-type mice. Overall, our data suggest that activation of either RIG-I/MAVS or STING pathways during acute intestinal tissue injury in mice resulted in IFN-I signaling that maintained gut epithelial barrier integrity and reduced GVHD severity. Targeting these pathways may help to prevent acute intestinal injury and GVHD during allogeneic transplantation.

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