

Hermansky-Pudlak syndrome (HPS) is a rare, autosomal immunodeficiency disorder in humans and is characterized by melanosome and platelet dysfunction. To date, 7 forms have been described and in every case, the molecular defect has been traced to a gene affecting lysosome trafficking. In mice, 16 mutant strains are currently described and serve as models for the human disease. Among them, 9 strains carry mutations in components of complexes termed BLOCs (Biogenesis of Lysosome-related Organelle Complexes) which act at different levels of vesicle function. In the course of our mouse germline ENU mutagenesis program, we identified a coat color mutant, *salt-and-pepper*, and traced the molecular defect to the *dysbindin* gene on chromosome 13. Dysbindin is a component of the BLOC-1 complex and mutations in the human ortholog are responsible for HPS-7. We investigated the innate immune response of these mutant animals and found a marked increased susceptibility to intracellular pathogens mouse cytomegalovirus (MCMV) and *L. monocytogenes*. Similar infections performed on mutant mice carrying other forms of Hermansky-Pudlak syndrome indicate that some, but not all, components of the vesicle trafficking machinery are required for the defense against viral and/or bacterial infections. These data reveal an important new physiological function for this class of proteins and will increase our understanding of the human syndromes.