Chronic Salmonella enterica Serovar Typhimurium-Induced Colitis and Cholangitis in Streptomycin-Pretreated Nramp1+/+ Mice.

Abstract:
Salmonella enterica subspecies 1 serovar Typhimurium is an enteric bacterial pathogen infecting a broad range of hosts. In susceptible Nramp1(-)/(-) (Slc11alpha1(-)/(-)) mice, serovar Typhimurium cannot efficiently colonize the intestine but causes a systemic typhoid-like infection. However, after pretreatment with streptomycin, these susceptible (C57BL/6 and BALB/c) mice develop acute serovar Typhimurium-induced colitis (M. Barthel et al., Infect. Immun. 71:2839-2858, 2003). It was not clear whether resistant Nramp1(+/+) (Slc11alpha1(+)/+) mouse strains would similarly develop colitis. Here we compared serovar Typhimurium infection in streptomycin-pretreated susceptible (C57BL/6) and resistant (DBA/2 and 129Sv/Ev) mouse strains: We found that acute colitis (days 1 and 3 postinfection) is strikingly similar in susceptible and resistant mice. In 129Sv/Ev mice we followed the serovar Typhimurium infection for as long as 6 weeks. After the initial phase of acute colitis, these animals developed chronic crypt-destructive colitis, including ulceration, crypt abscesses, pronounced mucosal and submucosal infiltrates, overshooting regeneration of the epithelium, and crypt branching. Moreover, we observed inflammation of the gall duct epithelium (cholangitis) in the 129Sv/Ev mice between days 14 and 43 of infection. Cholangitis was not attributable to side effects of the
streptomycin treatment. Furthermore, chronic infection of 129Sv/Ev mice in a typhoid fever model did not lead to cholangitis. We propose that streptomycin-pretreated 129Sv/Ev mice provide a robust murine model for chronic enteric salmonellosis including complications such as cholangitis.