Dendritic cells (DCs) and macrophages are critical to innate and adaptive immunity to the intestinal bacterial microbiota. Here, we identify a myeloid-derived mucosal DC in mice, which populates the entire lamina propria of the small intestine. Lamina propria DCs were found to depend on the chemokine receptor CX3CR1 to form transepithelial dendrites, which enable the cells to directly sample luminal antigens. CX3CR1 was also found to control the clearance of entero-invasive pathogens by DCs. Thus, CX3CR1-dependent processes, which control host interactions of specialized DCs with commensal and pathogenic bacteria, may regulate immunological tolerance and inflammation.