Pathogen sensing by receptors of the innate and adaptive immune system is essential host defense against infection. Moreover, immune cells are in principle also capable of recognizing and destroying cancer cells. Yet, aberrant immune signaling can also directly promote initiation and development of malignant disease by creating inflammatory environments and by suppressing natural antitumor immune responses. Furthermore, immune cells themselves can be targets of malignant transformation, and human lymphomas and leukemias are frequently driven by mutations influencing immune receptor signaling pathways. Along these lines, we will discuss new insights into the regulation and function of C-type lectin receptors (CLRs) and their associated signaling pathways in innate immunity and within tumor microenvironments and current results related to the mechanisms through which deregulated signals from antigen receptors promote lymphomagenesis.