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Characterization of the Expression and Function of the C-Type Lectin Receptor CD302 in Mice and Humans Reveals a Role in Dendritic Cell Migration

C-type lectin receptors (CLR) play important roles in immune cell interactions with the environment. We described CD302 as the simplest, single domain, type I CLR and showed it was expressed mainly on the myeloid phagocytes in human blood. CD302 co-localized with podosomes and lamellopodia structures so we hypothesized that it played a role in cell adhesion or migration. This study used mouse models to obtain further insights into CD302 expression and its potential immunological function. Mouse CD302 transcripts were, as in humans, highest in the liver followed by lungs, lymph nodes (LN), spleen and bone marrow. A detailed analysis of CD302 transcription in mouse immune cells revealed highest expression by myeloid cells, particularly macrophages, granulocytes and myeloid dendritic cells (mDC). Interestingly, 2.5-fold more CD302 was found in migratory compared to resident mDC populations. CD302 knockout (CD302KO) mice were generated. Studies on the relevant immune cell populations revealed a decrease in the frequency and numbers of migratory mDC within CD302KO LN compared to wild-type (WT) LN. In vitro studies showed CD302KO and WT DC had an equivalent capacity to undergo maturation, prime T cells, uptake antigens and migrate towards the CCL19/CCL21 chemokines. In vivo studies demonstrated that CD302KO migratory DC could exit skin tissue normally through lymphatic vessels, but exhibited reduced entry into the interfollicular channels of LN, confirming a functional role for CD302 in mDC migration.