Germinal centers (GCs) are specialized micro-environments that generate high affinity Ab-forming cells (AFCs) and memory B cells. Many B cells undergo apoptosis during clonal selection in GCs. The TAM (Tyro-3, Axl, and Mer) family receptor tyrosine kinases, including Mer, facilitate macrophage clearance of apoptotic cells. We previously showed that tingible body macrophages (TB MPs) in GCs express Mer. We observed that apoptotic cells (ACs) accumulated in GCs of mice deficient in Mer (Mer−/−), after immunization with T-dependent Ag. Accumulation of ACs in GCs of Mer−/− mice resulted in significantly increased AFCs, GCs, and Th1-skewed IgG2c Ab responses. We report here that increased GC response in Mer−/− mice compared to controls is due to increased proliferation of GC B cells. We also found that AC accumulation in Mer−/− GCs is not due to increased B cell apoptosis. We show that TB MPs express two other members (Tyro-3 and Axl) of TAM family receptors, which are similar in both Mer−/− and controls. TB MPs in GCs of both strains express similar levels of milk fat globule EGF factor 8 (Mfge8) and T cell immunoglobulin 4 (Tim-4), which are believed to aid AC clearance. These data indicate the critical role for Mer in the clearance of ACs in GCs. This is further strengthened by the efficient clearance of ACs from GCs in mice deficient in Axl (Axl−/−) in the presence of Mer. Together, these data demonstrate a pivotal role of Mer in regulating B cell response and in the maintenance of B cell tolerance.

**Methods and Results**

**Augmented anti-NP GC response in Mer−/− mice**

**Enhanced primary (short-lived) AFC responses in Mer−/− mice**

**Elevated Th1-skewed IgG2 Ab responses in Mer−/− mice**

**Expression of milk fat globule EGF factor 8 (Mfge8), a dual-function bridging molecule involved in the integrin pathway to clear ACs is not compromised in Mer−/− mice**

**Significantly increased number of apoptotic cells (ACs) accumulate in Mer−/− GCs**

**Significantly increased number of proliferating B cells in Mer−/− GCs**

**Accumulation of ACs is not due to increased cell death in Mer−/− GCs**

**Other members of the TAM family receptor tyrosine kinases are not altered in Mer−/− mice**

**No significant accumulation of ACs in GCs of Axl deficient (Axl−/−) mice in the presence of Mer**

**Conclusion**

- Significantly higher number of apoptotic cells (ACs) accumulate in GCs of Mer deficient (Mer−/−) mice
- Augmented anti-NP GC, AFC, and Th1-skewed IgG2 Ab responses in Mer−/− mice
- Significantly increased number of proliferating B cells in Mer−/− GCs
- Accumulation of ACs in Mer−/− GCs is not due to increased cell death
- ACs are largely cleared from GCs of Axl deficient (Axl−/−) mice, in the presence of Mer

We acknowledge support for this study from the National Institute of Health grants to Z.S.M.R. (RO3AR055701) and (RO1AI091670).