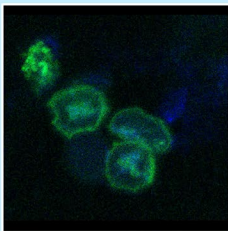


**WILL HARRIS**

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Myeloid-Derived Suppressor Cells (green:  
phospholipid membranes, blue: nuclei)

### **TAM RTK Inhibition Causes Contrasting Effects in Myeloid-Derived Suppressor Cells and Dendritic Cells**

While cancer immunotherapy presents the possibility of safe and effective treatments, a variety of factors may reduce the effectiveness of existing immunotherapies. Of particular note is the ability of cancer to activate cellular signaling pathways that ultimately suppress inflammatory responses. Two cell types thought to mediate cancer-related immunosuppression are myeloid-derived suppressor cells (MDSCs) and dendritic cells (DCs). The TAM family of receptor tyrosine kinases (*Tyros3-/-*, *Axl-/-*, and *Mer-/-*) is implicated in regulation of the immune system and the clearance of apoptotic cells. We hypothesize that TAM RTK signaling contributes to cancer-related immunosuppression by regulating the ability of MDSCs and DCs to suppress or stimulate the adaptive immune response. To determine the role of TAM RTKs in MDSC and DC function, we measured the expression level of various RNAs and proteins associated with the regulation of the immune system in MDSCs and DCs extracted from *Tyros3-/-*, *Axl-/-*, and *Mer-/-* mice. We also compare the ability of TAM knock-out and control DCs to stimulate T-cell proliferation. Due to the known role of nitric oxide signaling and arginase activity in MDSC-mediated suppression of the immune response, the immunosuppressive capabilities of MDSCs of both wildtype and TAM RTK knockout genotypes were assessed with enzymatic assays for nitric oxide synthase (iNOS) and arginase activity. We found that TAM RTK knockout MDSCs exhibited significant changes in RNA and protein expression and increased iNOS and arginase activity, indicating they have a reduced immunosuppressive capacity. Conversely, TAM RTK knockout DCs had a reduced capacity to induce an inflammatory T-cell response, along with changes in RNA and protein expression indicating a gain of immunosuppressive function. Thus, the role of TAM RTK signaling in immune responses may be more complex than previously believed. Further study is needed to evaluate whether inhibition of TAM RTKs would be effective in treating cancer, as drugs would reduce MDSC-mediated immunosuppression while attenuating the stimulation of T-cell activity by DCs.