Fundamental questions remain unresolved in the hematopoiesis field such as how hematopoietic stem cells balance proliferation, differentiation, and specialization steps to produce the vast repertoire of blood cell types required for proper immune function. We have tackled this rather complex problem using a multi-pronged approach that combines transcriptomics, genetics, and mutational analysis using the Drosophila hematopoietic system as a model. In the hematopoietic progenitor state, we find that cell-extrinsic signals play a major role in controlling both spatial and temporal aspects of the cell cycle and their differentiation into mature cell types. In particular, we discovered that blood progenitors are maintained in a non-proliferative state in the G2 phase of the cell cycle by Wnt- and hedgehog-dependent signaling pathways that link cell cycle progression to differentiation. Furthermore, our analysis of crystal cells, platelet-like cells involved in melanization, has uncovered new means by which Musashi and Numb affect canonical and non-canonical Notch signaling. We propose a model of how blood cells integrate various external inputs to determine cell cycle status and differentiation fate.