- **Gene regulation during T cell development**

T cells are the major organizers of the adaptive immune response, and a target of viruses such as HIV and HTLV-1 that cause currently incurable diseases. T cells develop from hematopoeitic stem cells that reside in the bone marrow. This process is governed by incompletely understood gene regulatory mechanisms that execute the T cell genetic program. Our laboratory investigates gene regulation during T cell development. We use both in vivo transgenic mouse models as well as newly developed technology for in vitro T cell development from embryonic stem cells. Our focus has been on the regulation of the gene locus encoding the alpha chain of the T cell receptor (TCRa), particularly its locus control region (LCR). Appropriately regulated expression of the TCRa gene is essential for the development of virtually all of the circulating T cells in the body. The TCRa LCR has powerful properties that provide a linked gene with a predictable pattern of gene expression, in terms of level, developmental timing and cell-type distribution. It also bears a strong, but poorly understood, insulation capacity that provides LCR-linked transgenes with integration site-independence when inserted into the genome. Our work to date has identified numerous sub-sequences of the TCRa LCR that support its various properties. Molecular investigations of these sequence elements (and their interactions) are expected to reveal components required for generating proper TCRa gene regulation in vivo and completion of T cell development. It will also provide tools to establish robust, predictable and reliable therapeutic gene expression in T cells via eventual gene therapy applications. Our lab's reagents and technologies have enabled us to additionally contribute to collaborations with other groups investigating important aspects of T cell development and function.