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Targeted Deletion of a High-Affinity GATA-binding Site in the GATA-1 Promoter Leads to Selective Loss of the Eosinophil Lineage In Vivo

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Article history

Transcription factor GATA-1 reprograms immature myeloid cells to three different hematopoietic lineages-erythroid cells, megakaryocytes, and eosinophils. GATA-1 is essential for maturation of erythroid and megakaryocytic precursors, as revealed by gene targeting in mice. Here we demonstrate that deletion of a high-affinity GATA-binding site in the GATA-1 promoter, an element presumed to mediate positive autoregulation of GATA-1 expression, leads to selective loss of the eosinophil lineage. These findings suggest that GATA-1 is required for specification of this lineage during hematopoietic development. Mice lacking the ability to produce eosinophils should prove useful in ascertaining the role of eosinophils in a variety of inflammatory or allergic disorders.

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However, in vivo, diminished GATA-1 activity results in normal homeostatic tissue mast cell levels and increased antigen-induced CD4+ Th2 and iMMC9 cell levels and heightened IgE-mast cell mediated reactions. Citation: Sharma S, Tomar S, Dharne M, Ganesan V, Smith A, Yang Y, et al. GATA-1, a zinc-finger protein, is expressed in a number of hematopoietic lineages such as mast cells, eosinophils, megakaryocytes, and erythroid cells [20, 21]. Sertoli cells are the only non-hematopoietic cells that express GATA-1 [22]. Loss of function studies have revealed an important role for GATA-1 in the development of megakaryocytes and erythroids [23–25]. GATA-1, the founding member of the GATA family of transcription factors, has been demonstrated to play crucial roles in the differentiation of erythroid cells, magakaryocytes, eosinophils, and mast cells. However, the role of GATA-1 in basophils remains elusive. Here we show that basophils abundantly express Gata1 mRNAs, and that siRNA-mediated knockdown of Gata1 resulted in impaired production of IL-4 by basophils in response to the stimulation with IgE plus antigens. Our findings demonstrate that GATA-1 plays a key role in the generation and function of basophils and underscore the need for careful distinction of the cell lineage responsible for each phenotype observed in ΔdblGATA mice. Targeted deletion of a high-affinity GATA-binding site in the GATA-1 promoter leads to selective loss of the eosinophil lineage in vivo . J. Exp. Med. Nature 455, 627–632 (2008)Showed that expression in the pancreas of a combination of three key regulators re-specifies one somatic cell type into another functional cell type, in vivo. ADS CAS Google Scholar. 67.