

# Regulatory T lymphocytes and Transplantation



## Themis modulates regulatory T cell suppressive functions

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Deciphering the genetic basis of human diseases and understanding the function of mammalian genes are among the main challenges for today's geneticists. In this regard, rodent models represent invaluable tools to identify new genes and to study the mechanisms of action of genes implicated in human diseases. Our team identified a spontaneous mutation of Themis gene responsible for high incidence of inflammatory bowel disease, which was associated with skewed cytokine secretion by effector CD4 T cells towards Th2 and Th17 and with impairment of the suppressive activity of the regulatory CD4 T cells (Treg). The contribution of Treg was further evidenced by experiments showing that transfer of Treg from normal BN rats to mutant animals prevented the occurrence of bowel lesions. The genetic dissection showed that the impact of Themis deficiency on Tregs depends on Vav1 variants. Together, these studies highlight the importance of Vav1 and Themis signaling hub in regulating the suppressive functions of Treg. Understanding the underlying molecular mechanisms may lead to advances in Treg biology and favor the identification of new pharmacogenetic markers and therapeutic targets in immune mediated diseases.

**Vav1 and Themis1 cooperate in controlling  
Treg functions and intestinal homeostasis**



**Vav1<sup>W63</sup>**

**Defective Tregs**

**IBD development**



**Vav1<sup>R63</sup>**

**Functional Tregs**

**No pathological manifestations**

