

Defective deletion and deviation in diabetes

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The NOD mouse strain, a popular model of type-1 diabetes, has a T-cell-intrinsic defect in clonal deletion of self-reactive thymocytes. Genetic intervals primarily controlling this deficit map to *chr 1* and *chr 3*. The *chr 3* interval also controls a NOD defect in clonal deviation of self-reactive thymocytes to the CD8 _{$\alpha\alpha$} and FoxP3⁺ CD4⁺ T regulatory lineages. This finding raises the speculation that the ineffectiveness of both central and peripheral tolerance in NOD mice may reflect, at least in major part, a single fault in T-cell signaling pathways.

References

Zucchelli S., Holler P., Yamagata T., Roy M., Benoist C. and Mathis D. Defective central tolerance induction in NOD mice: genomics and genetics. *Immunity* 22, 385-396 (2005).

Holler P., Yamagata T., Jiang W., Feuerer M., Benoist C. and Mathis D. The same genomic region conditions clonal deletion and clonal deviation to the CD8 $\alpha\alpha$ and Treg lineages in NOD vs C57Bl/6 mice. *J. Exp. Med.*, Submitted (2006).

Feurer M., Auyeung V., Hill J., Holler P., Jiang W., Benoist C. and Mathis, D. Enhanced thymic selection of FoxP3⁺ regulatory T cells in the NOD mouse model of autoimmune diabetes. In preparation (2007).