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## **T CELL BEHAVIOR IN AN ENGINEERED MODEL: PERIPHERAL TOLERANCE MECHANISMS**

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To examine mechanisms of T cell tolerance induction to an antigen expressed exclusively in the periphery, we have developed a double-transgenic mouse model wherein the expression of a neo-antigen,  $\beta$ -galactosidase ( $\beta$ -gal), is induced solely in pancreatic islet beta cells following administration of the tetracycline derivative, doxycycline (dox); expression of the antigen is extinguished following the removal of dox. This provides the opportunity to assay T cell tolerance induction under a variety of circumstances within a single model.

Our experiments thus far have revealed little evidence of tolerance within the CD4<sup>+</sup> T cell compartment toward this antigen, irrespective of when it is first expressed. Mice have been challenged with the  $\beta$ -gal antigen under four separate conditions of antigen expression. These are: 1) when the antigen has never been expressed (i.e., no dox treatment); 2) when it is synthesized throughout life; 3) when it is synthesized only in adulthood; and 4) when it is expressed for only a short time in adulthood, but then turned off.

Future applications of this model include an assessment of tolerance within the CD8<sup>+</sup> T cell compartment, an examination of epitope spreading, an evaluation of the influence of genetic background and coupling with  $\beta$ -gal-reactive TCR transgenes.