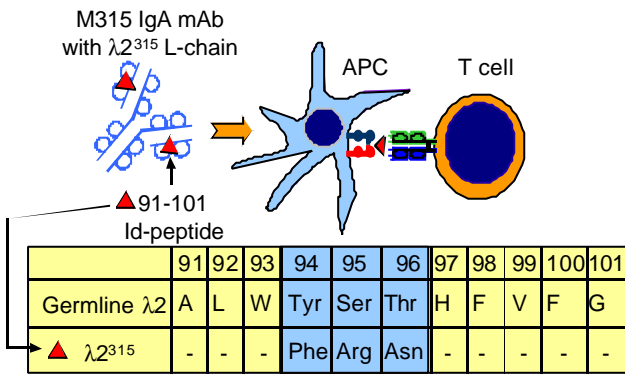


Background information. The $\lambda 2^{315}$ model system

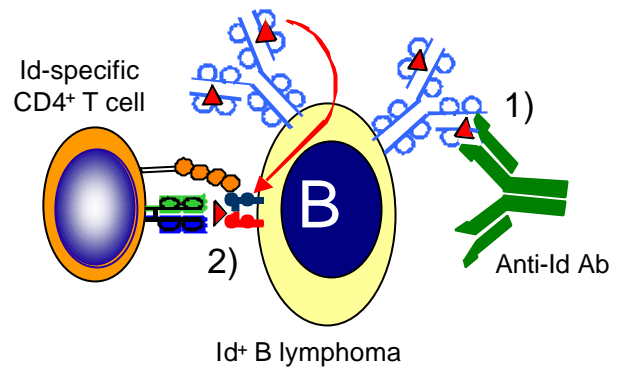
What role does T cell recognition of antibody variable (V)-region peptides have in regulation of the immune system and in eradication of B cell cancers? It has been difficult to answer these questions because Id-specific T cells have such low frequencies. We solved this problem by cloning Id-specific CD4⁺ T cells and defining their specificity. Then, to obtain measurable populations of Id⁺ B cells and Id-specific T cells, we made two complementary sets of transgenic mice. Below is given a brief account of this model system that we have established, with the most important references.

Id-specific, MHC-restricted T cell clones. BALB/c T cells which recognize an Id on the BALB/c $\lambda 2^{315}$ Ig L-chain in the context of the class II MHC molecule I-E^d have been cloned (Bogen *et al.*, *Eur J Immunol* 1986a). The T cells recognize a synthetic peptide containing the 91-101 amino acids of the $\lambda 2^{315}$ sequence; this stretch corresponds to the third hypervariable region. Phe⁹⁴ Arg⁹⁵ Asn⁹⁶ residues, unique to $\lambda 2^{315}$ due to somatic mutations, are important for Id expression (Bogen *et al.*, *Eur J Immunol*, 1986b, Bogen & Lambris, *EMBO-J* 1989). T cell clones which cross-react between synthetic Phe⁹⁴ and Tyr⁹⁴ peptide analogues use an extremely conserved receptor (V α 3, J α 1, V β 6, J β 1.1) (Snodgrass *et al.*, *Eur J Immunol*, 1992).

Professional antigen presenting cells endocytose, process and present Id⁺ immunoglobulin. Id⁺ Ig (with $\lambda 2^{315}$ L-chains) is processed by professional APC, and Id-peptide presented on MHC class II molecules to T cells. (Weiss & Bogen, *Proc. Natl. Acad. Sci.* 1989).

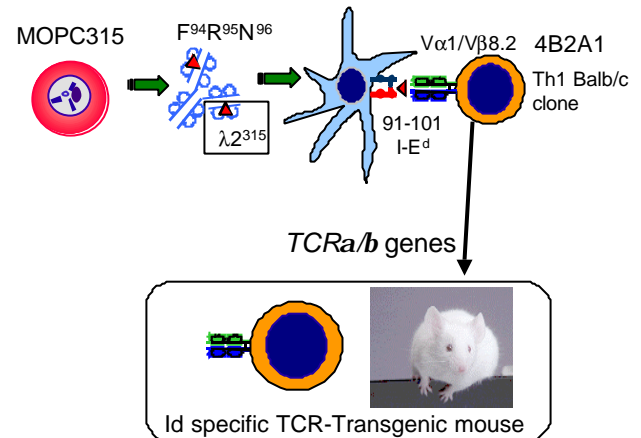


B lymphoma cells spontaneously process Id⁺ Ig and present Id-peptide on class II molecules. Transfected B lymphoma cells process their endogenously produced $\lambda 2^{315}$ (Weiss & Bogen, *Proc. Natl. Acad. Sci.* 1989). Nascent $\lambda 2^{315}$ is processed in the endoplasmic reticulum or Golgi part of the secretory pathway (Weiss & Bogen, *Cell* 1991). Thus, B cells constitutively process their own Ig and present V region peptides on MHC class II molecules to Id-specific T cells. In conclusion, both exogenous and endogenous Id⁺ Ig are processed and presented on MHC molecules. This implies that B cells will generally express two types of Id. ¹Id on BCR that can be recognized by anti-Id Ab, and ²Id-peptides on MHC class II molecules that can be recognized by Id-specific CD4⁺ cells.



Id-specific T cell receptor transgenic mice. The α - and β -chain genes of the 4B2A1 T cell clone (V α 1, J α 19; V β 8.2, J β 1.2) have been cloned and a transgenic strain on a BALB/c background has been established and characterized (Bogen *et al.*, *Eur J Immunol* 1992). This characterization was greatly facilitated by employing a clonotypic mAb that we produced (Bogen *et al.*, *Eur J Immunol*, 1990).

The $\lambda 2^{315}$ Id-specific TCR transgenic mouse



Id⁺ Ig transgenic mice. Mice were made transgenic for the $\lambda 2^{315}$ gene and bred onto a BALB/c background (Bogen and Weiss, *Eur J Immunol*. 1991).

The $\lambda 2^{315}$ Id⁺ L-chain transgenic mouse

