

Spontaneous eye disease in C57BL/10-background mice lacking $\gamma\delta$ T cells

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Mice lacking $\gamma\delta$ T cells due to genetic inactivation of the TCR-C δ gene are largely healthy animals when reared under standard conditions. However, they show an increased susceptibility to a number of different infectious agents, and show an impaired ability to heal epithelial tissues, including the skin and lung epithelium. This implies that $\gamma\delta$ T cell function is mainly of importance during disease. On the FVB background, however, TCR δ ^{-/-} mice were found to spontaneously develop dermatitis, implying that $\gamma\delta$ T cell function may under certain circumstances also be needed to maintain immune balance. We now report that C57BL/10 (B10) background mice lacking $\gamma\delta$ T cells frequently develop blindness in the absence of any deliberate provocation. By 4-5 months of age, 75% of B10-TCR δ ^{-/-} female mice display white opaque eyes, resulting from corneal inflammation (keratitis), although B6-TCR δ ^{-/-} mice (of the closely related C57BL/6 background) strain are not susceptible. The keratitis is often characterized by centralized hyperplasia of the corneal epithelium. Preliminary evidence indicates that neonatal reconstitution of B10-TCR δ ^{-/-} mice, using B10-derived hematopoietic precursors capable of producing $\gamma\delta$ T cells, can reduce both the incidence and severity of the keratitis. Unexpectedly, B10-TCR δ ^{+/-} females also developed keratitis, although their disease is comparatively delayed, implying that a full complement of $\gamma\delta$ T cells is necessary for protection against this spontaneous disease. Our observation underlines the importance of the role of $\gamma\delta$ T cells in normal regulation of immune and inflammatory responses, and serves as additional evidence that $\gamma\delta$ T cells are critical in maintaining the unique immunology of the eye. We are currently investigating whether the spontaneous keratitis originates from infectious or autoimmune processes, and examining the role of female hormones in development of this disease.