

The structure of the marsupial $\gamma\mu$ T cell receptor defines a third T cell lineage in vertebrates

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Most T cells found in jawed vertebrates express functional heterodimeric receptors (TCRs) on their surface formed by either α and β or γ and δ chains. Each chain possesses two domains, an amino-terminal variable domain (V) and a constant domain (C) on the carboxy-terminus (V-C pattern). In most cases, the ability of T cells to recognize diverse antigens relies on the surface (or paratope) located within $V\alpha - V\beta$ or $V\gamma - V\delta$ segments. Recent genomic studies of non-eutherian mammals identified clusters of genes that resemble the classical TCR loci but surprisingly contain an additional variable segment. The functional product common for marsupials and monotremes called ‘ μ chain’ was predicted to contain two variable ($V\mu$ and $V\mu_j$) and one constant ($C\mu$) domains. Single cells analysis of blood and spleen from *Monodelphis domestica* showed that some of the splenic T cells co-express the μ and γ chains suggesting that both polypeptides could form a novel type of T cell receptor, the $\gamma\mu$ TCR. Using obtained sequences, we generated and structurally characterized two different $\gamma\mu$ TCRs. Here, we present the novel and unusual architecture of a third lineage of T cell receptor found in marsupials and monotremes [1].

[1] Morrissey K.A., Wegrecki M., Praveena T., Hansen V.L., Bu L., Sivaraman K.K., Darko S., Douek D.C., Rossjohn J., Miller R.D., Le Nours J. The molecular assembly of the marsupial T cell receptor defines a third T cell lineage. *SCIENCE*, 371, 1383-1388, 2021.

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