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A V δ 3+ subset of MR1 reactive $\gamma\delta$ T cells recognise the side of the MR1 molecule

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T cells are broadly categorised by their expression of either an $\alpha\beta$ or $\gamma\delta$ T cell receptor (TCR). Whilst $\alpha\beta$ T cells are comprehensively understood $\gamma\delta$ T cells are ill-defined but are increasingly realised to be an important T cell subset that display both innate- and adaptive-like immune functions. The MHC class 1 related protein (MR1), presents bacterial vitamin B metabolites to $\alpha\beta$ mucosal associated invariant T cells (MAIT). MAIT cell TCR' bind atop MR1 in a conventional fashion, contacting the $\alpha 1$ and $\alpha 2$ helices which comprise the MR1 antigen presenting pocket, as well as contacting the ligand directly. Recently, published in Science we identified that $\gamma\delta$ T cells recognised MR1 but did so irrespective of the ligand being presented. Analysis of a V δ 1+ $\gamma\delta$ TCR in complex with MR1 revealed, an unusual docking mode binding underneath the MR1 antigen presenting groove. This was in stark contrast to the conventional MAIT TCR-MR1 interactions and all other TCR complex structures to date. Here, we present biochemical and structural analysis of a V δ 3+ MR1 restricted TCR which bound along the side of MR1, adopting another novel TCR docking topology and making no contacts with the presented antigen. Ultimately, our results expand the knowledge of MR1 restricted $\gamma\delta$ TCR's shedding further light on the unusual docking modes that $\gamma\delta$ TCR's likely employ more broadly.

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