Study reveals T-cell coreceptors are well endowed with kinases

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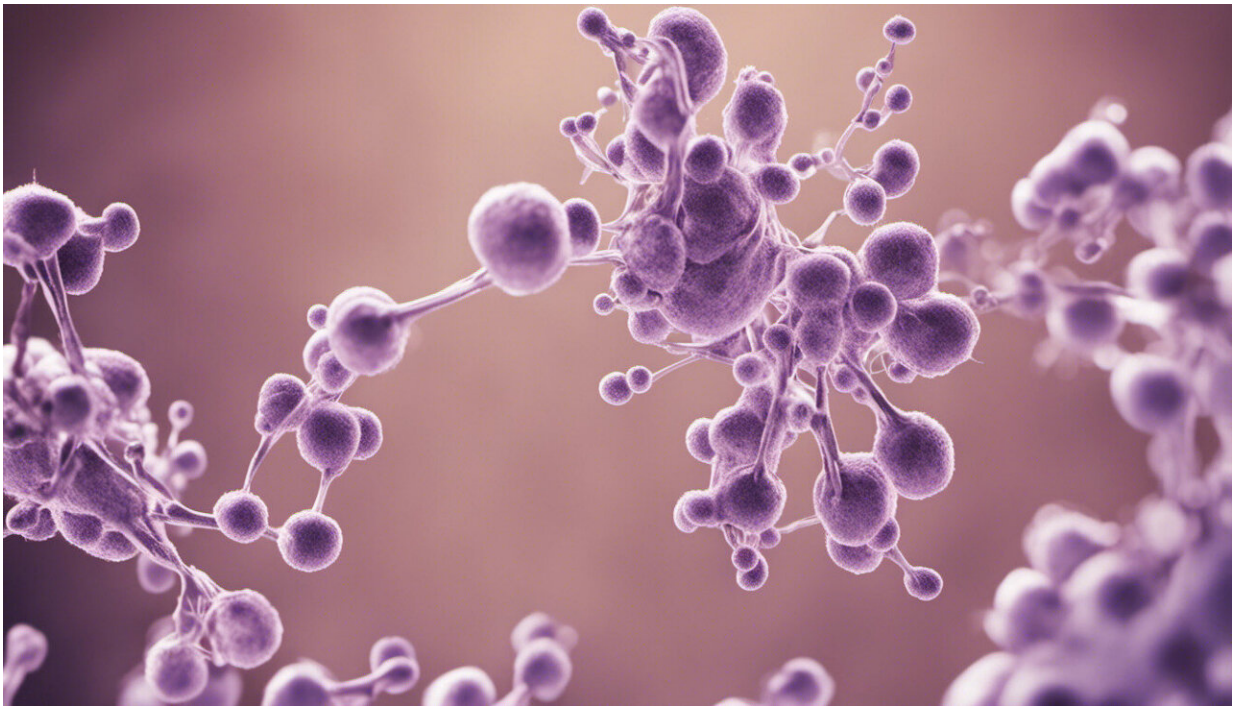

Credit: AI-generated image (disclaimer)

The kinase occupancy of CD4 and CD8 coreceptors is high, according to a new study published in *PNAS*.

Researchers at the Kennedy Institute and the MRC Weatherall Institute of Molecular Medicine (WIMM) have shed light on an important and

intensely debated puzzle in T cell biology—the partnership between coreceptors and Lck, the kinase responsible for signal initiation. CD4 and CD8 boost the sensitivity of T cells to signs of infection and cancer, and this discovery upends some earlier models of how they work.

For the first time, DPhil student Alex Mørch, working with Professors Michael Dustin (Kennedy) and Simon Davis (MRC WIMM), took advantage of technologies developed at Oxford to address the question in living cells. They used non-invasive fluorescence correlation spectroscopy to study in situ interactions between molecules and were able to demonstrate that Lck interacts with nearly all CD4 molecules and also with the majority of CD8 molecules in both T cells, thymocytes and model cells.

Commenting on the study, published in *PNAS*, Alex said, "These findings help settle the question of kinase occupancy in T cells. This point was controversial with some earlier studies suggesting that only a small minority of CD4 and CD8 had Lck associated. Our findings could have important implications for developing improved T cell-based therapies since Lck kindles critical signaling reactions."

More information: Alexander M. Mørch et al, The kinase occupancy of T cell coreceptors reconsidered, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2213538119

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