CD4+/CD8+ double-positive T cells: more than just a developmental stage?
CD4+/CD8+ DP thymocytes are a well-described T cell developmental stage within the thymus. However, once differentiated, the CD4+ lineage or the CD8+ lineage is generally considered to be fixed. Nevertheless, mature CD4+/CD8+ DP T cells have been described in the blood and peripheral lymphoid tissues of numerous species, as well as in numerous disease settings, including cancer. The expression of CD4 and CD8 is regulated by a very strict transcriptional program involving the transcription factors Runx3 and ThPOK. Initially thought to be mutually exclusive within CD4+ and CD8+ T cells, CD4+/CD8+ T cell populations, outside of the thymus, have recently been described to express concurrently ThPOK and Runx3. Considerable heterogeneity exists within the CD4+/CD8+ DP T cell pool, and the function of CD4+/CD8+ T cell populations remains controversial, with conflicting reports describing cytotoxic or suppressive roles for these cells. In this review, we describe how transcriptional regulation, lineage of origin, heterogeneity of CD4 and CD8 expression, age, species, and specific disease settings influence the functionality of this rarely studied T cell population.

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