PHENOTYPIC IDENTIFICATION OF NASCENT MEMORY CD8 T CELLS AND MATHEMATICAL MODELING ALLOW EARLY PREDICTION OF LONG-TERM MEMORY CELL COUNTS

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Résumé

The elucidation of the process and molecular regulation of CD8 T cell differentiation towards short-term cytotoxic effector and long-term protective memory cells is an important goal of vaccine research. It has long been hampered by the lack of phenotypic markers allowing discrimination between those subsets. We herein highlight by transcriptome analysis the existence of two steps in the effector phase of a primary response. Moreover, by CD44/Mki67/Bcl2 co-expression we clearly label cells corresponding to the naive, early effector, late effector and memory differentiation stages and identify nascent memory cells within co-existing differentiation stages during the effector phase. Finally, thanks to formal mathematical modeling, we show most cells follow a linear naive -> early effector -> late effector -> memory differentiation pathway and we predict long-term memory cell numbers from a few early measurements. We thus provide means to investigate the mechanisms of primary responses through the phenotypic identification of cells along the differentiation process and to speed-up candidate vaccine screening by early prediction of memory cell counts.

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