TRANSCRIPTOME ANALYSIS OF CD8+ RESIDENT MEMORY T CELLS REVEALS ORGAN-LEVEL ENVIRONMENTAL ADAPTATION AND FUNCTIONAL DIVERSITY IN T CELL MEMORY

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Recent research focusing on CD8+ memory T lymphocytes suggests the existence of several, highly specialized organ-resident memory T cell (Trm) subsets. CD8+ Trm cells are instructed to preferentially home to, subsequently become resident in, and rapidly respond upon recall antigen challenge within distinct organ environments.

Although there is consensus that all CD8+ Trm cell subsets are characterized by integrin alphaE (CD103) expression, they are also known to express unique markers in an organ-restricted fashion. Hence, it is possible that Trm cells of distinct organs adapt to the surrounding environment or even differ in functional terms. Nevertheless, the full spectrum of these markers is unknown, leaving room for speculation about possible differences in the characteristics and functions of CD8+ Trm cells in individual organs.

In this study we sought a better understanding of these questions using a hypothesis-free approach. We show that pure fractions of intact, viable murine CD8+ CD103+ Trm cells can be isolated from various organs using automated tissue processing followed by two-step MACS multisorting. Using circulating CD8+ CD62L- T effector memory (Tem) cells as reference, we also present initial findings obtained from whole-genome gene expression profiling describing common features of, and organ-specific differences discriminating between murine CD8+ Trm cell subsets of the small intestine, lung and liver.

Our preliminary findings suggest that individual CD8+ Trm subsets of given organs display clear differences in the usage of various genes potentially affecting homing, signal recognition and responsibility, T cell activation and effector functions. Validation of these findings by independent methodologies and functional assays is currently under way to test whether CD8+ T cell memory displays a previously unknown functional heterogeneity becoming apparent at the organ-level.