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203.LYMPHOCYTES AND ACQUIRED OR CONGENITAL IMMUNODEFICIENCY DISORDERS

Altered Cellular Dynamics and Surface Expression Promote Long-Lived Plasma Cell Survival

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Serological memory following vaccination decline with aging, indicating reduced survival of new plasma cells (PCs). We report that with age, bone marrow (BM) PC pool is enriched in long-lived plasma cells (LLPCs), leading to reduced PC turnover, suggesting increased competition. Using in vivo imaging, we find that LLPCs are highly organized into April-dependent clusters. Based on bulk RNA sequencing, and flow-based surface phenotyping, LLPCs exhibit unique transcriptome and proteome, fine tuning expression of key cell surface molecules, including CD93, CD81, CXCR4, CD326, CD44 and CD48, important for adhesion and homing. To test their functional role, *Cxcr4* was conditionally deleted in PCs following immunization, which led to rapid mobilization from the BM, reduced survival of antigen-specific PCs, and accelerated decay of antibody titer. Analysis of endogenous LLPCs BCR repertoire exhibits reduced diversity, reduced somatic mutations, and increased public clones and IgM isotypes, particularly in young mice, suggesting non-random selection into the LLPC pool that is age-dependent.

Disclosures No relevant conflicts of interest to declare.

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