The human bone marrow is a reservoir for polyfunctional memory T lymphocytes in old age

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INTRODUCTION

Immunological memory is a hallmark of the adaptive immune system. Memory T lymphocytes are generated after the first contact with a pathogen and provide long-lasting immunity. The bone marrow (BM) has been attributed a key role in the homing and long-term survival of memory T lymphocytes in mice (Tokoyoda et al., Immunity, 2009; Di Rosa and Santoni, Eur J Immunol, 2002). However, little is still known about memory T lymphocytes in the human BM and how aging affects their frequency and function. We therefore performed a comprehensive analysis of T lymphocytes in the BM of healthy young and elderly persons. We also performed immunofluorescence stainings to identify the “survival niches” for memory T lymphocytes in the human BM.

RESULTS

Polyfunctional T cells accumulate in the BM and are maintained during aging

Memory T cells reside in the human bone marrow (BM), display a non-senescent phenotype and are in a heightened activation state

A higher frequency of effector-memory T cells resides in the bone marrow (BM) compared to the peripheral blood (PB).

A lower number of senescent CD27 - CD57+ T cells resides in the BM compared to the PB.

A higher number of T cells expressing the activation marker CD69 in the BM compared to the PB.

Memory T cells reside on interleukin-15-expressing BM stroma cells

The human BM hosts T cells specific against a broad variety of pathogens

Composition of the TCR CDR3 Vβ repertoire of T cells in the BM and PB from young and elderly persons is shown. CDR3 length distributions of BM and PB TCR Vβ segments are shown.

Our results indicate that human effector-memory T lymphocytes preferentially home to the bone marrow (BM) and are in a heightened activation state. T lymphocytes in the BM display a non-senescent phenotype and are specific against a broad variety of pathogens. Yet, polyfunctional memory T lymphocytes are maintained during aging in the human BM despite a low grade pro-inflammatory milieu. In conclusion, the BM microenvironment promotes the survival of polyfunctional memory T lymphocytes during human aging.

SUMMARY & CONCLUSIONS

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