A population of innate myelolymphoblastoid effector cell expanded by inactivation of mTOR complex 1 in mice

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Adaptive autoimmunity is restrained by controlling population sizes and pathogenicity of harmful clones, while innate destruction is controlled at effector phase. We report here that deletion of Rptor in mouse hematopoietic stem/progenitor cells causes self-destructive innate immunity by massively increasing the population of previously uncharacterized innate myelolymphoblastoid effector cells (IMLECs). Mouse IMLECs are CD3-B220-NK1.1-Ter119- CD11clow/-CD115-F4/80low/-Gr-1- CD11b+, but surprisingly express high levels of PD-L1. Although they morphologically resemble lymphocytes and actively produce transcripts from Immunoglobulin loci, IMLECs have non-rearranged Ig loci, are phenotypically distinguishable from all known lymphocytes, and have a gene signature that bridges lymphoid and myeloid leukocytes. Rptor deletion unleashes differentiation of IMLECs from common myeloid progenitor cells by reducing expression of Myb. Importantly, IMLECs broadly overexpress pattern-recognition receptors and their expansion causes systemic inflammation in response to Toll-like receptor ligands in mice. Our data unveil a novel leukocyte population and an unrecognized role of Raptor/mTORC1 in innate immune tolerance.

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