Osteoblastic mTORC1 accelerates acute myeloid leukemia growth via IL-6 signaling

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Although there is increasing evidence that bone forming osteoblasts provide a microenvironment for leukemic stem cells (LSCs) and play a critical role in the maintenance and retention of LSCs, how those cells contribute to leukemia growth remains largely unclear. The mTOR complex 1 (mTORC1), a member of the serine/threonine kinases, is known to regulate the cellular function in various cell types. Using an MLL-AF9 acute myeloid leukemia (AML) mouse model, we found that AML cells enhance the mTORC1 activity in osteoblasts *in vivo* and *in vitro*. The osteoblast specific inactivation of *Tsc1*, a negative regulator of mTORC1, drives differentiation of hematopoietic stem cells (HSCs) toward myeloid lineage during steady state and promotes AML growth. Among the secretory factors examined, interleukine-6 (IL-6) was the most upregulated gene in *Tsc1*-deficient osteoblasts. Genetic inhibition of IL-6 receptor in AML cells significantly rescued tumor growth in osteoblast specific *Tsc1*-deficient mice. Collectively, our studies suggest mTORC1/IL-6 axis in osteoblastic niche could be a novel therapeutic target for AML.