

## Targeting the MYB Proto-Oncoprotein as a Therapeutic Strategy for Acute Myeloid Leukemia

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Abstract: The transcription factor MYB is an essential regulator of normal hematopoiesis and a proto-oncogene that is widely deregulated in leukemias and lymphomas through various mechanisms. There is considerable interest in developing agents capable of inhibiting MYB functions as a therapeutic strategy for cancers driven by deregulated MYB, with emphasis on AML. The proposed research integrates expertise from the collaborating labs to i) optimize novel MYB-modulatory agents in hand for pre-clinical studies, ii) define molecular modes of action for these novel agents, and **iii)** evaluate optimized agents in preclinical AML models. Optimized agents will serve as starting points for lead candidates for clinical development, while optimized probes will immediately, together with structurally related inactive analogs, be made available to the wider research community without encumbrance. Through these efforts, we will provide new tools for understanding the biological mechanisms underlying MYB-driven cancers, such as AML, and to define new molecular avenues for therapeutic intervention.