

# miR-142 orchestrates a network of actin cytoskeleton regulators during megakaryopoiesis

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## Abstract

Genome-encoded microRNAs (miRNAs) provide a posttranscriptional regulatory layer that controls the differentiation and function of various cellular systems, including hematopoietic cells. miR-142 is one of the most prevalently expressed miRNAs within the hematopoietic lineage. To address the *in vivo* functions of miR-142, we generated a novel reporter and a loss-of-function mouse allele. We show that miR-142 is regulating a network of targets that collectively control actin filament homeostasis. This network ensures proper execution of actin-dependent cytoskeletal functions, which are critical for megakaryopoiesis and erythropoiesis. Genetic ablation of miR-142 resulted in limited megakaryocyte polyploidization, abnormal proplatelet formation, and thrombocytopenia. Erythrocyte impairments resulted in severely-disrupted red blood cell membrane, enhanced sensitivity to hemolytic stress and anemia. The pivotal role for miR-142 activity in maturation and function of blood cells, illustrates how the critical contribution a single miRNA gene can orchestrate cytoskeletal dynamics in the erythroid and megakaryotic lineages.