Targeting the EIF2AK1 Signaling Pathway Rescues Red Blood Cell Production in *SF3B1* Mutant Myelodysplastic Syndromes With Ringed Sideroblasts

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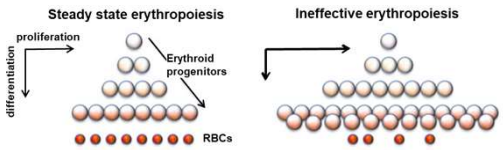
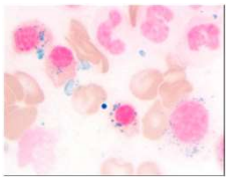
SF3B1^{MT} MDS-RS at the Single Cell Level

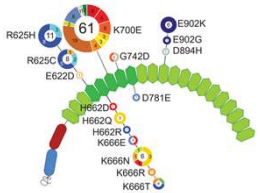
Ineffective erythropoiesis



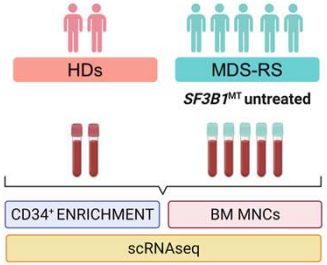
Ringed Sideroblasts



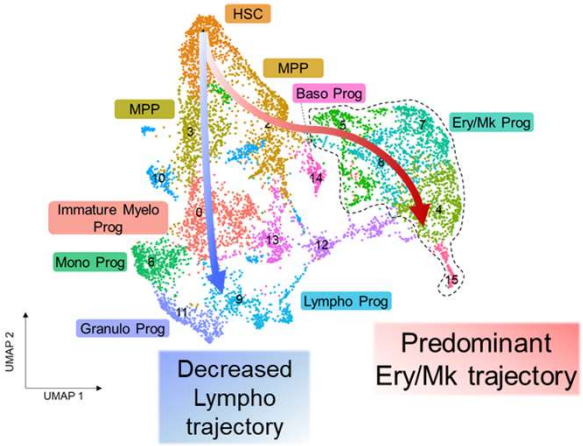
SF3B1^{MT}



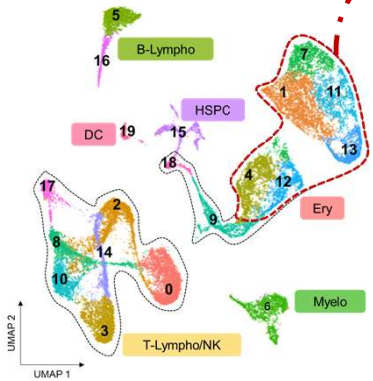
We profiled the hematopoietic landscape of ***SF3B1***^{MT} **MDS-RS** at the **single-cell level**

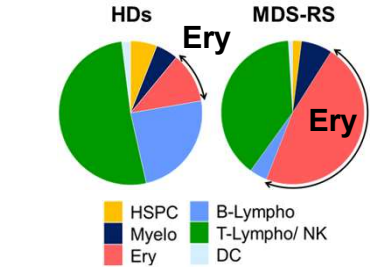


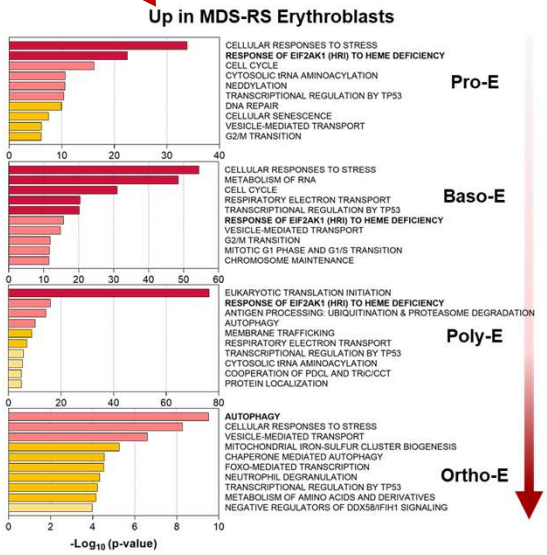
Lin^{-}CD34^{+} HSPCs

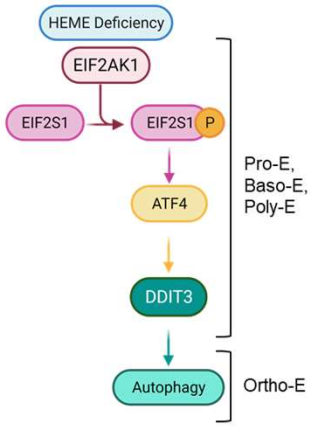


BM-MNCs









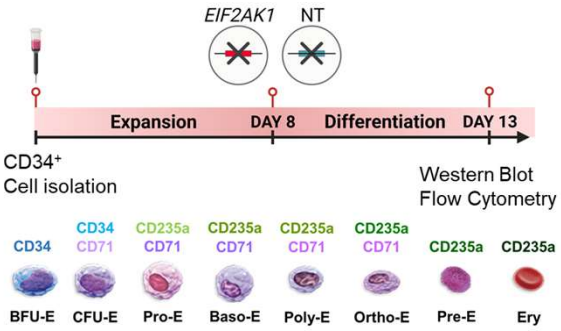
SF3B1^{MT} Lin^{-}CD34^{+} HSPCs:

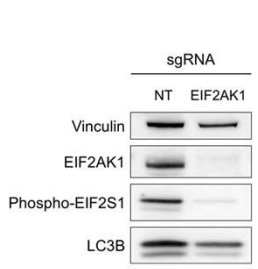
- ✓ Increased Ery/Mk differentiation
- ✓ Metabolic activation in *SF3B1*-mutant cells

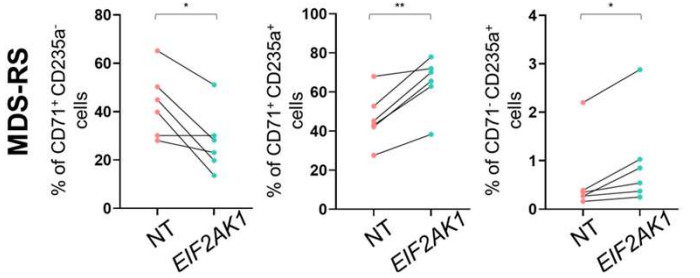
SF3B1^{MT} MNCs:

- ✓ Increased Erythroblast at the Orthochromatic stage

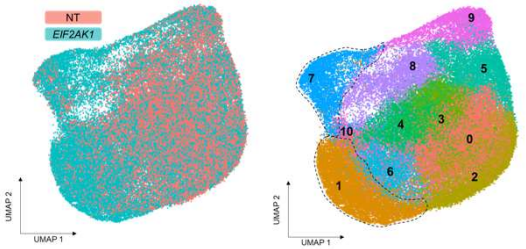
EIF2AK1 Depletion Overcomes *SF3B1*^{MT}- Induced Arrest in Terminal Erythroid Differentiation

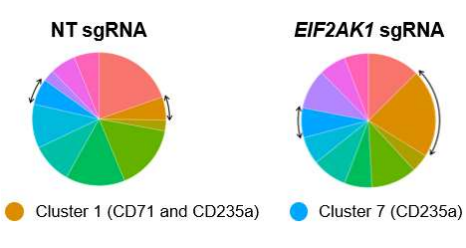


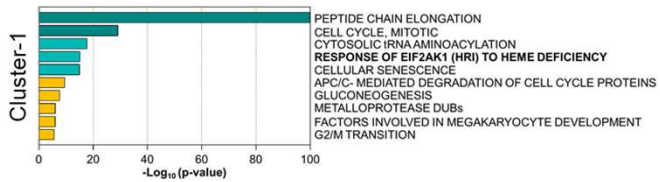


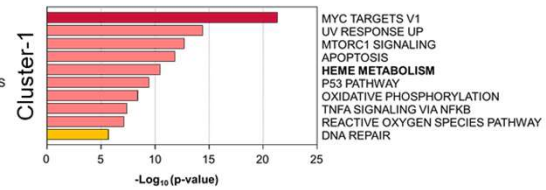


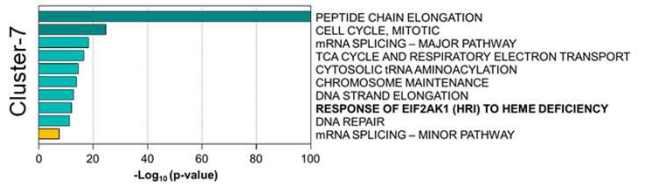
Terminally differentiated cells

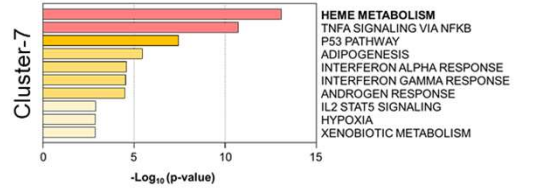






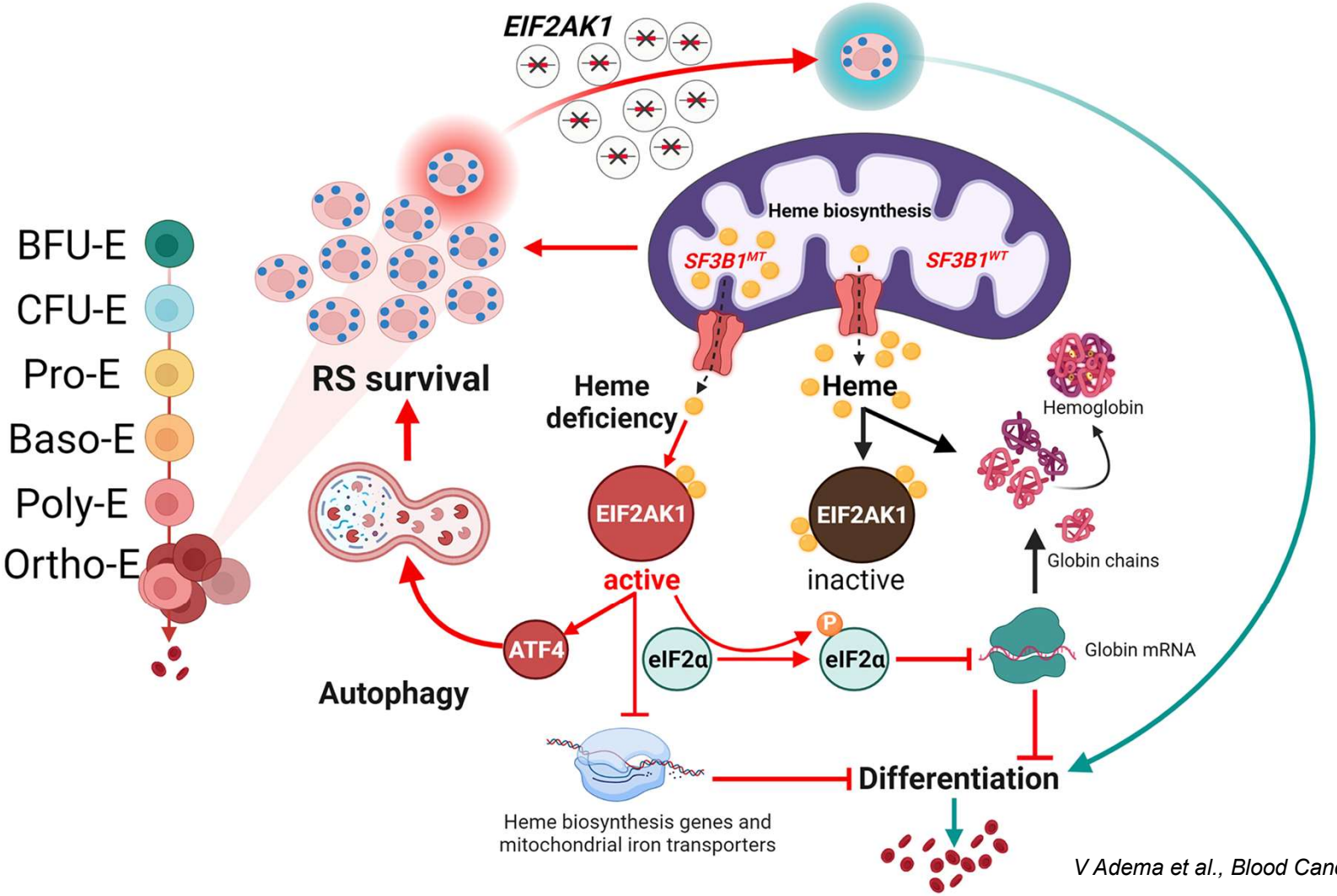






Depletion of EIF2AK1 induces differentiation of ringed sideroblasts. EIF2AK1 as a new pharmacological target for patients with MDS-RS with *SF3B1* mutations

Summary



V Adema et al., Blood Cancer Discov 2022