Role of CD43 in erythroid differentiation

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INTRODUCTION

Erythropoiesis primarily occurs in the bone marrow (BM) and involves the differentiation of erythroblasts within erythroblastic islands (EBIs). EBIs are the functional units of erythropoiesis, consisting of a central nurse macrophage surrounded by differentiating erythroblasts that gradually condense and eventually extrude their nuclei to form enucleated red blood cells. Recently, CD43 has been shown to interact with CD169 (Siglec-1) on macrophages and erythroblasts, facilitating cell adhesion and supporting erythropoiesis. While erythropoiesis typically occurs in the BM under homeostatic conditions, stress or extramedullary erythropoiesis is activated in the spleen when BM production is insufficient.

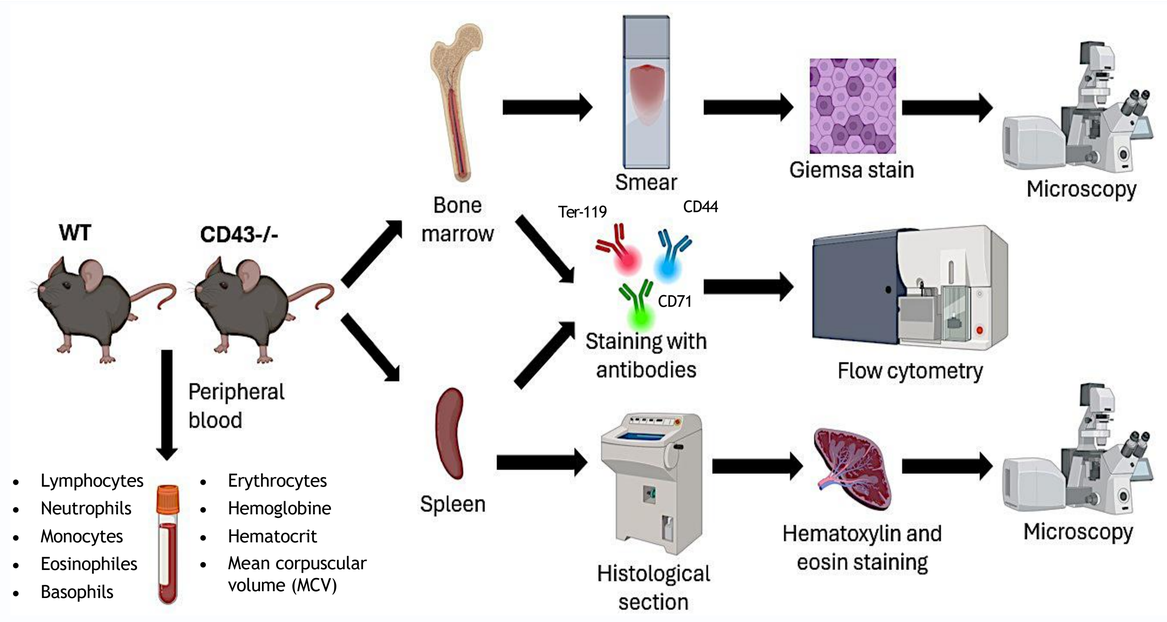
Given that CD43 is expressed very early during erythropoiesis, we hypothesized that it may play a role in erythroid differentiation and EBI organization, ultimately participating in various stages of erythropoiesis. In this study, we aimed to evaluate the role of CD43 in the organization of erythroblastic islands and in erythroid differentiation, with potential effects on erythroid cell proportions in bone marrow, spleen, and peripheral blood.

Given CD43's early expression during erythropoiesis, it is plausible that it plays a crucial role in erythroid differentiation and island organization. This study aimed to investigate the role of CD43 in erythroblastic island organization and erythroid differentiation, with potential implications for erythroblast proportions in the bone marrow, spleen, and peripheral blood.

OBJECTIVES

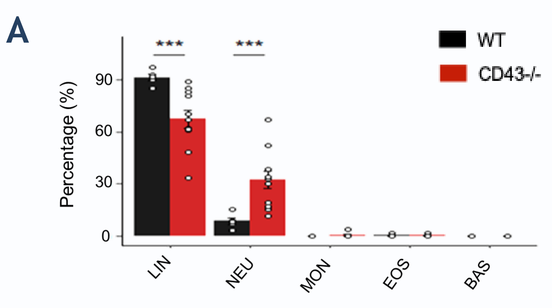
- ❑ Analyze the effects of CD43 in peripheral blood components.
- ❑ Quantify the proportions of different stages of erythroid cells in the bone marrow and spleen.
- ❑ Evaluate the role of CD43 in EBI composition and structure in the bone marrow.

METHODS



RESULTS

CD43 deficiency affects multiple hematopoietic lineages



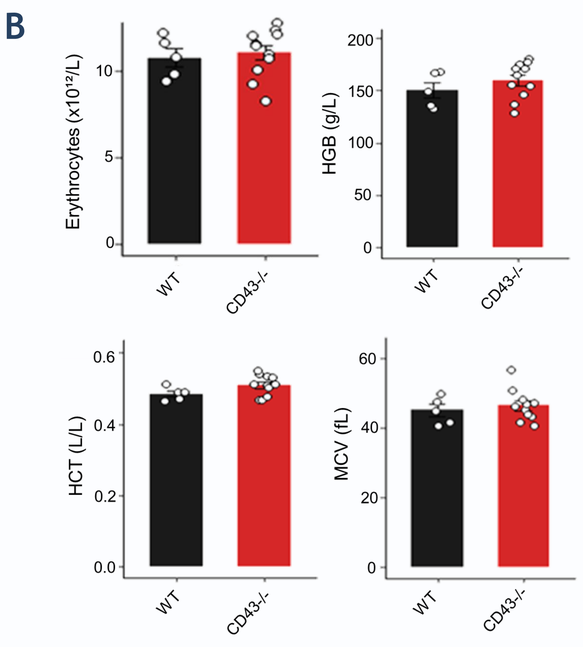
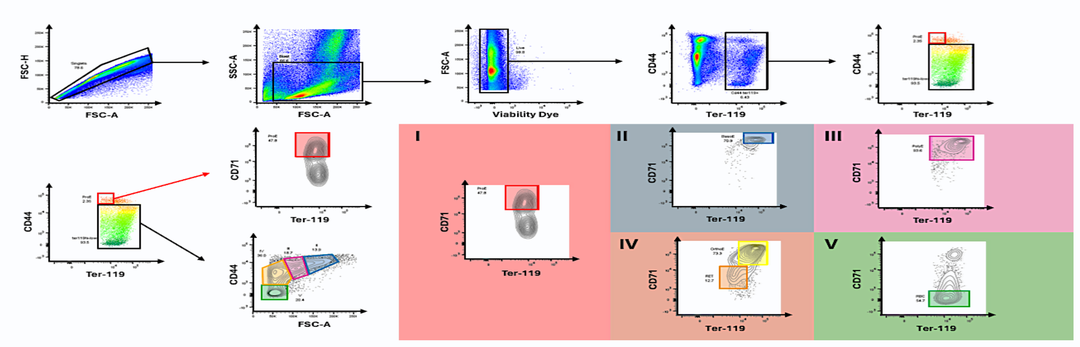
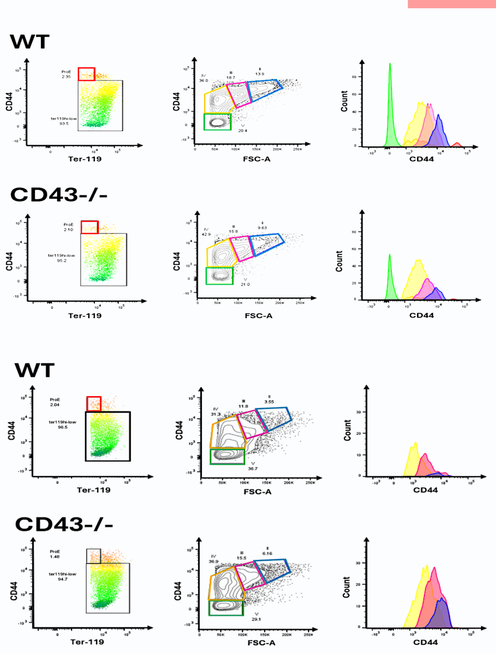
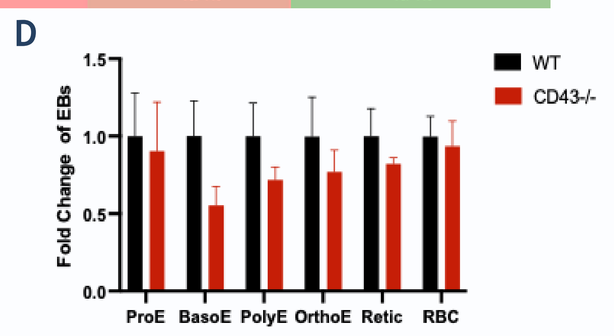


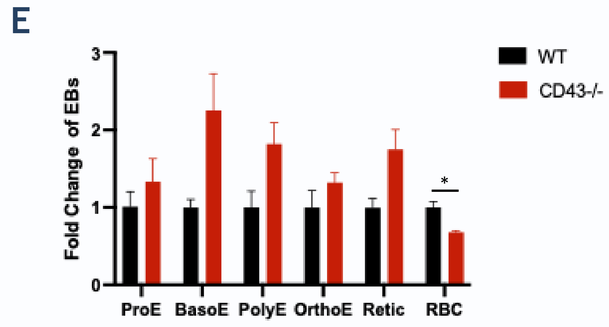
Figure 1. A) Percentage of neutrophils (NEU), lymphocytes (LIN), monocytes (MON), and eosinophils (EOS) in peripheral blood from WT and CD43KO mice. B) Erythrocyte count and red blood cell indices—hemoglobin (HGB), hematocrit (HCT), and mean corpuscular volume (MCV). n= 5 (wT) and 10 (KO). Wilcoxon rank-sum test, p-value ≤ 0.001

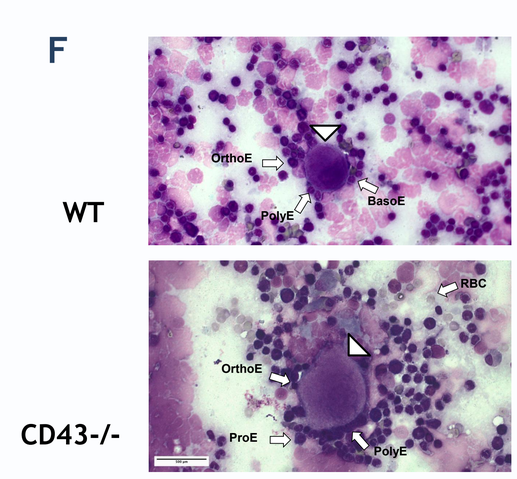
CD43 loss disrupts bone marrow erythroblastic island organization and maturation, while driving compensatory splenic EMH with increased erythroid output











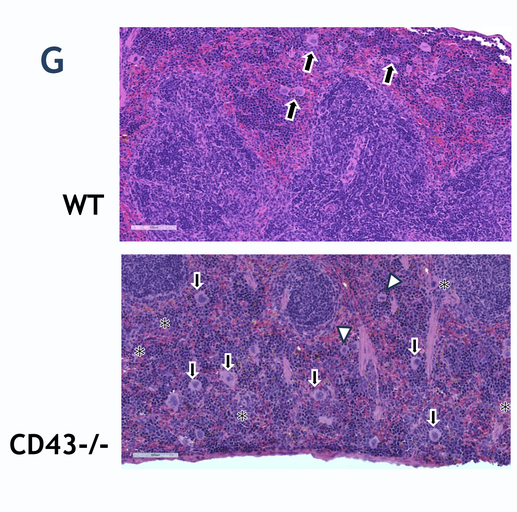


Figure 2. A) Erythroid lineage analysis strategy: progressive loss of CD44 and CD71 with a concomitant increase in Ter119 defines maturation from proerythroblast to mature erythrocyte in bone marrow and spleen from WT and CD43KO mice. B, C) Classification (gating) of erythroid populations—proerythroblast, basophilic, polychromatic, and orthochromatic erythroblasts, reticulocytes and mature erythrocytes (RBC), based on size and differential CD44 expression in bone marrow and spleen. D–E) Quantification of erythroblast subpopulations and mature erythrocytes in bone marrow and spleen. Wilcoxon rank-sum test, p-value ≤ 0.06. F) Giemsa staining of bone marrow. Shown are erythroblastic islands: a central macrophage (arrowhead) surrounded by erythroblasts. Scale bar: 100 µm G) H&E-stained splenic sections (WT vs. KO). Show megakaryocytes (arrow), erythroblastic islands (arrowhead), and myeloid precursor cells (asterisks). Scale bar: 100 µm.

CONCLUSIONS

- ❑ CD43 deficiency results in neutrophilia with lymphopenia, thereby elevating the NLR and indicating an immune imbalance, while baseline RBC indices remain unchanged.
- ❑ In the bone marrow, CD43KO mice exhibit fewer Basophilic/ Erythroblastic/Polyerythroblastic/Orthochromatic Erythroid Islands and disorganized erythroblastic islands, suggesting that CD43 is involved in island architecture/adhesion, and orderly maturation.
- ❑ The spleen of CD43KO mice displays expanded erythroid precursors and reticulocytes with megakaryocytes, along with erythroid/myeloid clusters, consistent with extramedullary hematopoiesis (EMH).
- ❑ Collectively, erythropoiesis is rerouted from marrow to spleen as a compensatory EMH mechanism, indicating that CD43 supports immune homeostasis and erythroid island organization.

REFERENCES AND ACKNOWLEDGEMENTS

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