

YOUNG SCIENCE FORUM: IL FUTURO NASCE IN LABORATORIO

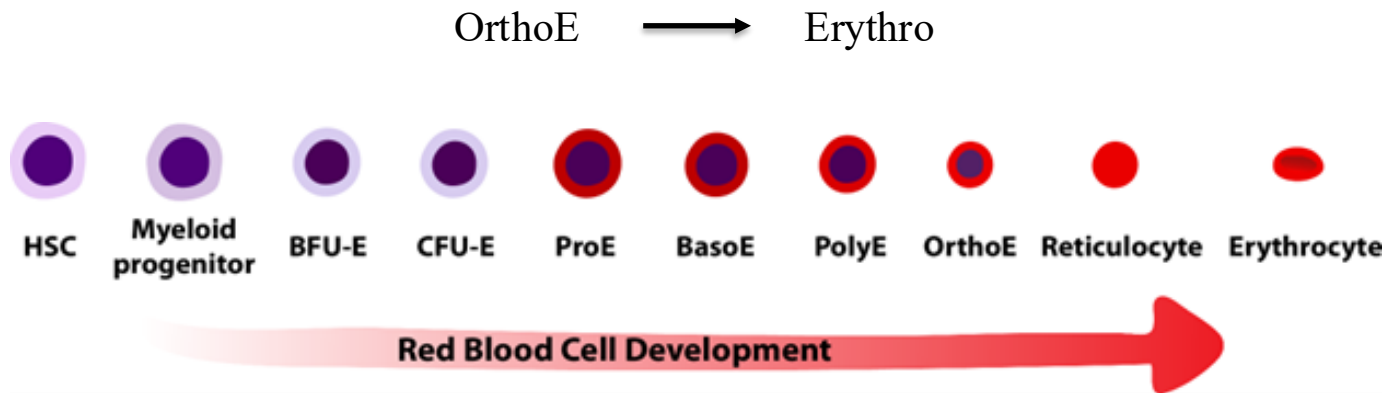


UBE2O AS A KEY REGULATOR OF DRUG-INDUCED ERYTHROPOIESIS IN THE CONTEXT OF MYELODYSPLASTIC SYNDROMES

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Extensive proteome remodeling and enucleation happen during terminal erythroid differentiation resulting in highly specialized, anucleate cells known as red blood cells.



Cha, H. J. Erythropoiesis: insights from a genomic perspective. Exp Mol Med 56, 2099–2104 (2024).

Review

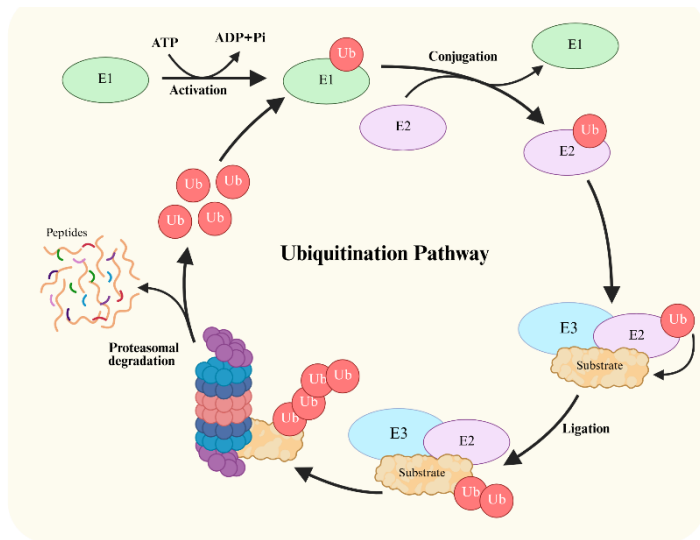
The Ubiquitin-Conjugating Enzyme E2 O (UBE2O) and Its Therapeutic Potential in Human Leukemias and Solid Tumors

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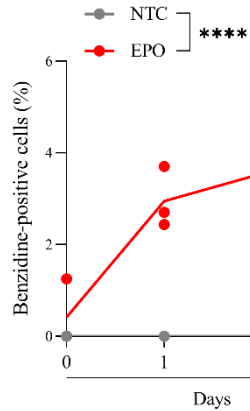
Published: 3 September 2024



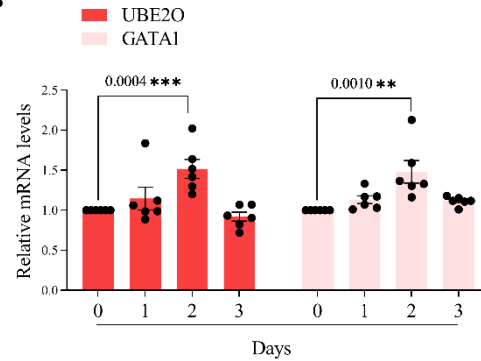
- ❖ UBE2O is an E2 enzyme
- ❖ Ubiquitination is essential for proteostasis and protein turnover
- ❖ UBE2O is involved in proteome remodelling during erythroid differentiation in mice
- ❖ Nguyen et al, <https://www.science.org/doi/10.1126/science.aan0218>

Induction of erythroid differentiation promotes UBE2O expression

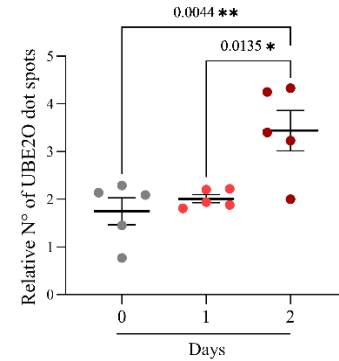
A



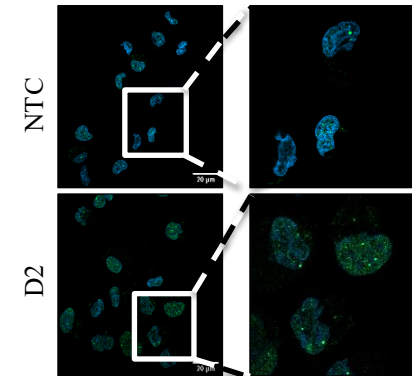
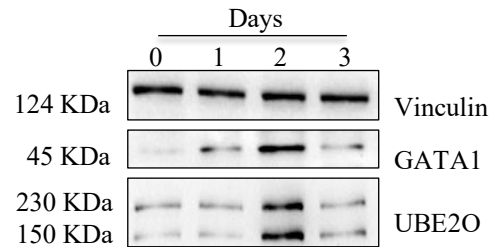
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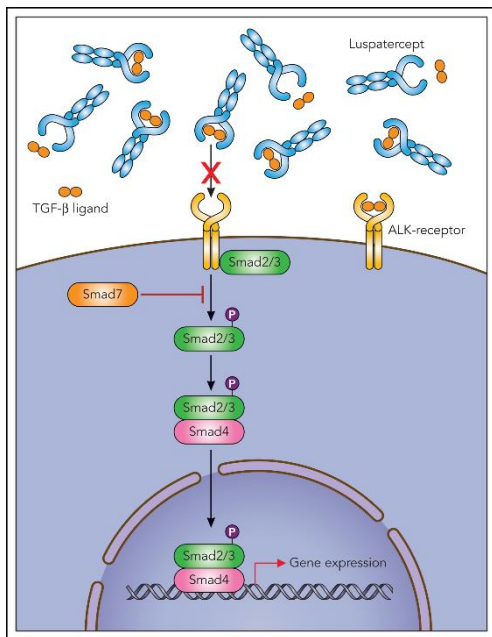
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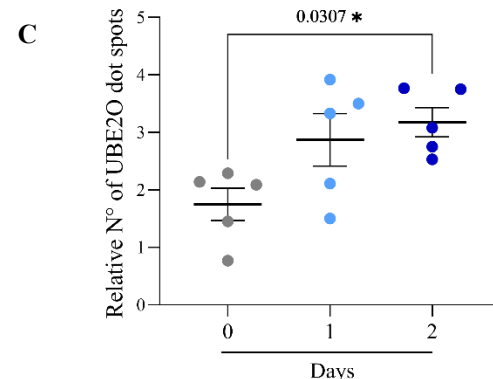
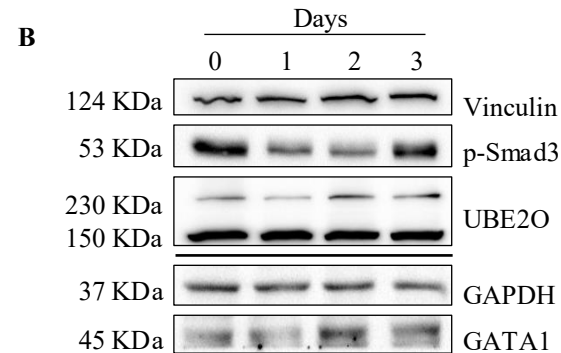
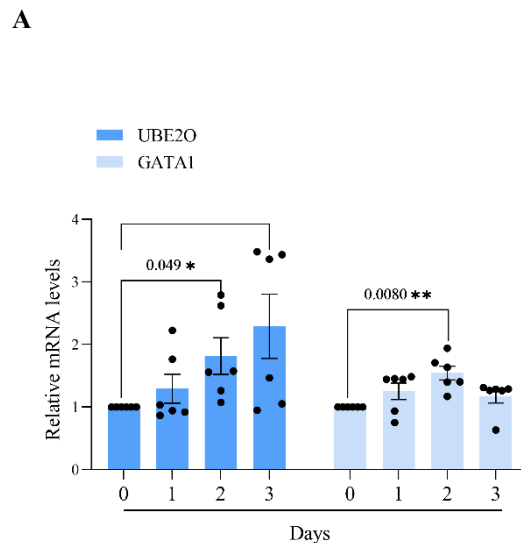
D



Luspatercept-induced erythroid differentiation promotes UBE2O expression



Kubasch AS, Fenaux P, Platzbecker U. Development of luspatercept to treat ineffective erythropoiesis. *Blood Adv.* 2021;5(5):1565-1575. doi:10.1182/bloodadvances.2020002177



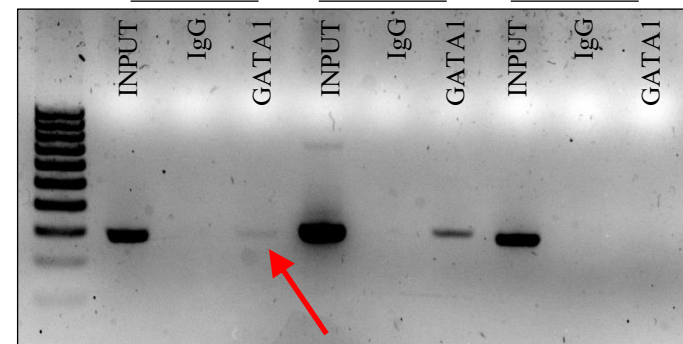
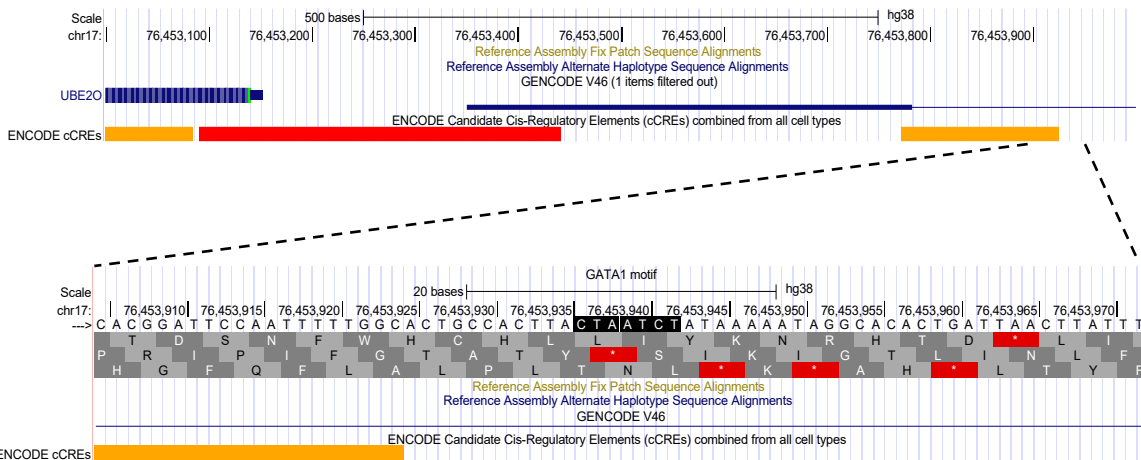
K562

Maffeo, et al. <https://doi.org/10.1182/bloodadvances.2025017340>

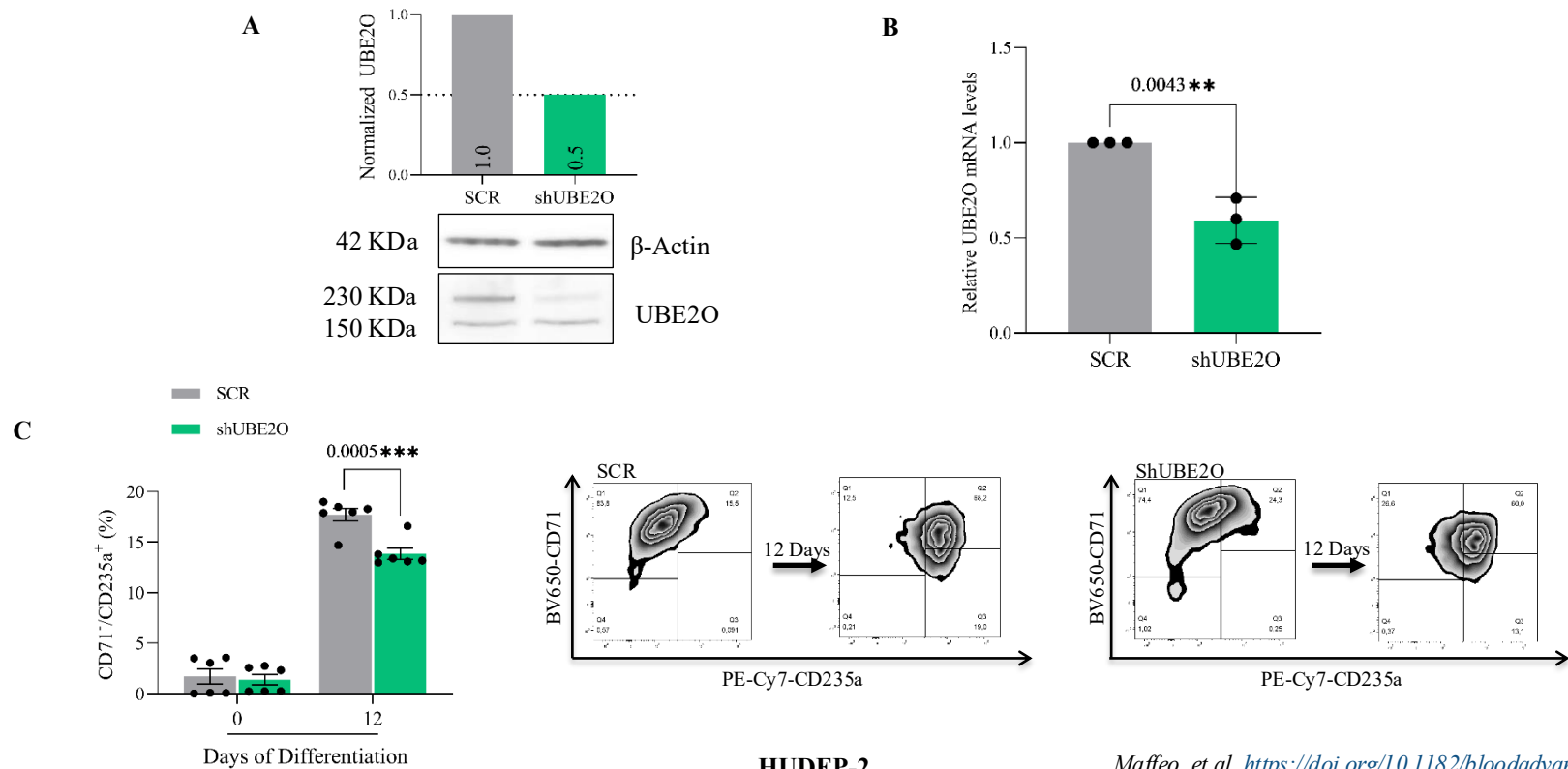
GATA1 regulates UBE2O transcription during erythroid differentiation

A

B



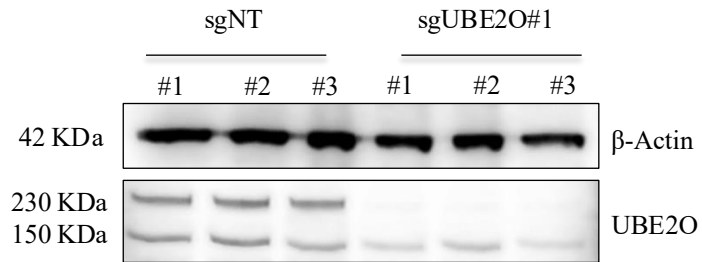
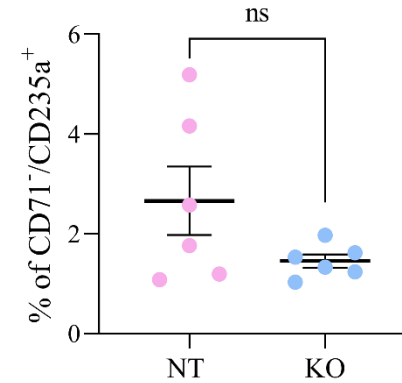
UBE2O silencing reduces erythroid differentiation of HUDEP-2 cells



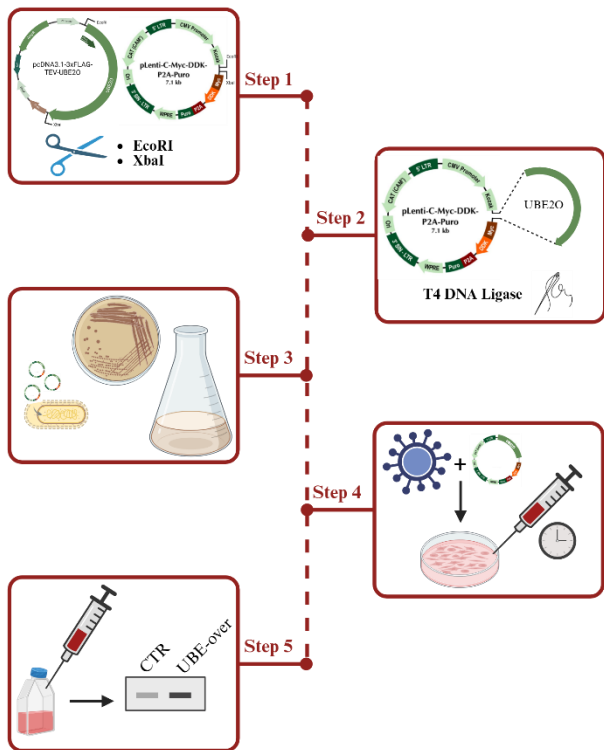
HUDEP-2

Maffeo, et al. <https://doi.org/10.1182/bloodadvances.2025017340>

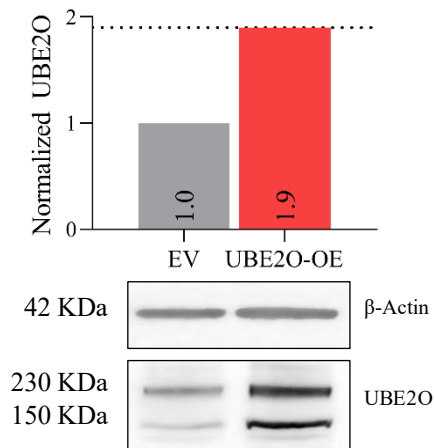
Functional validation of UBE2O loss in primary CD34⁺ hematopoietic cells

A**B**HD CD34⁺

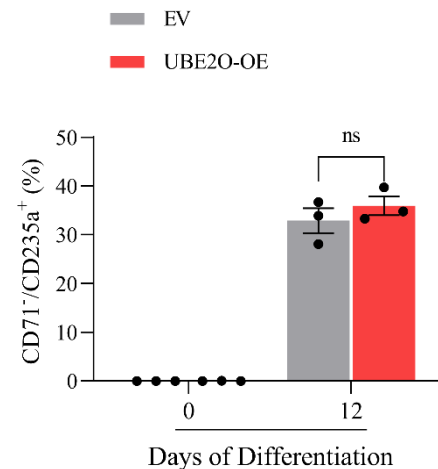
Overexpression of UBE2O in HUDEP-2 cells is not sufficient to enhance terminal erythroid maturation



A



B



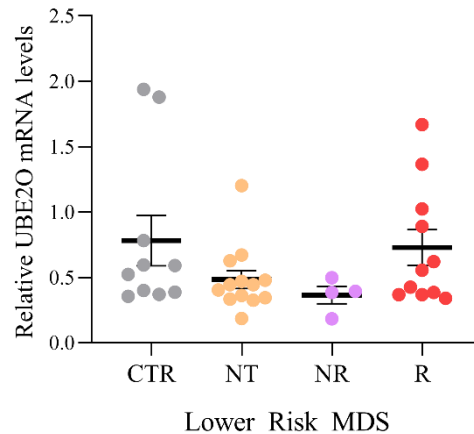
HUDEP-2

Erythroid stimulation upregulates UBE2O expression in MDS patients' samples

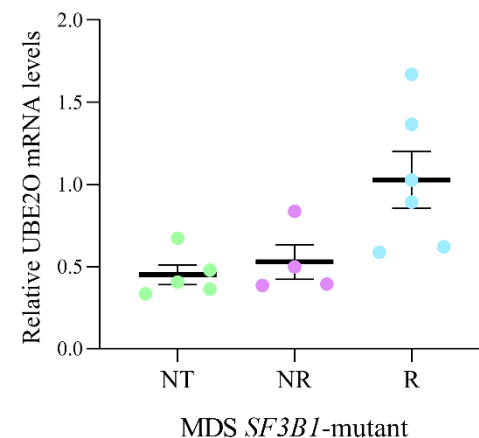
MDS

- ❖ MDS is a malignant myeloid clonal disorder
- ❖ Bone marrow dysplasia, genetic abnormalities and ineffective erythropoiesis
- ❖ Lower risk MDS are clinically treated with erythropoiesis inducing agents to correct anemia

A



B



PBMCs

Conclusion

- ❖ UBE2O is a key regulator of erythroid maturation
- ❖ UBE2O deficiency affects erythroid differentiation capacity
- ❖ GATA1 directly regulates UBE2O transcription
- ❖ Erythropoietin and luspatercept converge on the GATA1/UBE2O axis
- ❖ UBE2O could represent a biomarker of treatment response in MDS

REGULAR ARTICLE

 blood advances

UBE2O as a key regulator of drug-induced erythropoiesis in the context of myelodysplastic syndromes

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Data are available from the corresponding author, Beatrice Maffeo (beatrice.maffeo@unito.it), on request.

The full-text version of this article contains a data supplement.

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