



## The 65th ASH Annual Meeting Abstracts

## ONLINE PUBLICATION ONLY

## 602.MYELOID ONCOGENESIS: BASIC

**U2AF1 S34F Mutation Promote Megakaryopoiesis and Fibrogenesis in MDS**Wenjun Zhang<sup>1</sup>, Jinqin Liu<sup>1</sup>, Lin Yang<sup>1</sup>, Yiru Yan<sup>1</sup>, Tiejun Qin<sup>2</sup>, Zefeng Xu<sup>1,2</sup>, Gang Huang, PhD<sup>3</sup>, Bing Li<sup>1,2</sup>, Zhijian Xiao<sup>4,2,5</sup><sup>1</sup> State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China<sup>2</sup> MDS and MPN Centre, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China<sup>3</sup> Divisions of Experimental Haematology and Cancer Biology, Cincinnati Children's Hospital Medical Center, San Antonio, OH<sup>4</sup> State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China<sup>5</sup> Hematologic Pathology Centre, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China**Aims:** Exploring the clinical and pathological characteristics of MDS patients with U2AF1 mutation and investigating the impact of mutation on hematopoietic stem and progenitor cells.**Methods:** Nine hundred and eighty-nine consecutive subjects with MDS who underwent targeted next generation sequencing (NGS) from August 2016 to September 2022 were included in this study. Clinical and pathological characteristics were collected and analyzed. U2AF1<sup>S34F</sup> retroviral murine model was used to evaluate changes of hematopoiesis in the bone marrow and spleen.**Results:** Among the 989 MDS patients, U2AF1 mutation occurs in 23% of them. Within the subgroup of patients diagnosed with MDS with fibrosis (MDS-f) according to the updated WHO 2022 criteria, the frequency of U2AF1 mutation rose to 42%. Patients with U2AF1 mutation exhibited lower levels of hemoglobin and higher degrees of fibrosis, along with a significant increase in megakaryocyte counts in bone marrow biopsy and smear (**Figure A**).Our U2AF1<sup>S34F</sup> retroviral murine model also had MDS-like phenotype with pancytopenia in the peripheral blood and the significantly increased proportion of LSK, ST-HSCs and MPPs in bone marrow and spleen. A notable finding was the significant increase in the proportion of megakaryocyte progenitor cells (MkP). HE staining and CD41 immunohistochemistry staining demonstrated a pronounced elevation and clustering of megakaryocytes both in bone marrow and spleen (**Figure B**).**Conclusion:** Our study suggested that U2AF1<sup>S34F</sup> mutation enhancing megakaryocytic differentiation in vivo. This finding may be associated with specific clinically and pathologically features in patients, including a significant increase of megakaryocytes and higher fibrosis grades, it could be a promising therapeutic target in fibrosis.

Bing Li and Zhijian Xiao are Co-corresponding authors.

**Disclosures** No relevant conflicts of interest to declare.

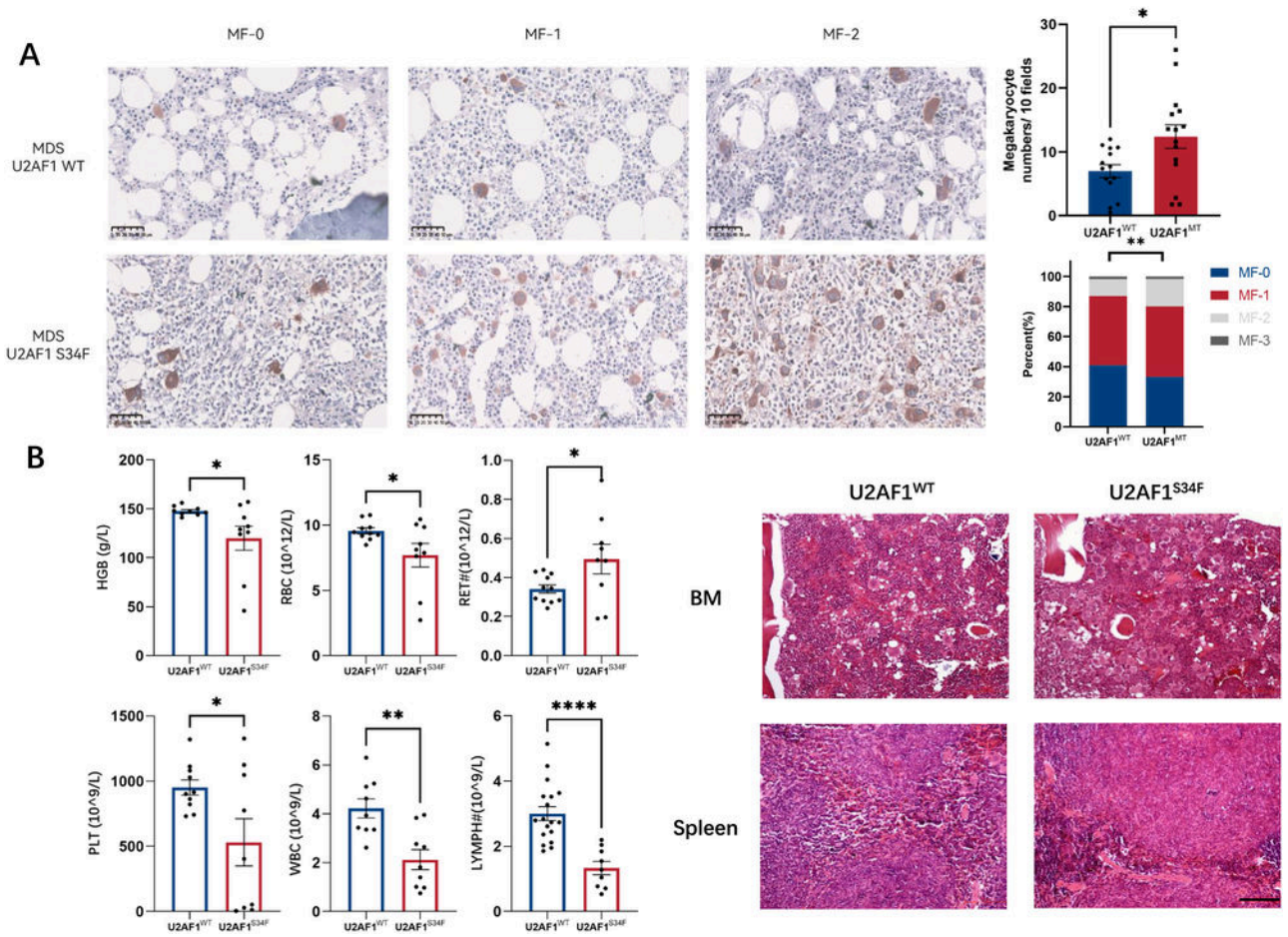


Figure 1

<https://doi.org/10.1182/blood-2023-185678>

Downloaded from [http://ashpublications.net/blood/article-pdf/142/Supplement\\_1/5685/2190439/blood-2285-main.pdf](http://ashpublications.net/blood/article-pdf/142/Supplement_1/5685/2190439/blood-2285-main.pdf) by guest on 18 May 2024