INVESTIGATING GENDER-BASED DIFFERENCES IN THE MOLECULAR PROFILE OF MYELOID NEOPLASMS: INSIGHTS FROM AN INSTITUTIONAL GENOMIC DATABASE

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Introduction

Men with myeloid neoplasms show higher rates of high-risk somatic mutations, particularly in chromatin and DNA repair pathways, contributing to poorer outcomes[1].

Aim

To investigate gender-specific differences in the frequency of high-risk somatic mutations in myeloid neoplasms using our institutional genomic database.

Objectives

- To compare the frequency of high-risk mutations between men and women.
- To identify mutation patterns associated with prognosis and disease progression.
- To provide insights that may guide risk stratification and treatment strategies.

Methods

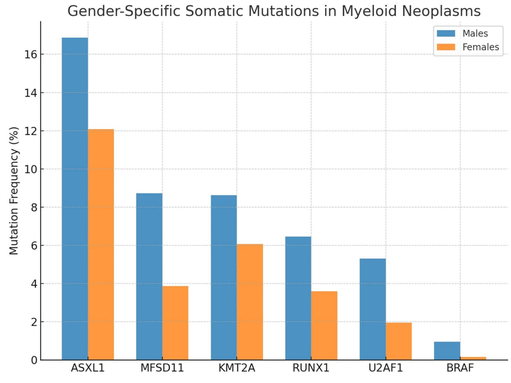
- We performed a retrospective analysis of our hematologic NGS dataset (cBioPortal) to evaluate gender-based differences in driver mutations, tumor suppressors, and oncogenes.
- ASXL1, RUNX1, TP53, IDH1/2, FLT3, NPM1, and CEBPA mutations were deemed high-risk due to faster leukemic progression, poor prognosis, and variable treatment response.
- U2AF1, SRSF2, NRAS, KRAS, EZH2, and MLL mutations are high-risk, as they are recurrently altered in myeloid neoplasms and linked to adverse outcomes, progression, and poor prognosis.
- Statistical analysis used chi-square tests with significance at $p < 0.05$ and FDR $q < 0.05$.

Results

In a cohort of 2107 men and 1940 women, somatic mutations in **ASXL1, MFSD11, KMT2A, RUNX1, U2AF1, and BRAF** were significantly more frequent in men.

- **ASXL1:** 16.9% vs 12.1%
- **MFSD11:** 8.7% vs 3.9%
- **KMT2A:** 8.6% vs 6.1%
- **RUNX1:** 6.5% vs 3.6%
- **U2AF1:** 5.3% vs 2.0%
- **BRAF:** 1.0% vs 0.2%

All differences were statistically significant ($p < 0.001$).



Summary

- Men with myeloid neoplasms showed higher rates of high-risk mutations (**ASXL1, MFSD11, KMT2A, RUNX1, U2AF1, BRAF**) than women.
- These differences may contribute to worse outcomes and highlight the need for gender-specific risk assessment and treatment strategies.

Discussion

- Men with myeloid neoplasms harbored significantly higher rates of **ASXL1, RUNX1, and U2AF1**, mutations linked to aggressive disease and poor outcomes.
- These findings support prior reports of gender-based disparities in mutational biology and prognosis.
- The enrichment of chromatin remodeling, splicing, and DNA repair mutations in men may explain survival differences.
- Understanding gender-specific mutation patterns could improve **risk stratification, prognostic models, and therapeutic decisions**.
- Larger studies are needed to validate these findings and explore underlying biological mechanisms.

References

1. Gender-related differences in the outcomes and genomic landscape of patients with myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes, BJHaem

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