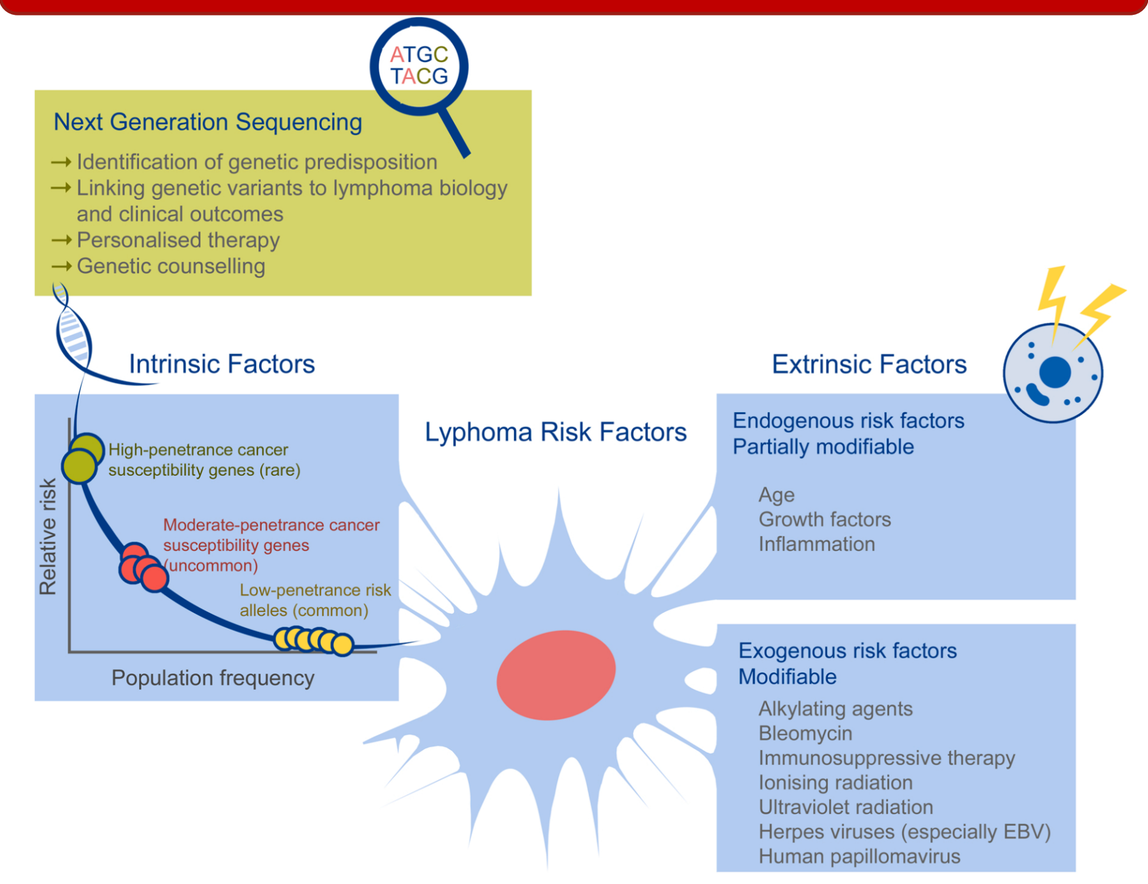
SOHO 2025 Young Investigator Scholarship

WHO SHOULD WE SCREEN FOR GERMLINE CANCER PREDISPOSITION IN PEDIATRIC LYMPHOMA?

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(Affiliations are provided in the abstract)

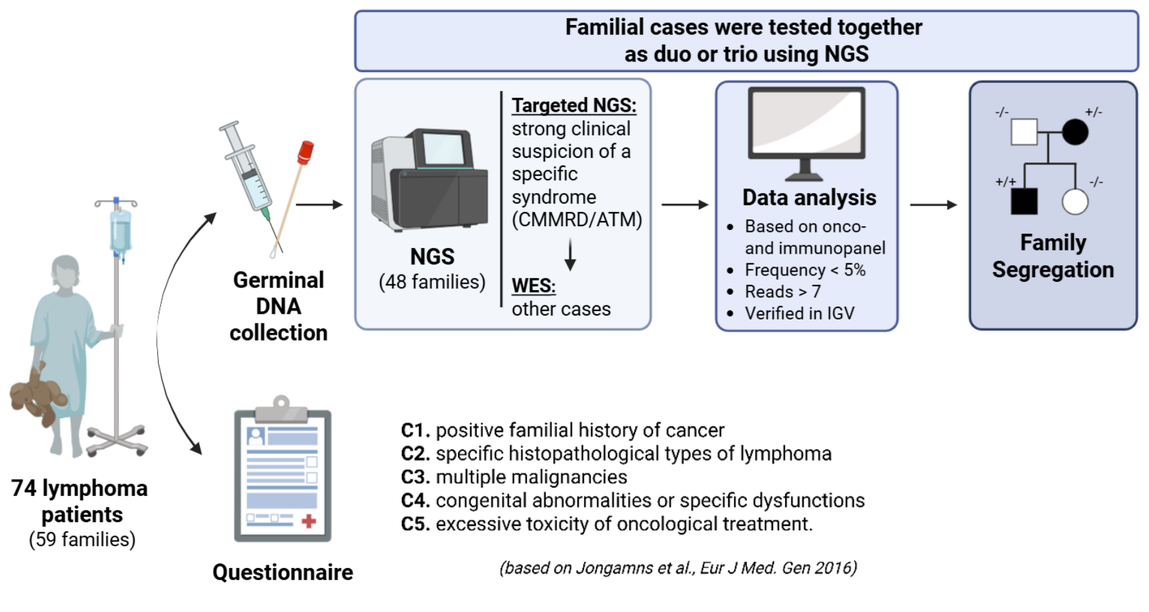
Introduction



Objectives

To test simplified cancer predisposition screening form tailored for pediatric patients diagnosed with lymphoma and evaluate its application in an NGS-based diagnostic setting.

Methods



Results (1)

Patients' characteristics

50 males (68%)

- Median age at lymphoma diagnosis was 8 years (IQR: 5-13)
- Histopathological diagnosis: **(1)** Hodgkin lymphoma (HL; 27 patients, 36%); **(2)** T-cell lymphoblastic lymphoma (T-LBL; 13 patients, 18%); **(3)** Diffuse large B-cell lymphoma (DLBCL; 11 patients, 15%).

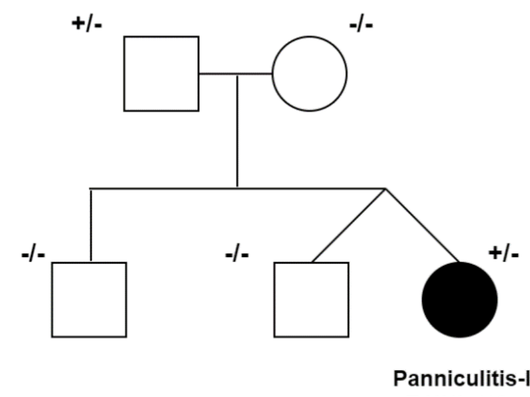
Inclusion criteria

Inclusion criterion	% of families
C2. specific histopathological types of lymphoma	**33 (56%)**
C4. congenital abnormalities or specific dysfunctions	**22 (37%)**
C1. positive family history of cancer	**18 (31%)**
C3. multiple malignancies	**16 (27%)**
C5. excessive toxicity of oncological treatment*	**9 (15%)**

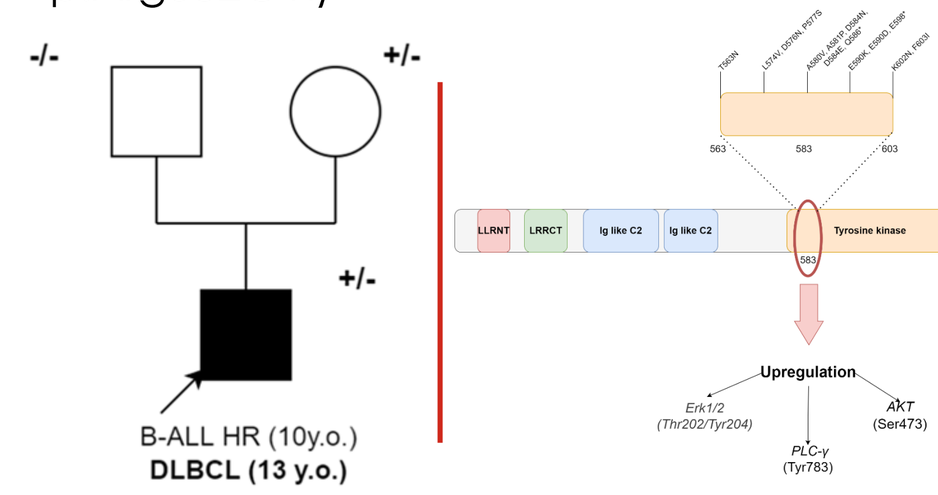
Results (2)

Genetic results

- In total, 58 patients from 48 (81%) families underwent genetic testing for CPS.
  - Causative variants: 10 (21%) families
    - MMR genes (4 families)
    - Biallelic *ATM* variants (2 families)
    - Single patients carrying pathogenic variant within *BLM*, *CXCR4*, *TP53* and *CHEK2*
  - Candidate variants: 9 (19%) families
    - monoallelic variant within *BRCA1* gene (2 families), *PALB2* (NM_024675:c.110G>A; p.Arg37His)
  - No germline predisposition: 29 (60%)
  - The most promising candidate variants:
    - *LCK* (NM_005356.5:c.1176C>G; p.Asn392Lys)

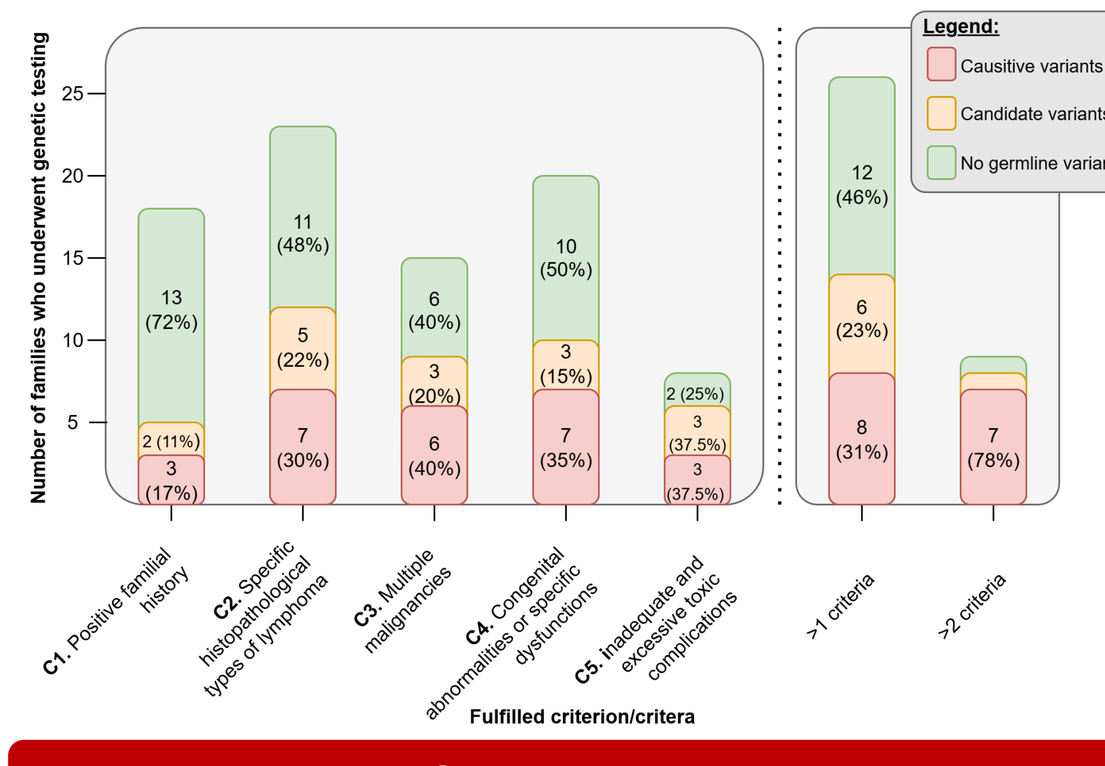


    - *NTRK3* (NM_001012338.2:c.1745G>A; p.Arg582Gln)



    - *CHD8* (NM_001170629:c.6614delC; p.Pro2205LeufsTer57)

The incidence of causative variants with respect to inclusion criteria



Summary

Meeting at least three criteria increased the likelihood of detecting a germline cancer predisposing variant over sevenfold. When the patient met one criterion, excluding positive family history, the probablility to uncover genetic susceptibility to lymphoma raised three- to fourfold.

References

1. Jongmans et al. Recognition of genetic predisposition in pediatric cancer patients: An easy-to-use selection tool. Eur J Med Genet 2016.
2. Bakhuizen et al. Comparison of clinical selection-based genetic testing with phenotype-agnostic extensive germline(…). Lancet Child Adolesc Heal 2024.
3. Szmyd et al. Genetic predisposition to lymphomas: Overview of rare syndromes and inherited familial variants. Mutat Res Mutat Res 2021.

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