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Aurora-A and Polo-Like Kinases are Important Diagnostic and Therapeutic Markers in Hodgkin Lymphoma and Mimics

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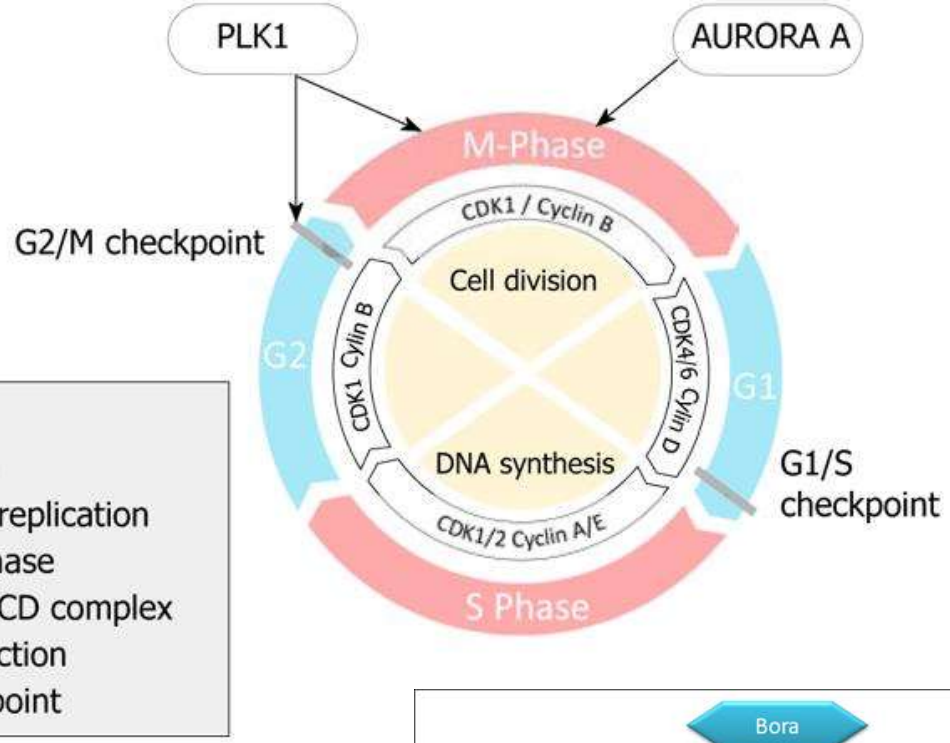
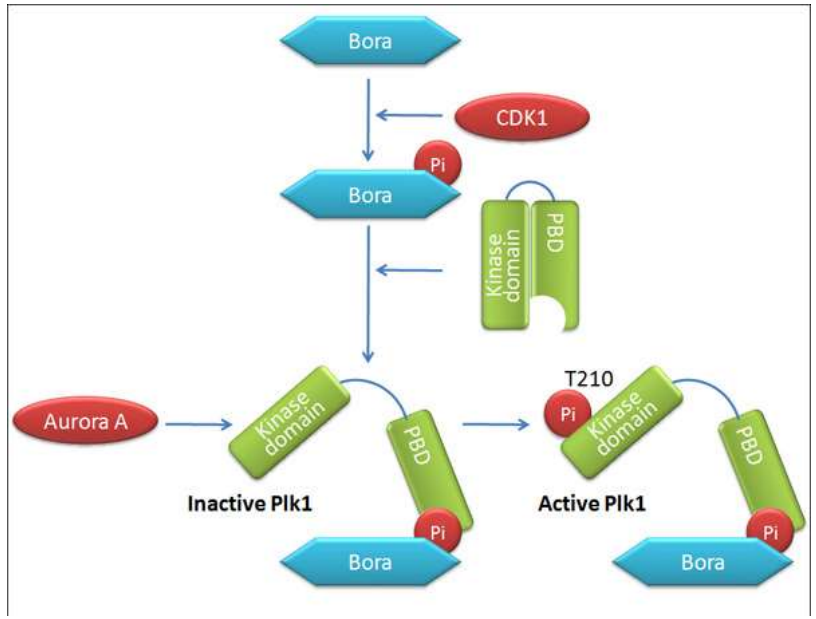
Background

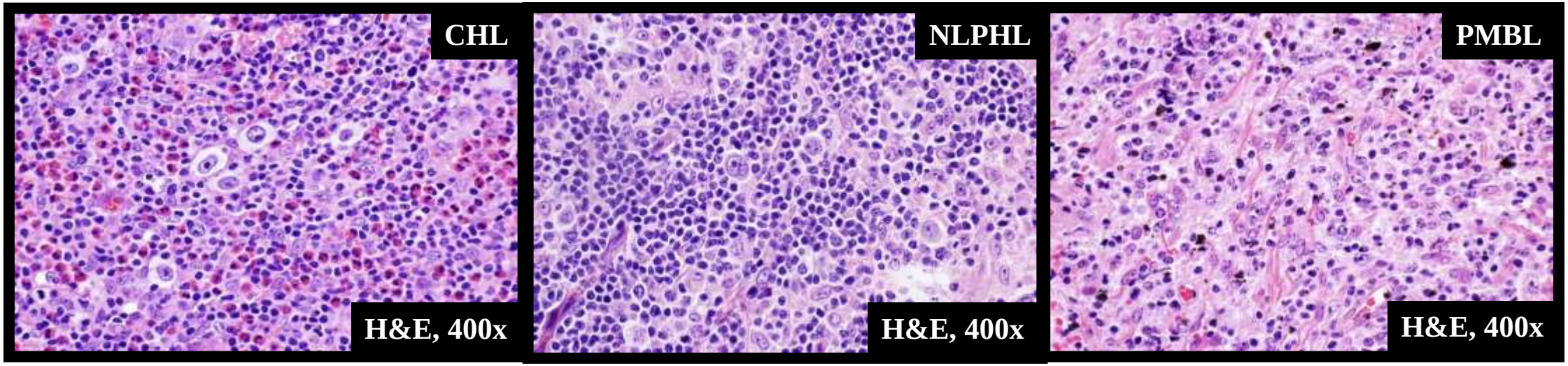
- Aurora-A kinase (AA) and Polo-like kinase (PLK) are implicated in the tumorigenesis of solid tumors and, recently, in B- and T-cell non Hodgkin lymphomas (NHL)
- They play a key role in tumor proliferation and disease progression in highly aggressive B-cell NHL
- They also serve as indicators of disease activity and are thus attractive therapeutic targets





Study Goals

- This study assesses AA and PLK expression in different Classic Hodgkin Lymphoma (CHL) types, such as nodular sclerosis type, mixed cellularity type, and lymphocyte rich type, and their mimics: nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) and primary mediastinal B-cell lymphoma (PMBL)



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Design

- 27 classic Hodgkin lymphoma cases, 16 nodular lymphocyte predominant Hodgkin lymphoma cases, and 8 primary mediastinal B-cell lymphoma cases were assessed for Aurora-A kinase and Polo-like kinase expression by immunohistochemistry (IHC)
- CHL cases included the following: 8 mixed cellularity CHL, 1 lymphocyte rich CHL, and 18 nodular sclerosis CHL
- A mouse monoclonal AA-antibody (1:1000 dilution, Abcam, UK) and a PLK-antibody (1:500 dilution, Cell Signaling Technologies, USA) were used
- Each case was semi-quantitatively graded for percentage of positive cells (<50% vs. >50%), for staining intensity (1-3+), and for localization (nuclear vs. cytoplasmic)
- IHC analysis was performed by 2 pathologists (KMH and KVI)
- Statistical analysis was performed using Fisher's exact test

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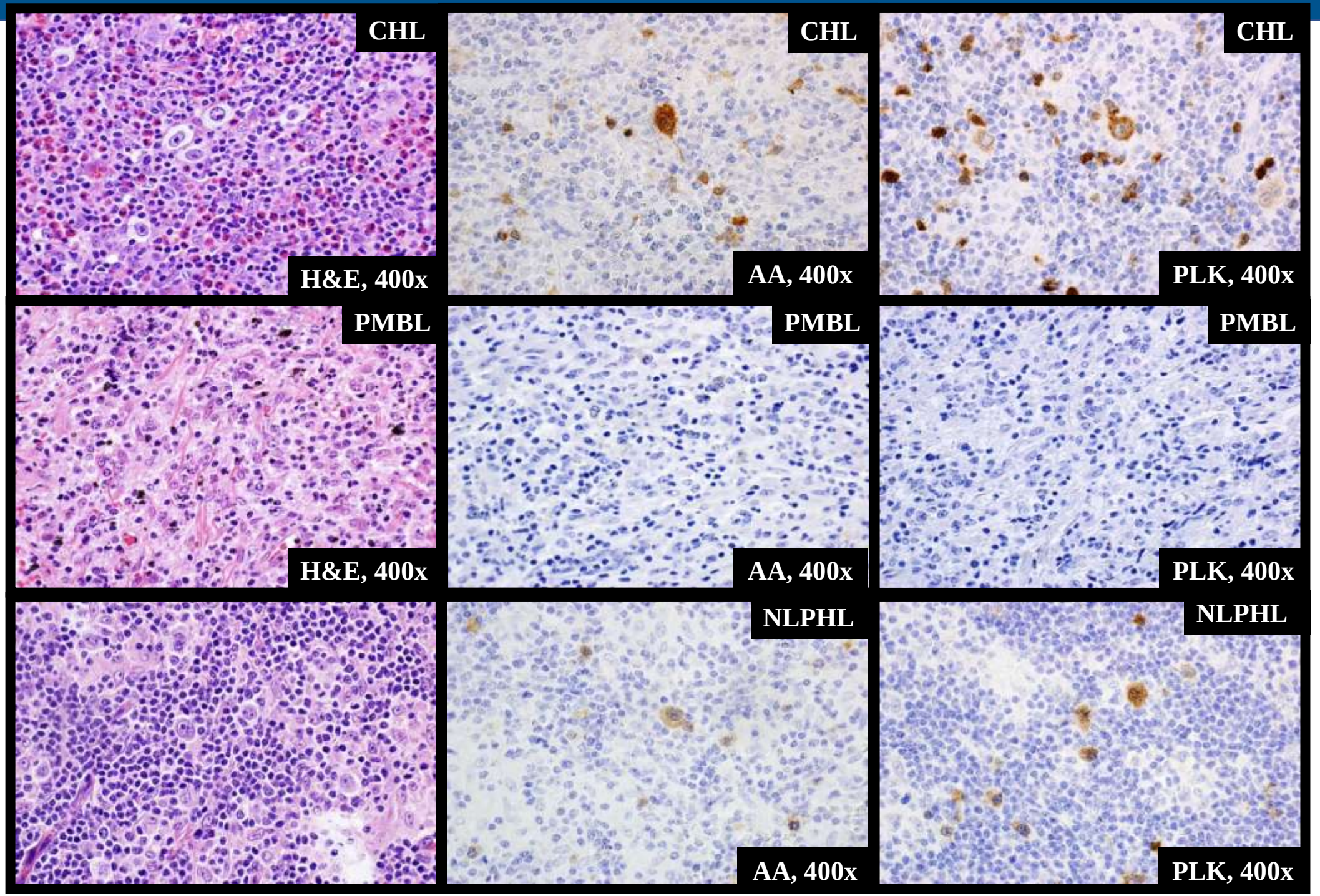
CHL
H&E, 400x
CHL
AA, 400x
CHL
PLK, 400x
PMBL
H&E, 400x
PMBL
AA, 400x
PMBL
PLK, 400x
NLPHL
AA, 400x
NLPHL
PLK, 400x

Aurora-A and Polo-like kinase were expressed in classic Hodgkin lymphoma but not primary mediastinal B-cell lymphoma

	Aurora-A Positive	Aurora-A Negative	
Classic Hodgkin Lymphoma	27	0	p = 0.0002
Primary Mediastinal B-cell Lymphoma	3	5	

	Polo-like Kinase Positive	Polo-like Kinase Negative	
Classic Hodgkin Lymphoma	26	1	p = 0.0009
Primary Mediastinal B-cell Lymphoma	3	5	

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Aurora-A and Polo-like Kinase were expressed in nodular lymphocyte predominant Hodgkin lymphoma but not in primary mediastinal B-cell lymphoma

	Aurora-A Positive	Aurora-A Negative	
Nodular Lymphocyte Predominant Hodgkin Lymphoma	16	0	p = 0.0013
Primary Mediastinal B-cell Lymphoma	3	5	

	Polo-like Kinase Positive	Polo-like Kinase Negative	
Nodular Lymphocyte Predominant Hodgkin Lymphoma	16	0	p = 0.0013
Primary Mediastinal B-cell Lymphoma	3	5	

Polo-like kinase expression correlated with higher stage disease at presentation in nodular lymphocyte predominant Hodgkin lymphoma

	Tumor Cells with <50% PLK Expression	Tumor Cells with >50% PLK Expression	
Low Stage Disease (I-II)	5	1	**p = 0.044**
High Stage Disease (III-IV)	1	8	

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Conclusion

- Aurora-A and Polo-like kinase are commonly expressed in classic Hodgkin lymphoma and nodular lymphocyte predominant Hodgkin lymphoma but not in primary mediastinal B-cell lymphoma. Thus, they are useful markers in the distinction of CHL or NLPHL from PMBL.
- PLK is a useful marker for the prognostication of NLPHL
- AA and PLK are attractive potential therapeutic targets in the treatment of CHL and NLPHL
- Additional studies are underway to characterize an array of hematopoietic lesions known to overlap with CHL

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Acknowledgements

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