The role of NPM/ALK kinase in the pathogenesis of anaplastic large cell lymphoma

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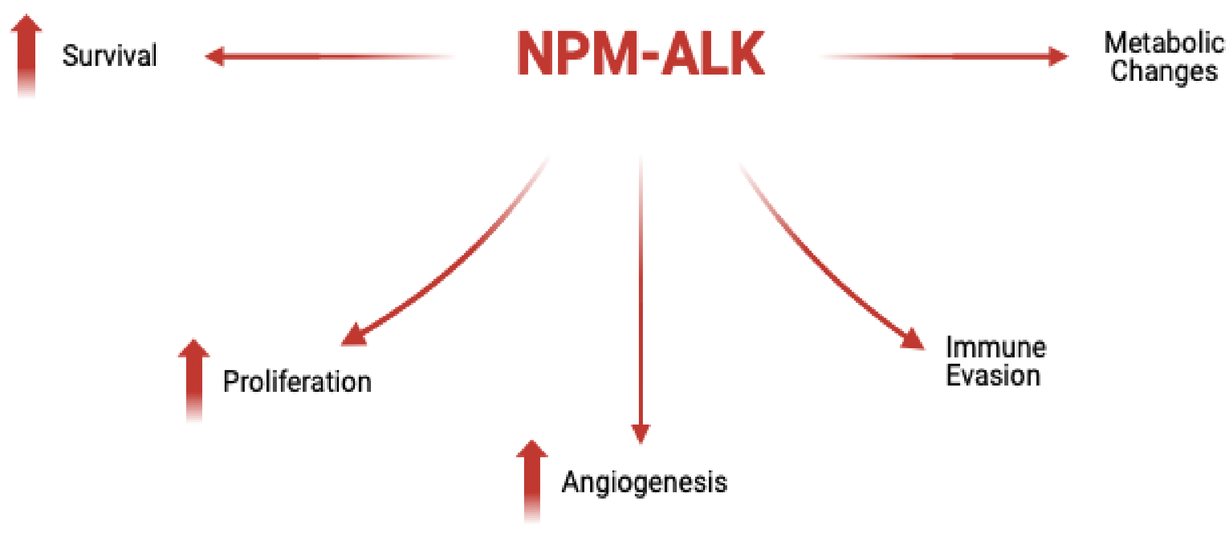
The research aim is to determine the role of NPM/ALK kinase in the pathogenesis of anaplastic lymphoma and to identify the cellular pathways responsible for inducing resistance to the Alk inhibitor

INTRODUCTION

- Anaplastic large cell lymphoma (ALCL) is a rare and aggressive non-Hodgkin's lymphoma arising from from peripheral T lymphocytes
- Between 60 and 80% of ALK+ ALCL cases contain the Nucleophosmin-Anaplastic Lymphoma Kinase (NPM-ALK) chromosomal translocation
- Among patients who have a high response to crizotinib monotherapy, about 30-40% of patients have developed further resistance to the drug



30-40% of ALK-positive patients develop resistance to Crizotinib

METHODOLOGY

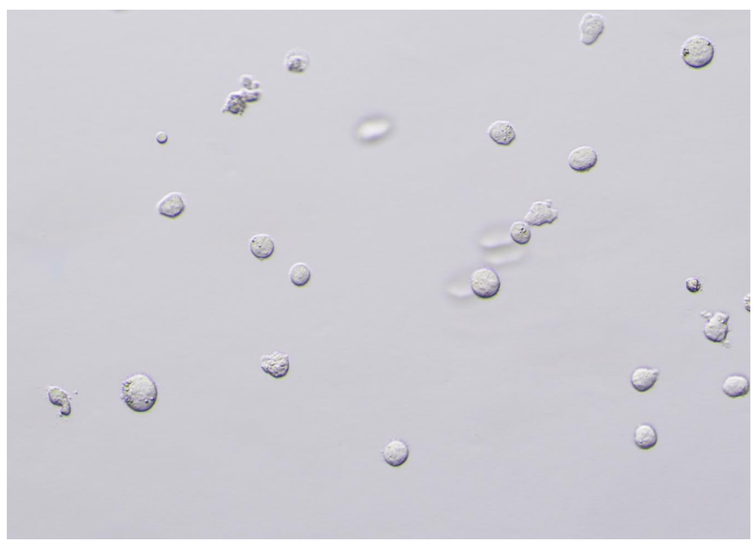
Milestone 1
Determine the effect of ALK inhibitor on the concentration of proteins such as STAT3, ALK, and phospho-ALK in ALCL Alk+ cell models

Milestone 2
Determine the effect of ALK inhibitor on the cumulative effect of reactive oxygen species in ALCL Alk+ cell models

Milestone 3
Determine which signaling pathway most influences the cumulative effect of reactive oxygen species in ALCL Alk+ cell models after ALK inhibitor treatment. Perform Western Blot assay to determine, the effect of ALK inhibitor in ALCL Alk+ cell models on activation of selected cellular pathways

Milestone 4
Repeat the study in ALCL Alk- cell models

Control
Positive control - not treated ALCL Alk+ cells
Negative control - not treated ALCL Alk- cells



ALCL ALK+ cell line SUP-M2

ALCL ALK+ cell line SR-786

PROGRESS

- ✓ The first author of the publication related to the dissertation topic 5.2 Impact Factor, 200 Ministerial score
- ✓ International collaboration with the Department of Pathology, Fox Chase Cancer Center, Temple University, USA
- ✓ Opinion of the bioethics committee
- ✓ Submission of the individual research plan
- ✓ Analysis of scientific literature related to the dissertation topic. Preparation of the research methodology and task schedule for the Individual Research Plan
- ✓ Purchase of necessary scientific reagents, including cell lines required for scientific research in the dissertation
- ✓ Conducting cell culture and creating a bank of cell lines needed for ongoing scientific research as part of the dissertation

REFERENCES

Wiese, W.; Barczuk, J.; Racinska, O.; Siwecka, N.; Rozpedek-Kaminska, W.; Slupianek, A.; Sierpinski, R.; Majsterek, I. PI3K/Akt/mTOR Signaling Pathway in Blood Malignancies—New Therapeutic Possibilities. Cancers 2023, 15, 5297. doi.org/10.3390/cancers15215297

Wang Y, He J, Xu M, Xue Q, Zhu C, Liu J, Zhang Y, Shi W. Holistic View of ALK TKI Resistance in ALK-Positive Anaplastic Large Cell Lymphoma. Front Oncol. 2022 Feb 8;12:815654. doi: 10.3389/fonc.2022.815654

El-Mallawany, N., Frazer, J., Van Vlierberghe, P. et al. Pediatric T- and NK-cell lymphomas: new biologic insights and treatment strategies. Blood Cancer Journal 2, e65 (2012). hdoi.org/10.1038/bcj.2012.8