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# Invitation for PhD defense

by Issa Ismail Issa



## Genetic determinants of drug response in diffuse large B-cell lymphoma

Friday 17<sup>th</sup> of May 2024

Time: 13:00

Auditorium A, Forsknings Hus, Aalborg Universitetshospital

## About the PhD thesis

Diffuse large B-cell lymphoma (DLBCL) is a common type of cancer arising from B-cells. Despite receiving first- or second-line treatments, many patients develop resistance and die. There is therefore a need for identification of genes and mechanisms affecting drug response within DLBCL tumor cells. The aim of this PhD is to elucidate the genetic determinants of drug response in DLBCL. This PhD project includes four experimental and bioinformatical studies:

**Study I** characterized the mutational landscape of DLBCL to identify genes associated with drug resistance to first-line treatment. This study revealed that *MYD88* mutations are associated with disease progression in DLBCL.

In **Study II**, a bendamustine resistance gene signature, able to assign probabilities of bendamustine resistance to different subtypes of DLBCL and MM patients, was developed.

In **Study III**, genes associated with response to platinum-based drugs were identified using genome-wide CRISPR/Cas9 screens. The study revealed that DNA damage response genes and *BTK* play essential roles in response to platinum-based drugs.

In **Study IV**, combination treatment with cisplatin and the Hsp90 inhibitor 17AAG was investigated. 17AAG sensitized DLBCL cells to cisplatin and resulted in increased levels of DNA damage and apoptosis.

The work presented in this PhD project contributes to our knowledge of drug response mechanisms in DLBCL. The genes identified from the analysis of DLBCL tumors and *in vitro* experiments lay the foundation for deeper investigation into their mechanistic roles in drug response and their targetability in clinical settings, aiming to improve treatment response and survival of DLBCL patients.

## Invitation for PhD defense

The Department of Clinical Medicine, Aalborg University and Aalborg University Hospital are pleased to invite to PhD defense by *Cand.Scient.Med.*, *Issa Ismail Issa*, who will defend the thesis entitled:

### Genetic determinants of drug response in diffuse large B-cell lymphoma

**The PhD defense will take place**

Friday 17<sup>th</sup> of May 2024

Time: 13:00

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After the defense there will be a reception. All are welcome.