Single-cell heterogeneity in Sézary syndrome

Heterogeneity as a driver of treatment resistance?

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Sézary syndrome

- **Skin homing CD4+ T cells**
- Monoclonal TCR
- Low CD7/CD26 expression
- Leukemic and peripheral involvement (can be sampled from blood)

![Image of a person with Sézary syndrome symptoms]

- Generalized erythroderma
- Suppressed immune system
- Recurrent or chronic infections
- Chronic inflammation
- ...

**Cancer growth**

- IFNα
- ECP
- Retinoids
- mAbs
- HDACi
- ...

**Resistance**

- Median life expectancy < 3 years
- No curative treatment
Surface marker heterogeneity

Single-cell surface marker screening by flow cytometry

BD Lyoplate
Malignant subpopulations

12 color flow cytometry
Surface marker heterogeneity
Transcriptional heterogeneity

Targeted single-cell RNA-seq

BD Precise
Transcriptional heterogeneity

BD Precise
Targeted single-cell RNA-seq
Single-cell heterogeneity
HDACi treatment effect on subpopulations

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CD197  CD26  CD62L  CD43  FSC.A  CD49b  CD39  CD49RA

CD279  CLA  CD70  CD164  CD7  CD3  PhenoGraph  Reduced

15 color flow cytometry
14-16 color flow cytometry
Heterogeneity may drive resistance
Conclusions

- Malignant T cells from Sézary syndrome patients have diverse expression profiles (both protein and mRNA)
- Single-cell heterogeneity is common and may represent distinct malignant subpopulations
- Treatment can selectively affect some subpopulations while allowing others to persist
Acknowledgements

Skin Inflammation & Cancer, SIC
University of Copenhagen, Denmark

Niels Ødum
Anders Woetmann
Andreas Willerslev-Olsen
Chella Krishna Vadivel
Claudia Nastasi
Edda Blümel
Lisa Harth
Maria Gluud
Martin Namini
Sana Ahmad
Sara Rosillo
Shayne Ford
Tengpeng Hu
Thomas Litman
Thorbjørn Krejsgaard
Veronica Stolearenco

T-cell biology group, ISIM
Past and present members
University of Copenhagen, Denmark

International and domestic collaborators

Leo Fondate
Est. 1984

Kræftens Bekæmpelse

Det Frie Forskningsråd
Danish Council for Independent Research

Novo Nordisk Fonden