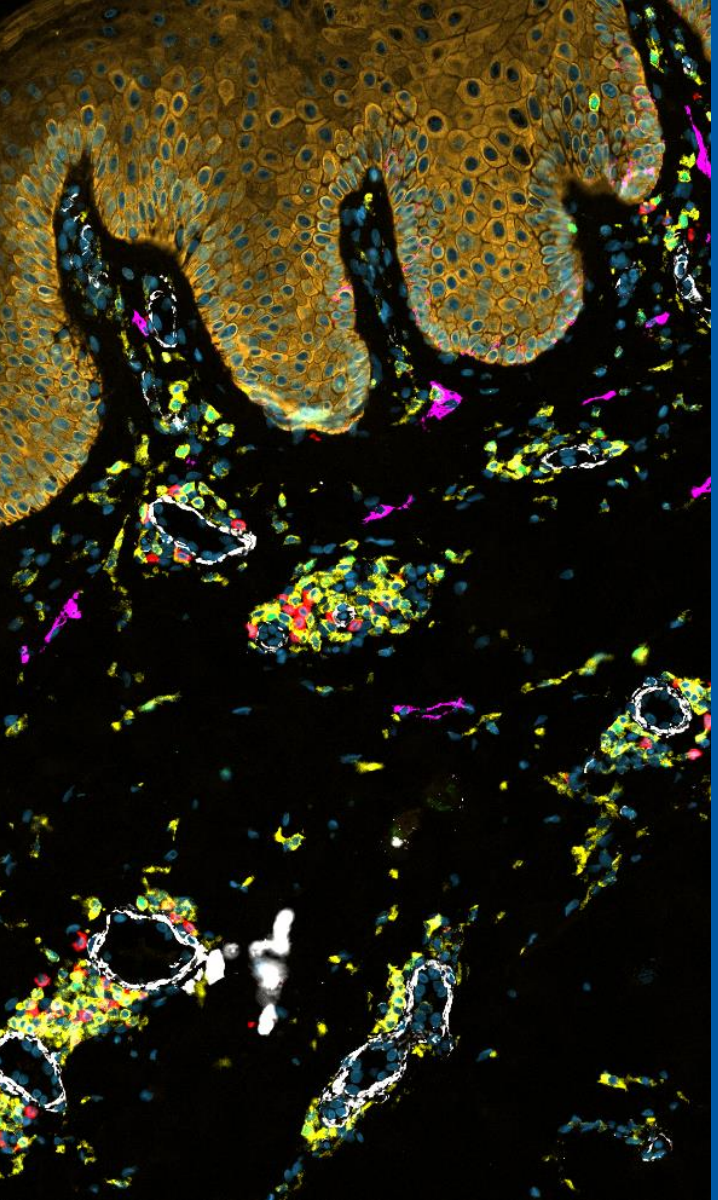


Spatial Biology Congress

| 2024-12-07

Spatial atlas of inflammatory skin disease and cutaneous T cell lymphoma

Pacôme Prompsy
Computational Biologist
Guenova Lab

CHUV | Unil UNIL | Université de Lausanne

Introduction

Benign Inflammatory skin disease

AD — *Eczema*

PS — ***Ps**oriasis*

LP — ***L**ichen **P**lanus*

DAR — ***Dar**ier Disease*

Benign

Malignant

Cutaneous **T** **C**ell **L**ymphoma (CTCL)

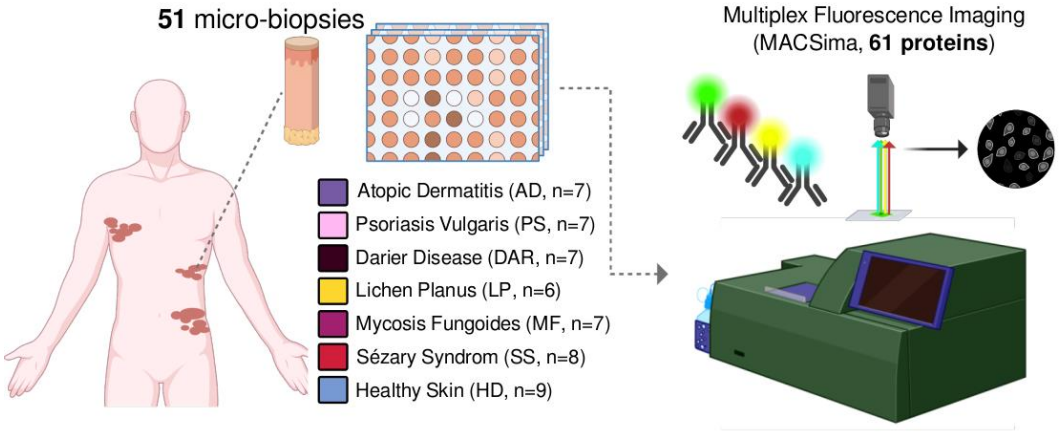
MF — ***M**ycosis **F**ungoides*

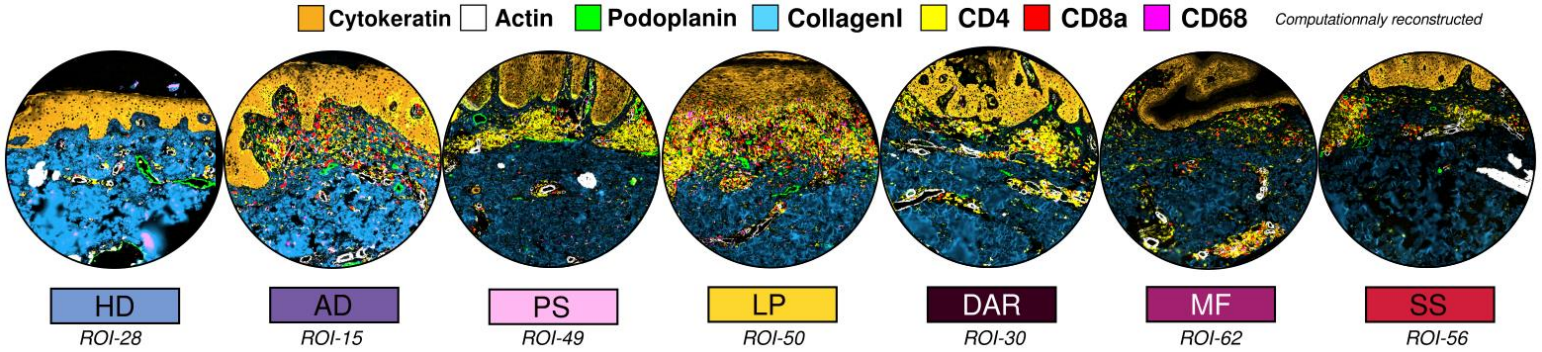
SS — ***S**ézary **S**yndrom*

- Benign inflammatory skin diseases and CTCL are both **deregulation of T cells in the skin**
- To improve cure of the malignant diseases, multiple challenges remain:
  - **Enhance diagnostic**
  - **Predict response in malignant disease**

Roediger et al., T cells in the skin: Lymphoma and inflammatory skin disease (2022)

Multiplexed protein imaging of skin diseases

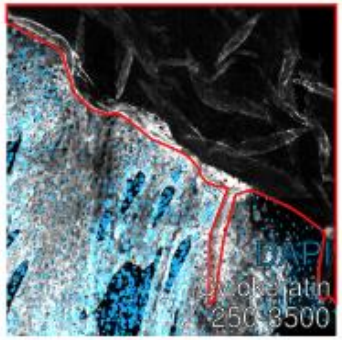


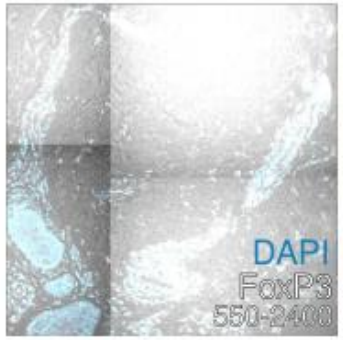


- 1) What characterizes malignant skin disease ?
- 2) Can we predict response to treatment ?

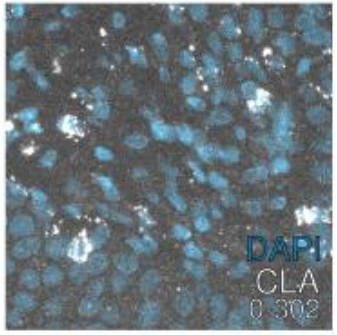
But … Challenges in analyzing highly multiplex fluorescence images

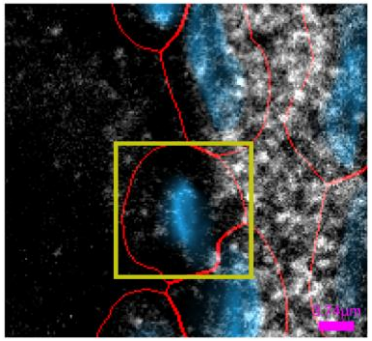
- Manageable artifacts
  - Folds
  - Stains
  - Whole punch spills

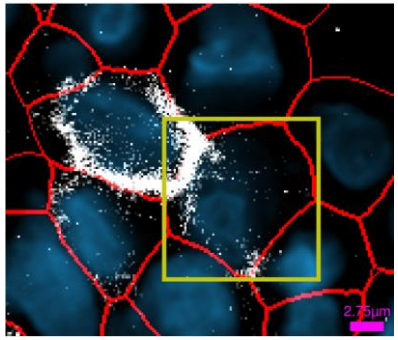




- More challenging artifacts
  - Varying intensity range
  - Low Signal/Noise
  - Spillover







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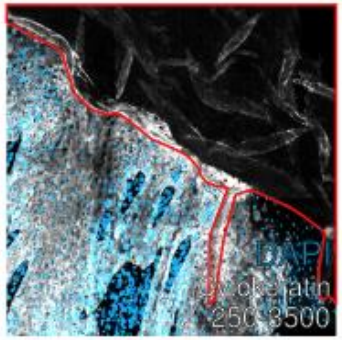

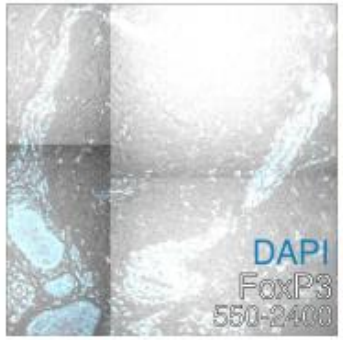

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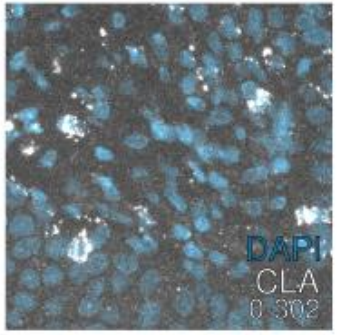
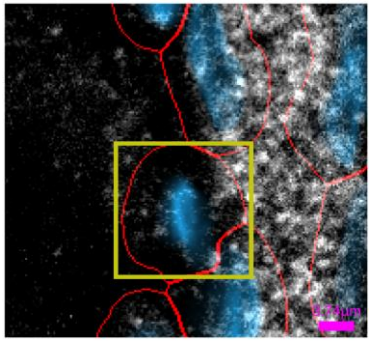




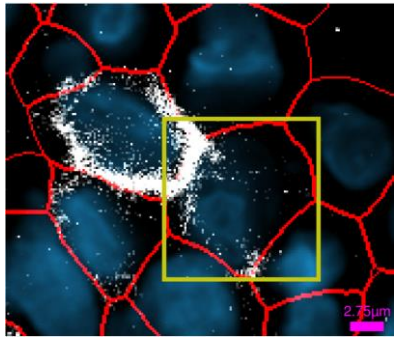
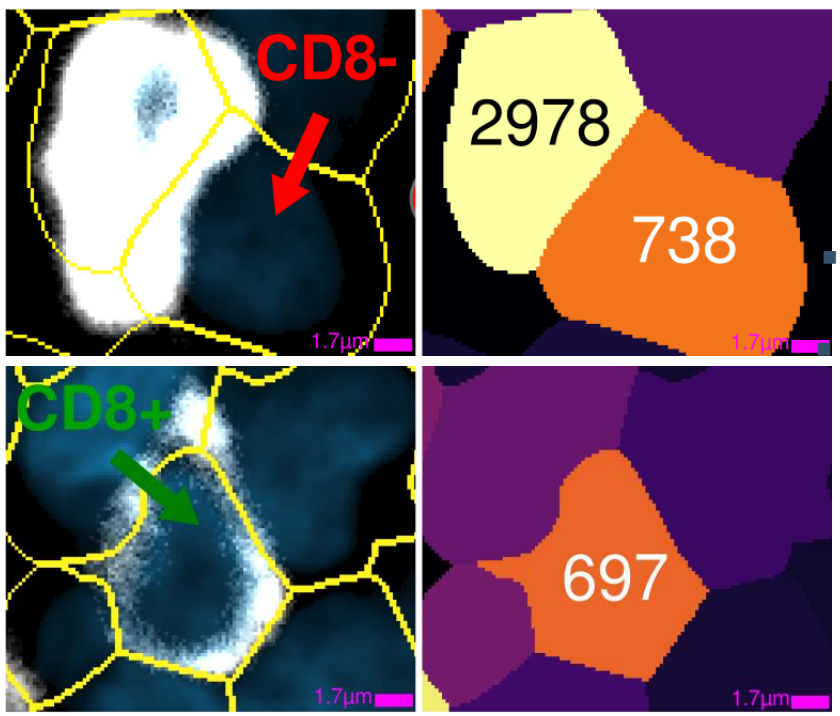


Image vs average intensity

- Image
- VS
- Average intensity

- Spillover



- Low intensity cell

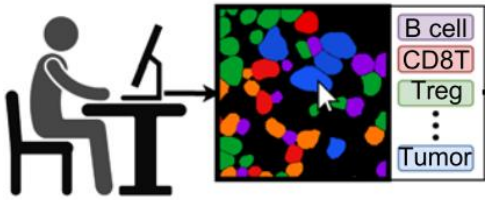
- Averaging intensity **hides the pattern**.

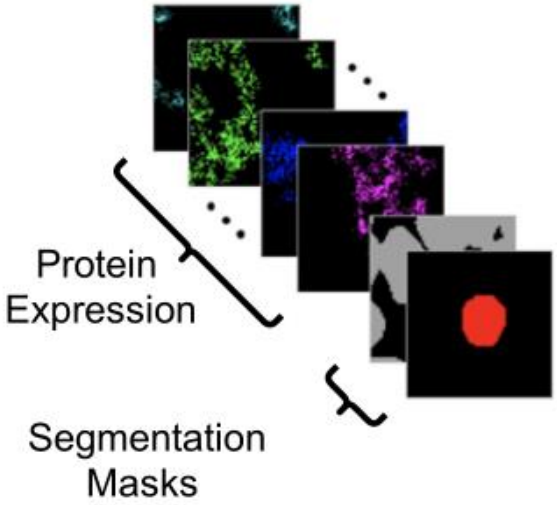
"Classical" tools, based on the average intensity suffer from this fact.

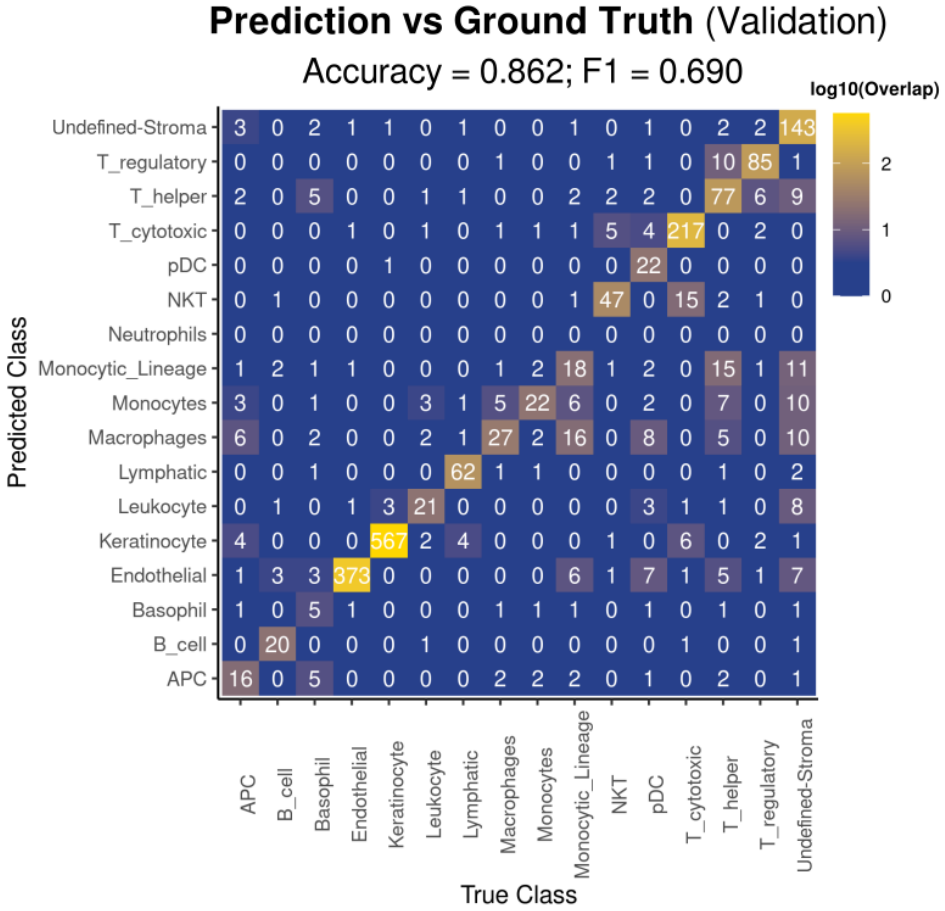
Deep-learning based cell phenotyping reveals heterogeneous cell composition

CellSighter[1]

Annotated 17 celltypes in 11 images (>8000 cells)

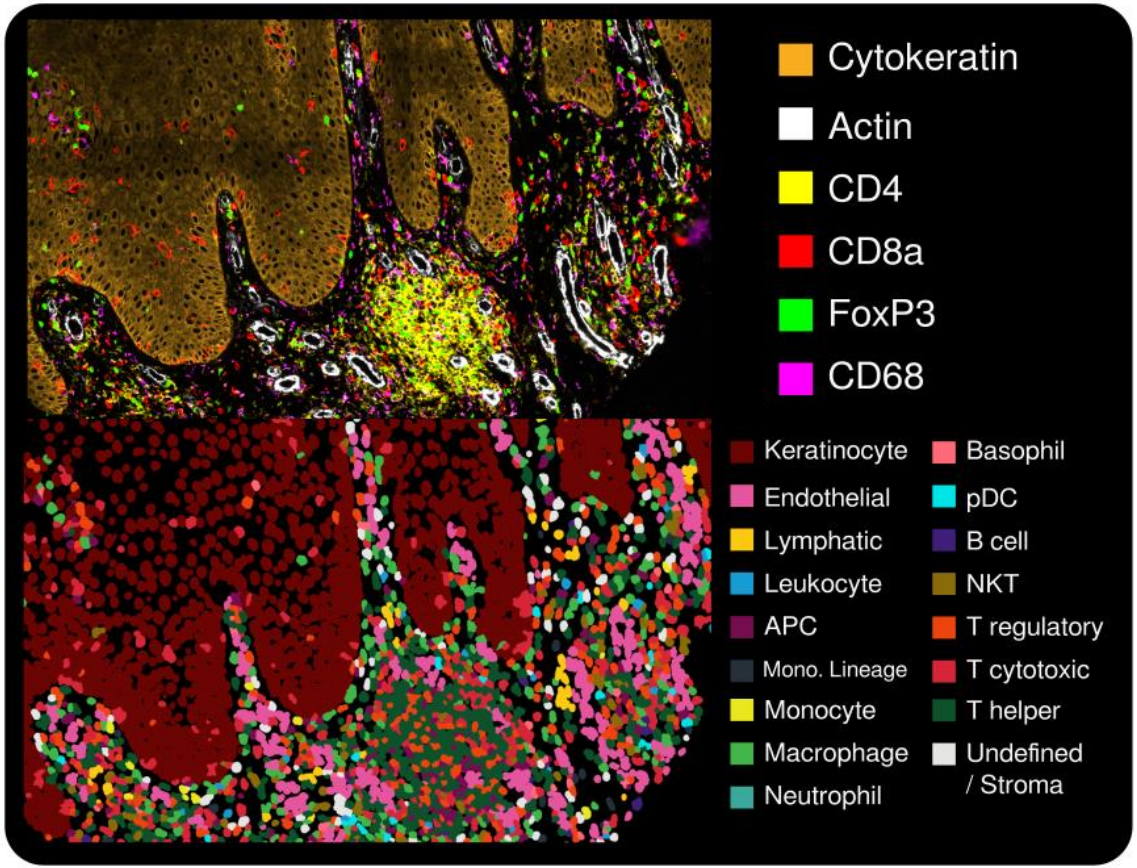




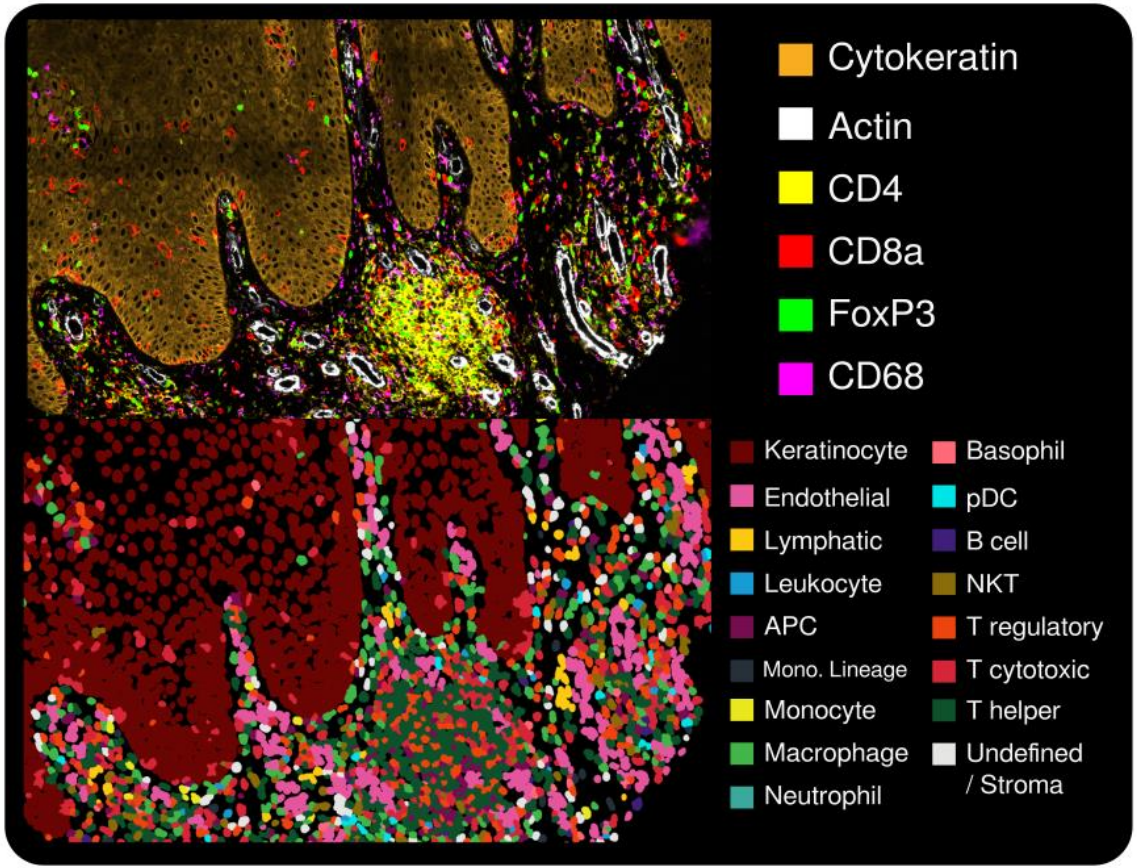


[1]CellSighter: a neural network to classify cells in highly multiplexed images, Amitay et al., Nat. Comm. (2022)

Deep-learning based cell phenotyping reveals heterogeneous cell composition

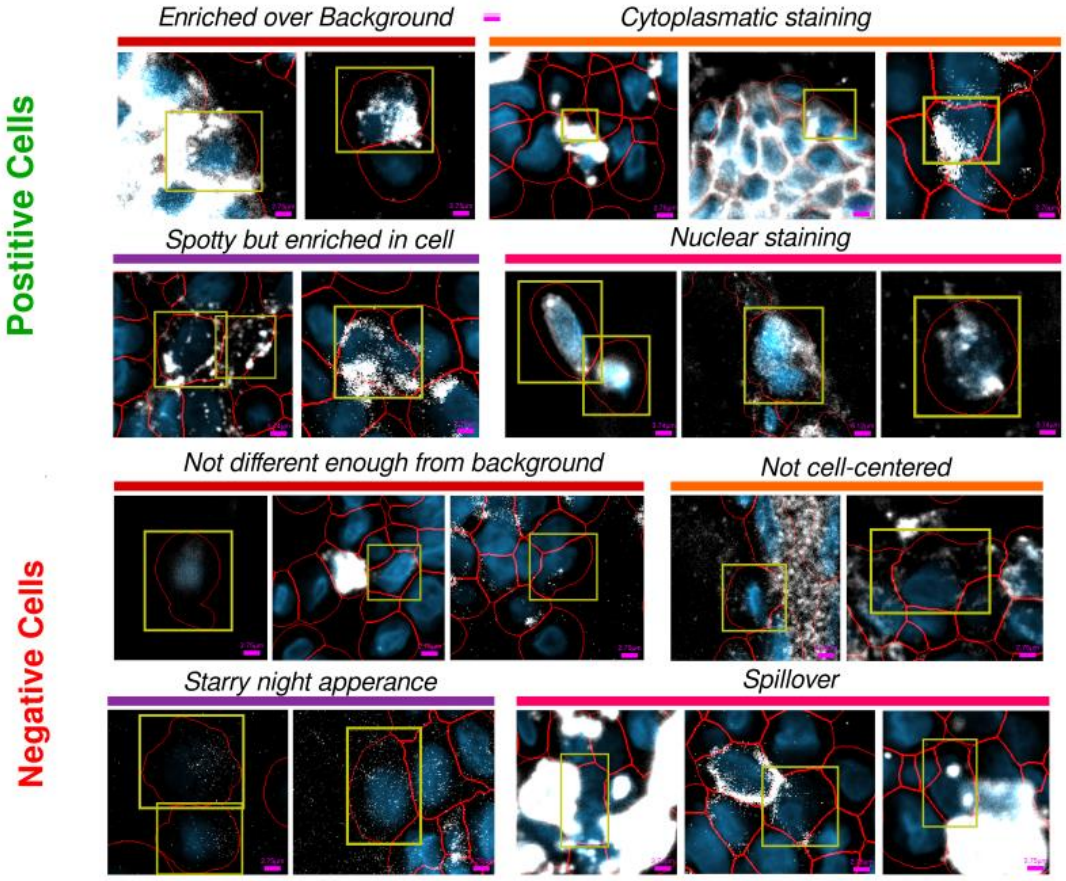


Deep-learning based cell phenotyping reveals heterogeneous cell composition



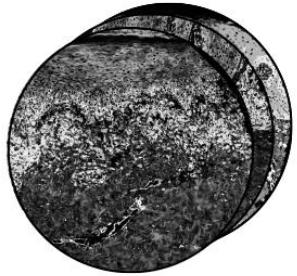
What about the markers ?

“Hacking” CellSighter for image-based positive marker detection



60 markers

Total annotated cells: 82134



Training

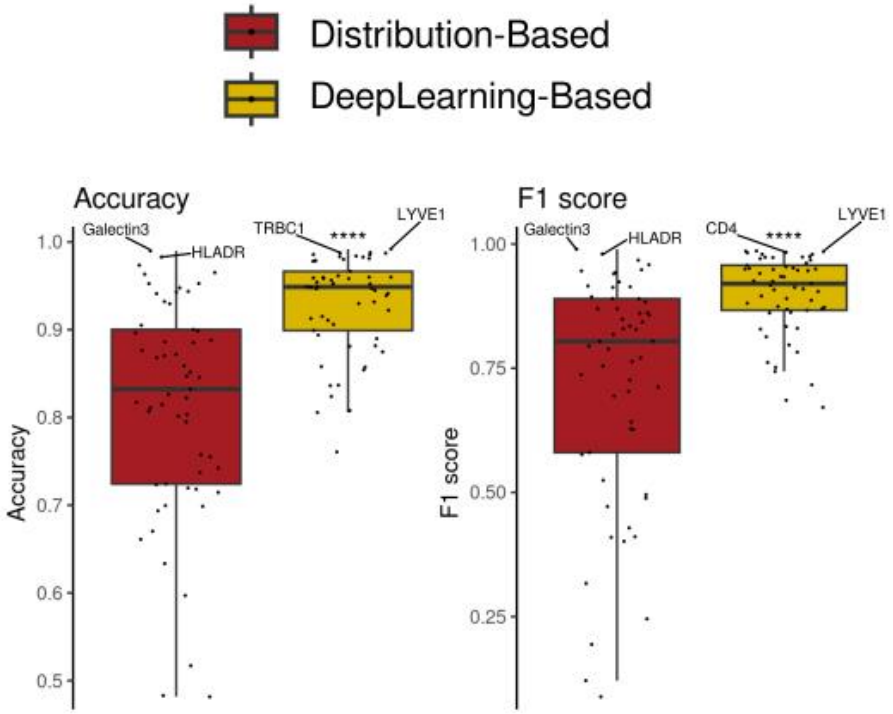
6 punches

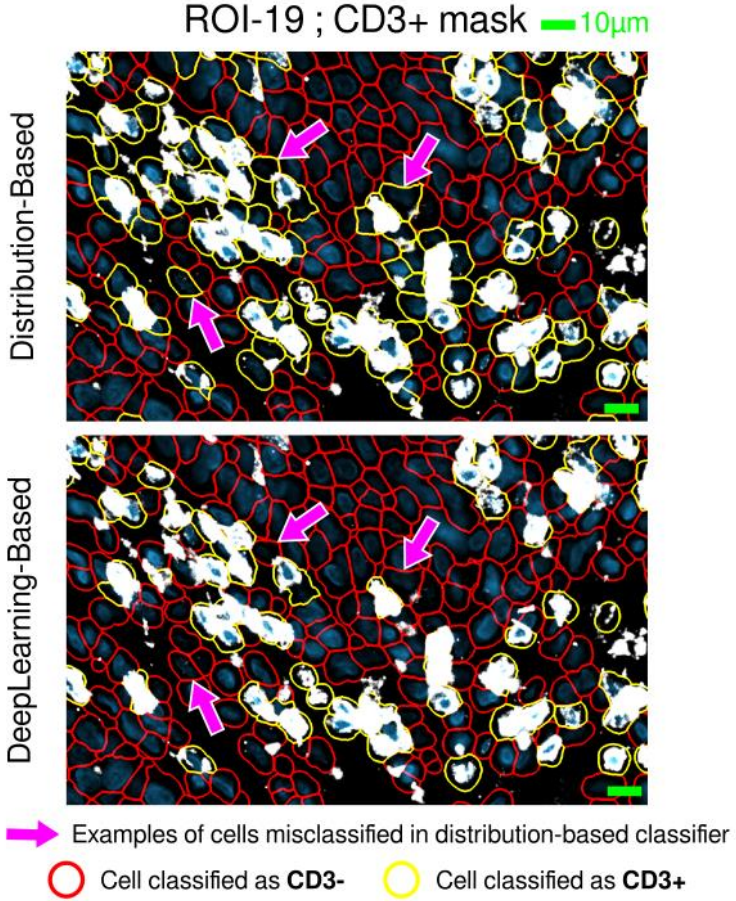
Validation

5 punches

[1]CellSighter: a neural network to classify cells in highly multiplexed images, Amitay et al., Nat. Comm. (2022)

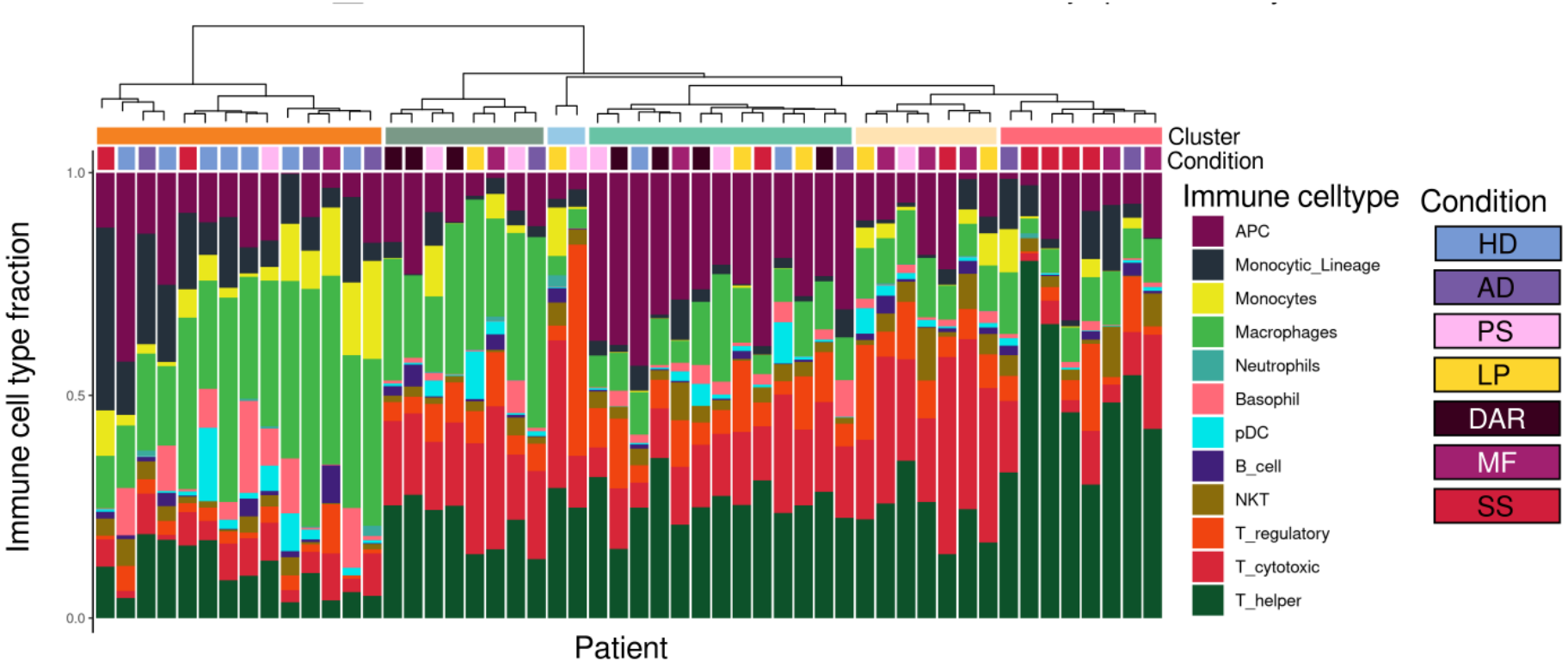
Leveraging deep-learning for positive marker detection





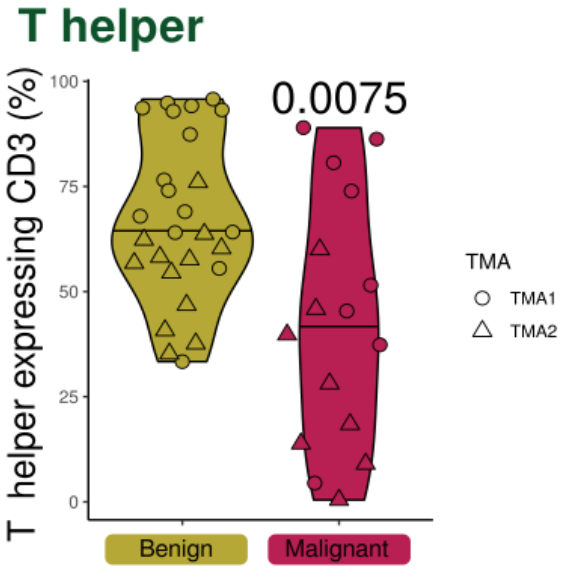
Back to the biology

Cell composition reveals strong heterogeneousity within diseases



- Strong heterogeneity of cell composition
- Some malignant patients have similar composition to healthy / benign

Increased T cell densities and CD3 loss in malignant skin disease



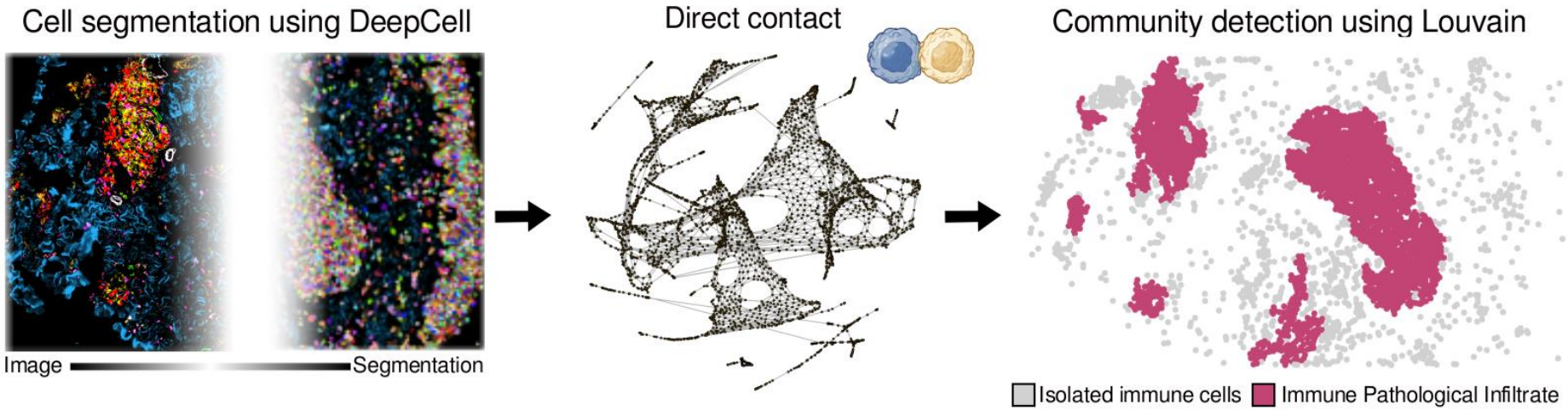
Migration / regulation of T cytotoxic & NK cells

- T cell activity / TCR signalling

- Strong reduction of the hallmark CD3 marker in T helper in malignant disease

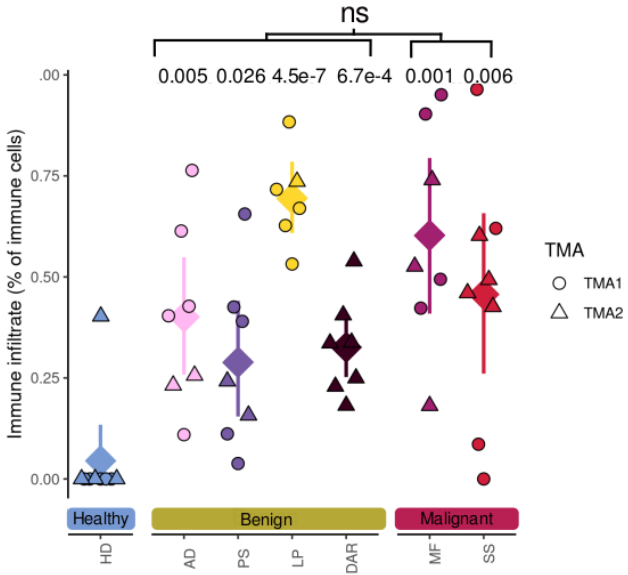
Sano et al., Immunological study on CD3 defective cutaneous T cell lymphoma cells from a patient with Sézary syndrome. Clin Exp Immunol. (1998)
Liu et al., Single-cell transcriptomics links malignant T cells to the tumor immune landscape in cutaneous T cell lymphoma. Nat Commun 13, 1158 (2022)

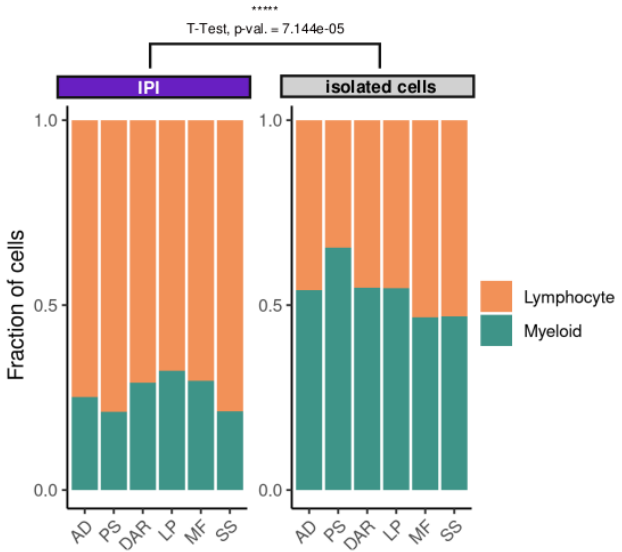
Spatial configuration : the «immune pathological infiltrate»

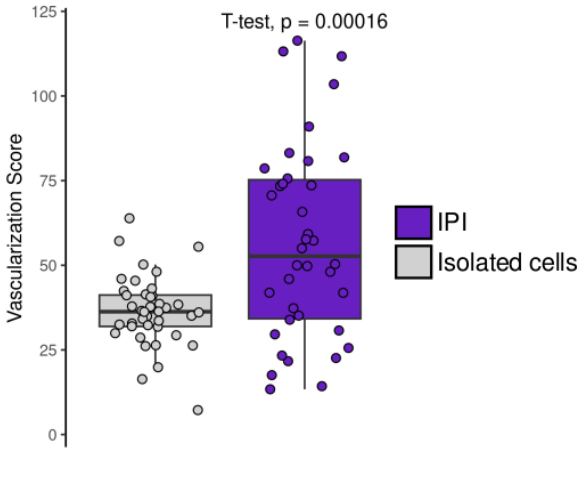


- Building from cell-in-contact network we find communities of immune cells using
- louvain clustering (keeping those > 30 cells).

Spatial configuration : the «immune pathological infiltrate»

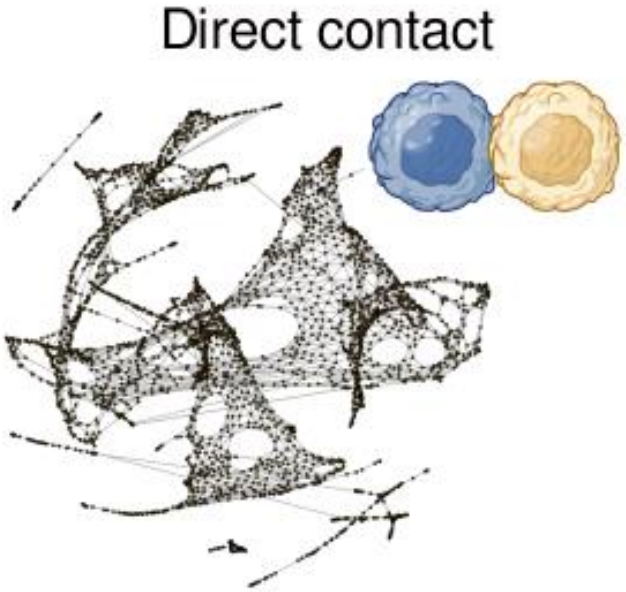






- The IPI is increased in malignant compared to most benign skin NCD.
- They are highly lymphocytic compared to the rest and are significantly more vascularized.

Diving further : finding «immunological synapses»



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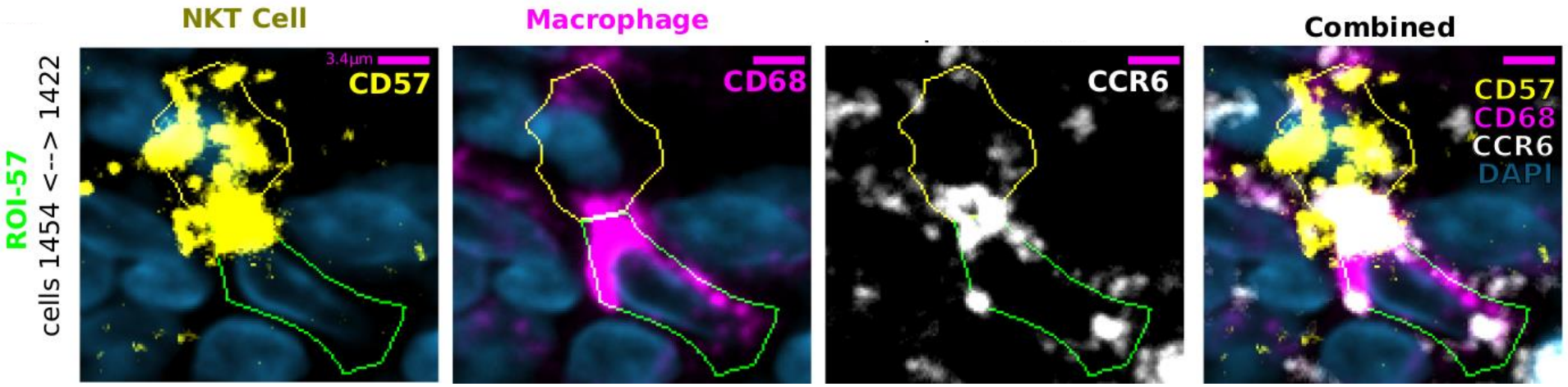

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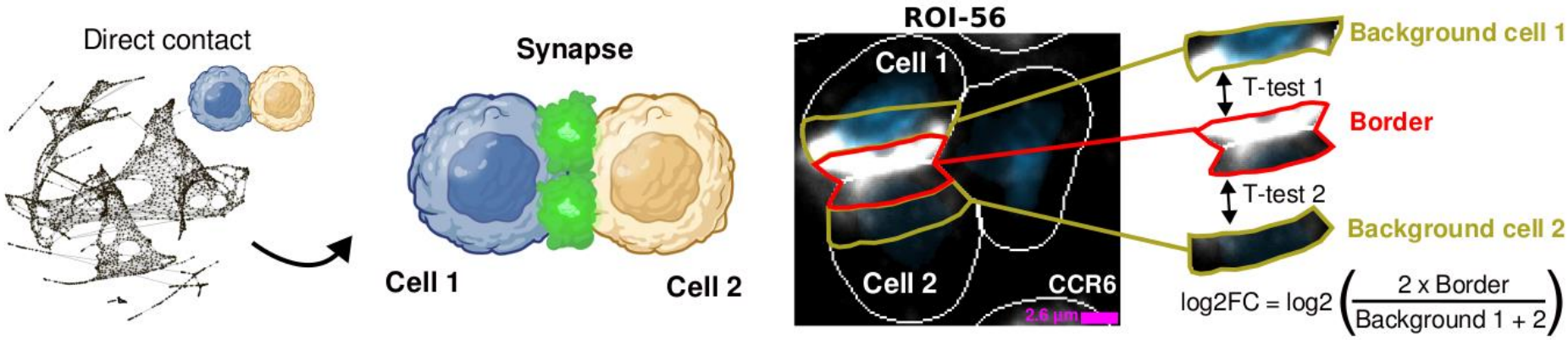
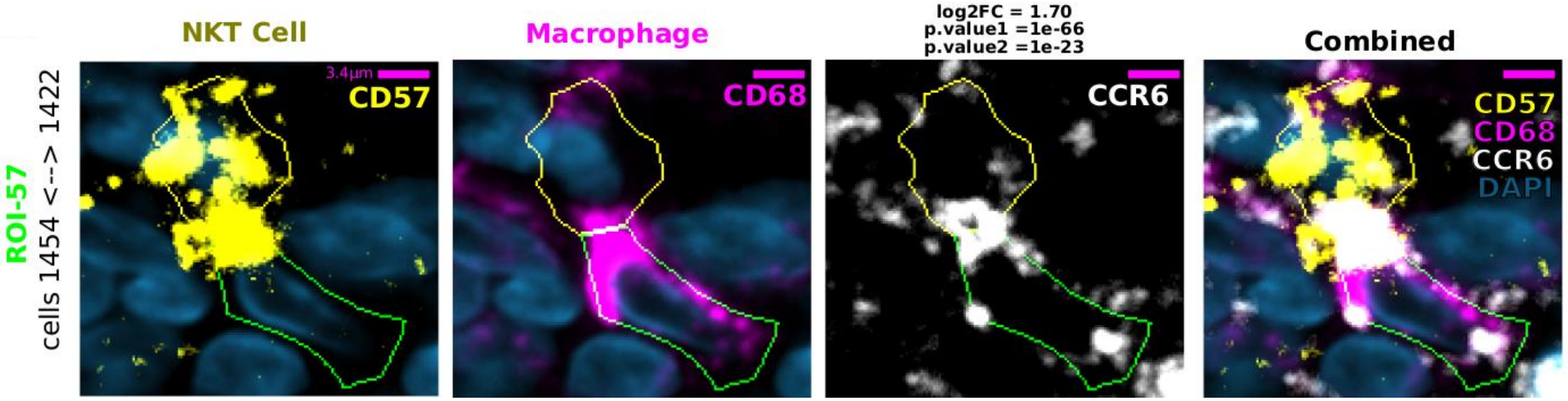
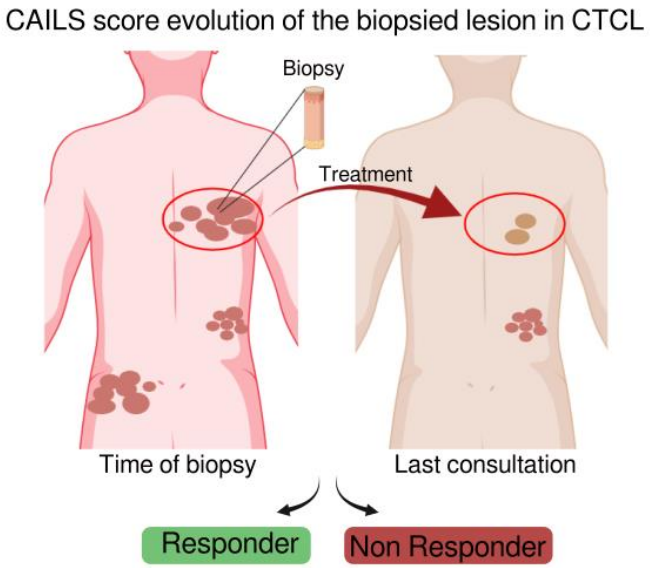
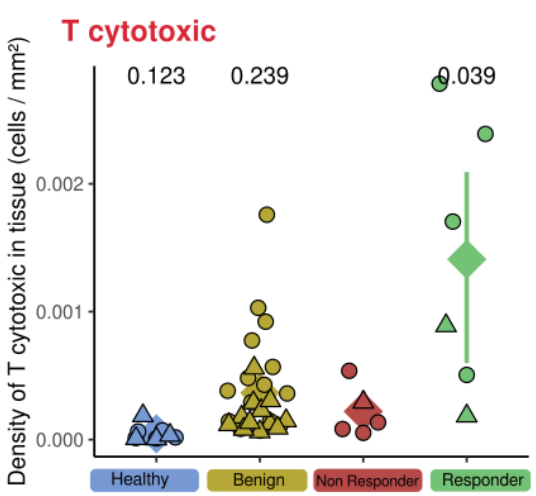
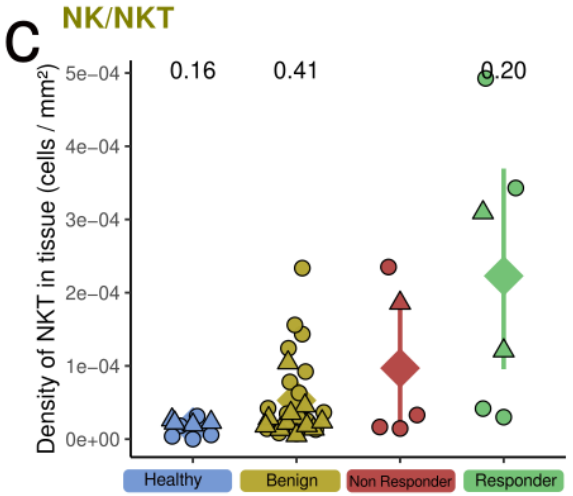




T cytotoxic fraction improves response to treatment







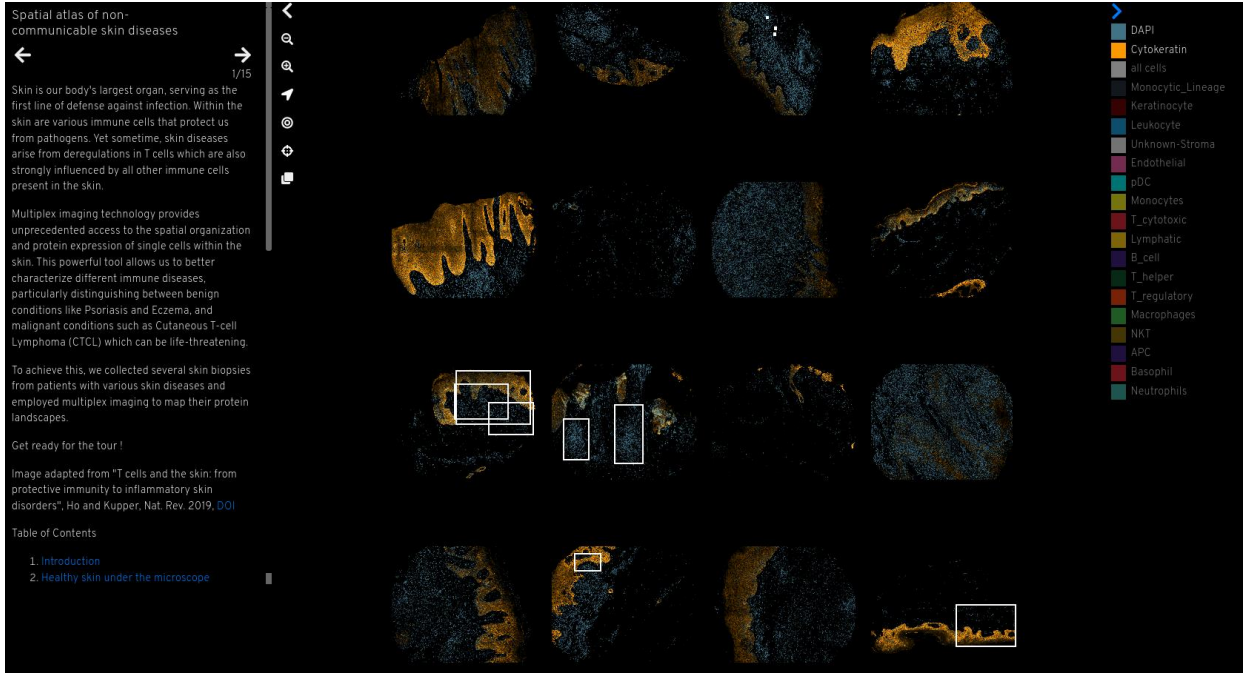
- Classifying patients according to evolution of CAILS score (Responder vs Non Responder)
- Responsive patients have in average **2-3 times greater proportions of cytotoxic**
- **T cells at time of biopsy** (validated on survival of additionnal 34 patients)

Conclusion

- We build a spatial atlas of immune skin diseases with precisely phenotyped cells and functional markers
- T helper cells in CTCL shift their program to evade immune surveillance by cytotoxic T cells
- The best predictor for lesion evolution is the fraction of cytotoxicic T cells at time of biopsy

See the story online

MINERVA



https://bit.ly/skin-atlas

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CHUV Dermatology

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CHUV

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Fondation Dind/Cottier