# Clinical multi-omics targeting melanoma and reproductive disorders

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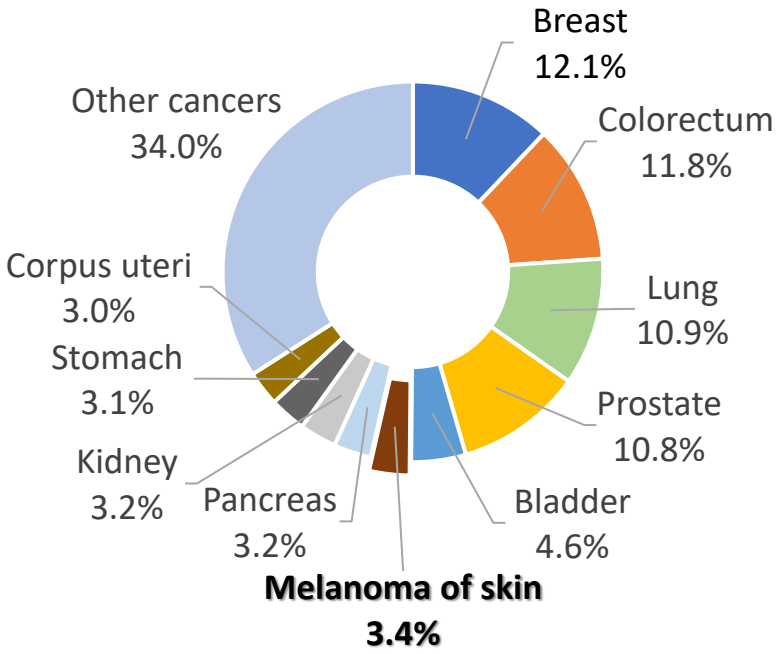
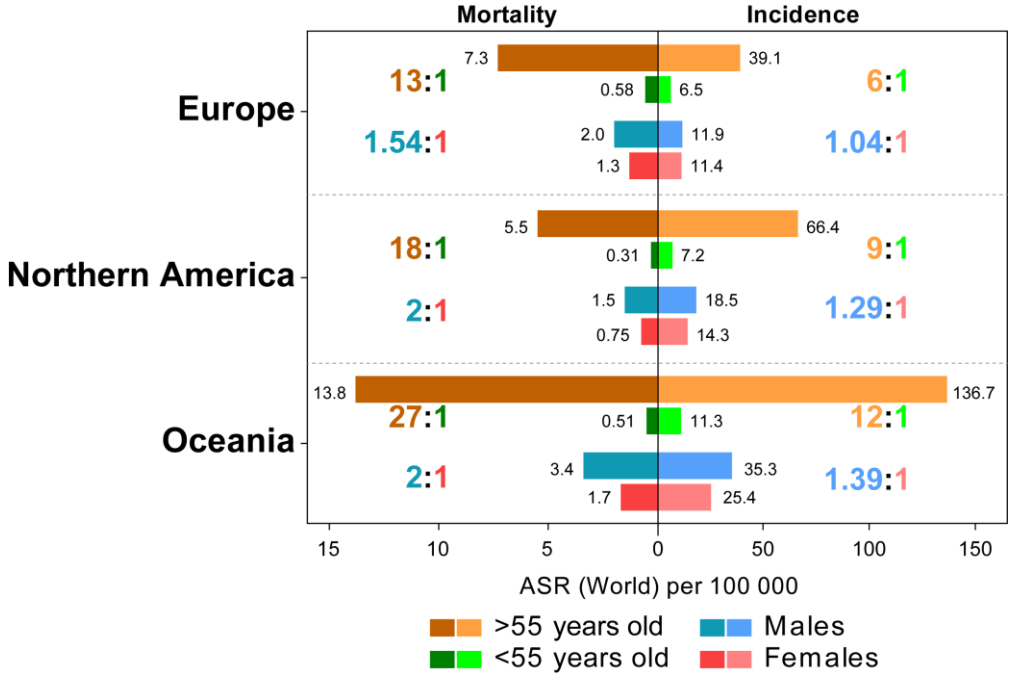
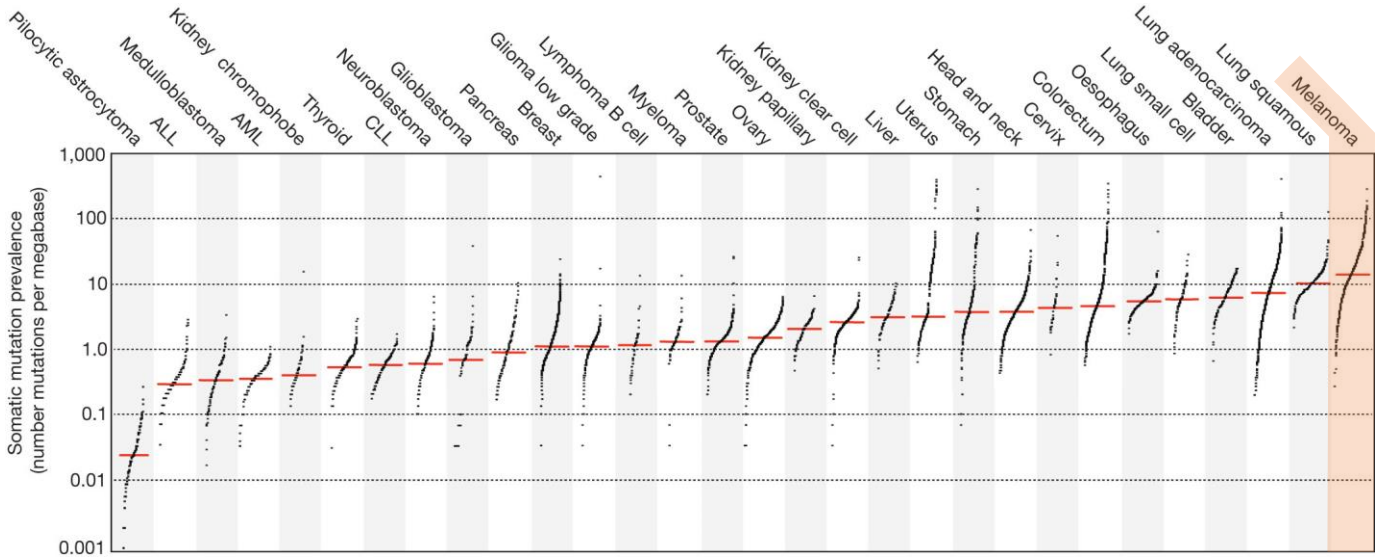
## Estimated number of melanomas in Europe




## Melanoma differentially affects populations

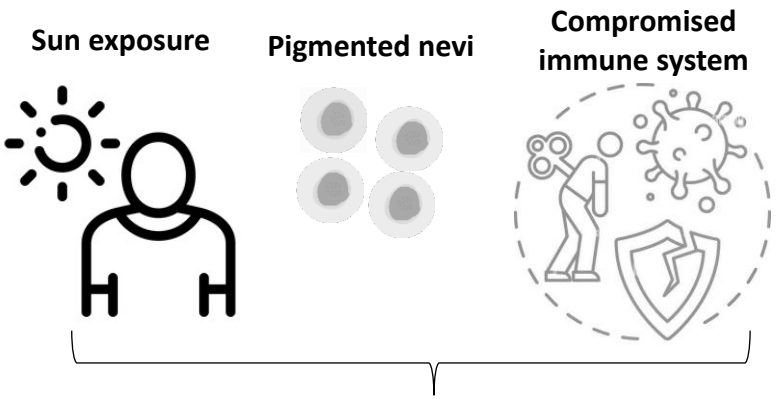


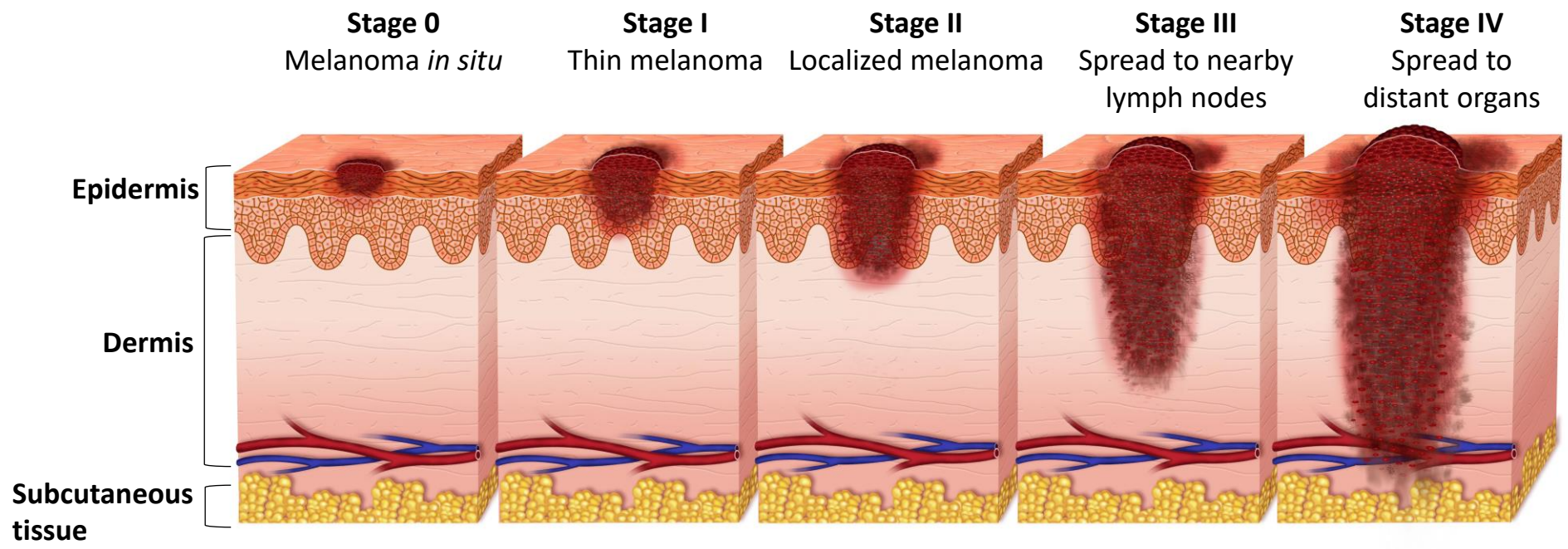

**Melanoma is the most genetically heterogenous of human cancers**

LB Alexandrov *et al. Nature* **000**, 1-7 (2013)

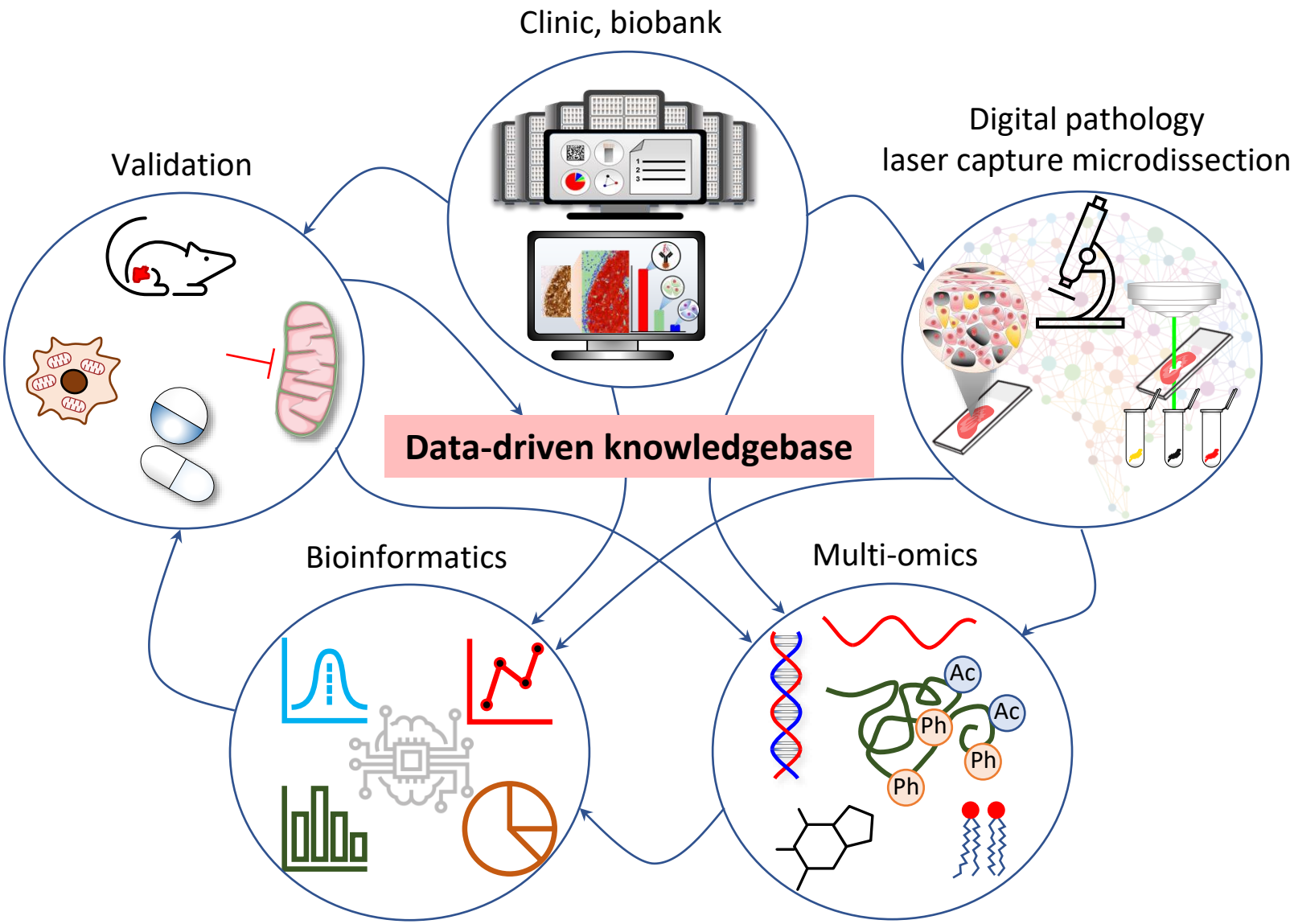
# Stages of melanoma



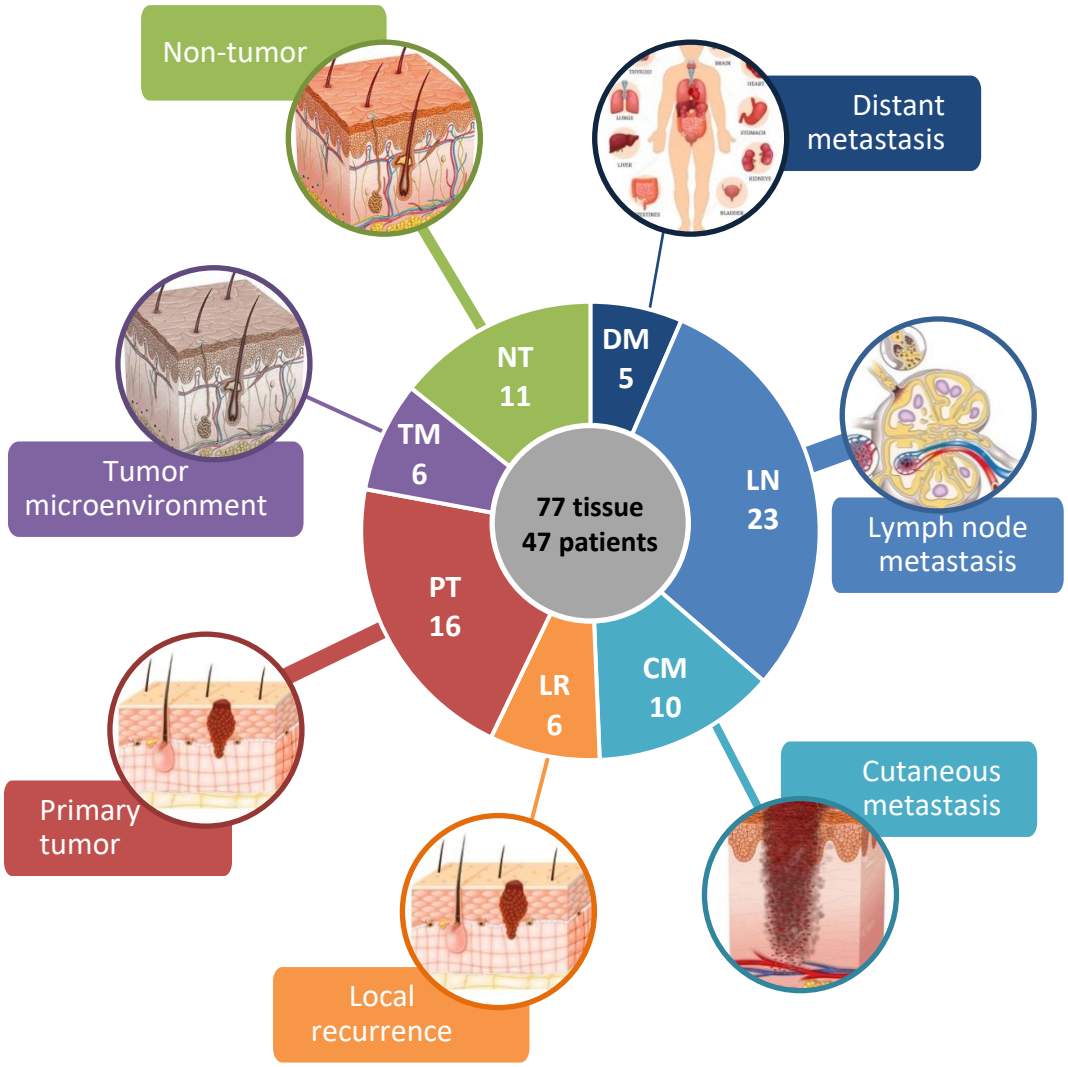

- **What are the molecular mechanisms responsible the pathogenesis of melanoma?**
- **What drives the recurrence and resistance to therapy?**
- **How can we impact the clinical decision-making towards precision medicine?**



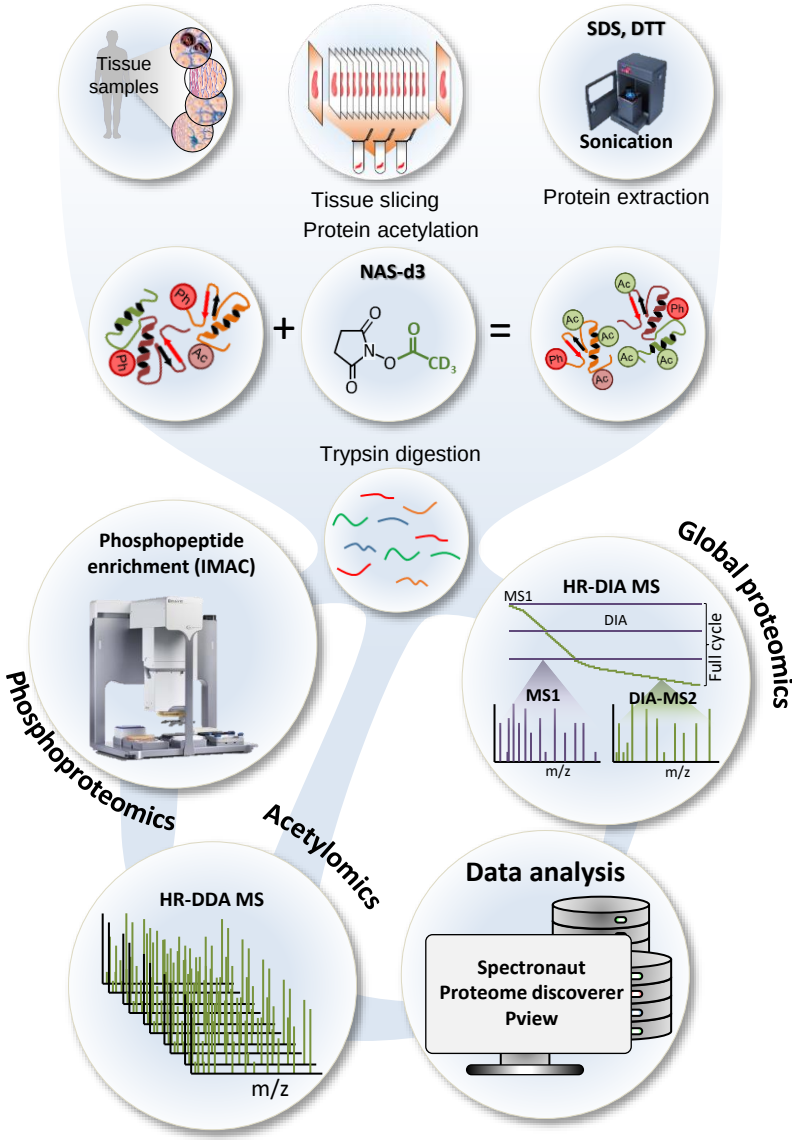
# Data-driven approach to understand molecular mechanism of melanoma



# Prospective melanoma cohort study (Cuarto study)

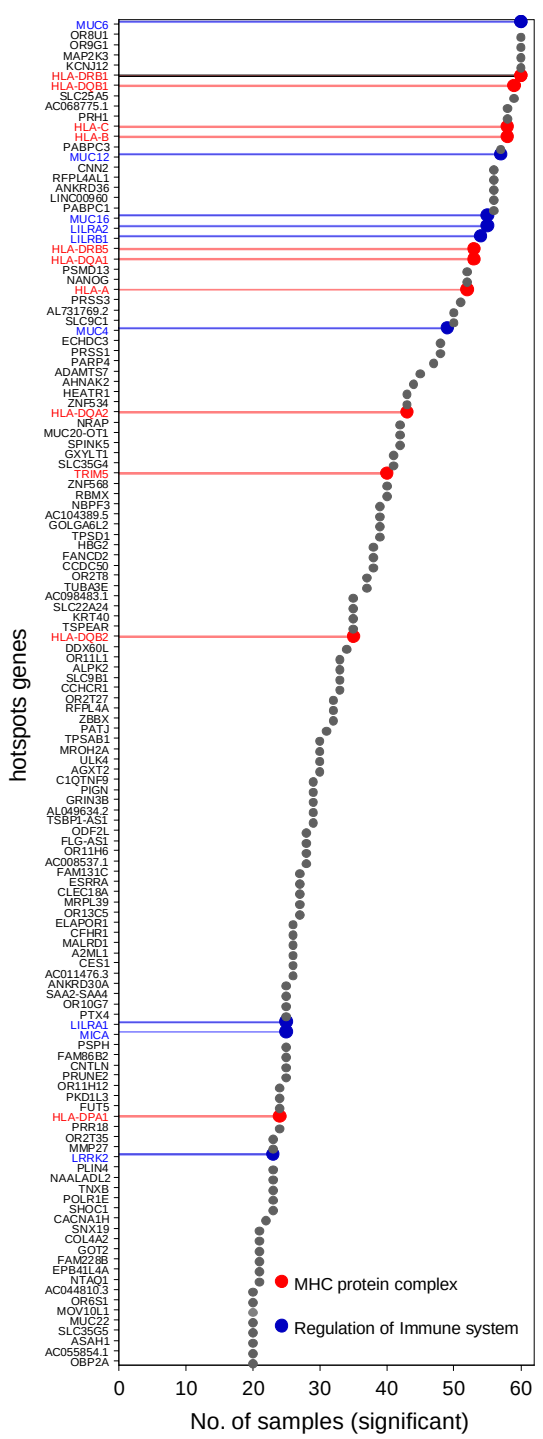


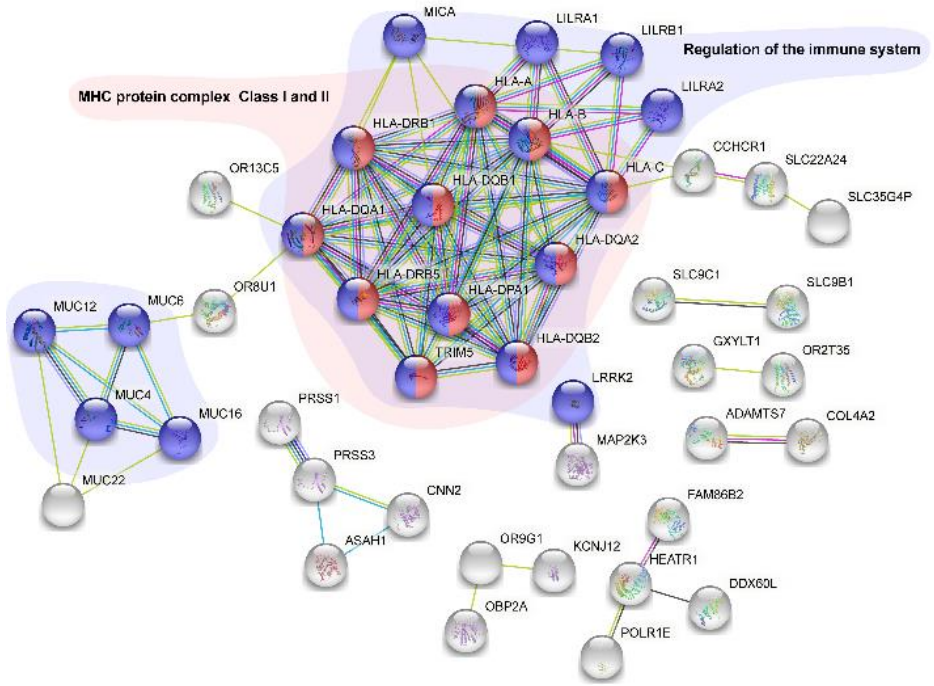

## Proteomics, PTMs analysis

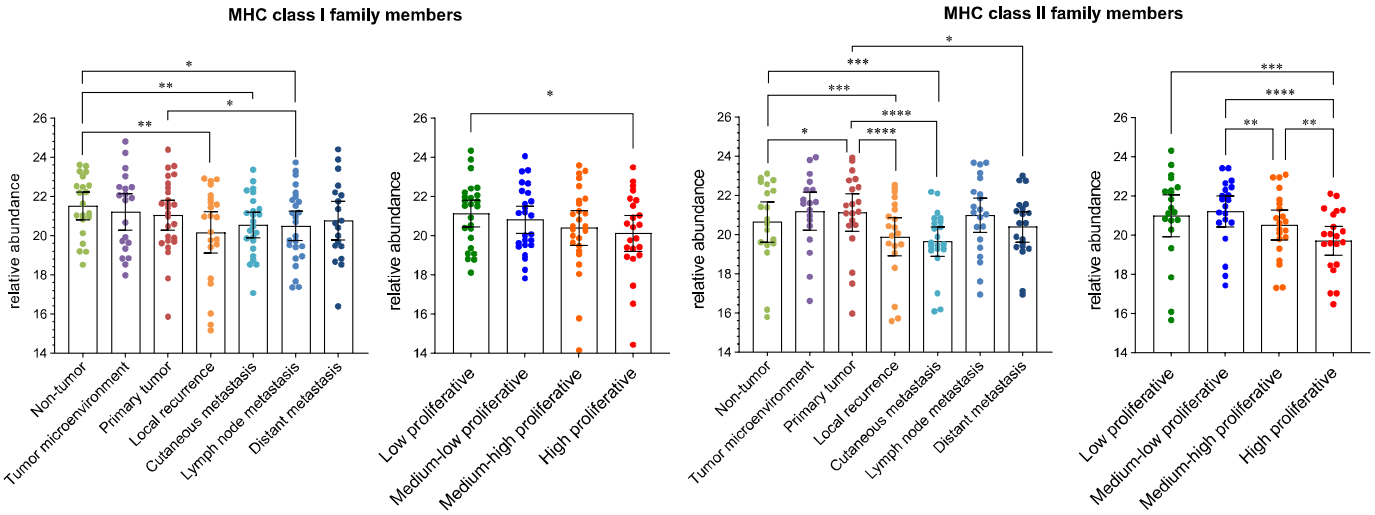



## Whole exome sequencing on tumor samples

# Antigen processing and presentation is heavily mutated and dysregulated in melanoma

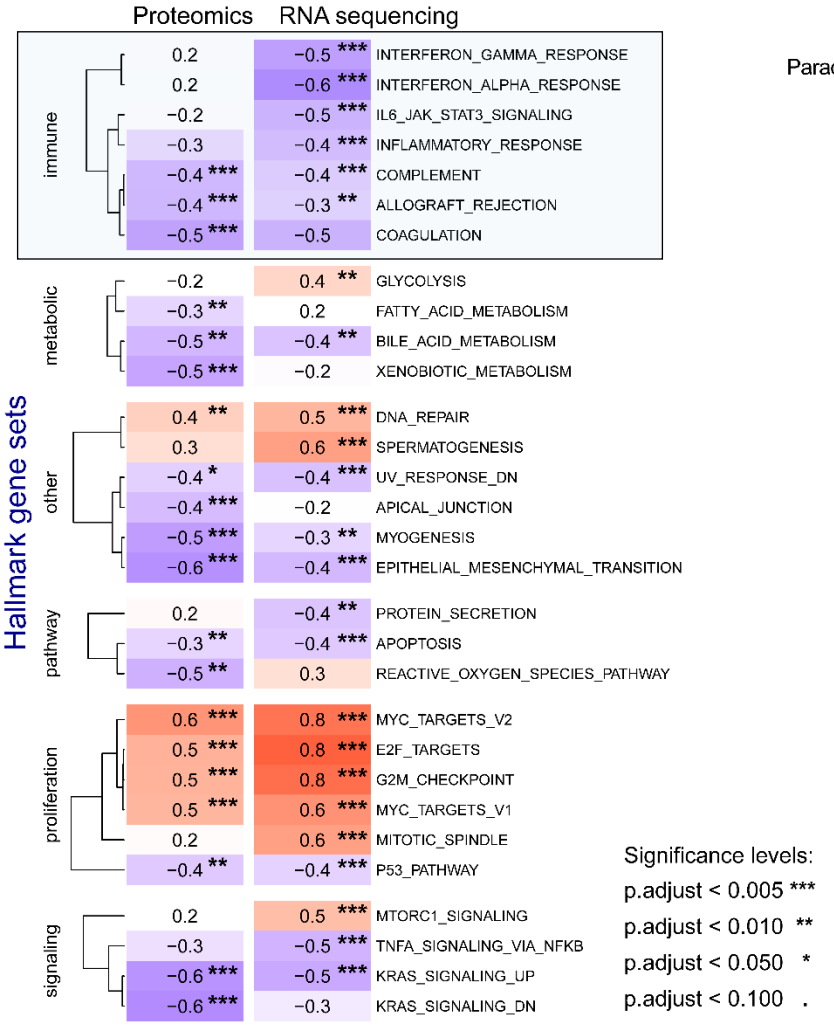


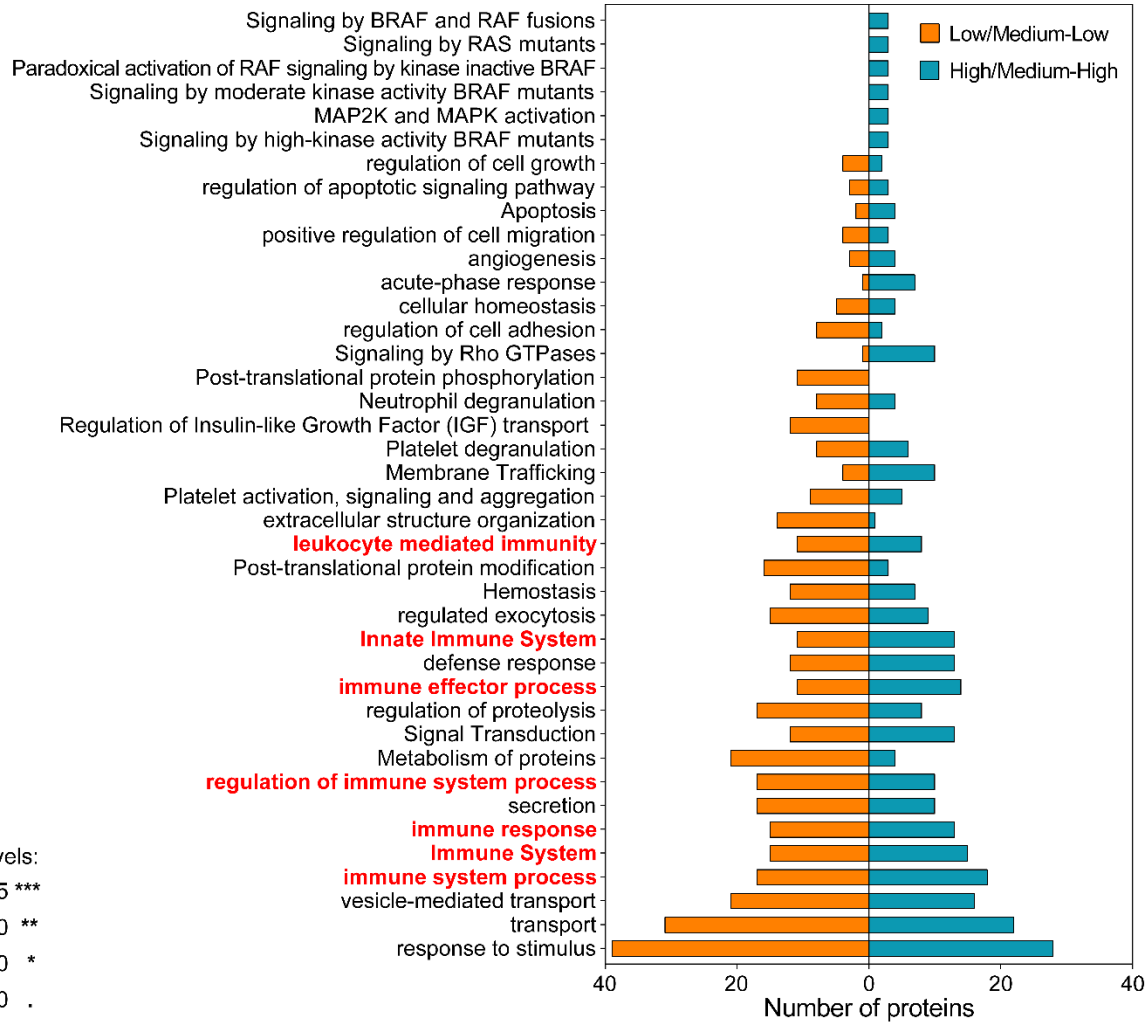



# Melanoma proliferation is supported by the modulation of the immune system at different molecular levels

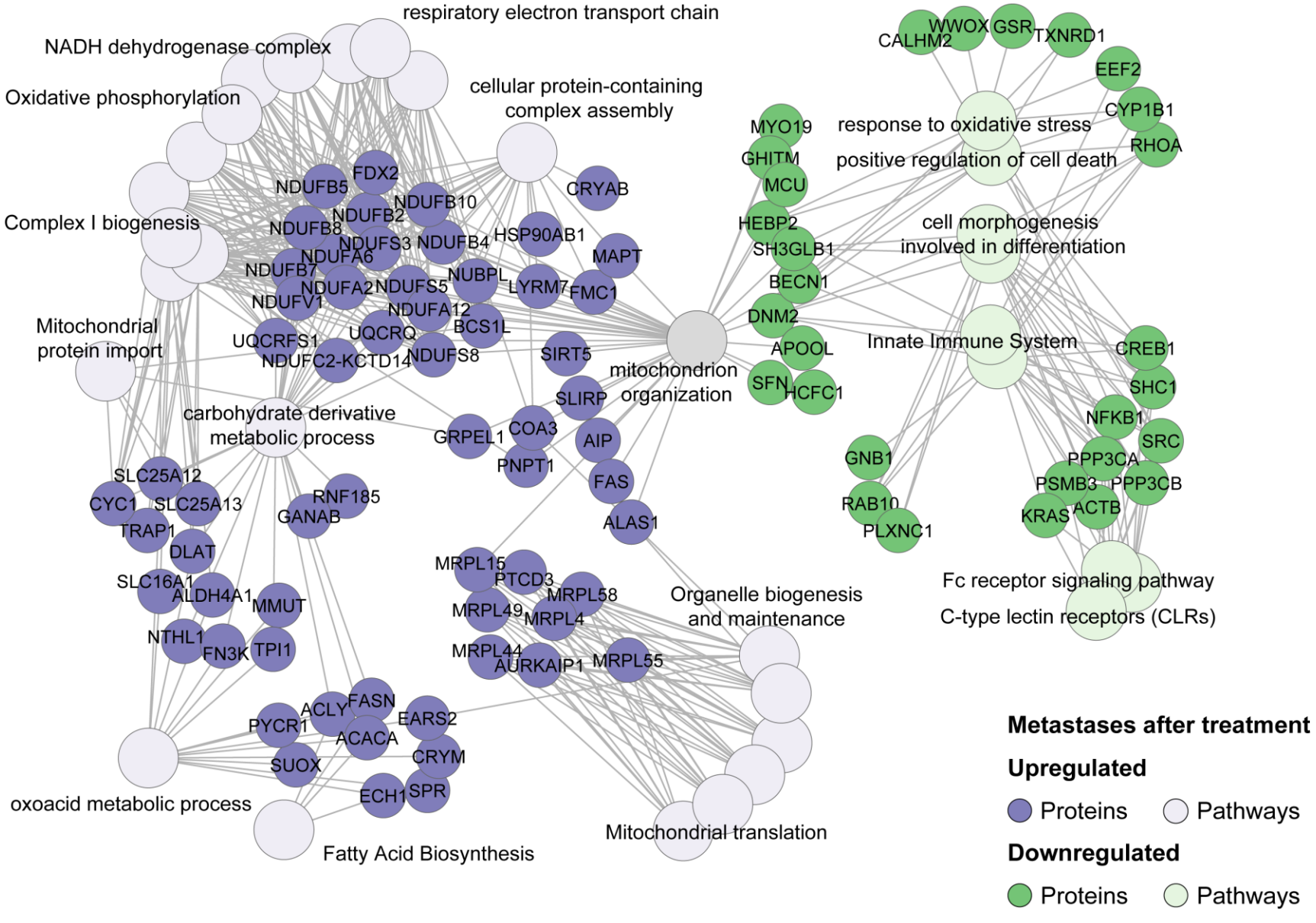
## Melanoma samples



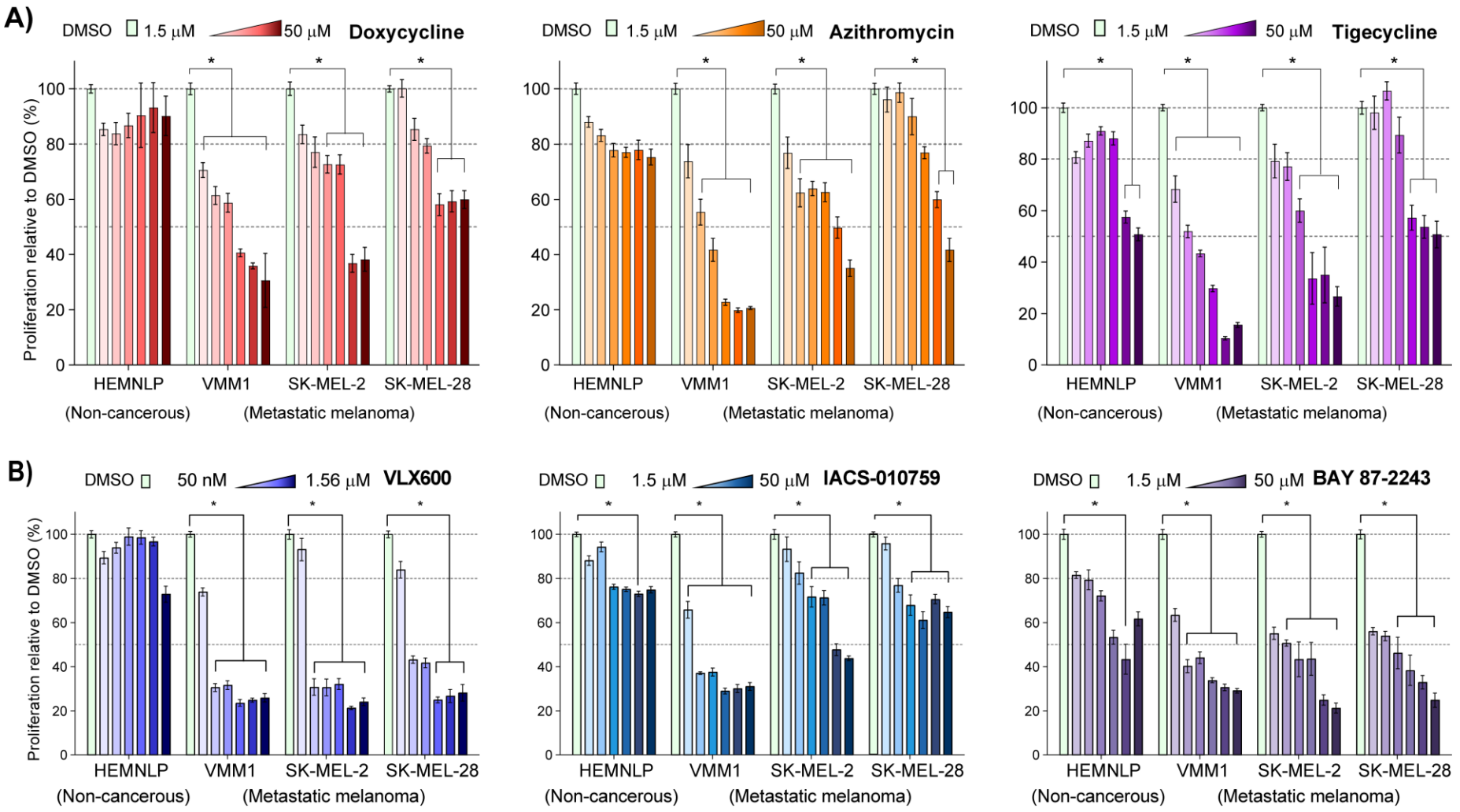

## Plasma proteome from melanoma patients



# Mitochondrial proteome in melanoma metastases

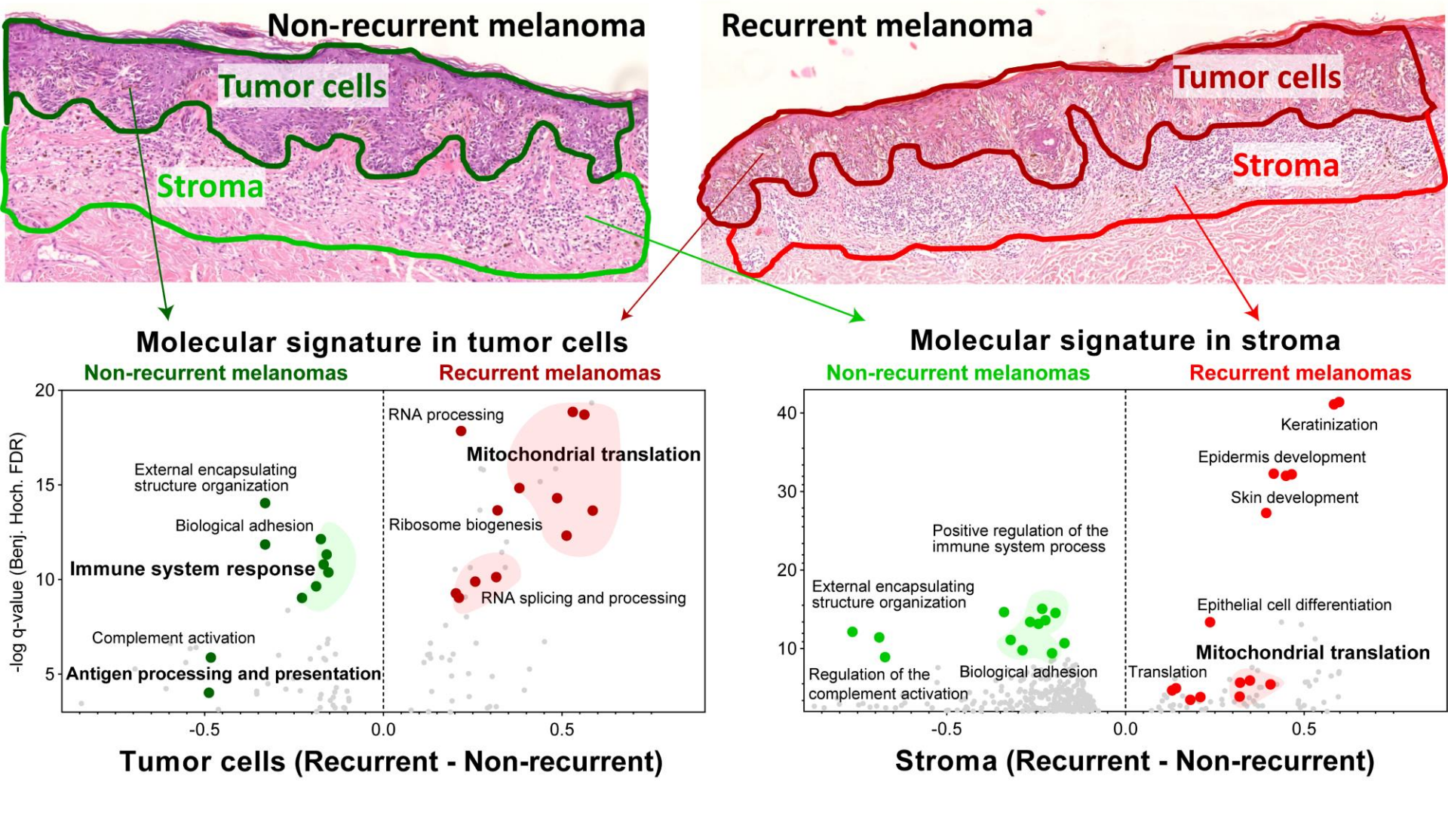


# Targeting the mitochondrial translation and OXPHOS impairs the proliferation of melanoma cells



# The alpha cohort study

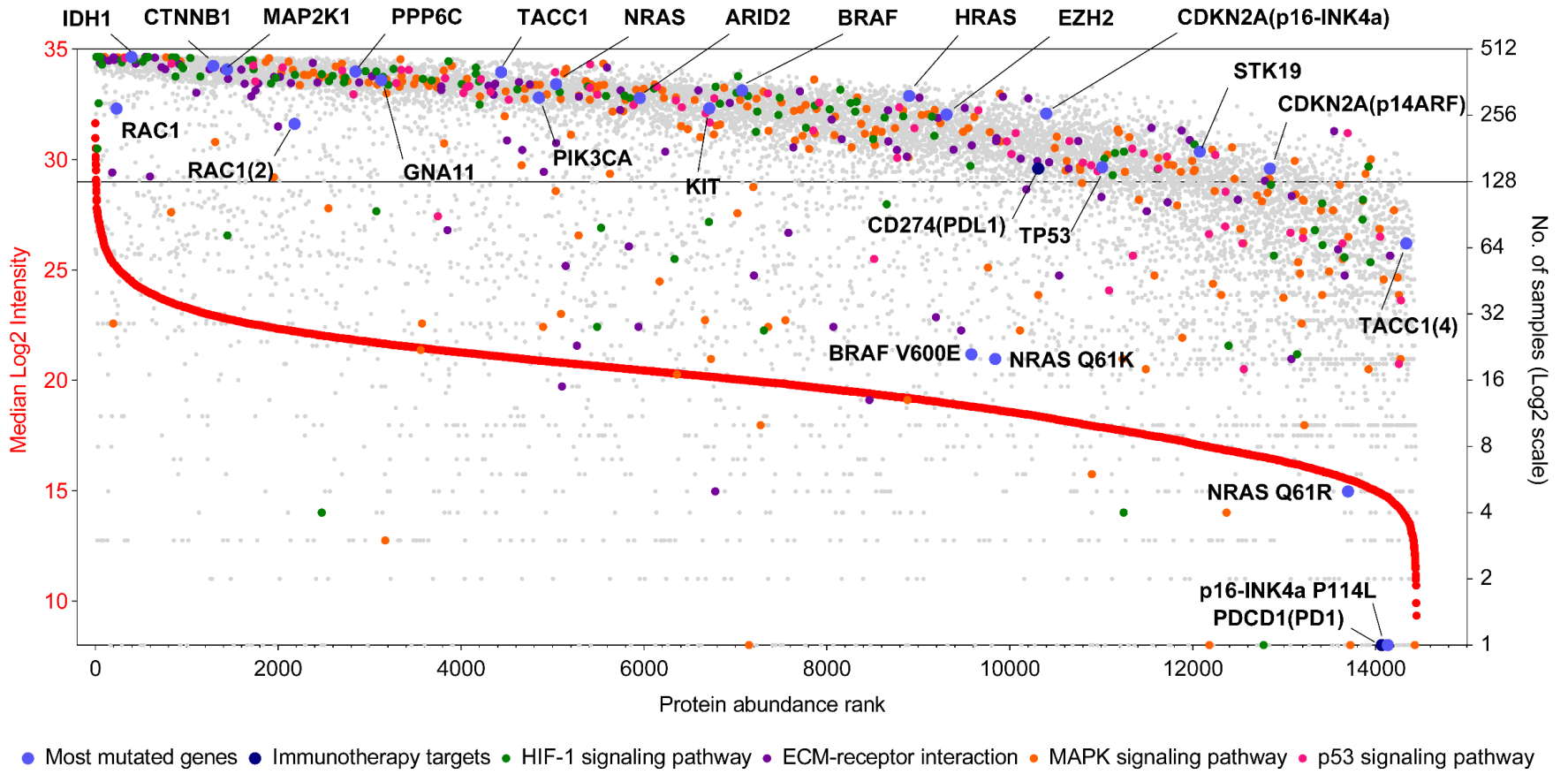
12 early-stage primary melanomas
n=6 non-recurrent; n=6 recurrent melanoma within 5 years



# The MM500 study
# covering to a large extent the melanoma disease presentation

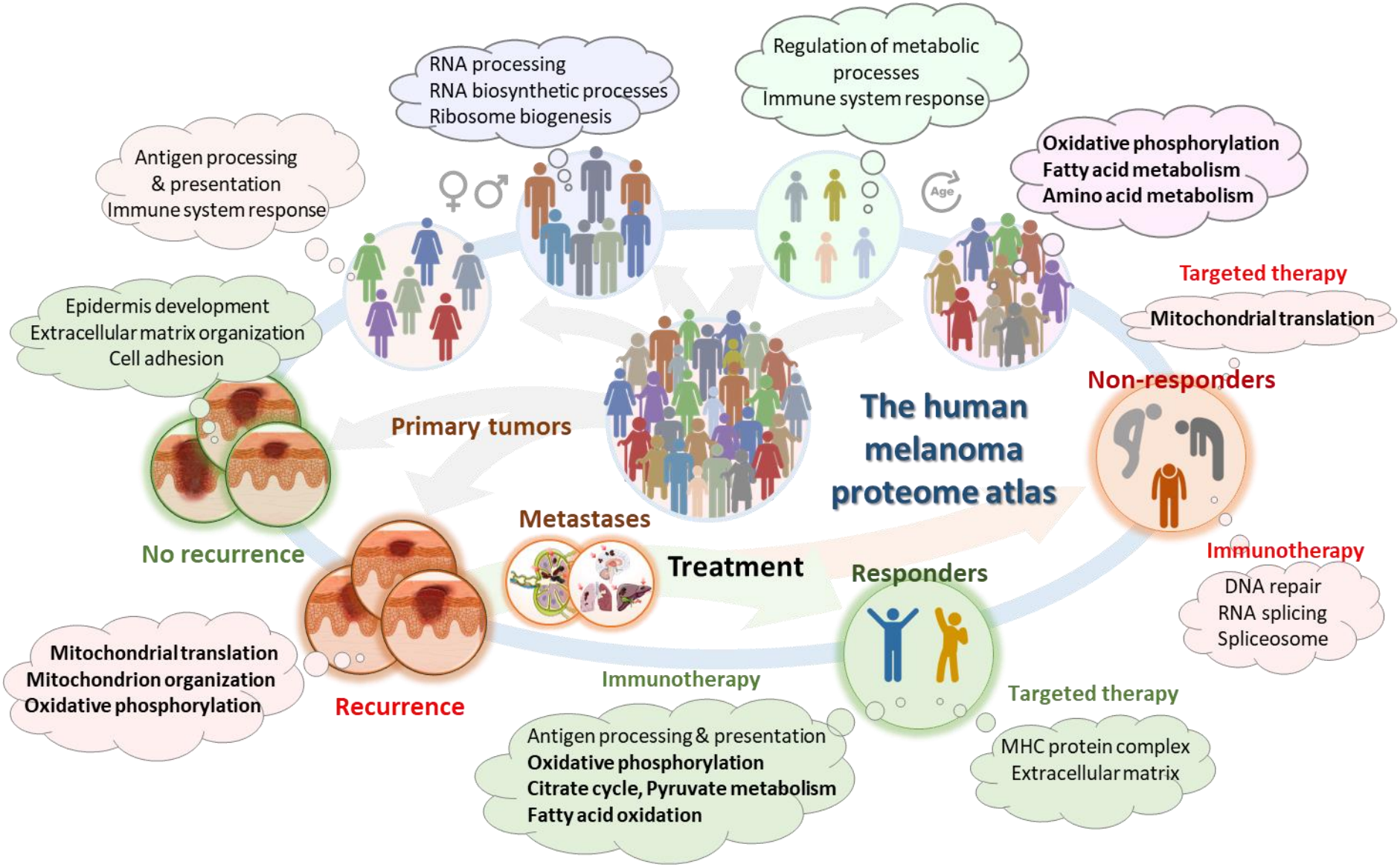
## The human melanoma proteome atlas

+16 000 proteins
50 000 phosphorylation sites
4 000 lysine acetylation sites

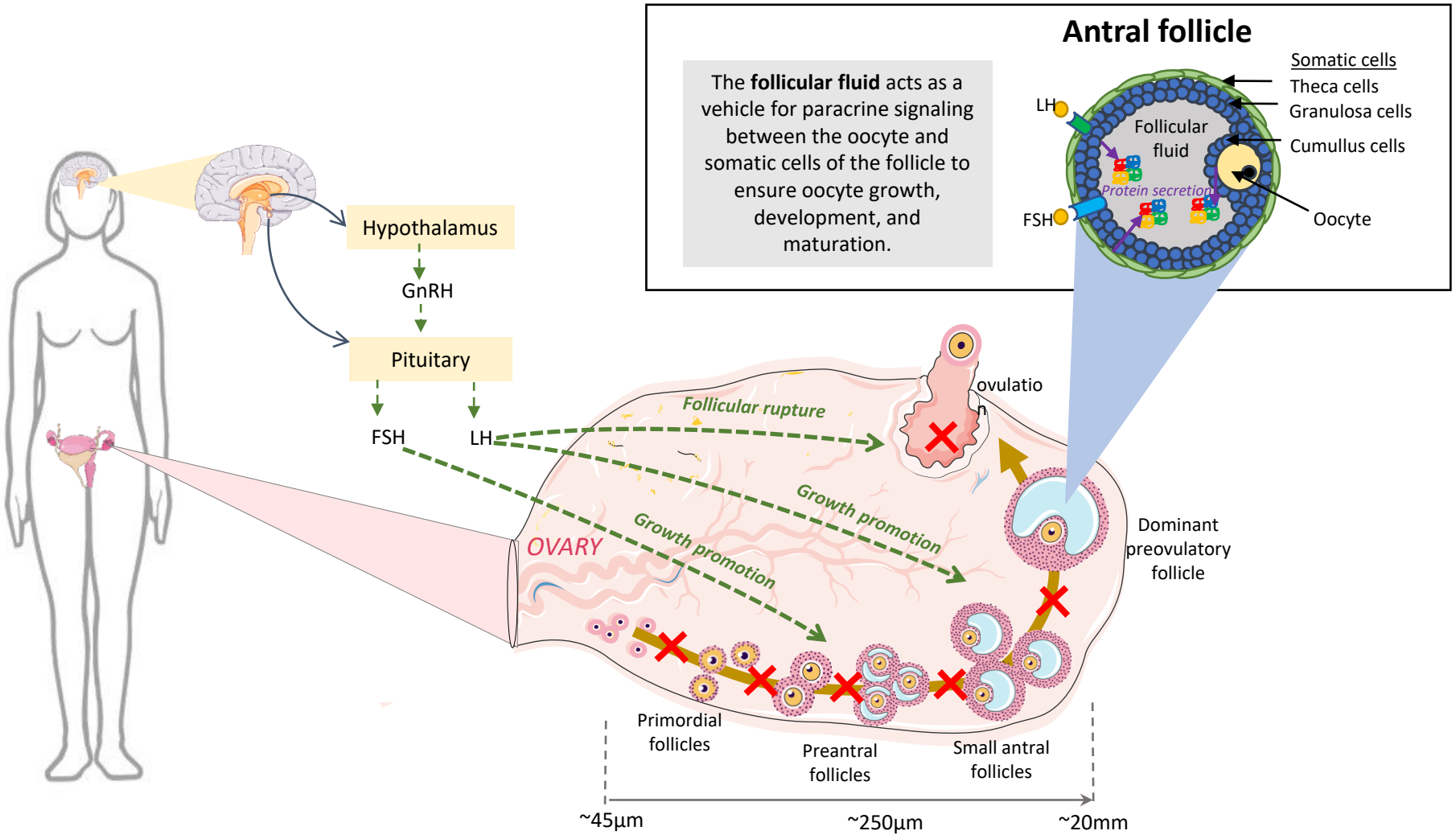



*Clin. Transl. Med.* 2021;11:e451. *Clin. Transl. Med.* 2021;11:e473.

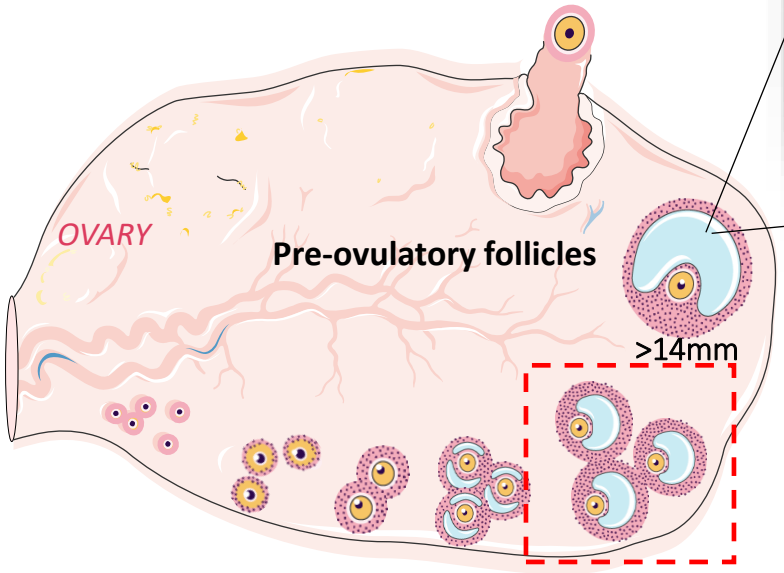
# The melanoma disease presentation at the functional proteome level

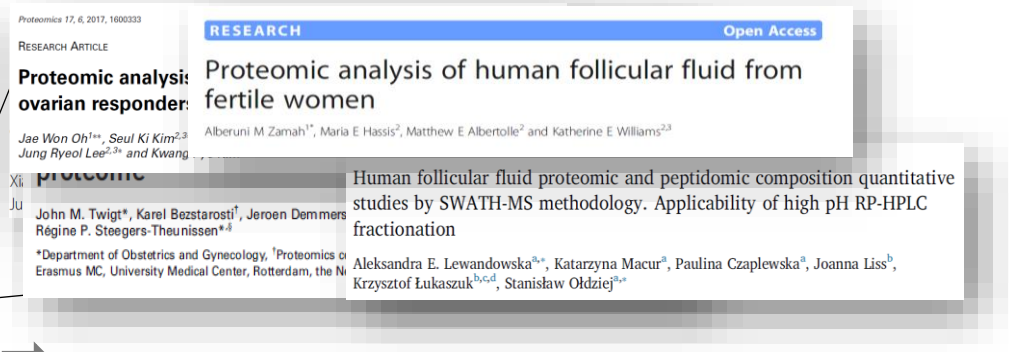


# Female reproductive system



# Previous proteomics studies in Follicular Fluid

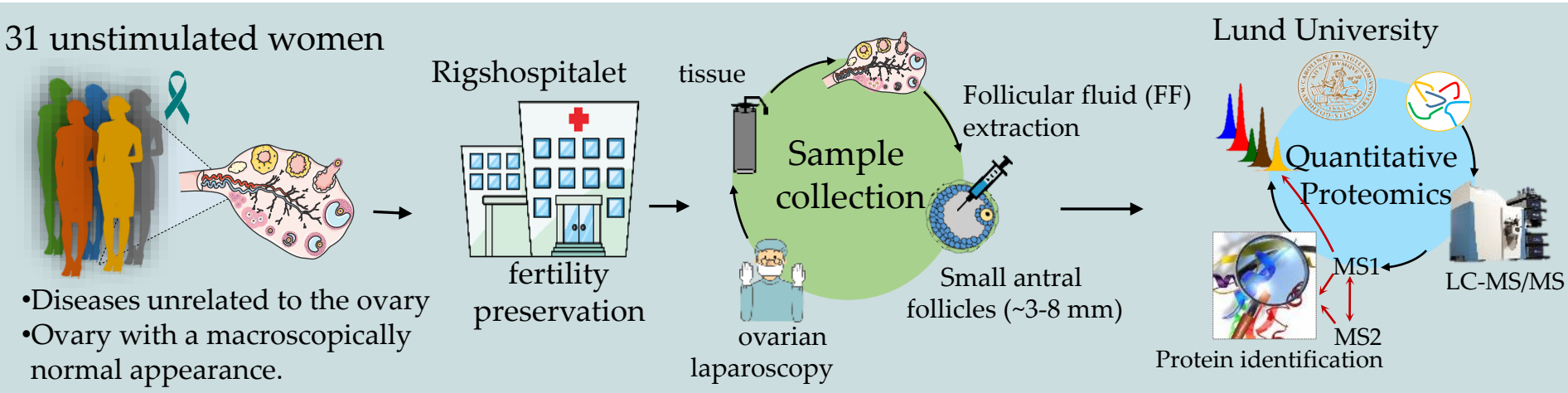


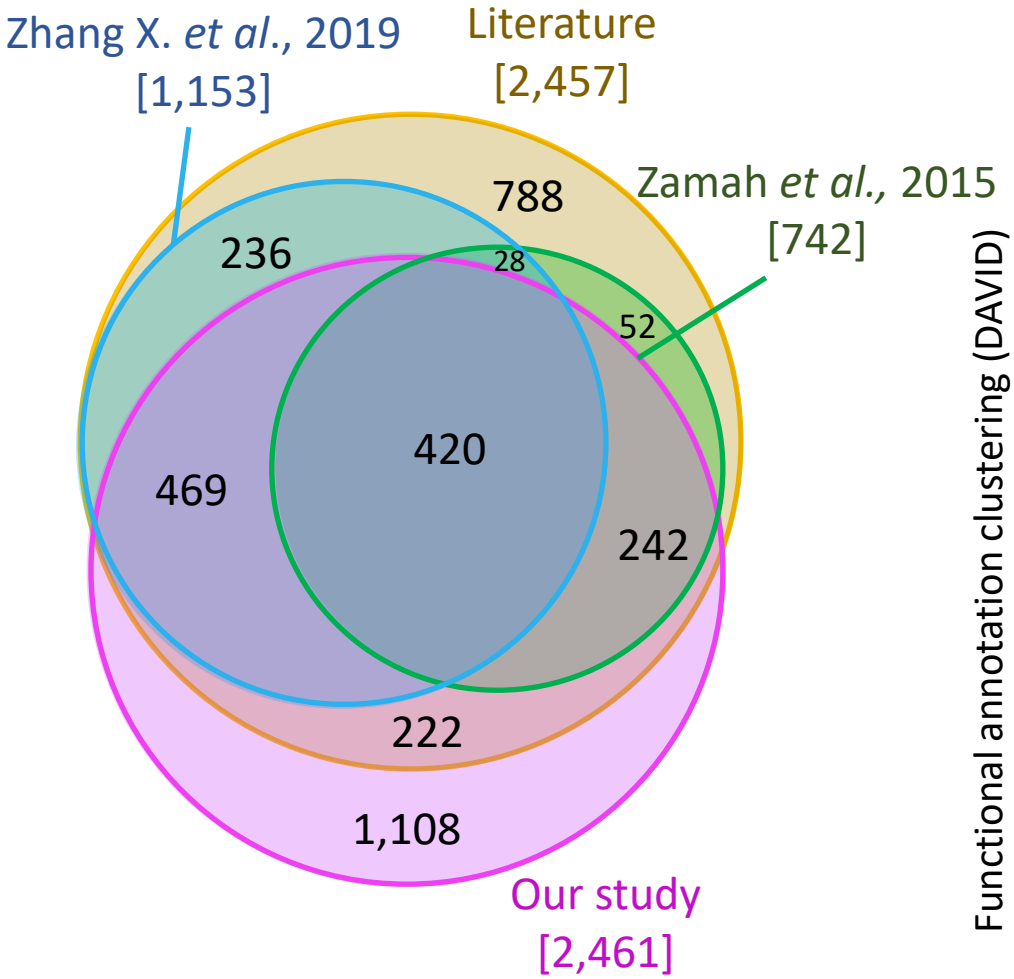

FF contains a high number of plasma constituents transferred through the follicular basal membrane as follicular expansion.

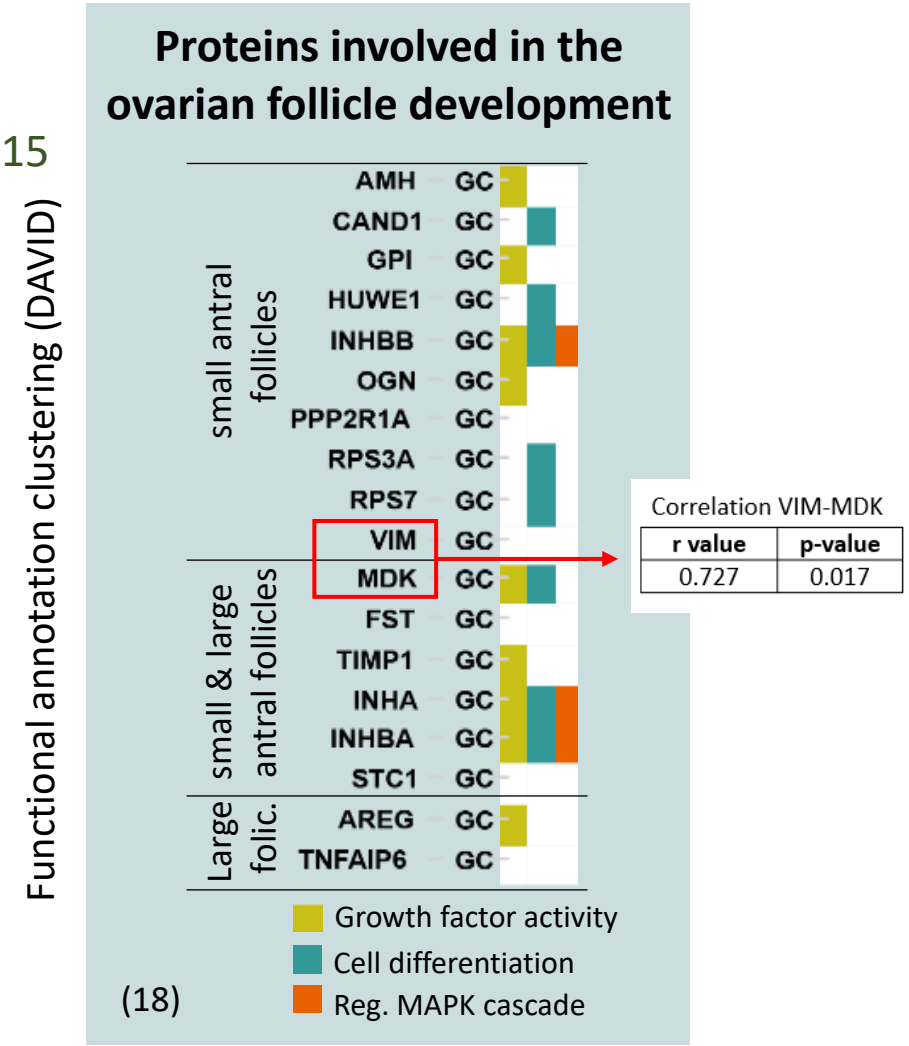
It attenuates the detection of low abundant proteins.

Is it possible to identify more proteins involved in folliculogenesis and oocyte development?



# Proteomics of follicular fluids



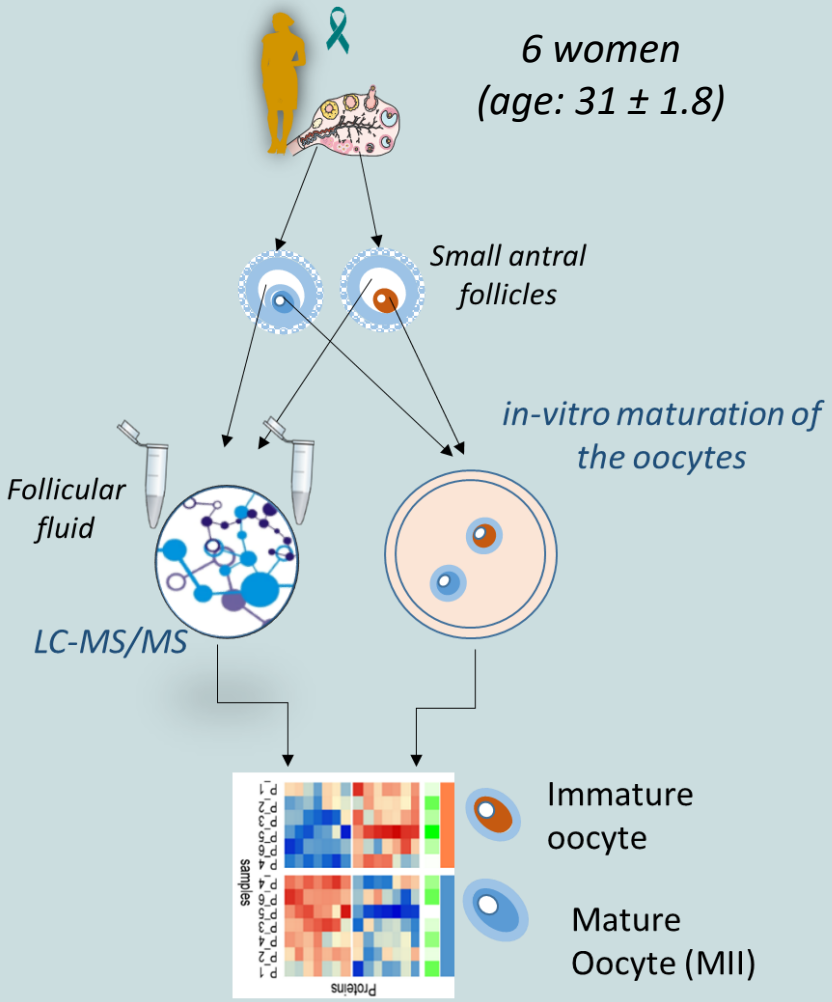



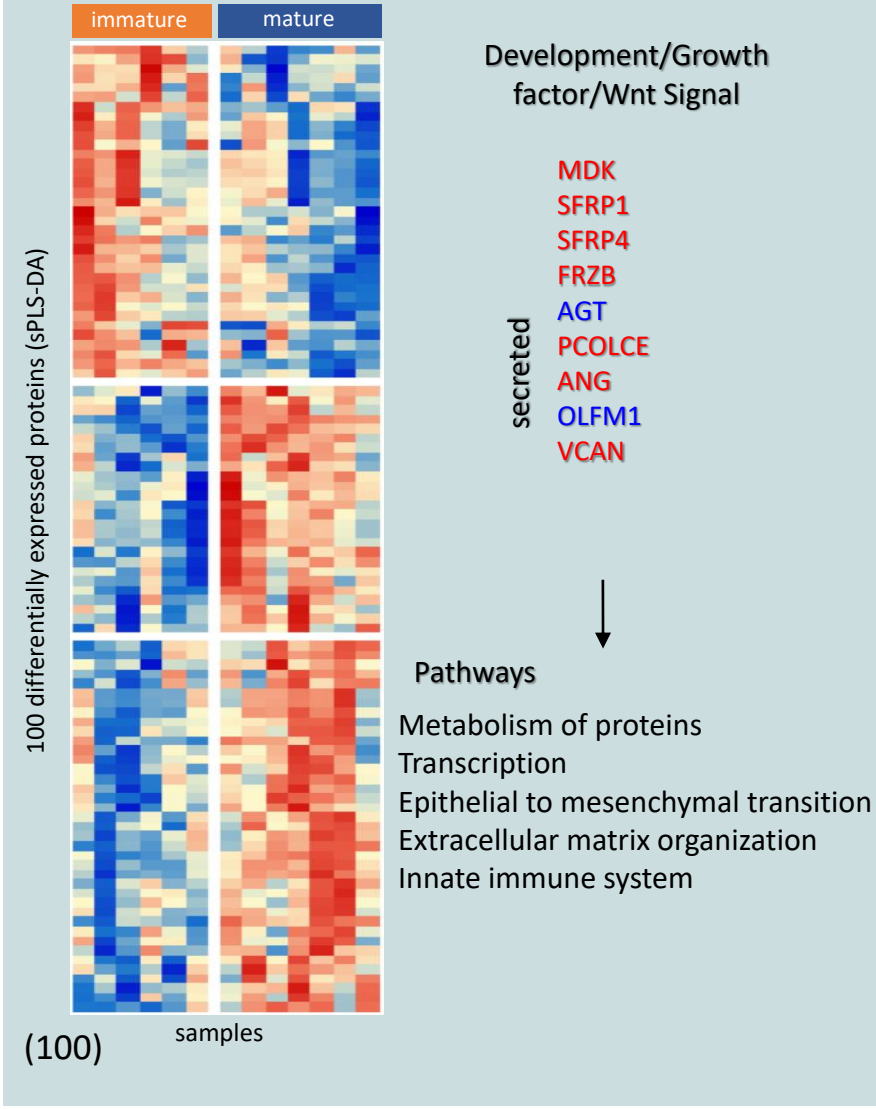

We reported the largest number of proteins identified in ovarian follicular fluid

Hum Reprod. 2021 Feb 18;36(3):756-770.

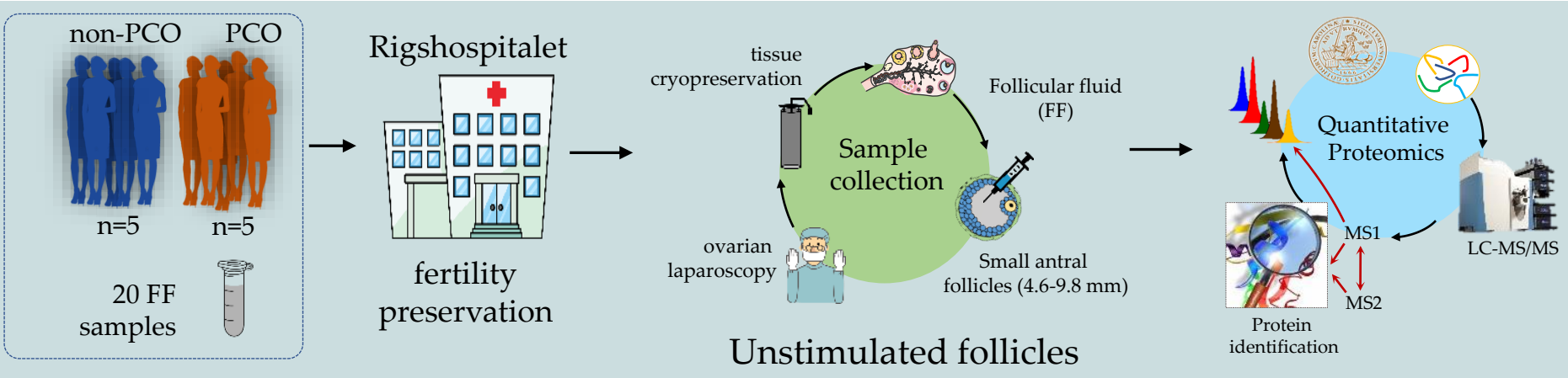
# Proteomics of follicular fluids

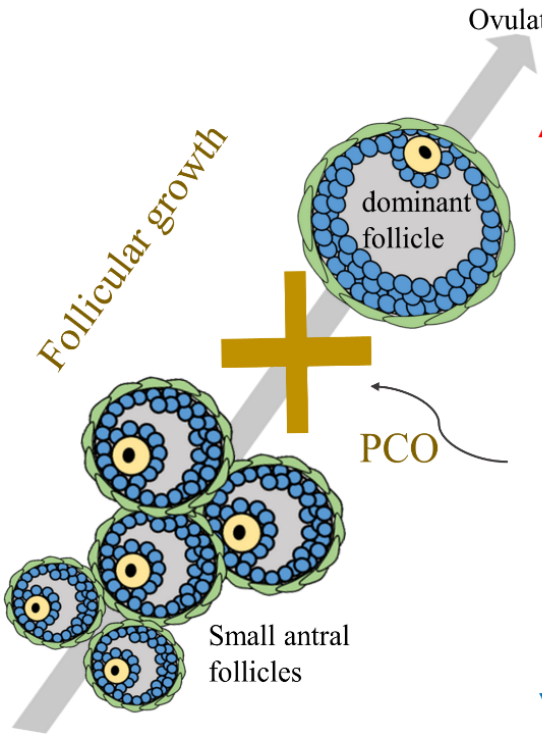
## Proteins related to upcoming oocyte maturation



# Polycystic ovarium syndrome study




## Disruption in follicular growth

- Immune System & Inflammatory Processes | S100A9, IGLC2,7, IGLVs IGHVs, IGKVs
- Cell Signaling & Communication | PSMB1, PSMB4, SFRP1, DAG1, INHBC, PFN2, HSP90AB1, MAPK8IP2, STRAP, PPP2CB, CDH3, PARP1
- ECM–receptor interaction | DAG1, COL5A2, THBS4
- Response to oxidative stress. | PRDX2, PPP2CB, P4HB, ATRN, PARP1
- Response to hormone & endogenous stimulus | DAG1, PPP2CB, SFRP1, COL5A2, PARP1
- Growth factor/hormone activities | DCN, FAP, THBS4, IL1RAP, INHBC

# Acknowledgements:





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