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Clinical multi-omics targeting melanoma and reproductive disorders

Jeovanis Gil

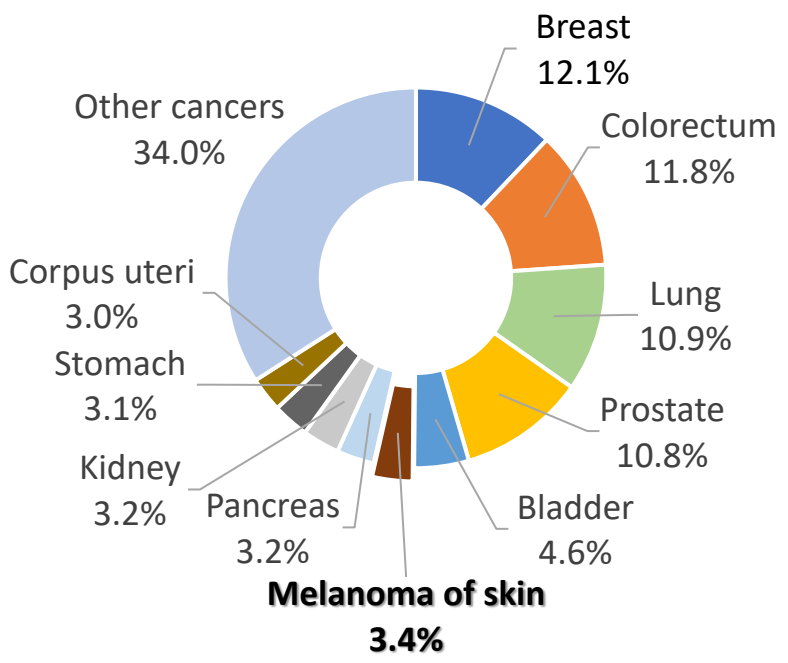
European Cancer Moonshot Lund Center

Department of Translational Medicine

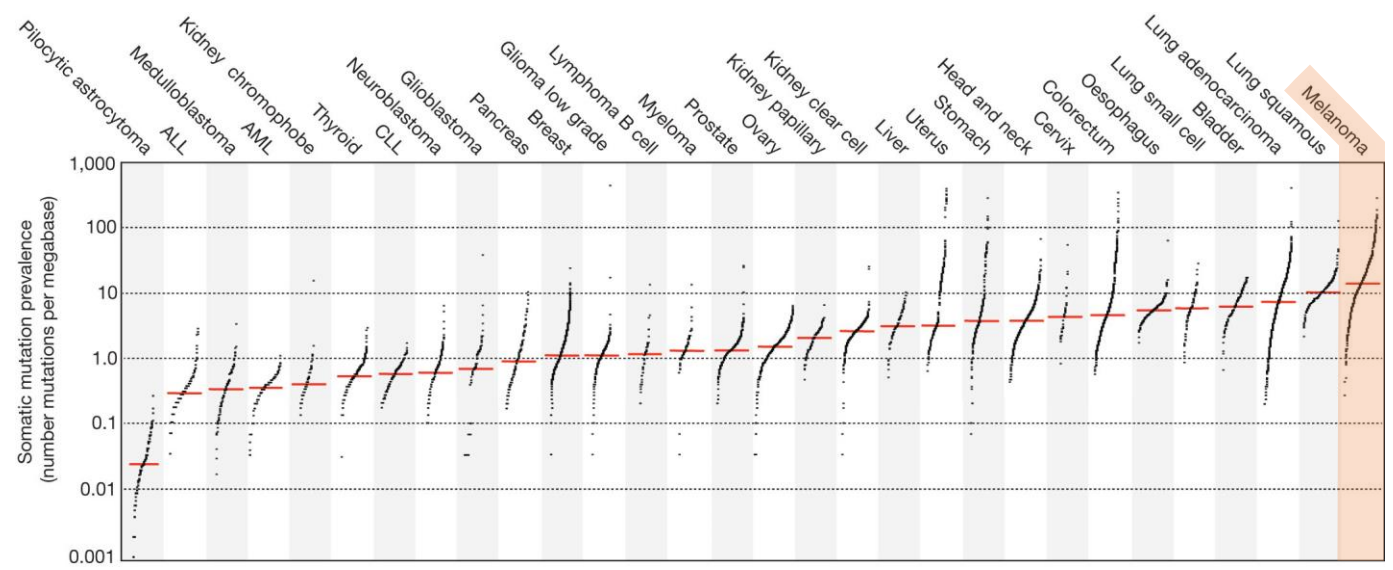
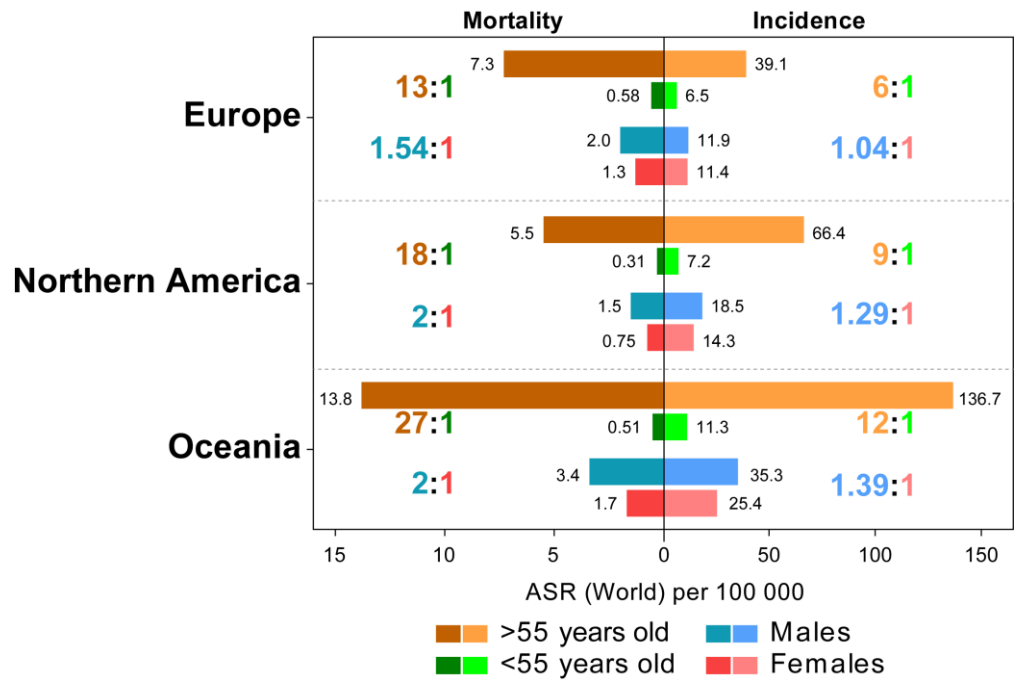
Lund University

Timișoara 2022

Estimated number of melanomas in Europe



Melanoma differentially affects populations



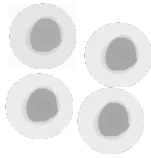
Melanoma is the most genetically heterogenous of human cancers

Stages of melanoma

Sun exposure

Pigmented nevi

Compromised immune system



- 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?

Stage 0

Melanoma *in situ*

Stage I

Thin melanoma

Stage II

Localized melanoma

Stage III

Spread to nearby lymph nodes

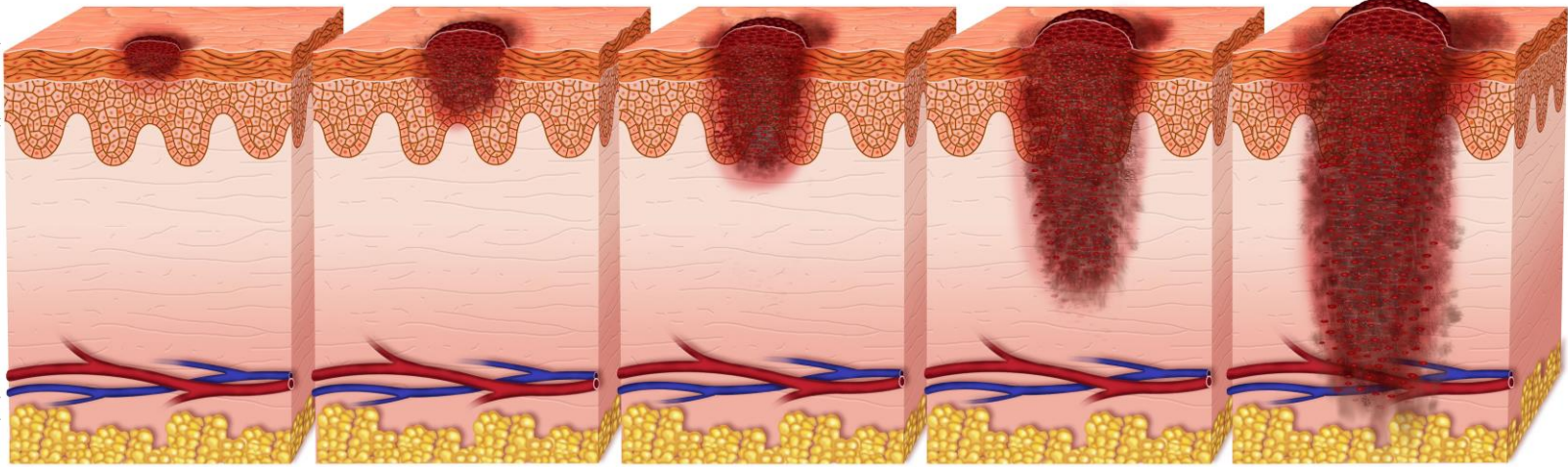
Stage IV

Spread to distant organs

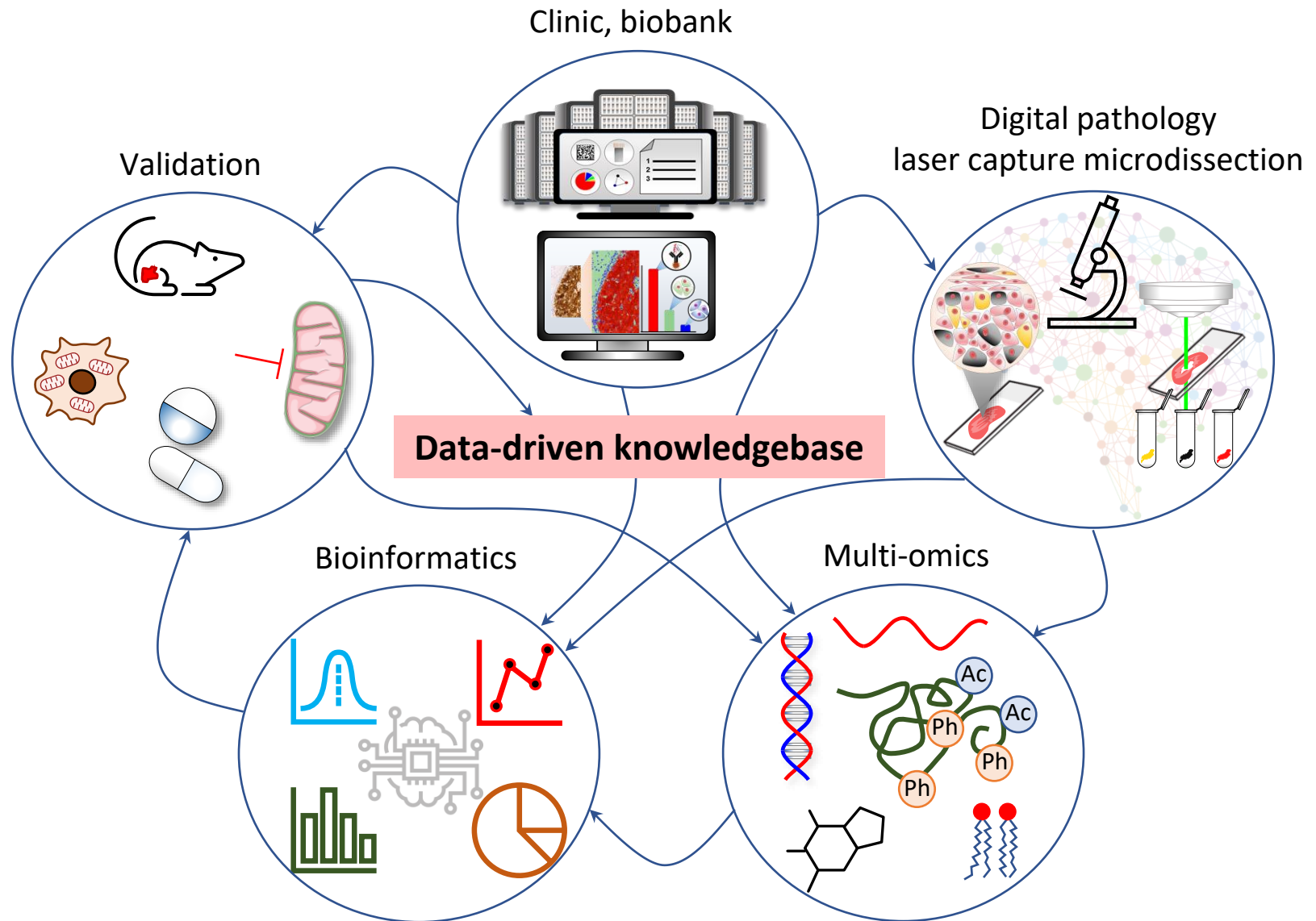
Epidermis

Dermis

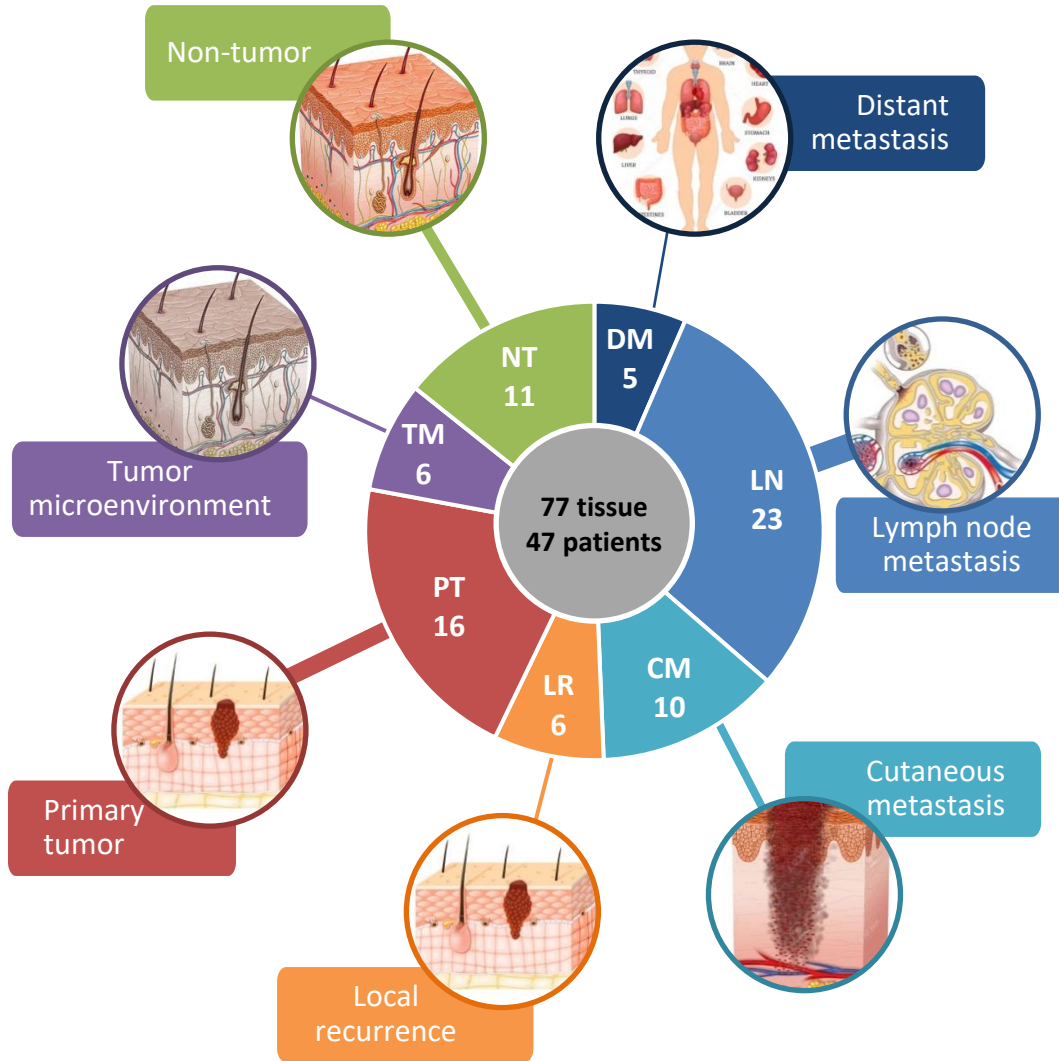
Subcutaneous tissue



Data-driven approach to understand molecular mechanism of melanoma

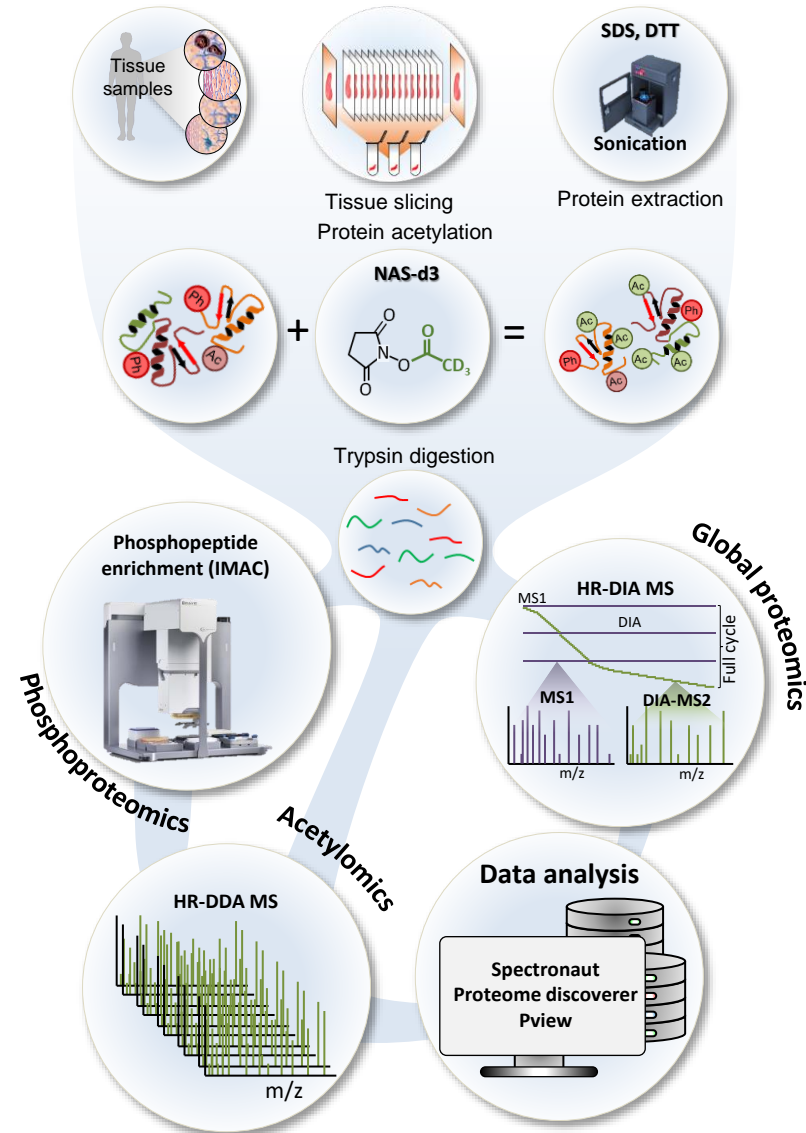


Prospective melanoma cohort study (Cuarto study)



Whole exome sequencing on tumor samples

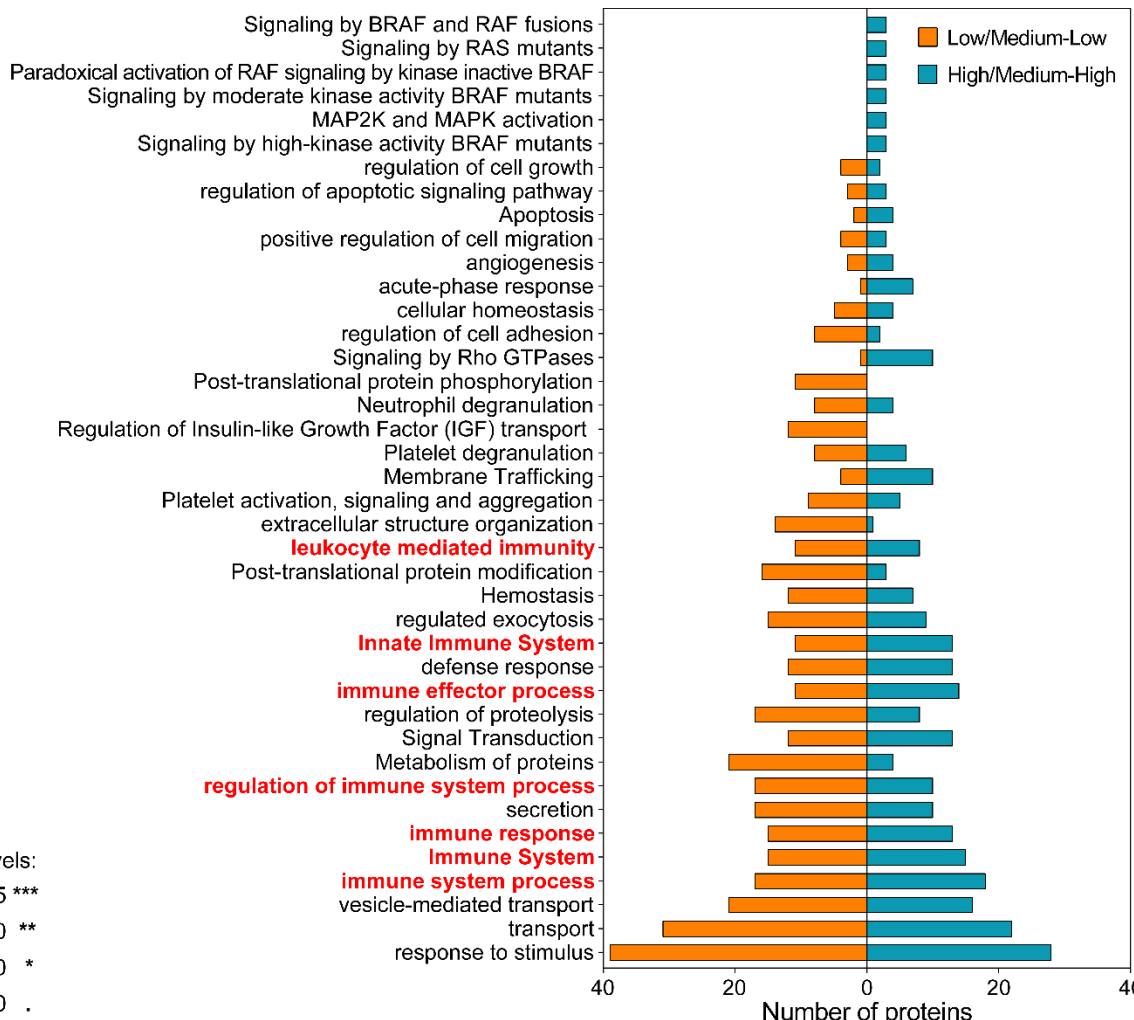
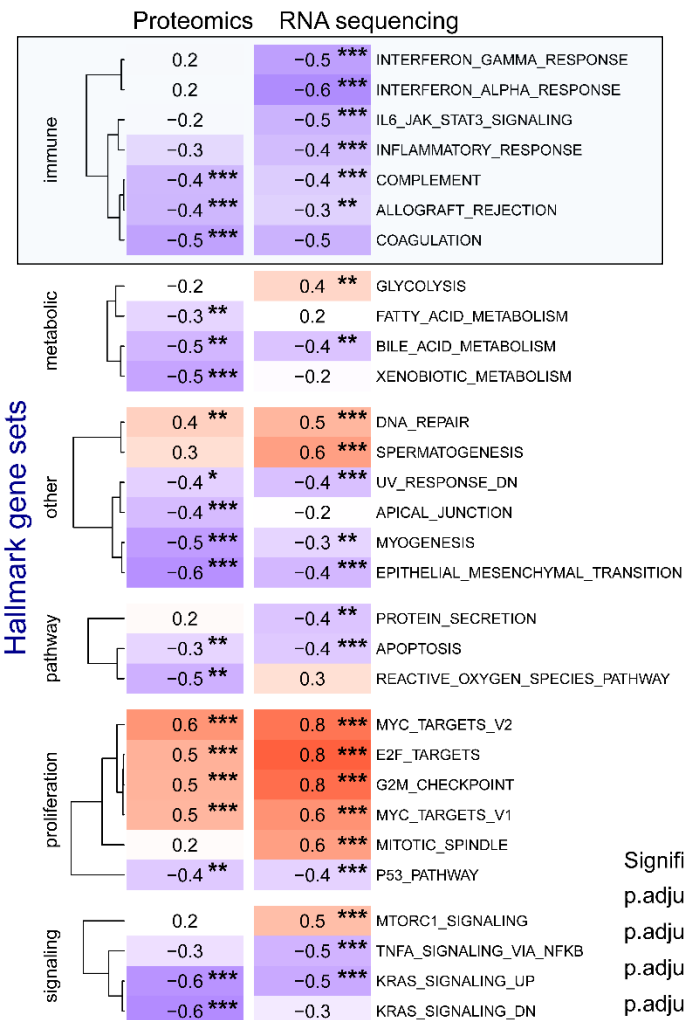
Proteomics, PTMs analysis



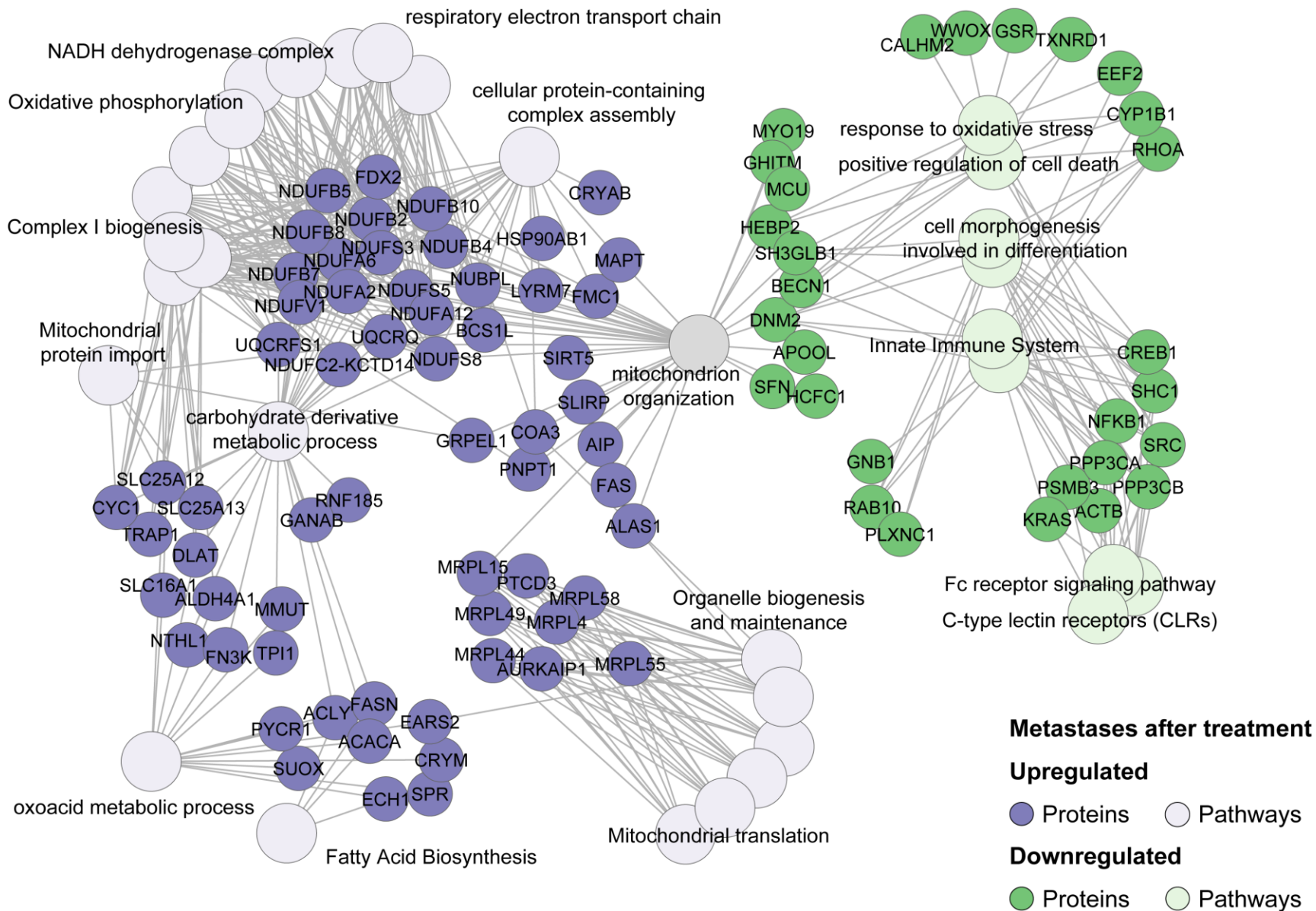
Melanoma proliferation is supported by the modulation of the immune system at different molecular levels

Melanoma samples

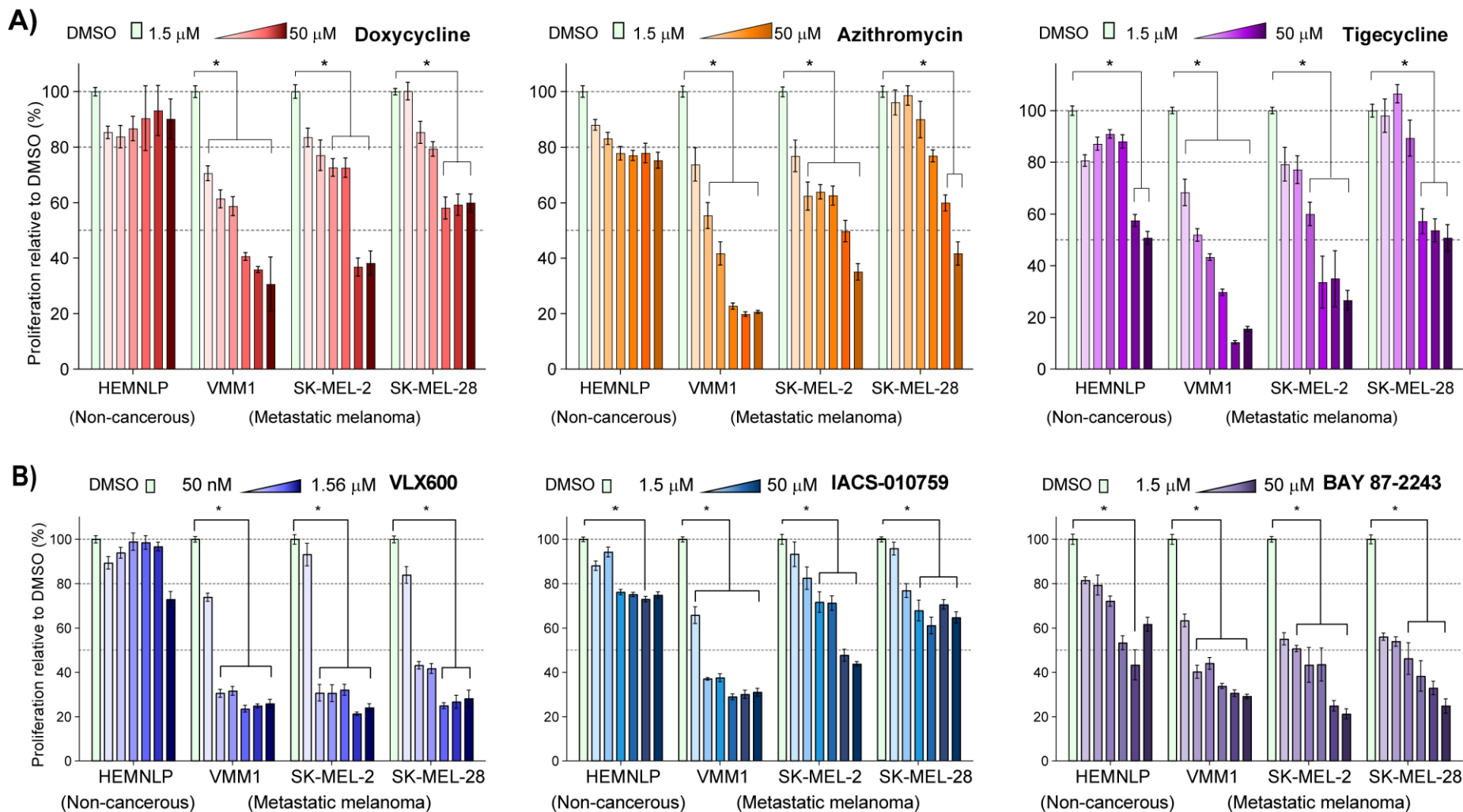
Plasma proteome from melanoma patients



Mitochondrial proteome in melanoma metastases

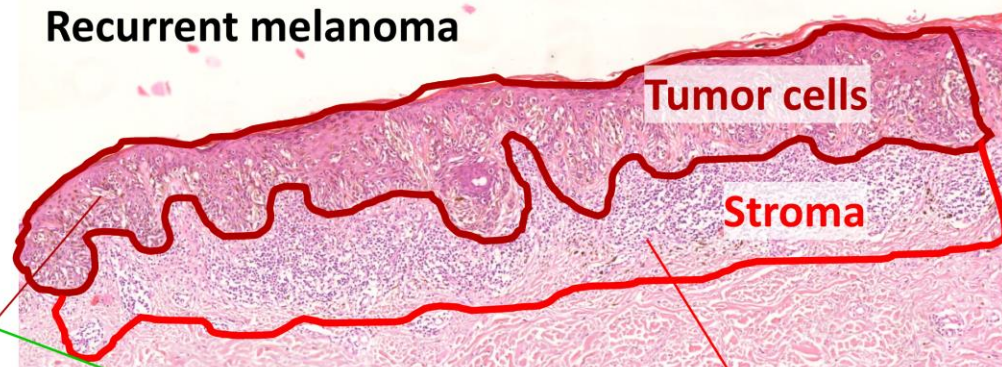
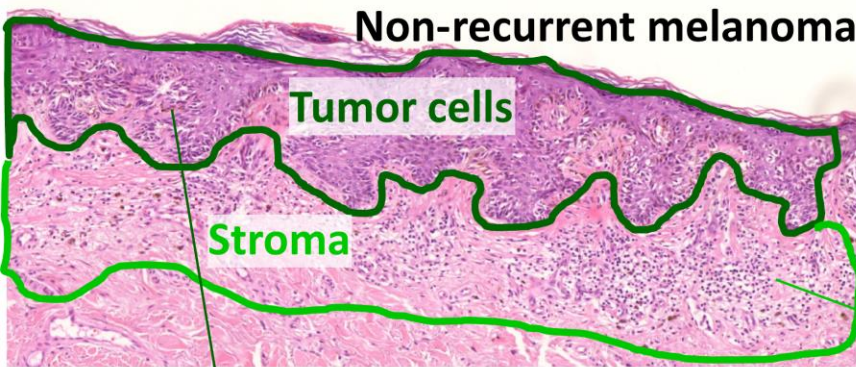


Targeting the mitochondrial translation and OXPHOS impairs the proliferation of melanoma cells



The alpha cohort study

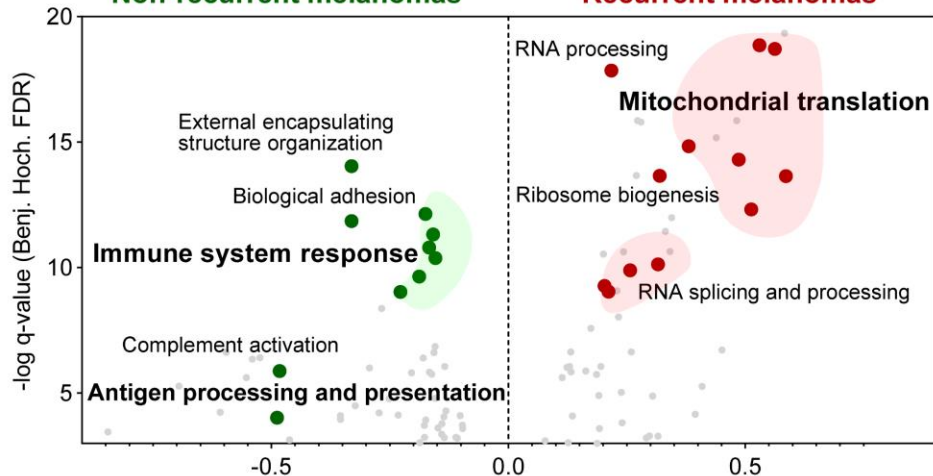
12 early-stage primary melanomas
n=6 non-recurrent; n=6 recurrent melanoma within 5 years



Molecular signature in tumor cells

Non-recurrent melanomas

Recurrent melanomas

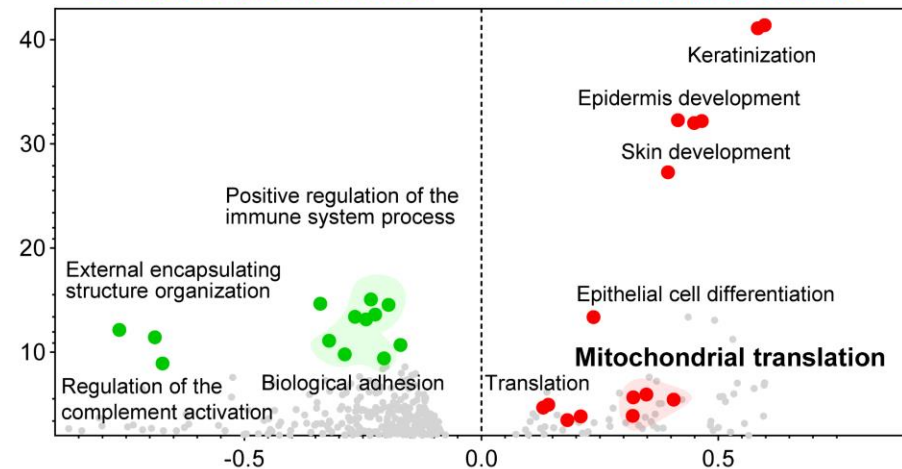


Tumor cells (Recurrent - Non-recurrent)

Molecular signature in stroma

Non-recurrent melanomas

Recurrent melanomas

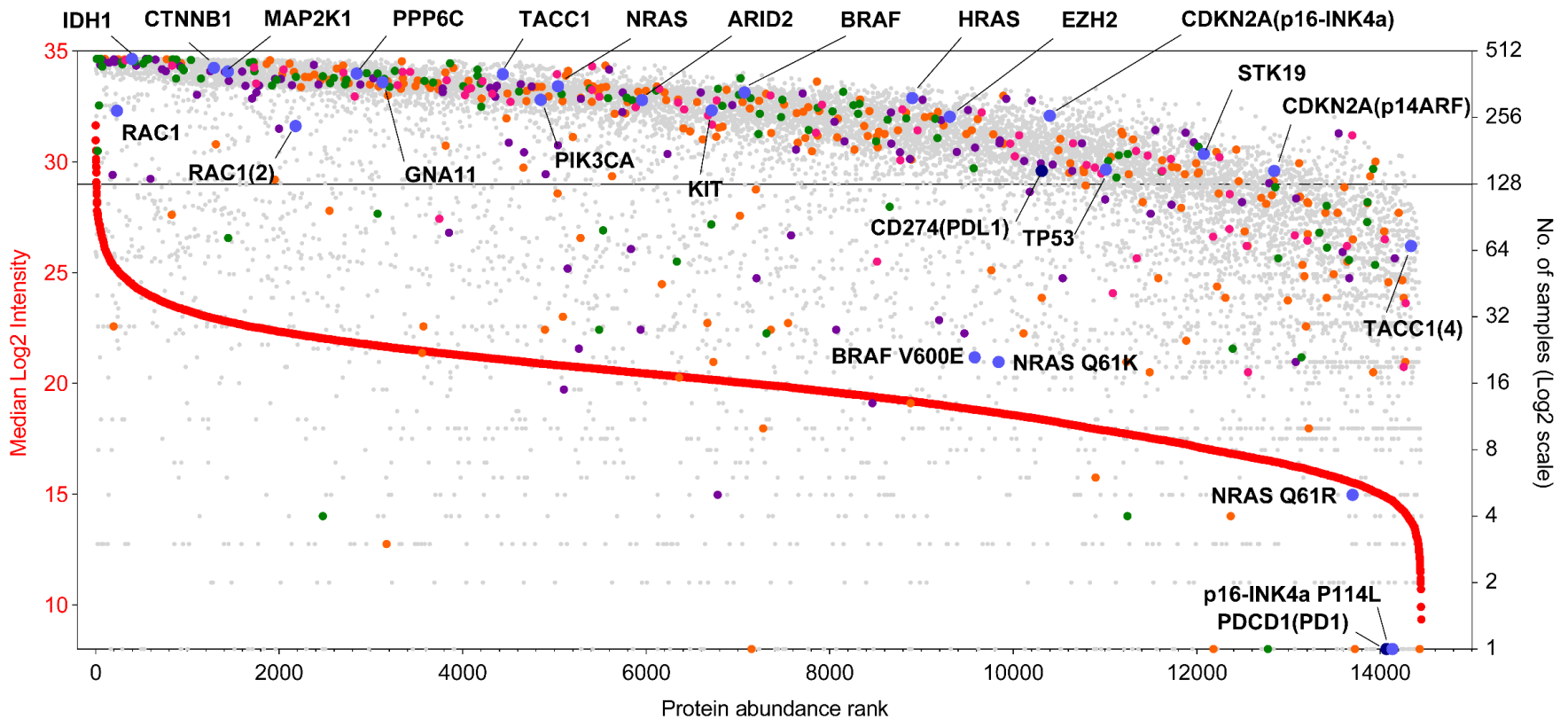


Stroma (Recurrent - Non-recurrent)

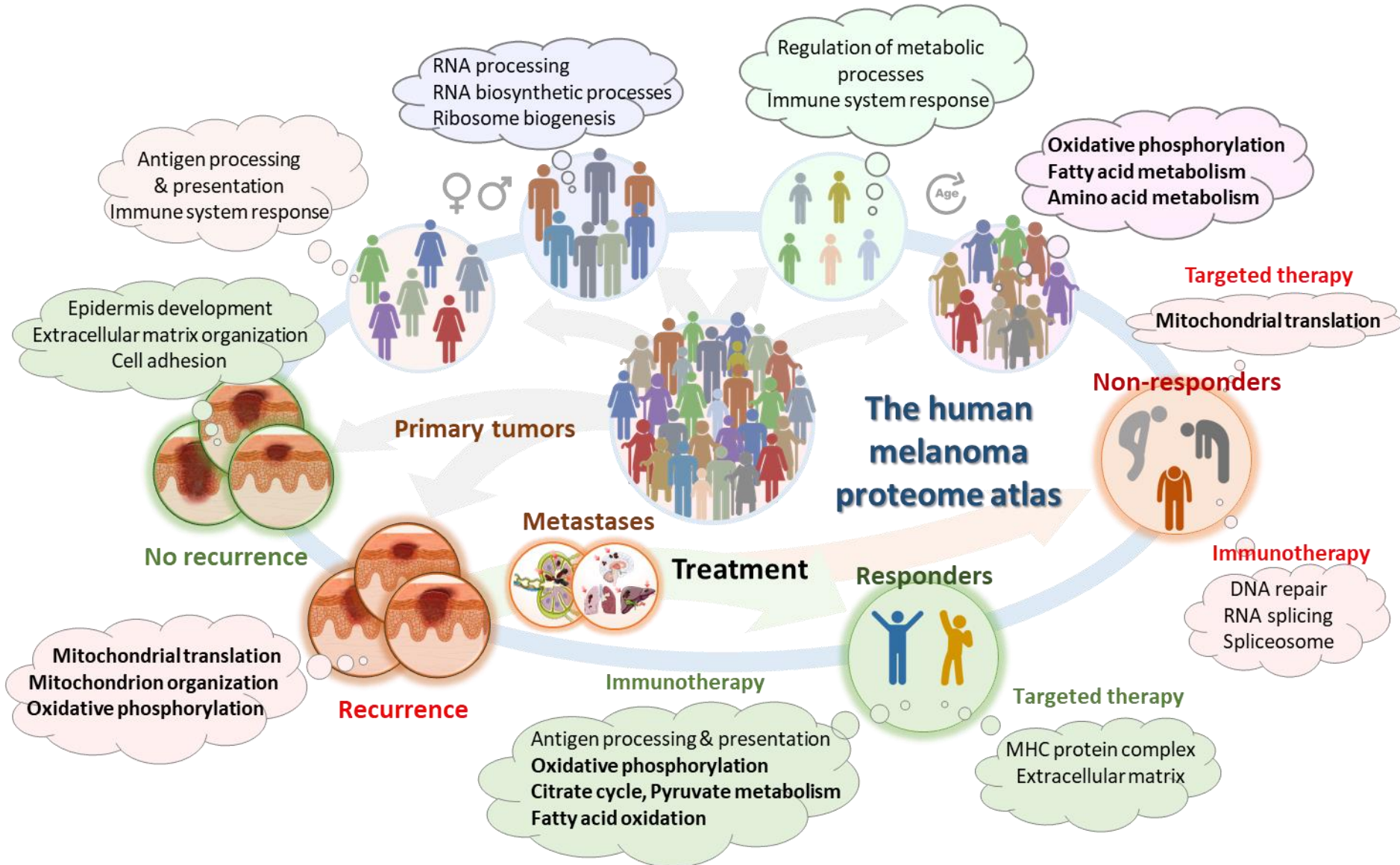
The MM500 study covering to a large extent the melanoma disease presentation

The human melanoma proteome atlas

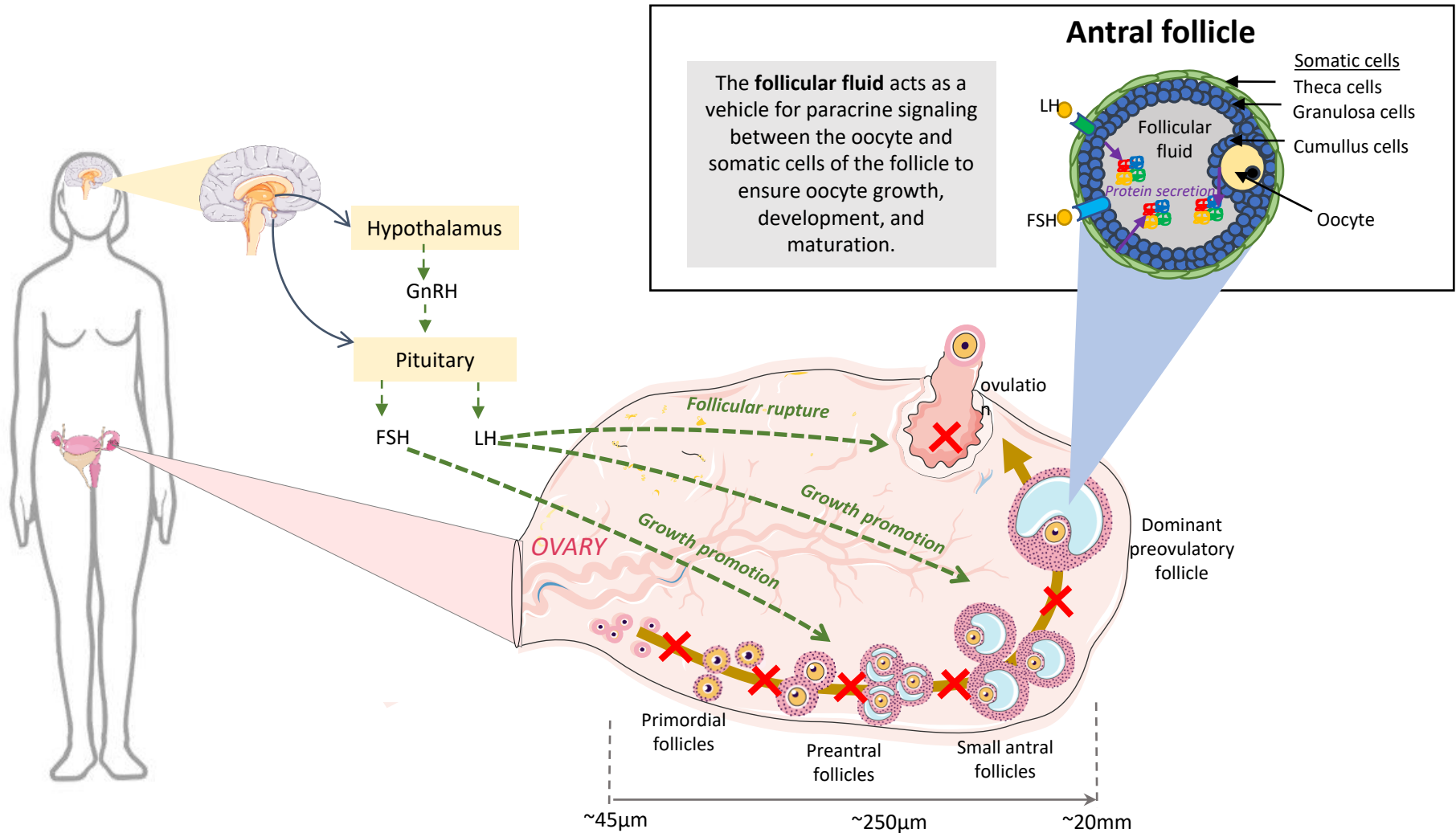
+16 000 proteins
50 000 phosphorylation sites
4 000 lysine acetylation sites



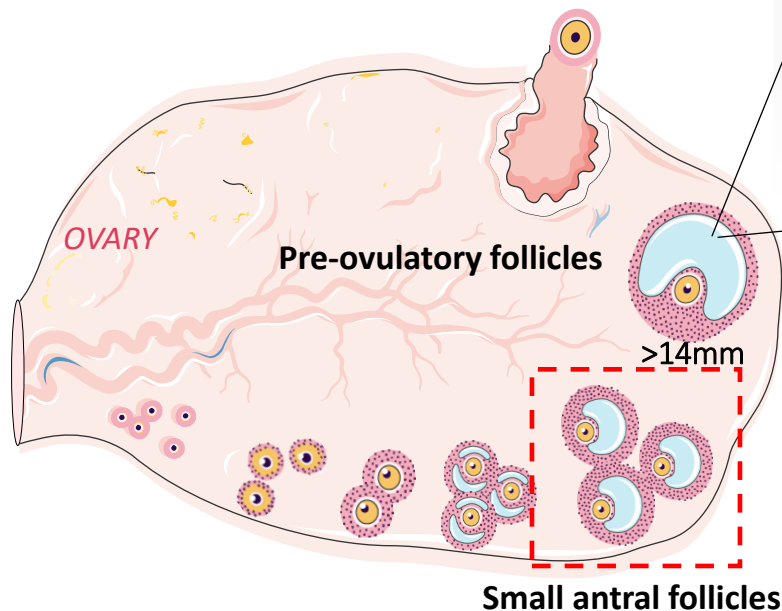
The melanoma disease presentation at the functional proteome level



Female reproductive system



Previous proteomics studies in Follicular Fluid



Proteomics 17, 6, 2017, 1600333

RESEARCH Open Access

RESEARCH ARTICLE
Proteomic analysis of ovarian responder: Proteomic analysis of human follicular fluid from fertile women
 Jae Won Oh^{1,a}, Seul Ki Kim^{2,3}, Alberuni M Zamah¹, Maria E Hassis², Matthew E Albertolle² and Katherine E Williams^{2,3}
 Jung Ryeol Lee^{2,a} and Kwang Ju

Human follicular fluid proteomic and peptidomic composition quantitative studies by SWATH-MS methodology. Applicability of high pH RP-HPLC fractionation

John M. Twigg⁴, Karel Bezstarosti¹, Jeroen Demmers¹, Régine P. Steegers-Theunissen^{4,5}
 Aleksandra E. Lewandowska^{6,a}, Katarzyna Macur⁶, Paulina Czaplowska⁶, Joanna Liss⁶, Krzysztof Łukaszuk^{6,c,d}, Stanisław Oldziej^{6,a}

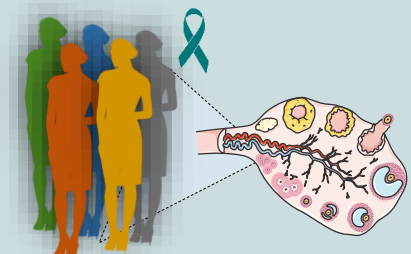
¹Department of Obstetrics and Gynecology, ²Proteomics of Erasmus MC, University Medical Center, Rotterdam, the N

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

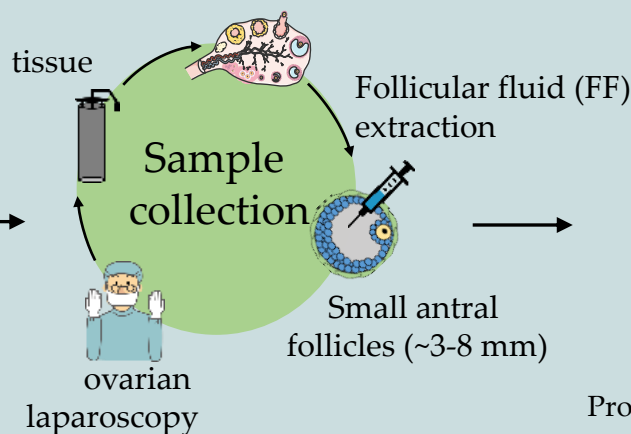
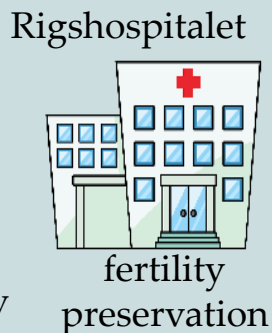
It attenuates the detection of low abundant proteins.

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

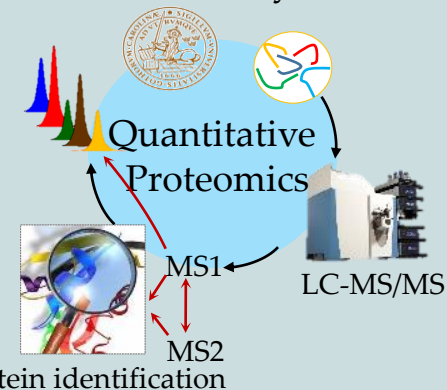
31 unstimulated women



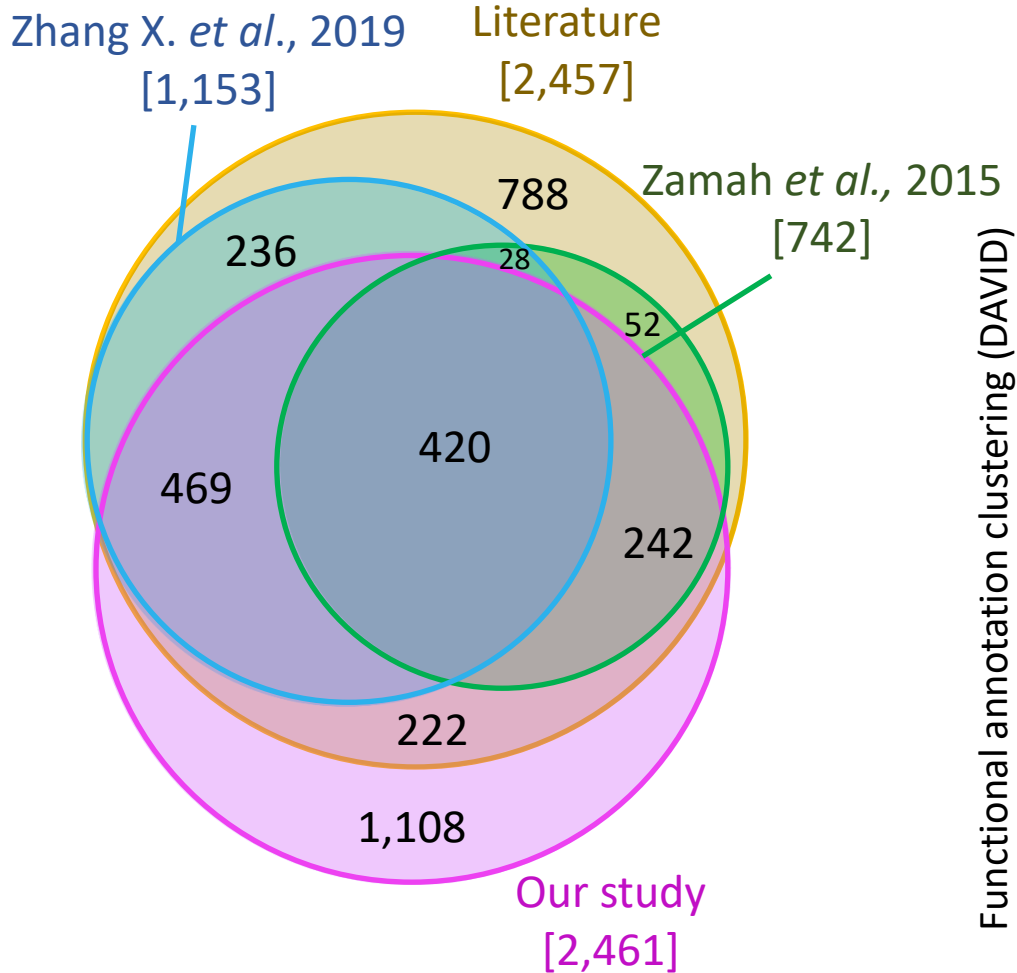
- Diseases unrelated to the ovary
- Ovary with a macroscopically normal appearance.



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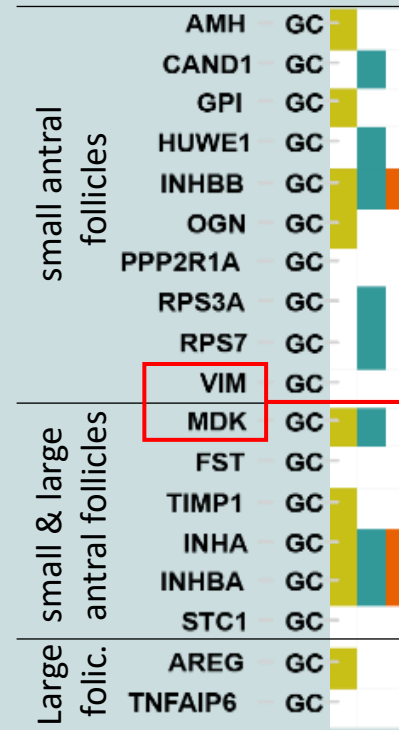


Proteomics of follicular fluids



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

Proteins involved in the ovarian follicle development



Correlation VIM-MDK

r value	p-value
0.727	0.017

(18)

Proteomics of follicular fluids

Proteins related to upcoming oocyte maturation

6 women
(age: 31 ± 1.8)

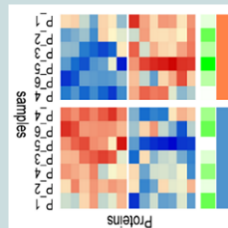


Small antral follicles

in-vitro maturation of the oocytes

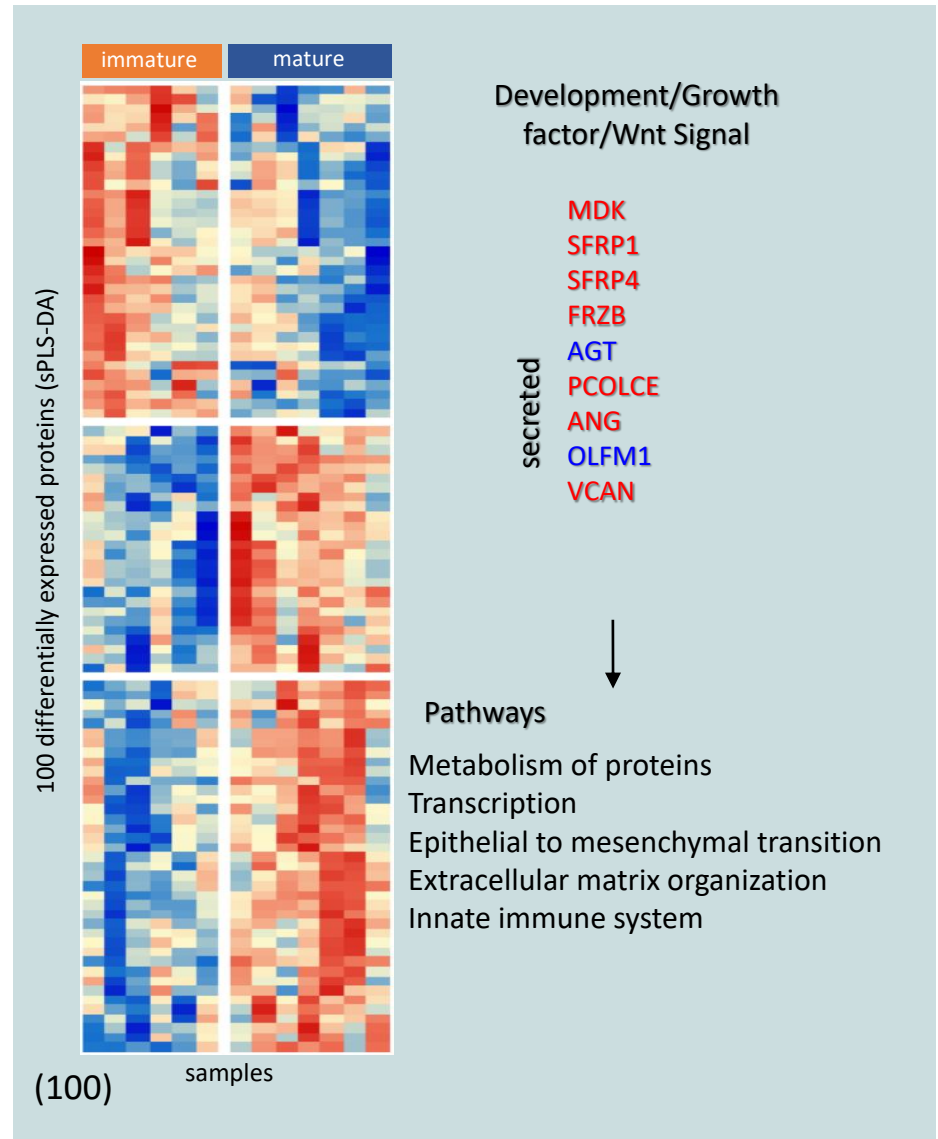
Follicular fluid

LC-MS/MS

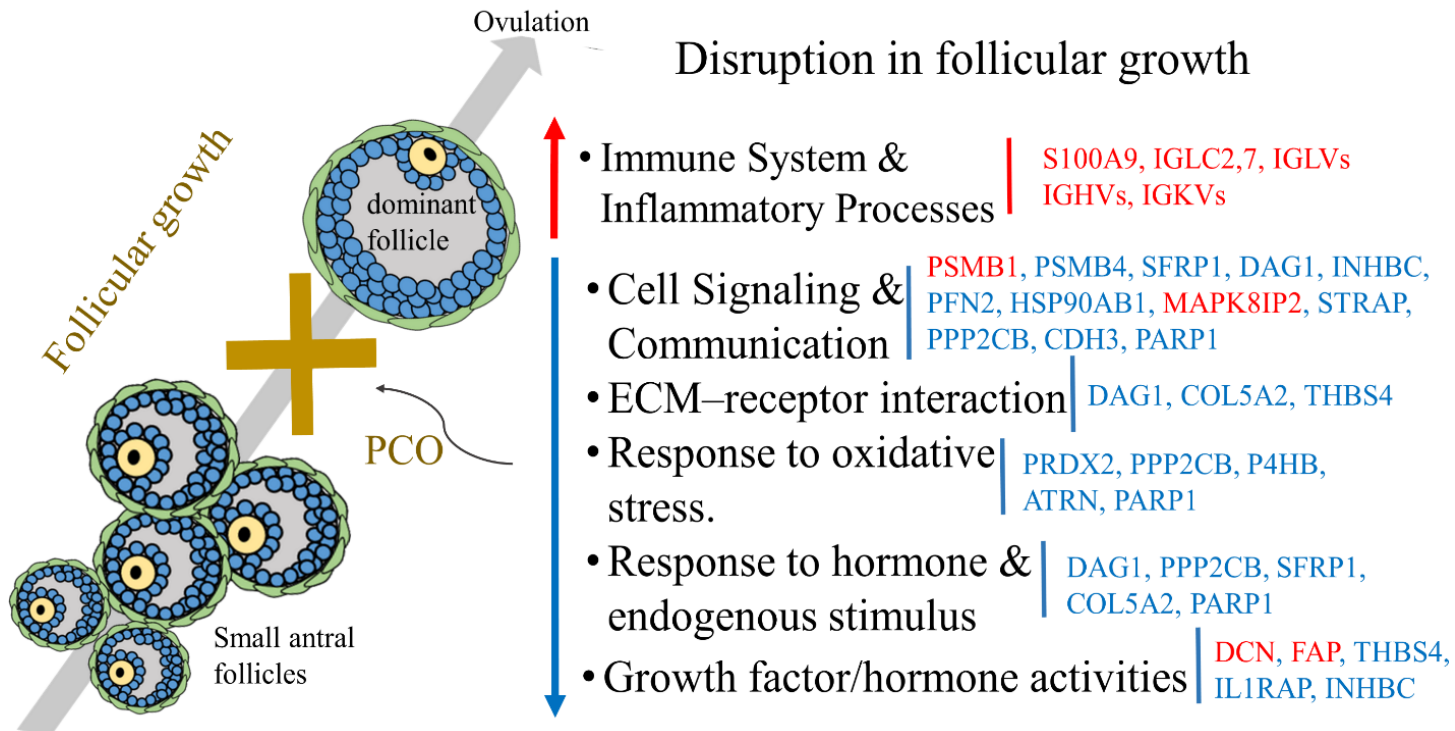
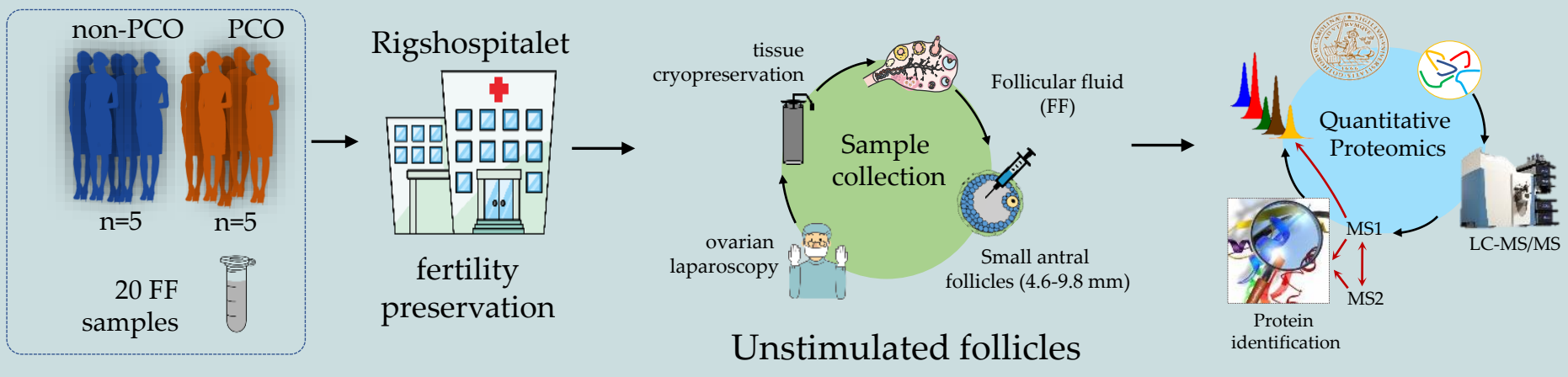


Immature oocyte

Mature Oocyte (MII)



Polycystic ovary syndrome study



Acknowledgements:



university of
 groningen

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Fru Berta
Kamprads
Stiftelse

