

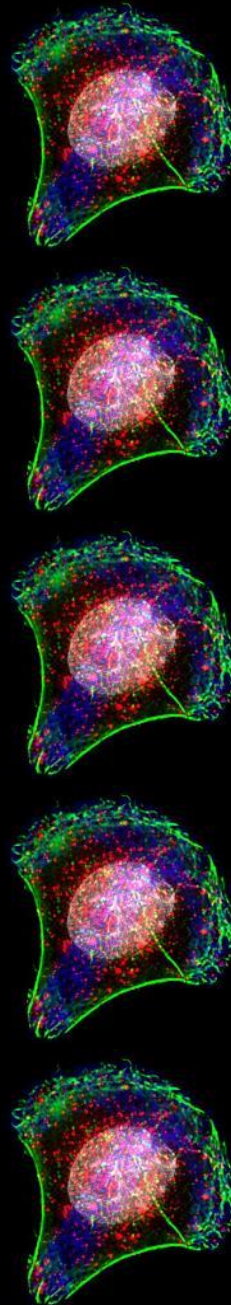
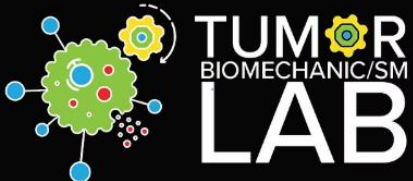
# Peripheral positioning of lysosomes supports melanoma aggressiveness

*Katerina Jerabkova-Roda*

*Postdoctoral researcher*

Tumor Biomechanics lab, Strasbourg, France

14e Forum du Cancéropôle Est, 28<sup>th</sup> November 2025





Why are some cells more aggressive than others?

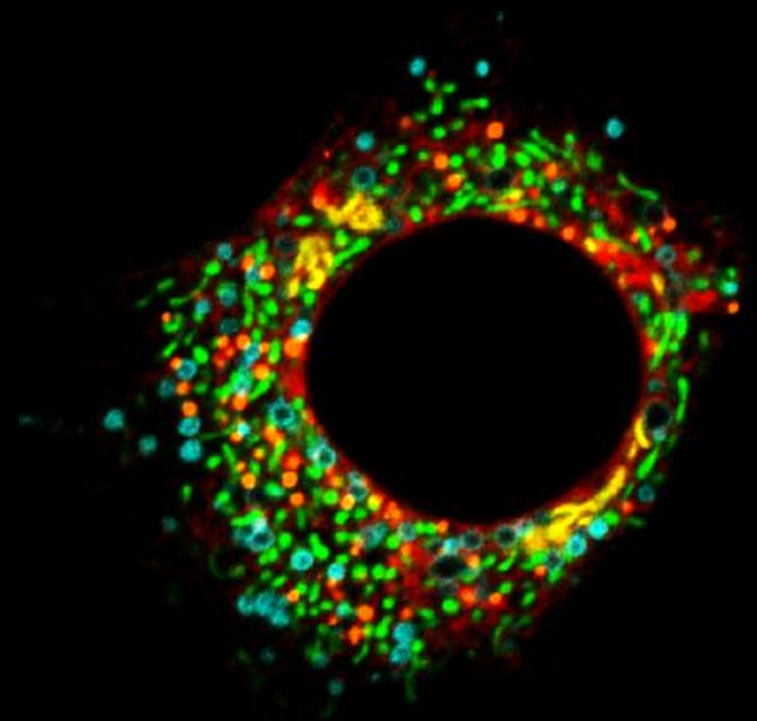
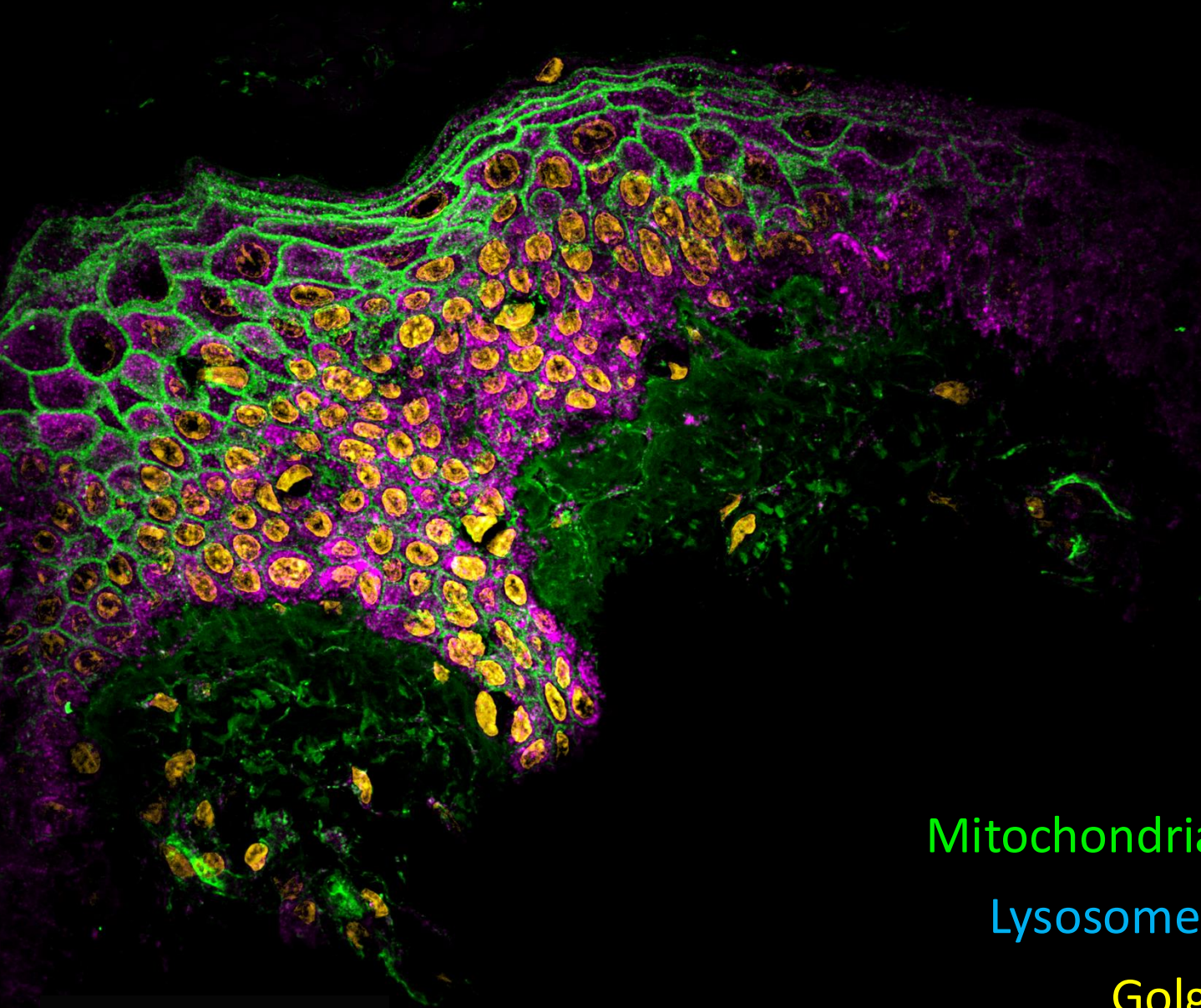
Transcriptional profiles  
Subcellular architecture

Mitochondria

Lysosomes

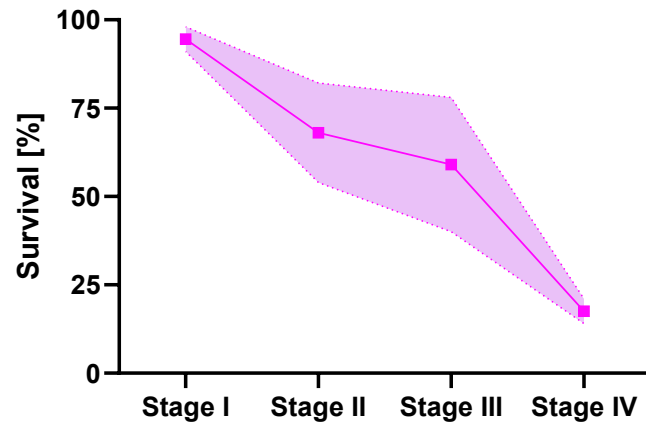
Golgi

ER



# Melanoma model to study phenotypic transitions

Patient 5-year survival



Stage 0-II. = 96%, Stage IV. = 15%-25%

No molecular marker for diagnosis

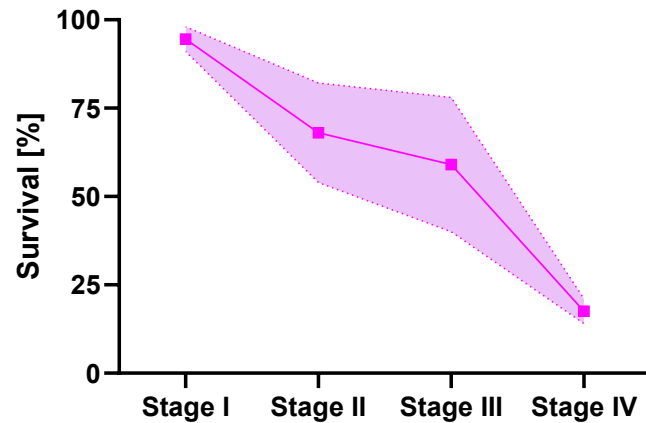


Main risk factor: UV radiation



# Melanoma model to study phenotypic transitions

Patient 5-year survival



Stage 0-II. = 96%, Stage IV. = 15%-25%

No molecular marker for diagnosis

Radial Growth

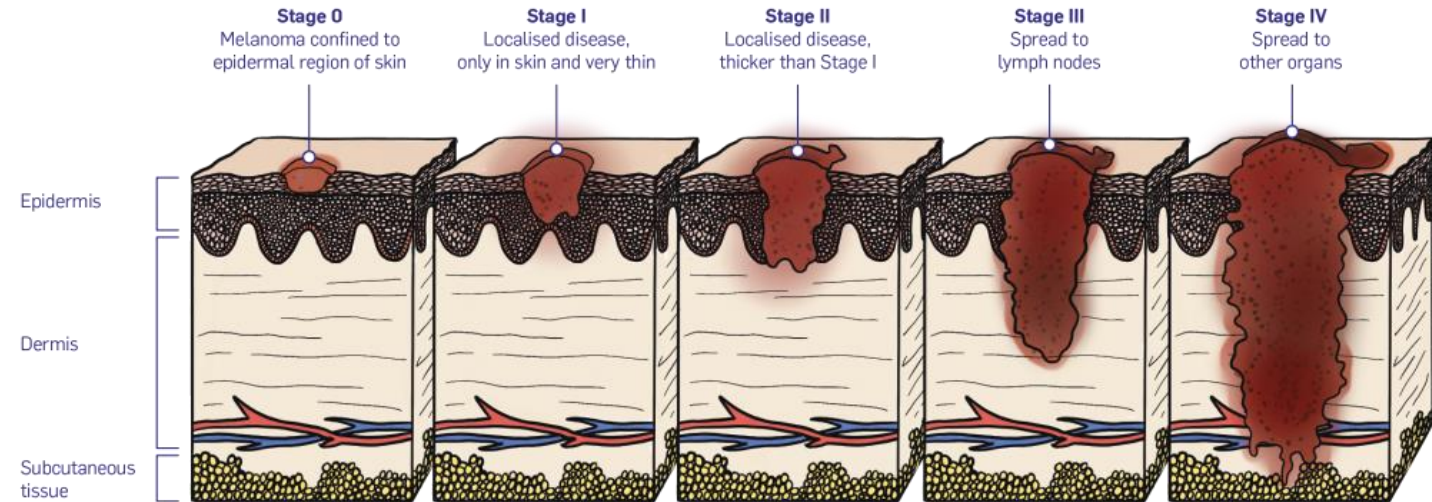
RGF

Vertical Growth

VGP

Metastatic

Met



*Melanoma and Skin Cancer Advocacy Network*

Panel of Patient-derived cells

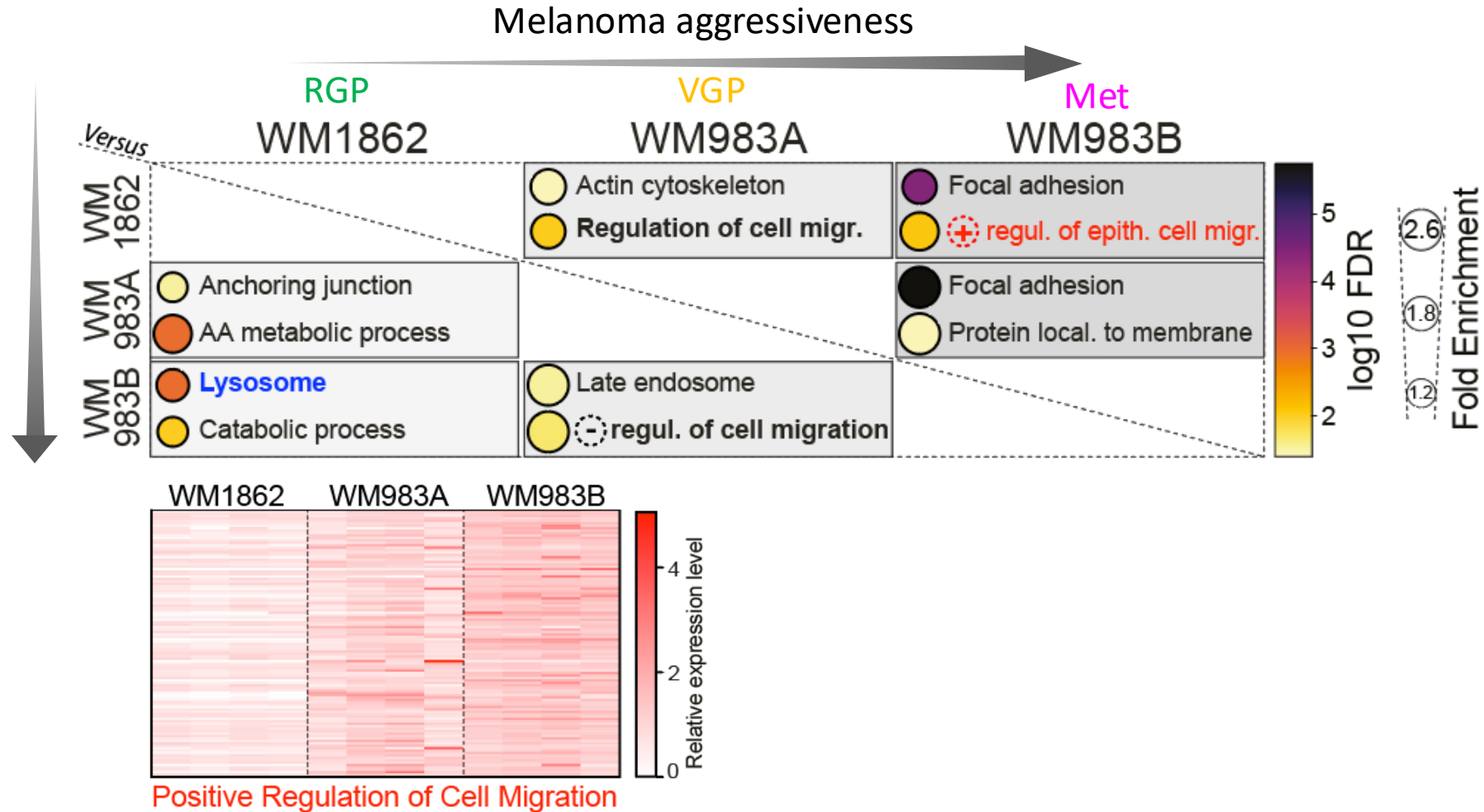
	Healthy	RGF		VGP		Metastasis	
Cell line	Melanocyte	WM1862	WM1552c	WM983A	WM115	WM983B	A375
Mutations	-	BRAF V600E	BRAF V600E PTEN	BRAF V600E	BRAF V600D PTEN	BRAF V600E	BRAF V600E CDKN2A



Main risk factor: UV radiation

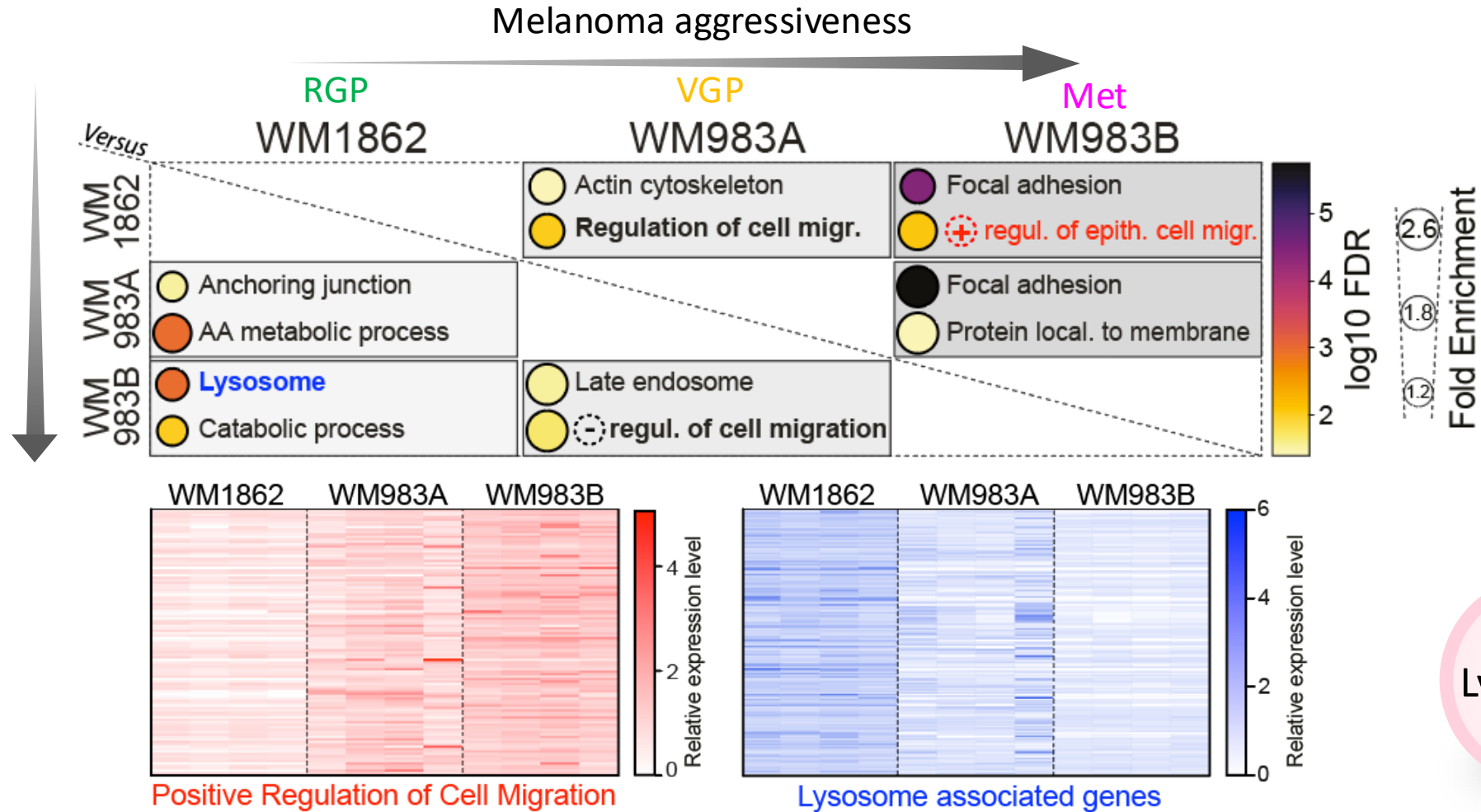
# What drives melanoma cell adaptation?

## Transcriptomics analysis

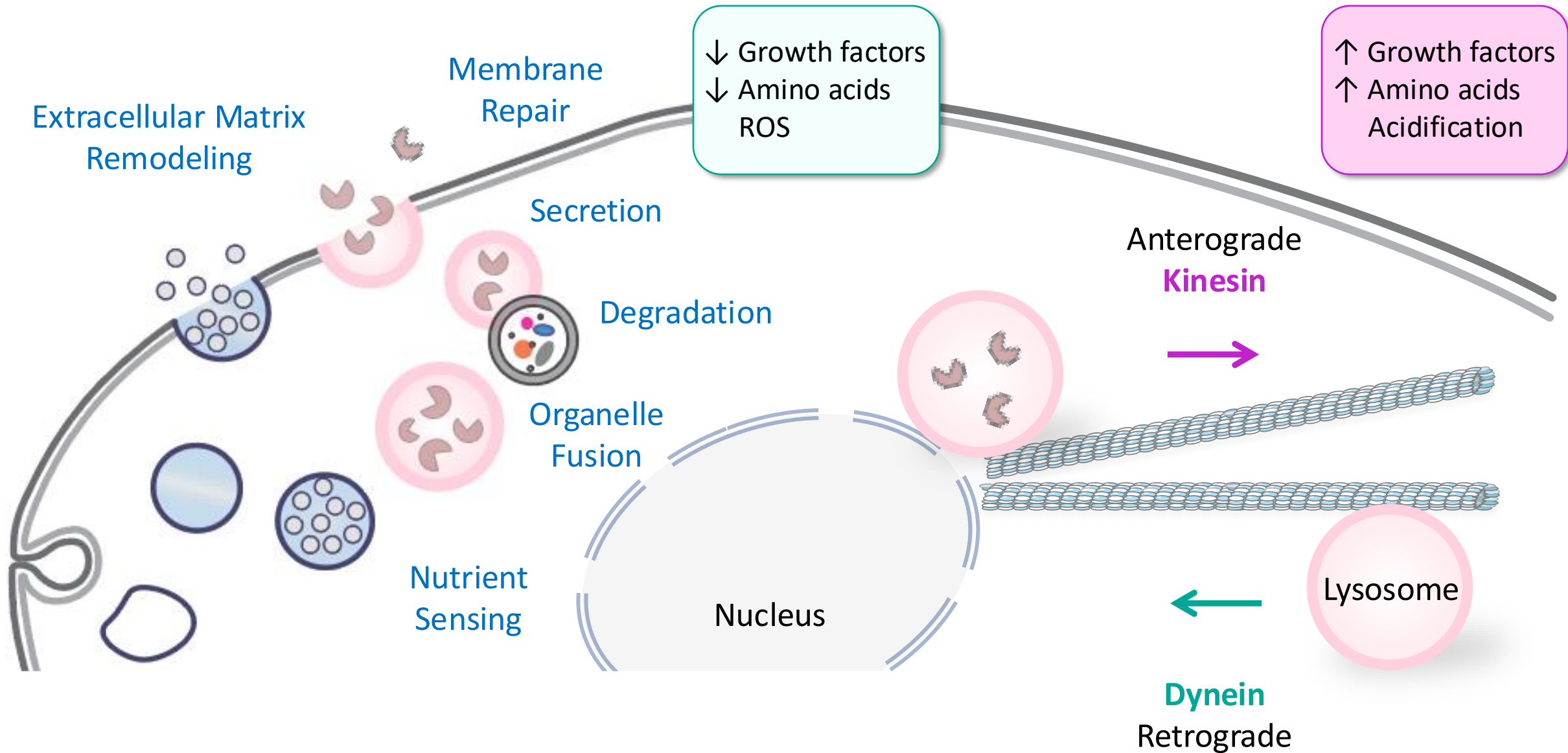


# What drives melanoma cell adaptation?

## Transcriptomics analysis

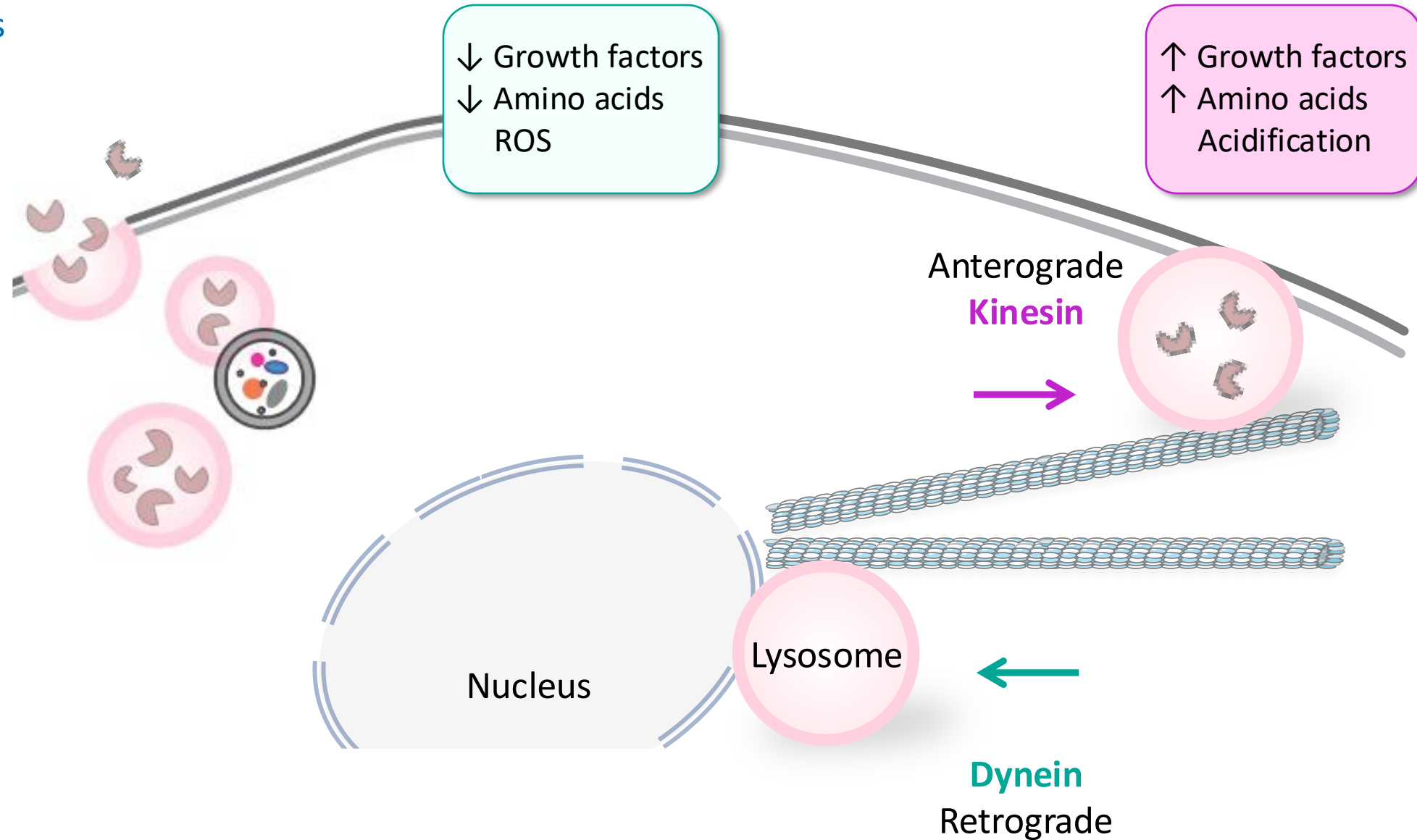
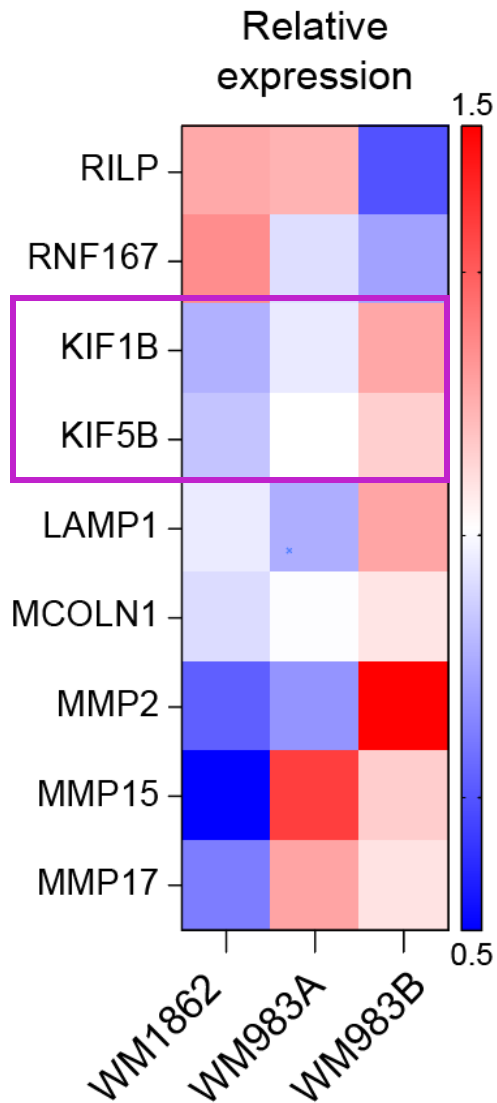


# Lysosomes are important signaling hubs of the cells



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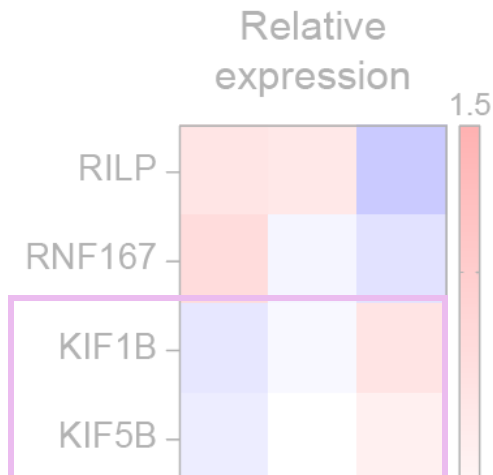
## Transcriptomics analysis



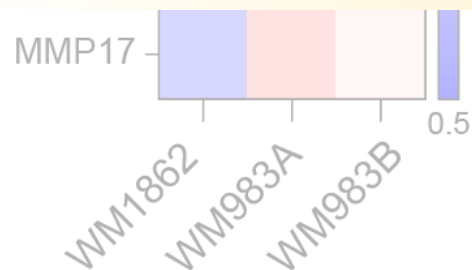


# Lysosomes are important signaling hubs of the cells

## Transcriptomics analysis



Is lysosome positioning changing along melanoma progression?



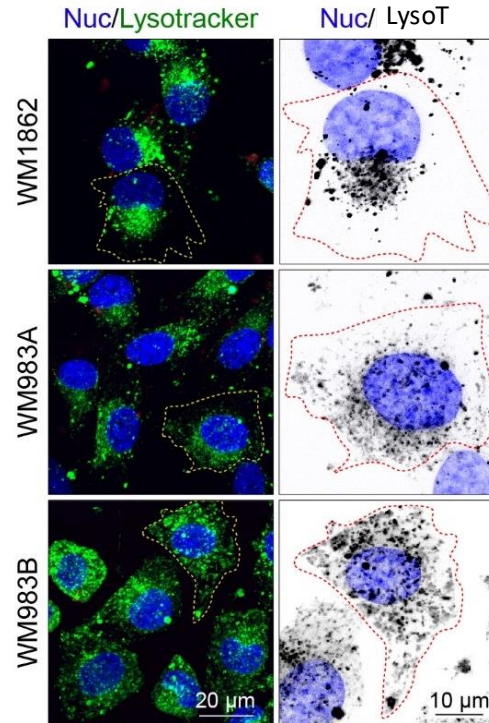
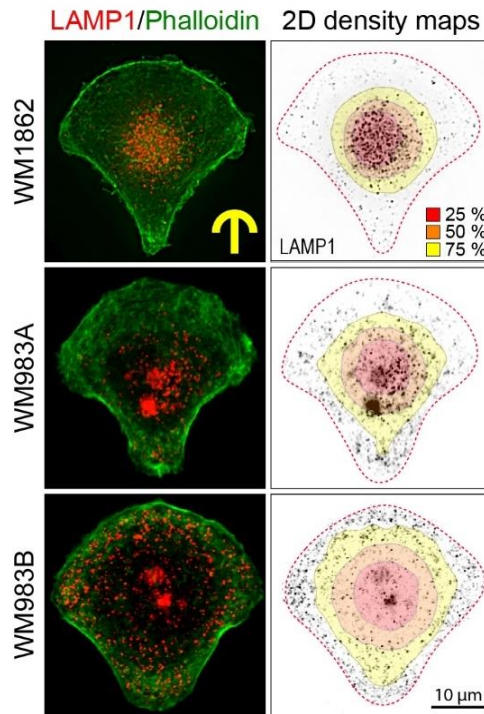
# Lysosome positioning in aggressive melanoma cells

Patient-derived melanoma cells

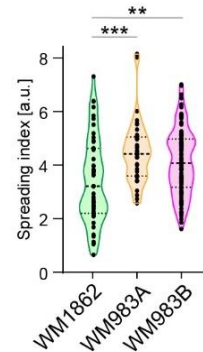
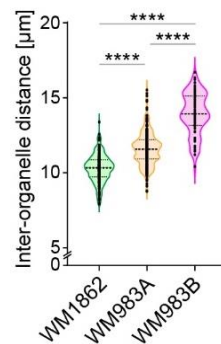
## Micropatterning

## Live imaging

Melanoma invasiveness



Peripheral lysosomes



# Lysosome positioning in aggressive melanoma cells

Patient-derived melanoma cells

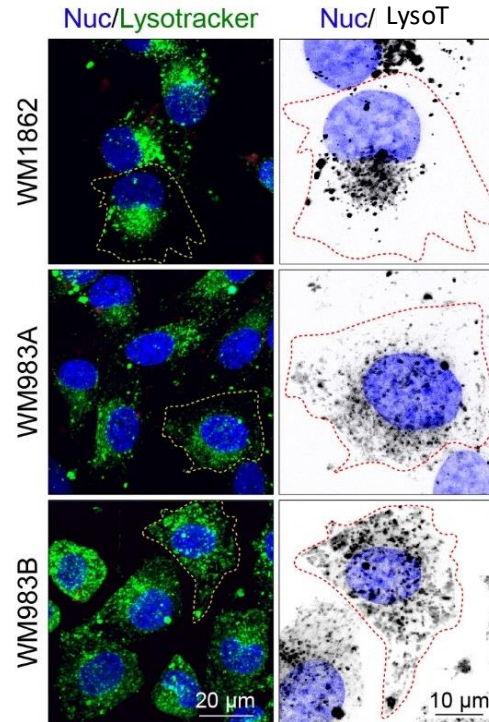
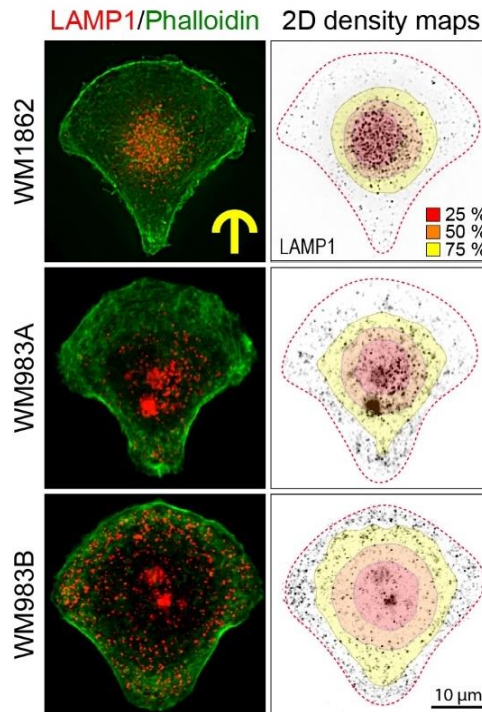
Patient tumor biopsies

## Micropatterning

## Live imaging

## Immunofluorescence

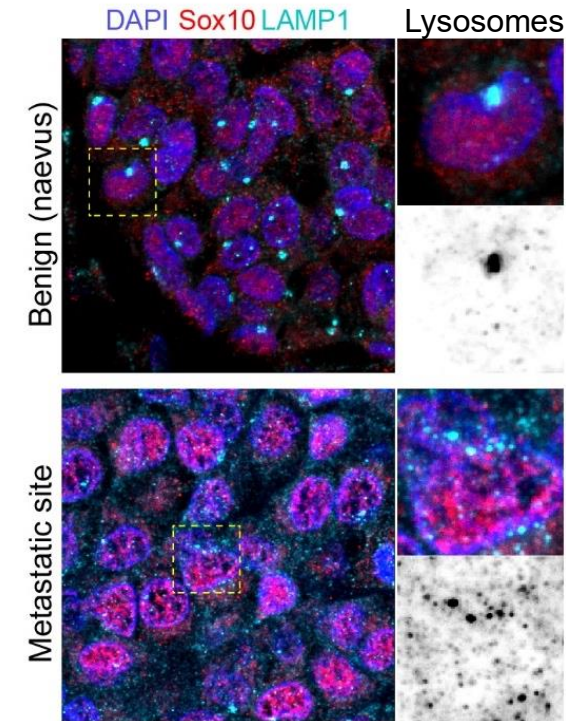
Melanoma invasiveness



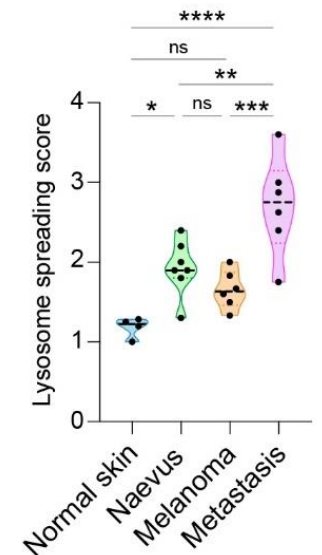
Benign (naevus)



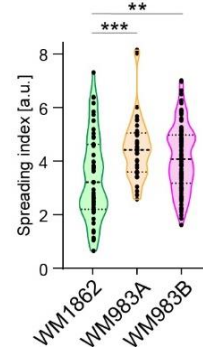
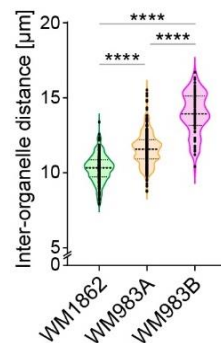
Metastatic site



Peripheral lysosomes



Peripheral lysosomes



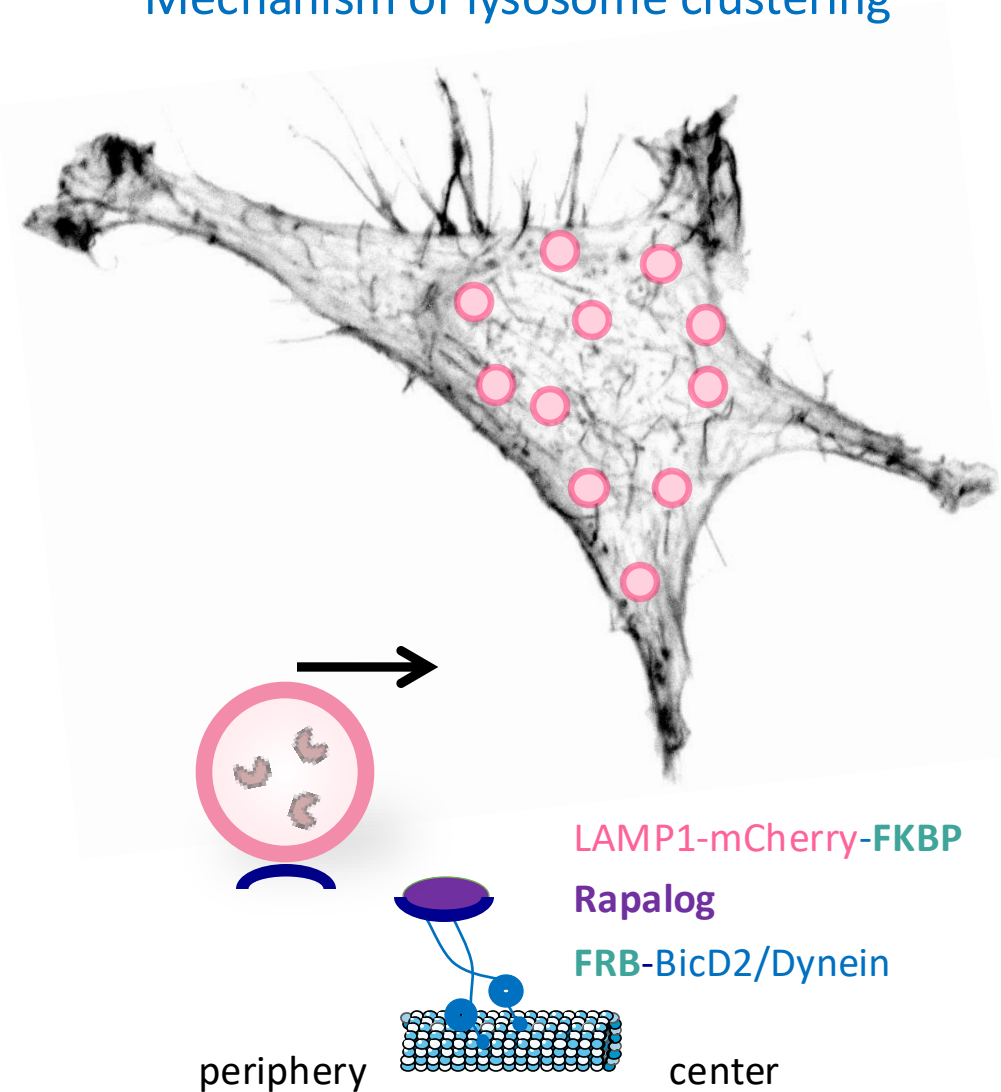
Aggressive cells = scattered lysosomes

Lysosomes are repositioned to cell periphery during melanoma progression



# Tuning lysosome positioning to study its impact on cell invasiveness

## Mechanism of lysosome clustering

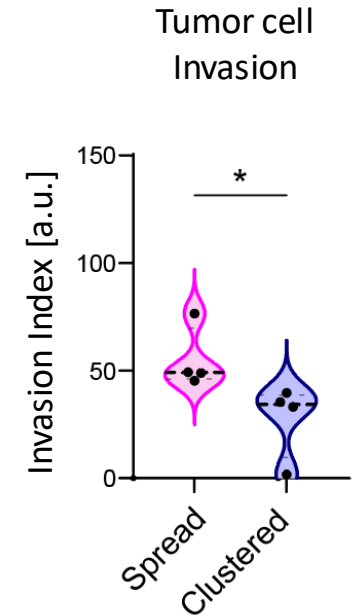
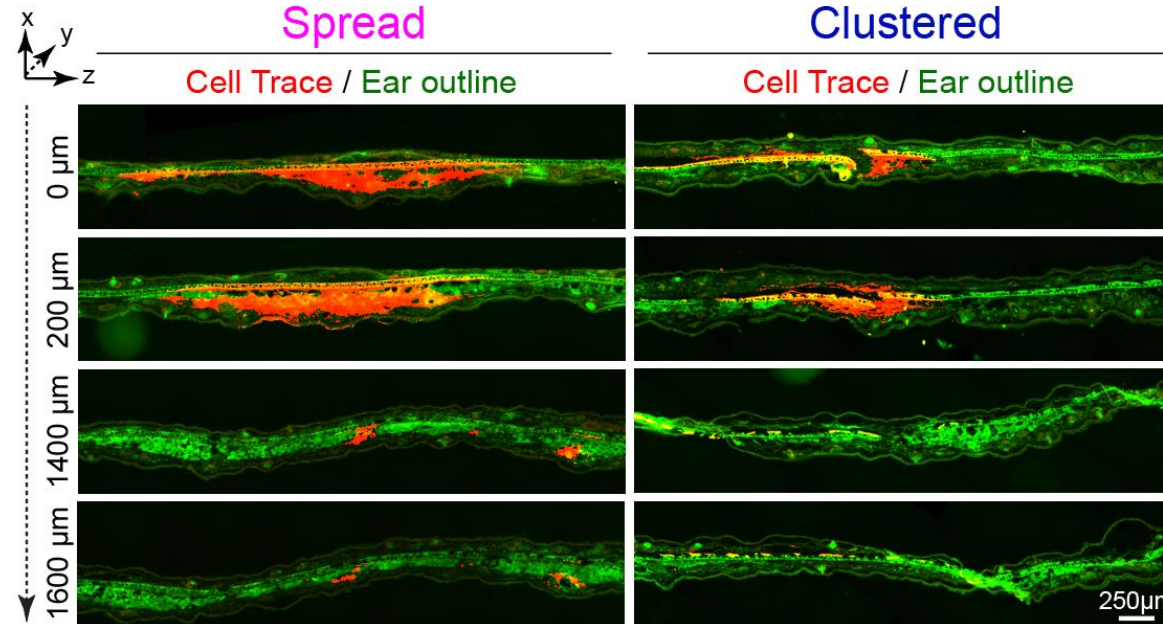
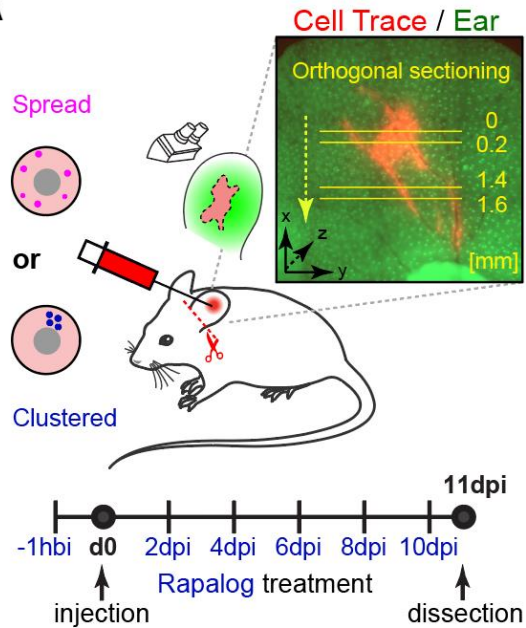


# *In vivo* implications of lysosome re-positioning



## Intra-dermal injection of melanoma cells in mouse ear

A

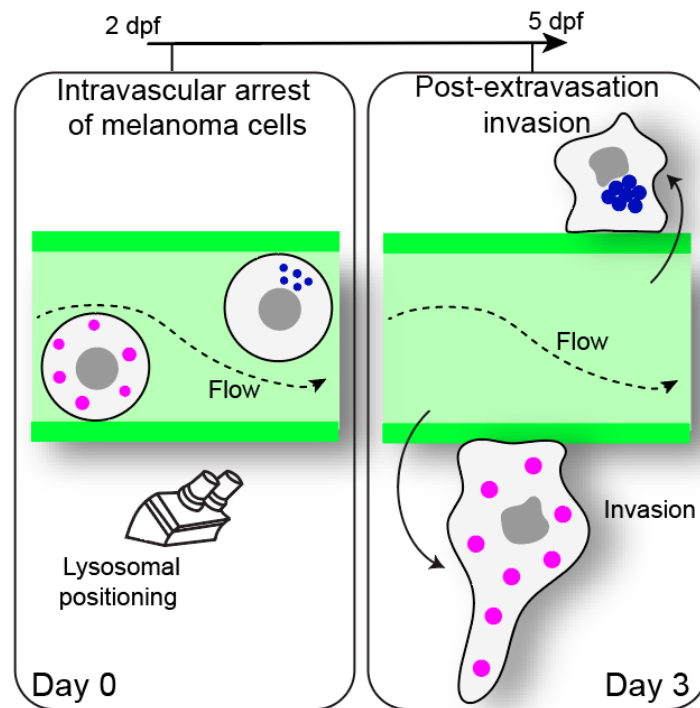
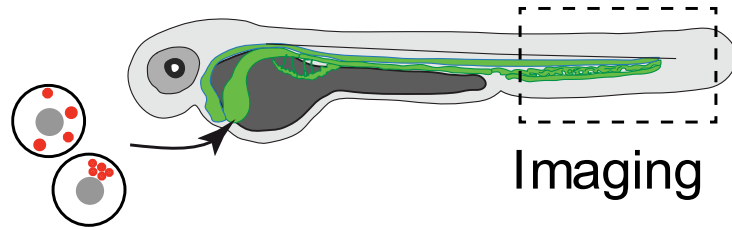


*In vivo* evidence: Peripheral lysosomes promote local cell invasion

# *In vivo* implications of lysosome re-positioning



## Zebrafish model: experimental metastasis

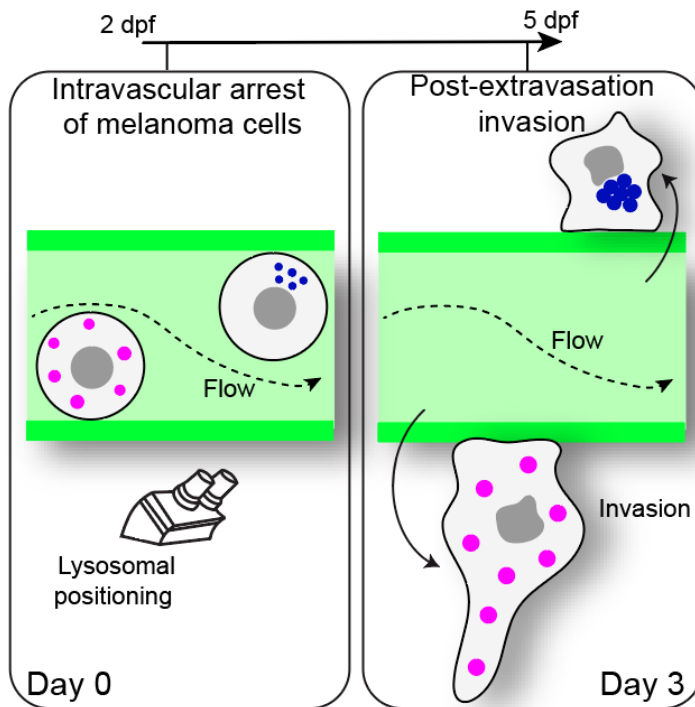
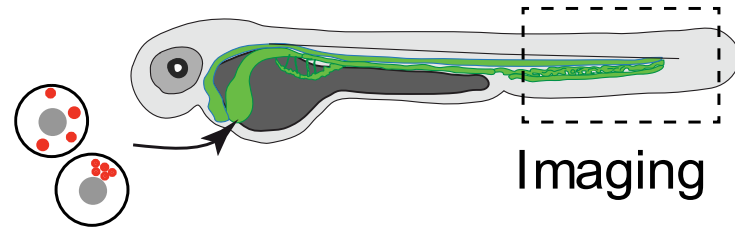




# *In vivo* implications of lysosome re-positioning



## Zebrafish model: experimental metastasis



Spread

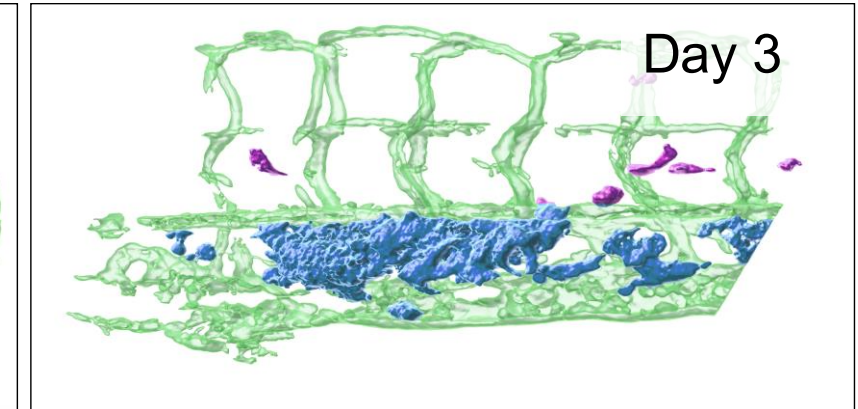
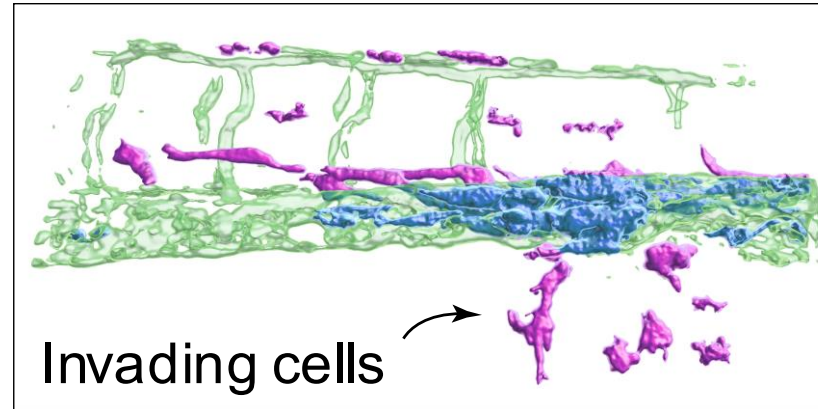
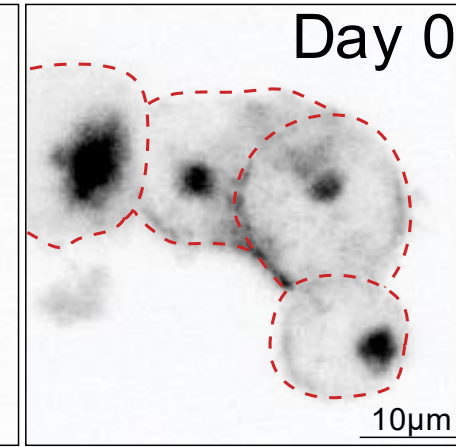
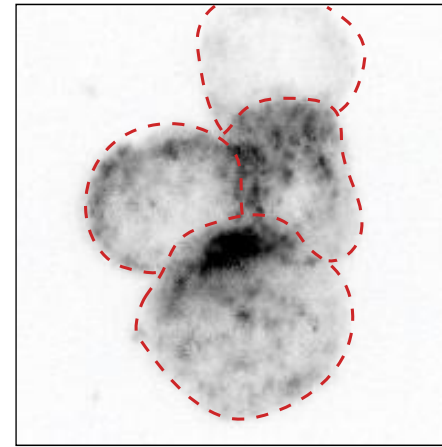
Clustered

Day 0

10μm

Day 3

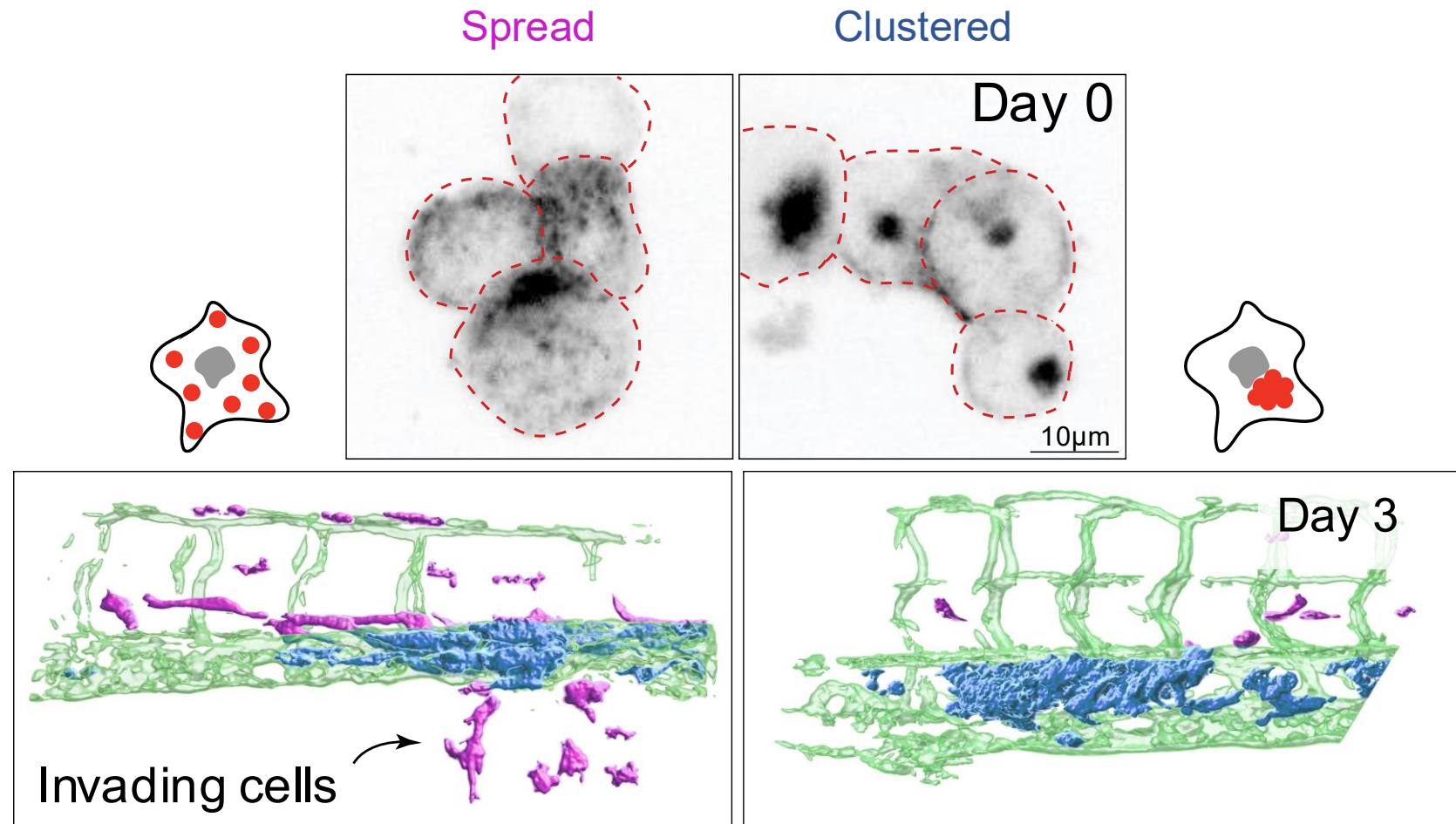
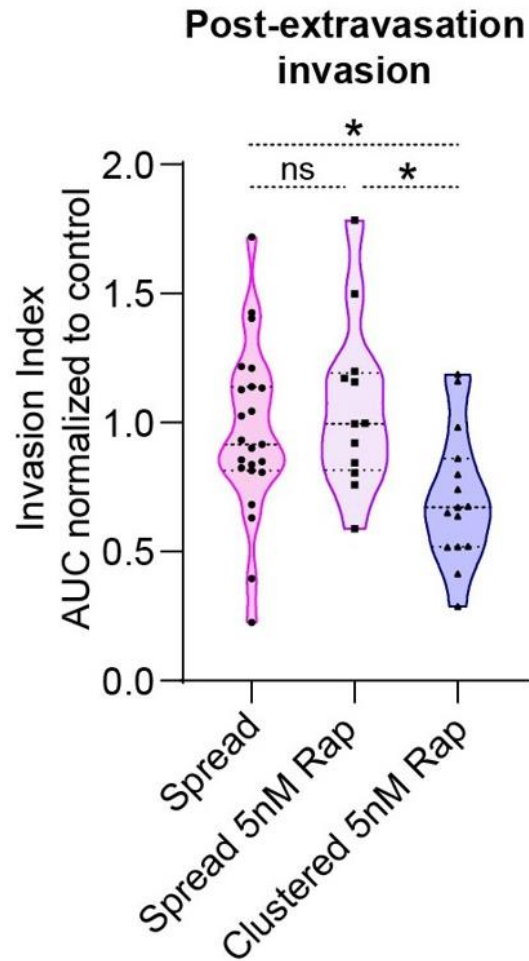
Invading cells



# *In vivo* implications of lysosome re-positioning



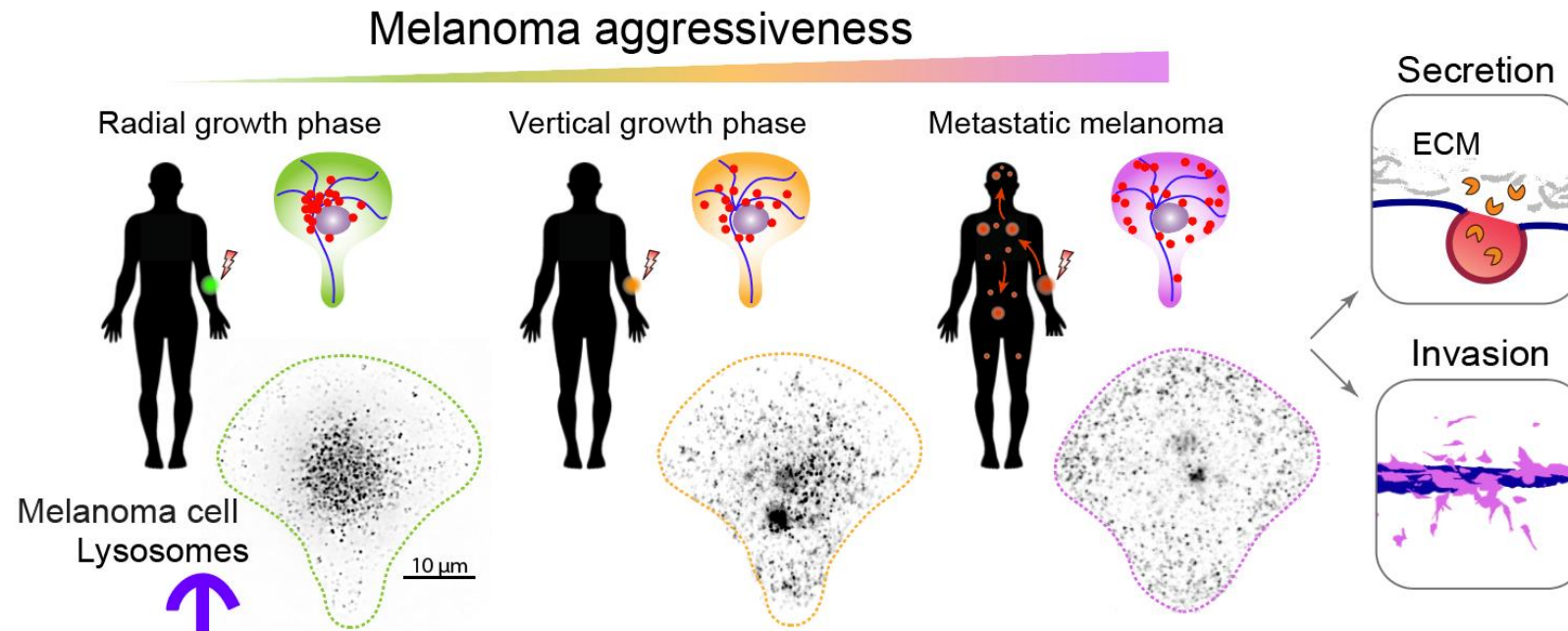
## Zebrafish model: experimental metastasis



Peripheral lysosomes have causal role in cell invasion

# Conclusions & Perspectives

## TAKE HOME MESSAGE:

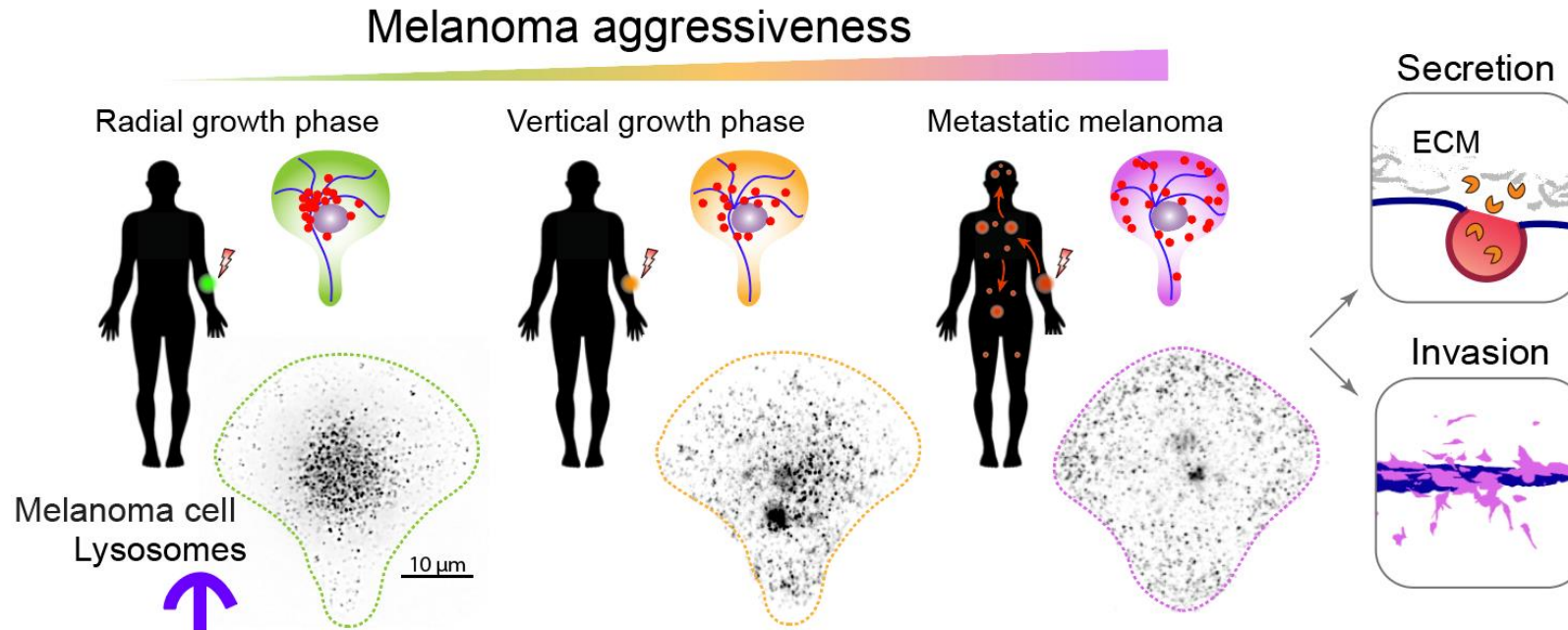


**Lysosomes** are re-positioned towards **cell periphery** in invasive melanoma  
→ increased cell secretion, matrix degradation and invasion



# Conclusions & Perspectives

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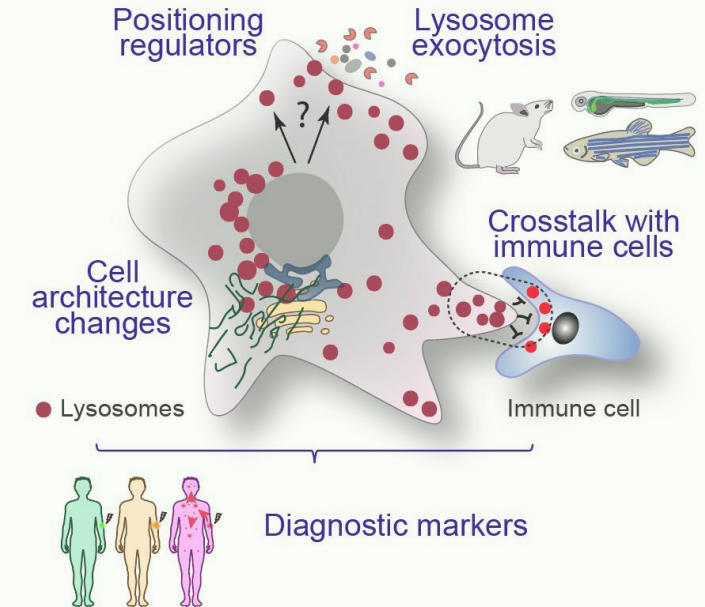


**Lysosomes** are re-positioned towards **cell periphery** in invasive melanoma  
→ increased cell secretion, matrix degradation and invasion

*Jerabkova-Roda et al. Nature Communications, 2025*

## FUTURE DIRECTIONS:

### Melanoma cell adaptation



Potential for **diagnostic/prognostic marker** of metastatic melanoma

Early melanoma detection  
saves lives



# Acknowledgements



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Philippe Ronde

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CRBS PIC-STRA, IGBMC QuEST,

PICT-IBiSA Curie

Genomax sequencing platform

LSMBO Proteomics facility

*Thank you for your attention!*   KatkaJerabkova

