Modelling the tumor microenvironment for therapeutic testing and target identification

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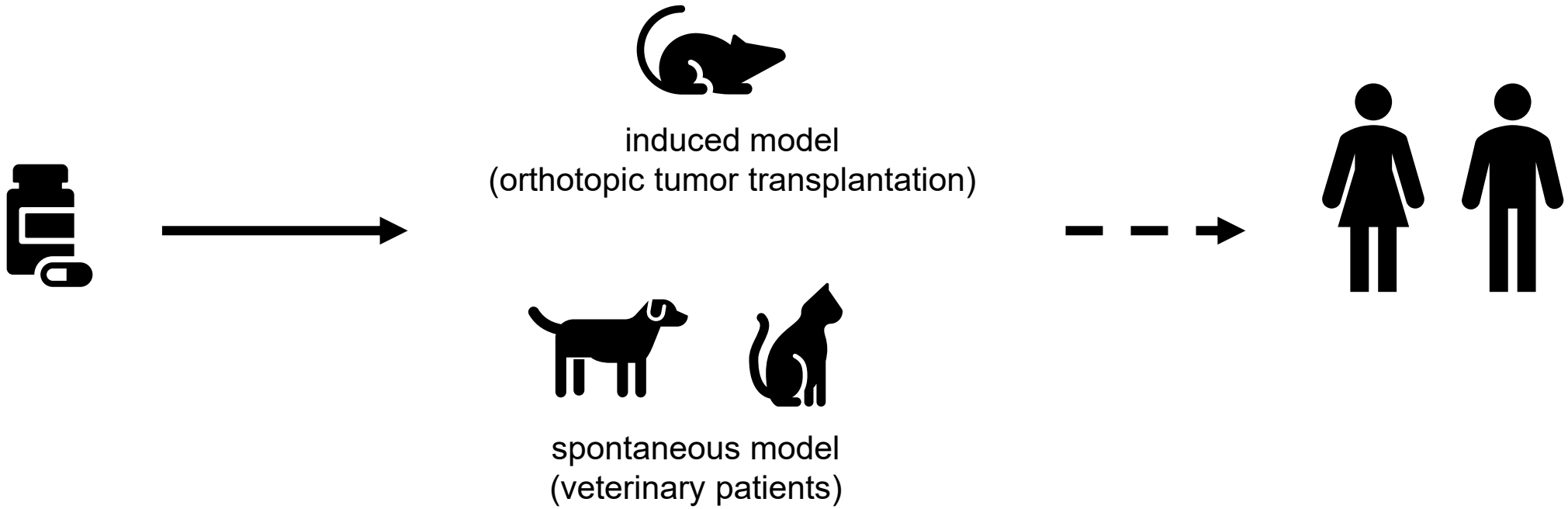
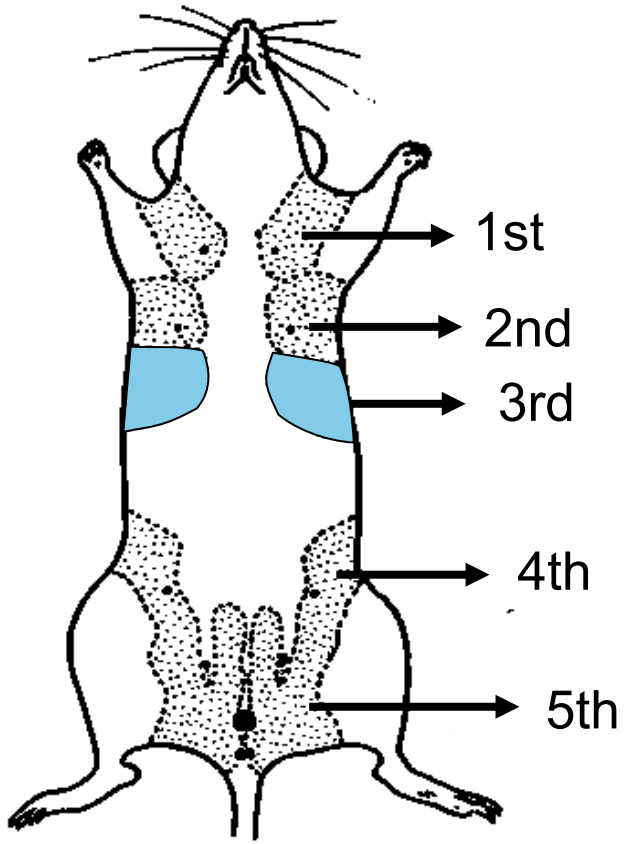
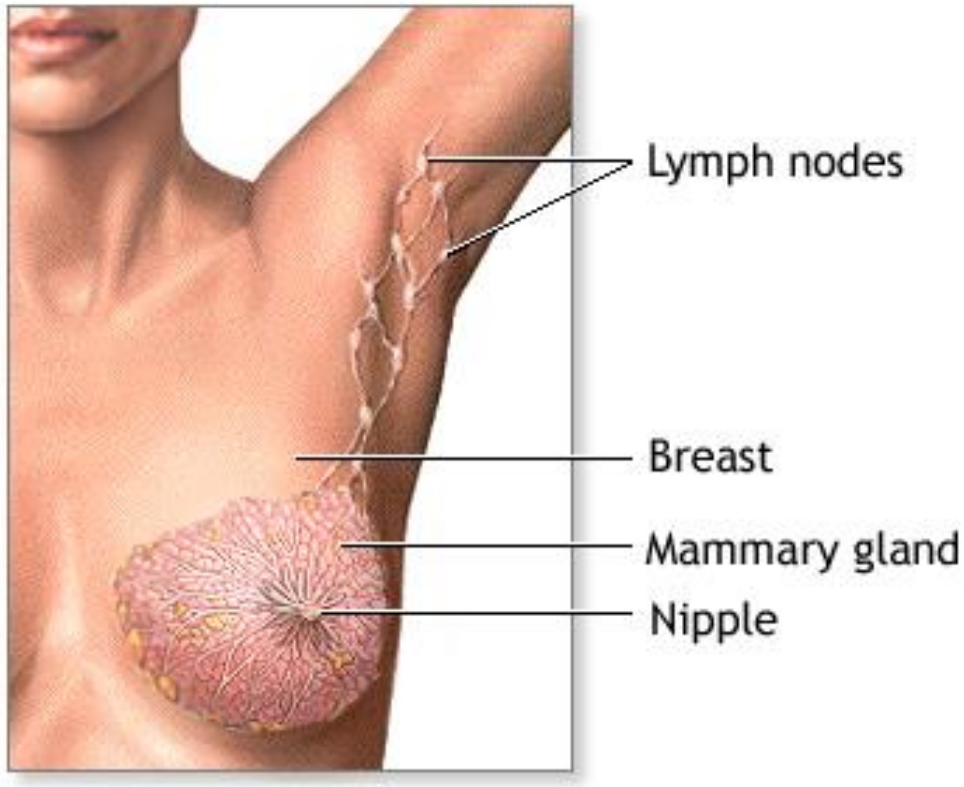
Animal cancer models for clinical translation to the human cancer patient



Orthotopic tumor transplantation: triple-negative breast cancer (TNBC) as an example

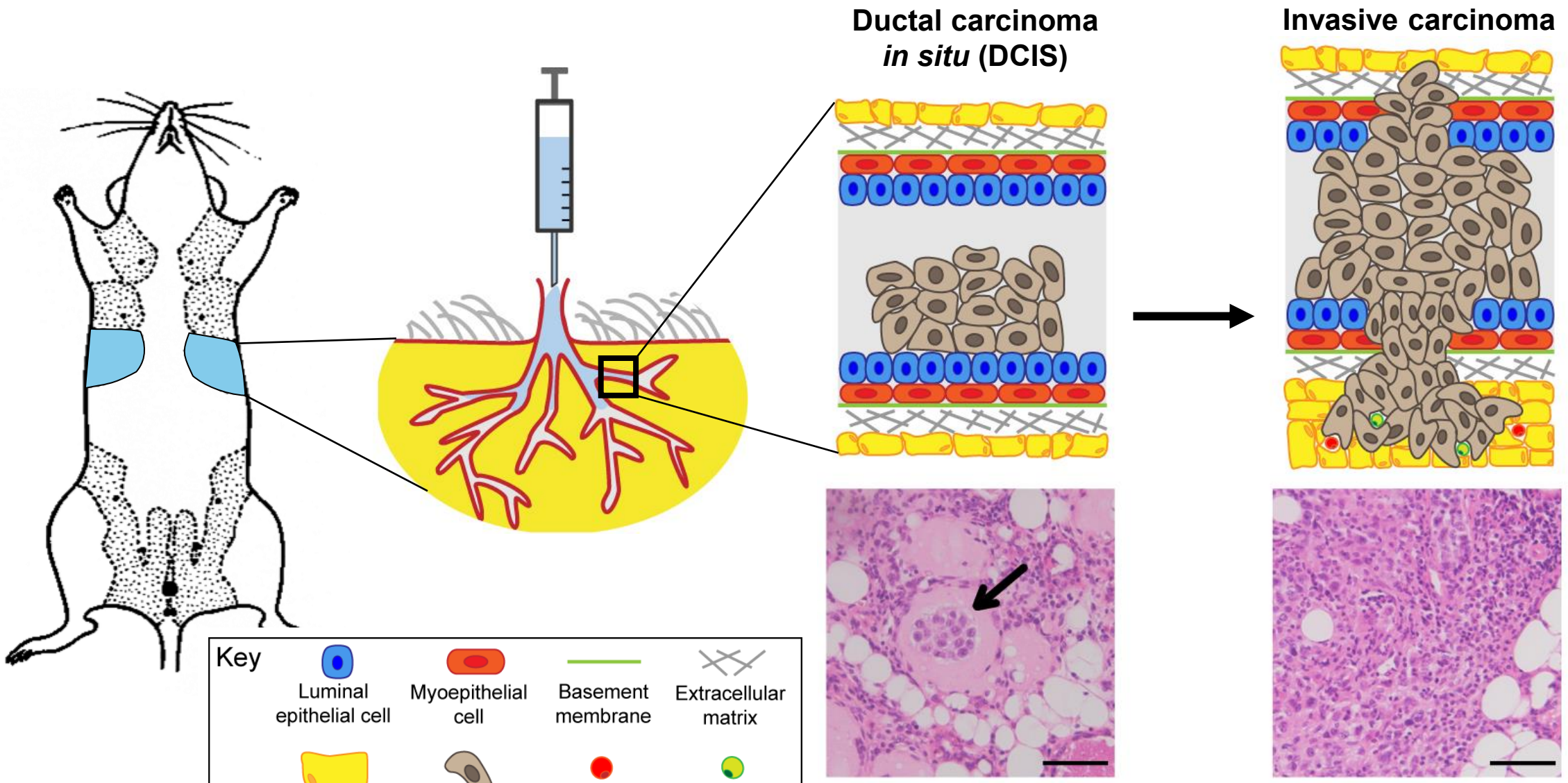
5 mammary gland pairs





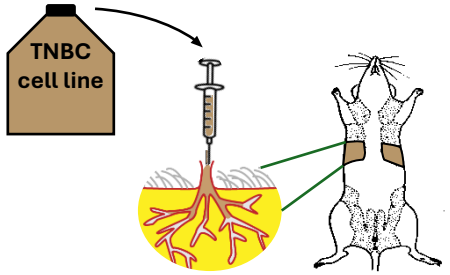
A.D.A.M. Medical Encyclopedia

Intraductally injected mammary tumor cells recapitulate early and late TNBC stages

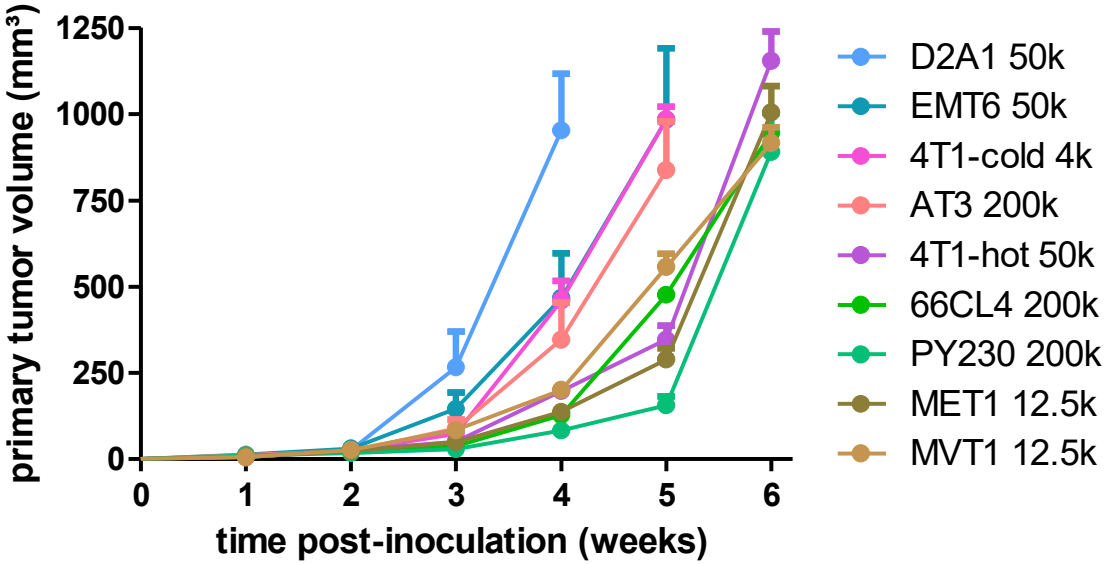


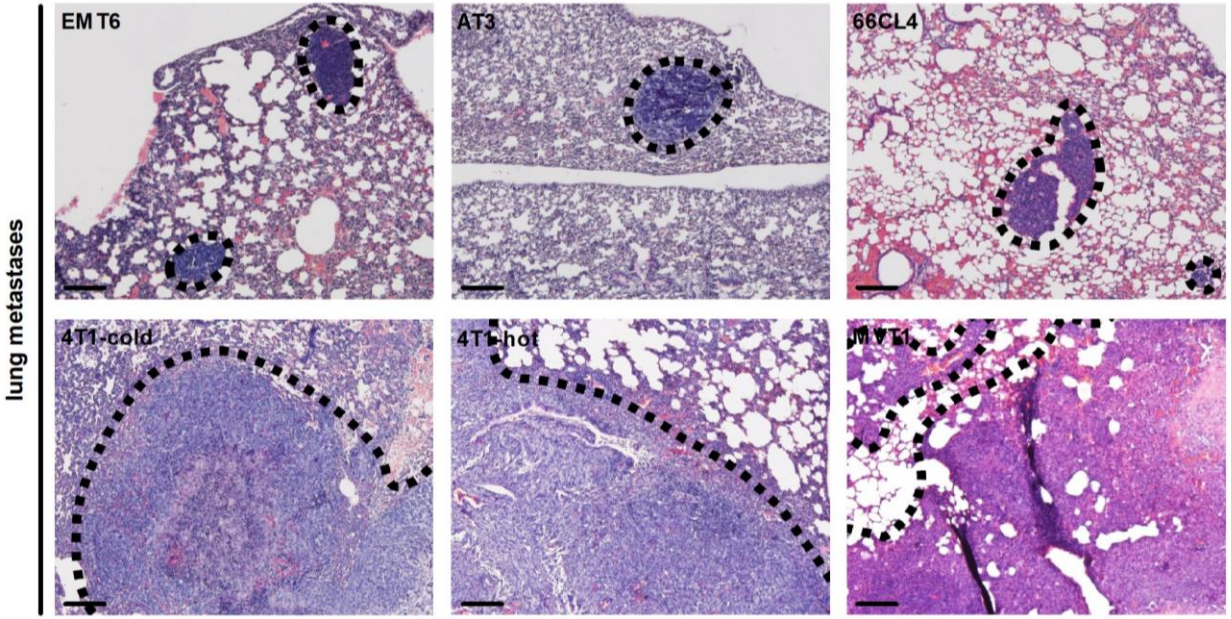
Boiy R & Steenbrugge J et al., Clin Exp Metastasis, 2018

Growth kinetics and metastatic behavior of mouse TNBC cell line-derived primary tumors



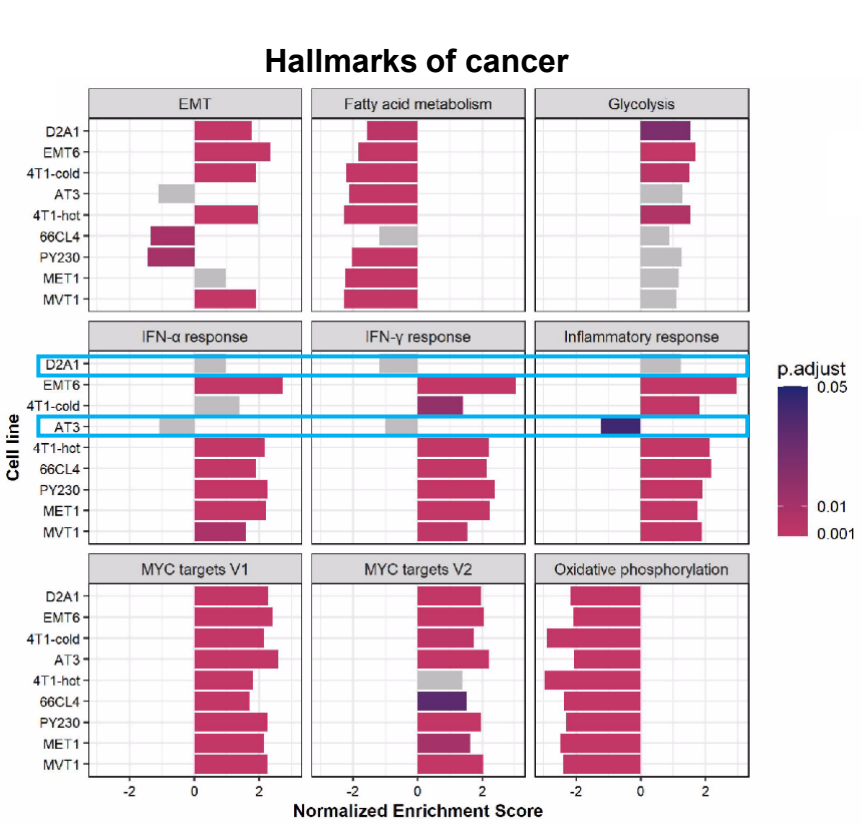
	Mouse TNBC cell line	Mouse strain	Inoculated cell number	Time to reach humane endpoint (weeks)	Lung metastases
1	D2A1	BALB/C	50k	4	- (8/8 mice)
2	EMT6	BALB/C	50k	5	+ (5/8 mice)
3	4T1-cold	BALB/C	4k	5	++ (9/9 mice)
4	AT3	C57BL/6	200k	5	+ (4/8 mice)
5	4T1-hot	BALB/C	50k	6	++ (6/6 mice)
6	66CL4	BALB/C	200k	6	+ (6/10 mice)
7	PY230	C57BL/6	200k	6	- (8/8 mice)
8	MET1	FVB/N	12.5k	6	- (13/13 mice)
9	MVT1	FVB/N	12.5k	6	++ (11/11 mice)

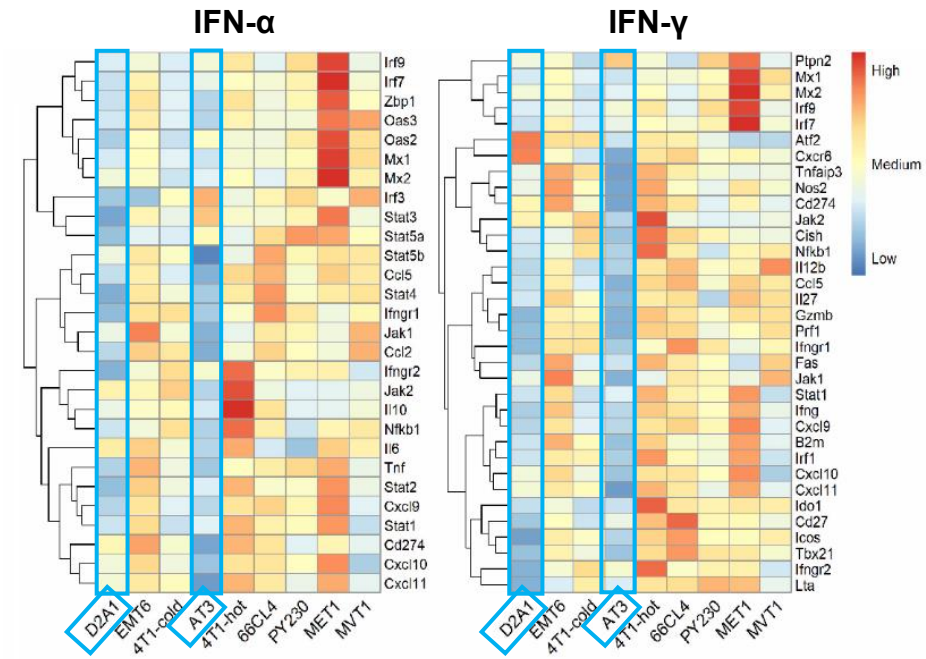


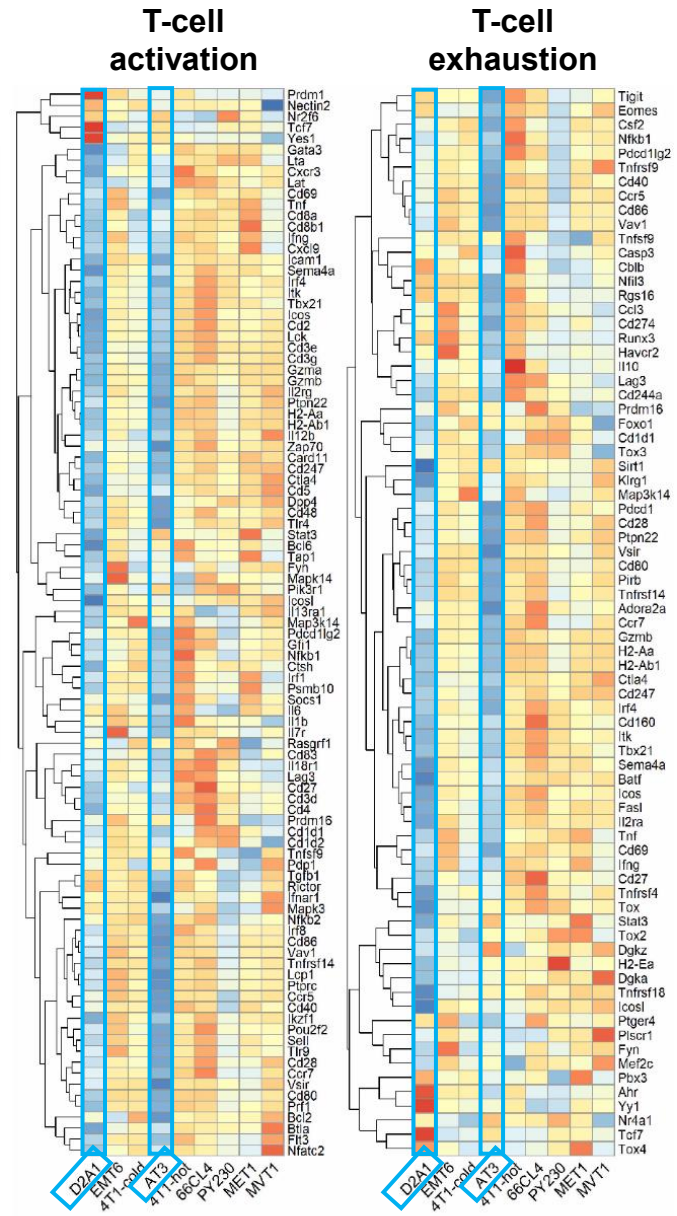


Salembier R et al., npj Breast Cancer, 2025 (manuscript under review)

Transcriptomic profiling of the mammary tumor microenvironment





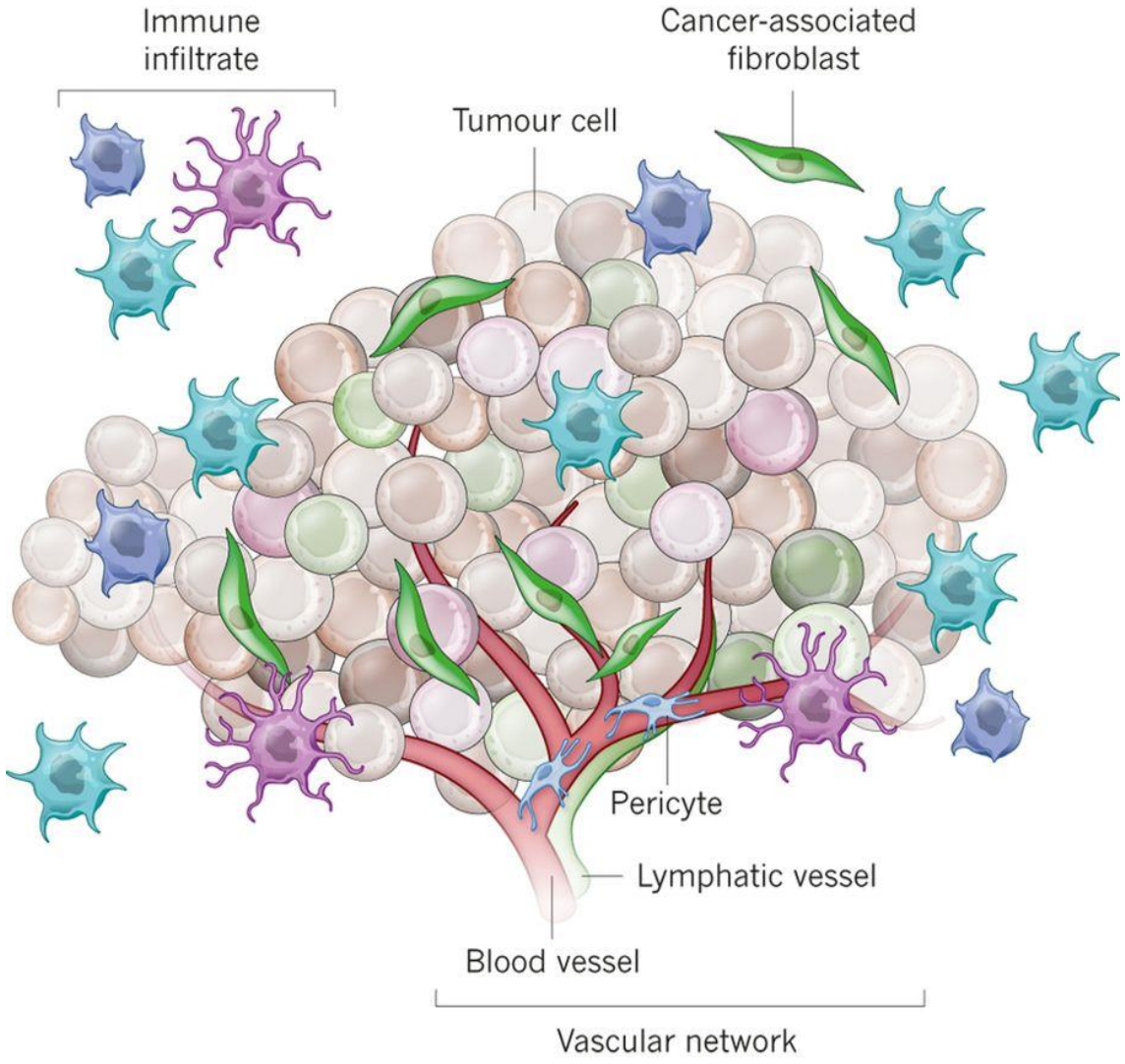


Used for:

- Experimental therapeutic testing (e.g. c-MET inhibitor: *npj Breast Cancer*, 2021)
- Optimizing chemotherapeutic efficacy (e.g. cisplatin: *Oncoimmunology*, 2022)
- Identifying (immuno)therapeutic targets (2021-now)

Salembier R et al., npj Breast Cancer, 2025 (manuscript under review)

Identifying immunotherapeutic targets in the mammary tumor microenvironment

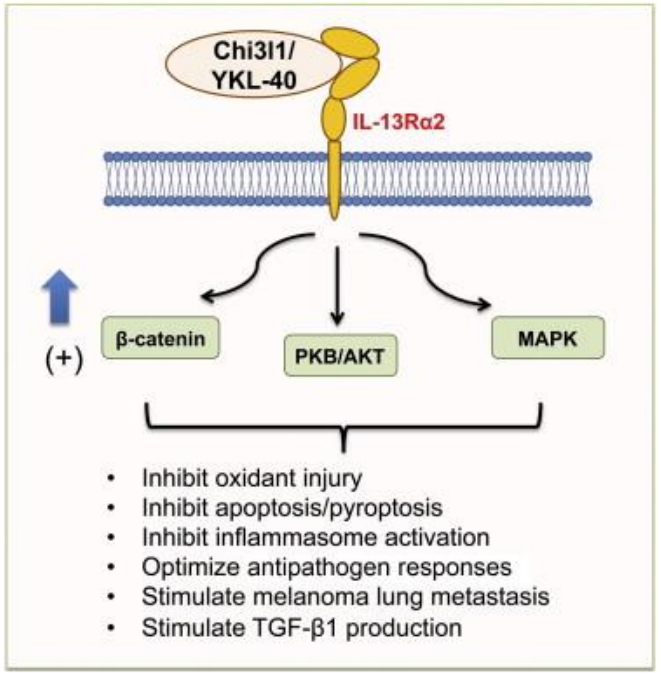


Current focus is on:

- Cancer-associated fibroblasts
- Extracellular matrix components
- **Immunosuppressive myeloid cells (neutrophils)**

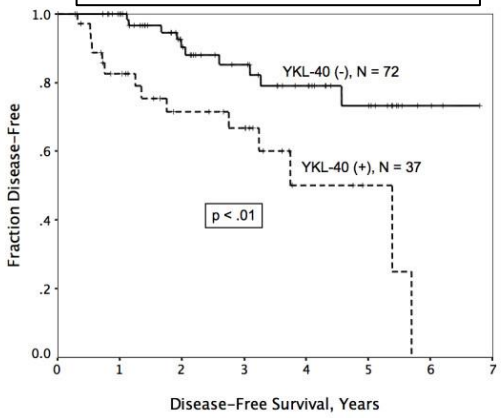
Junttila MR & de Sauvage FJ, Nature, 2013

Chitinase 3-like 1 (CHI3L1) as candidate (immuno)therapeutic target in TNBC



He CH et al., Cell Rep, 2013

Human



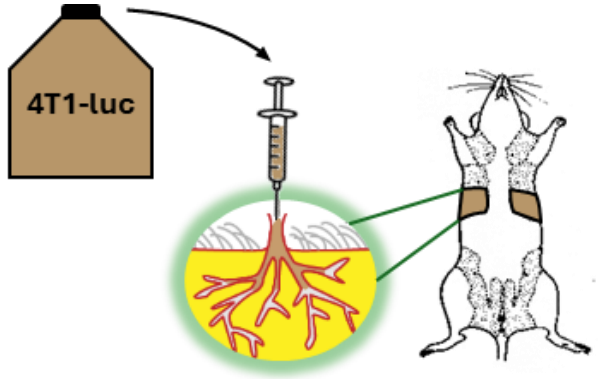
Kim SH et al., World J Surg Oncol, 2007

Mouse

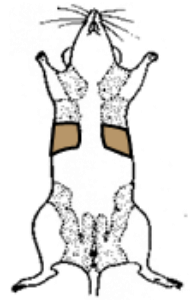
low CHI3L1 high CHI3L1

Ma B et al., Cancer Res, 2015

CHI3L1 deficiency reduces disease progression in the 4T1-based TNBC model

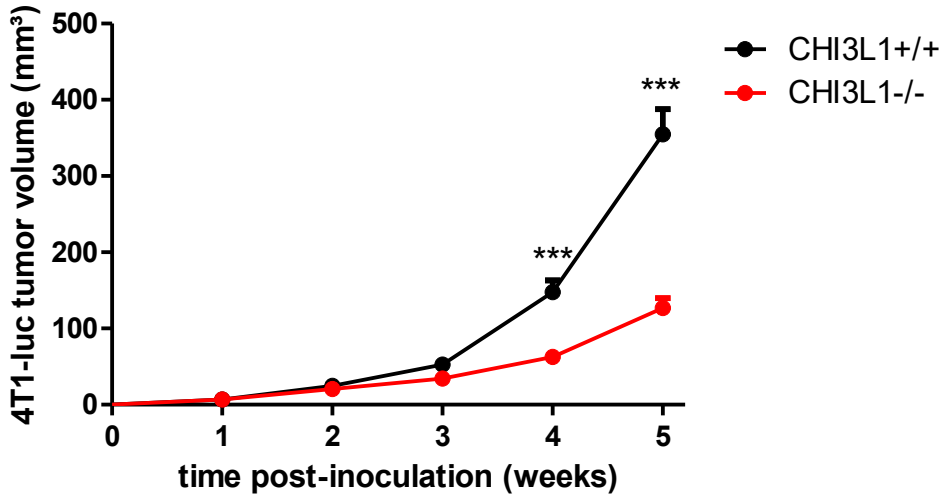


vs.

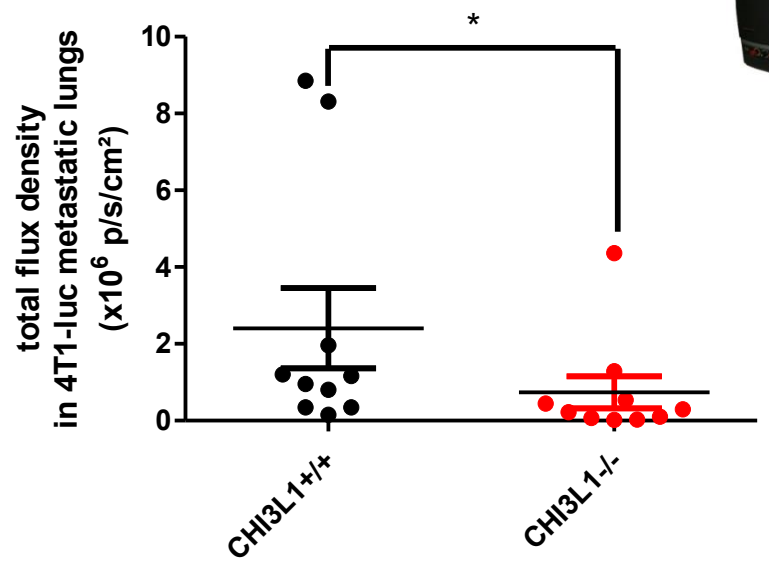


CHI3L1$^{+/+}$ CHI3L1$^{-/-}$

Caliper measurement



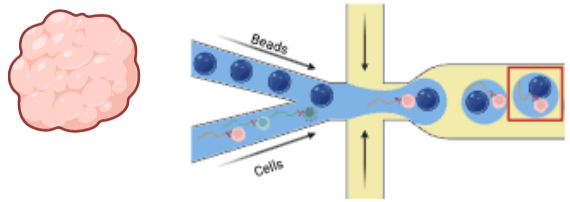
***Ex vivo* imaging (5 weeks p.i.)**

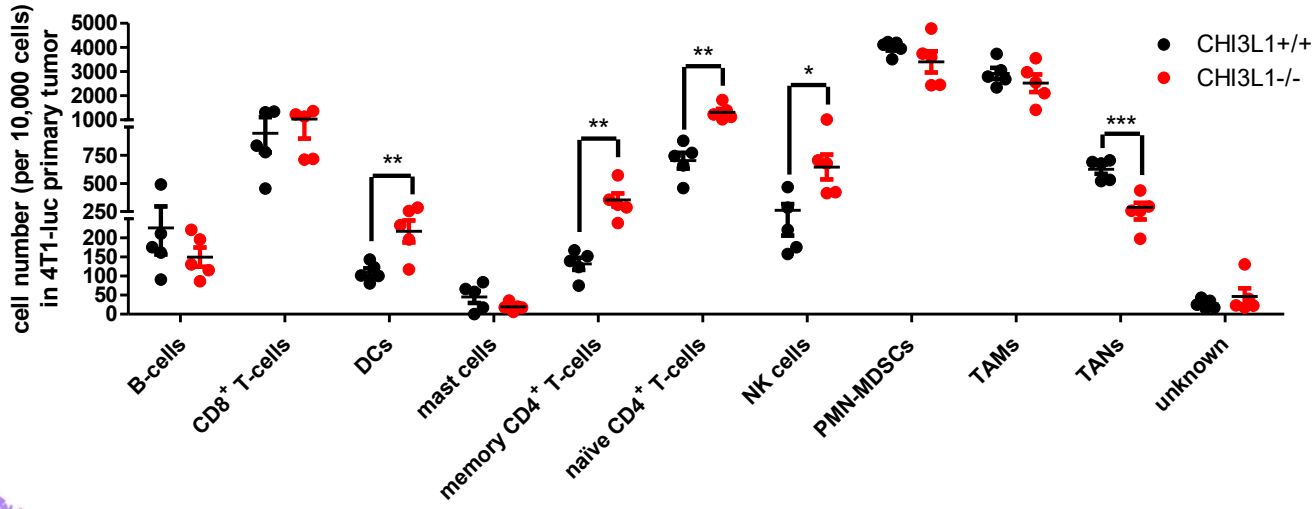


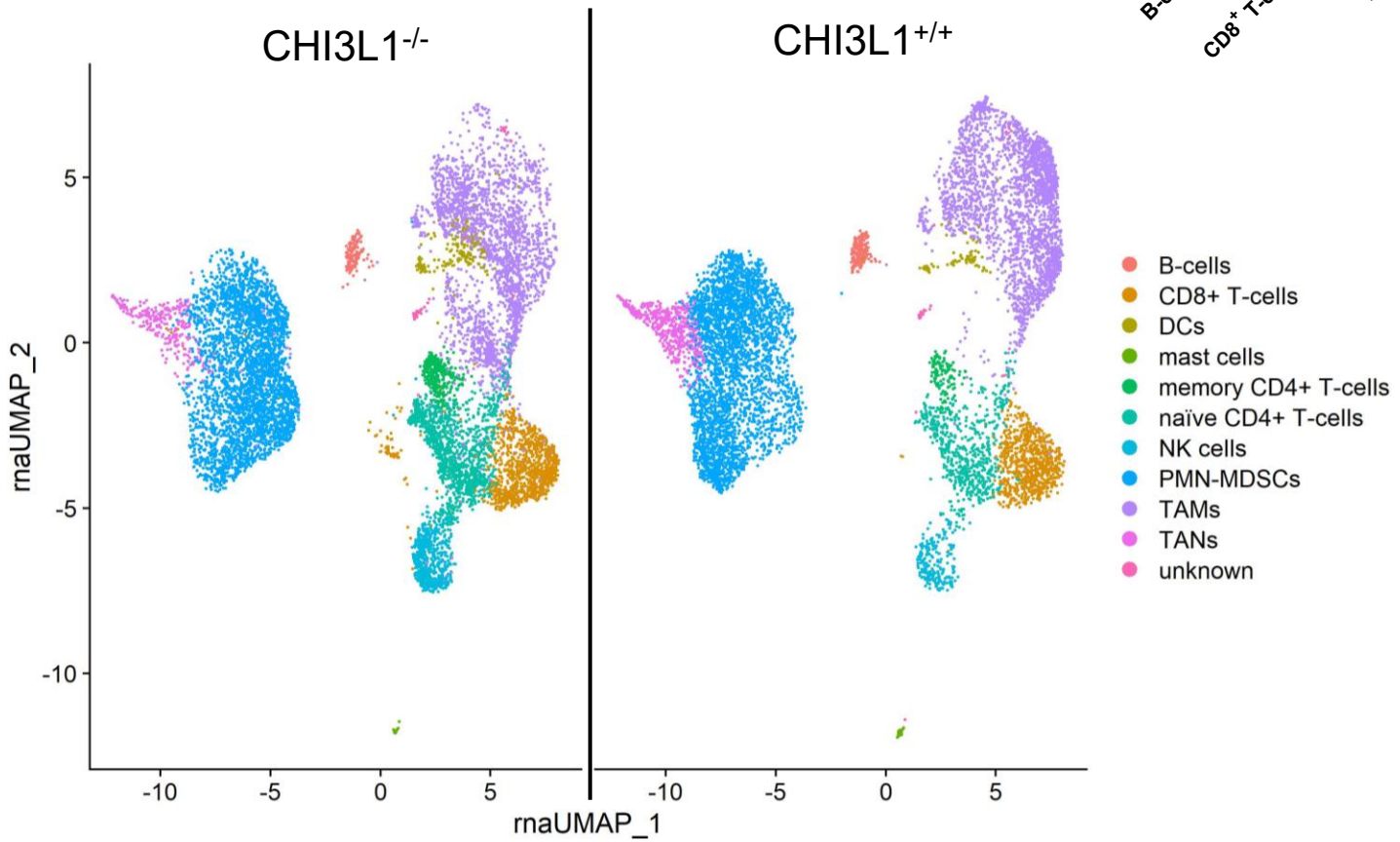
Salembier R et al., 2025 (manuscript in preparation)

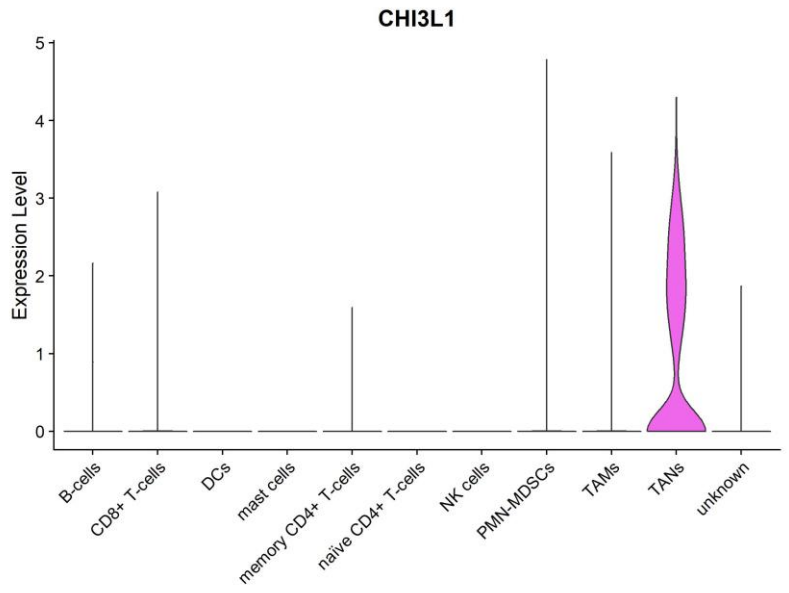
Neutrophil-derived CHI3L1 stimulates immunosuppression in the 4T1-based TNBC model

CITE-seq (5 weeks p.i.)









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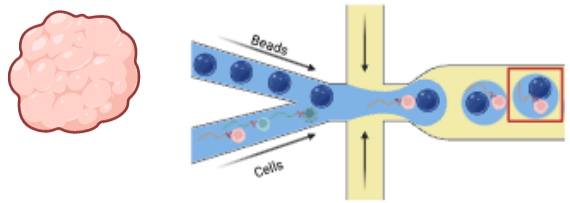
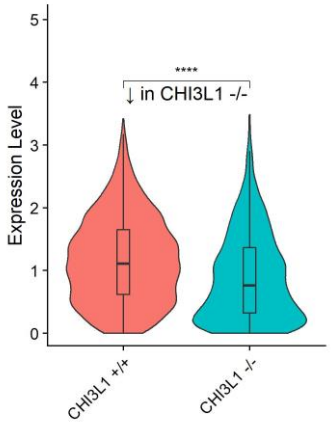
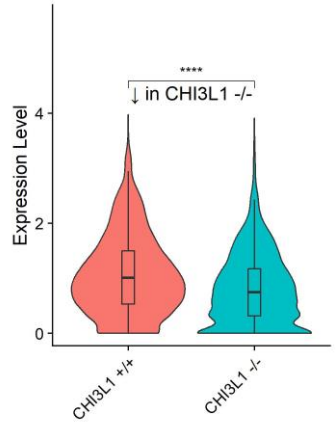


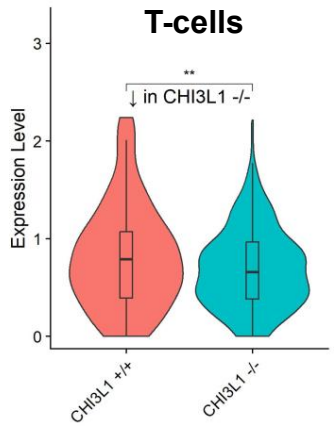
PD-L1 on TAMs



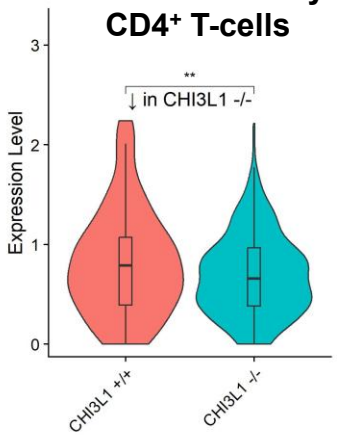
PD-L2 on TAMs



PD-1 on CD8⁺ T-cells

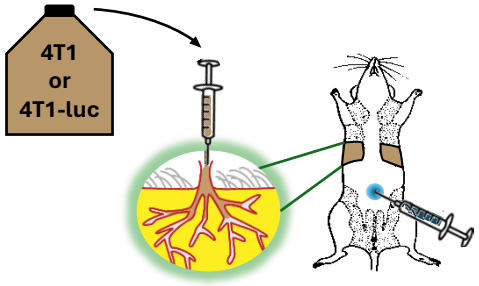


PD-1 on memory CD4⁺ T-cells



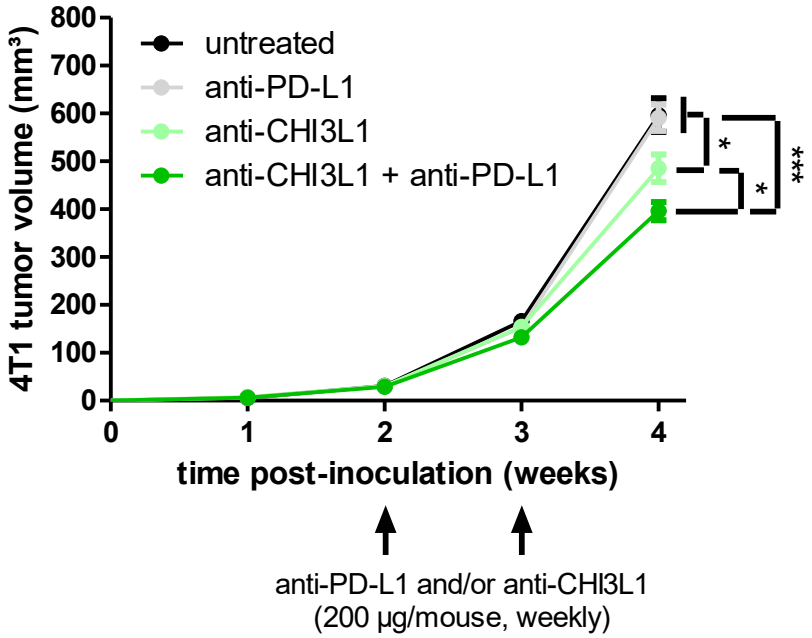
Salembier R et al., 2025 (manuscript in preparation)

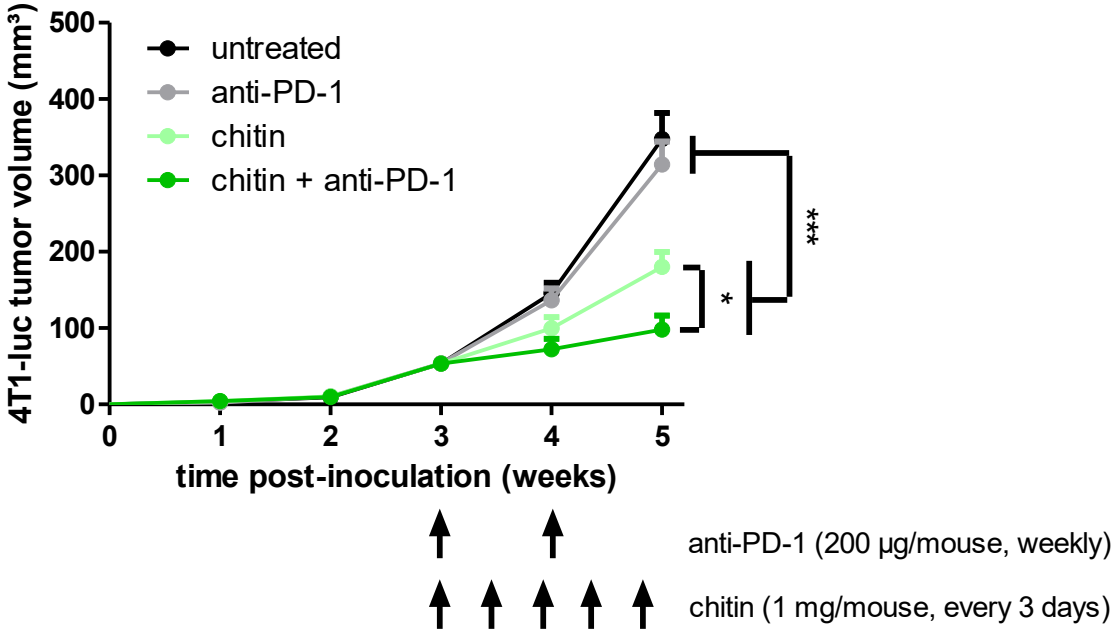
CHI3L1 blockade alleviates anti-PD-(L)1 resistance in the 4T1-based TNBC model



Intraperitoneal (i.p.) treatments

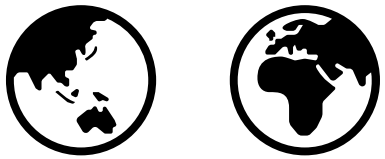
Caliper measurement





Salembier R et al., Breast Cancer Res, 2024
Salembier R et al., 2025 (manuscirpt in preparation)

Do you want to collaborate with us?



We are open for collaborations on:

- In vivo cancer models for **therapeutic testing**
- **Identifying and investigating targets of interest** in relevant cancer models
- Any other cancer-related subject that requires preclinical models

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University of Colorado Denver

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