Universitätsspital Basel

Universität Basel

Departement Biomedizin Basel

Tumors derived from PROCR-positive mammary stem cells give rise to claudin-low breast cancer with poor prognosis

Poster 11

Michal Kloc

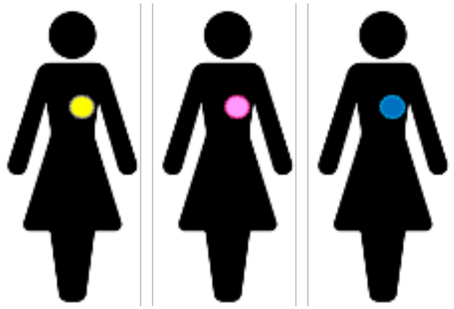
Bentires-Alj lab

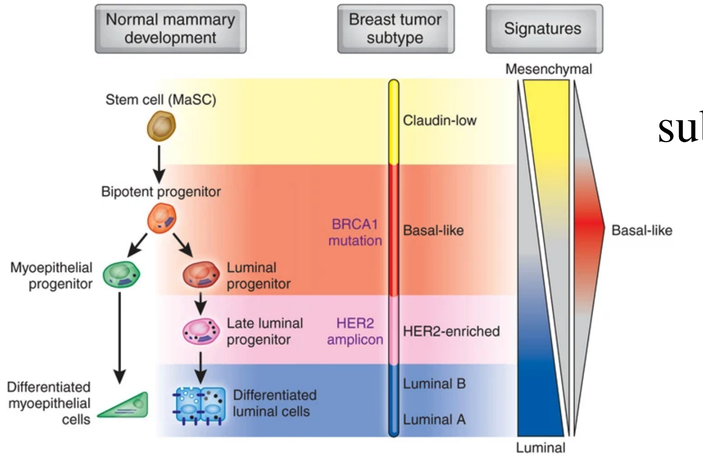
with Marion A. Salvador

Breast cancer heterogeneity is responsible for therapy failure

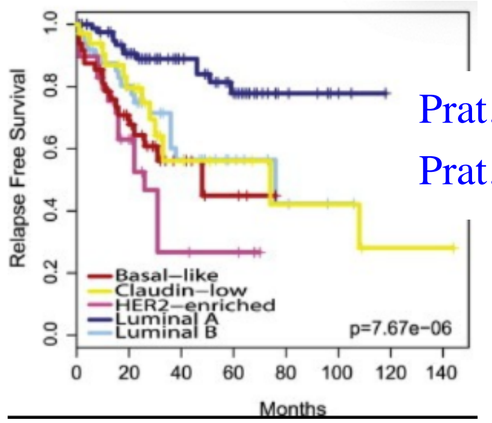
Cell of origin concept

inter-tumoral heterogeneity





Association between breast cancer (BC) molecular subtypes and differentiation status of healthy mammary cells based on gene expression profiling

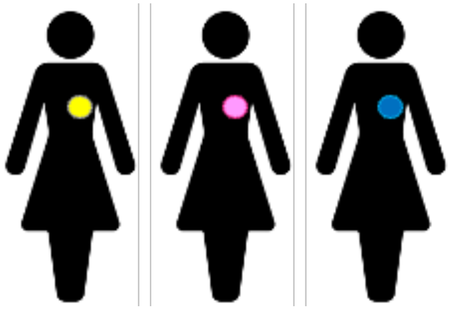


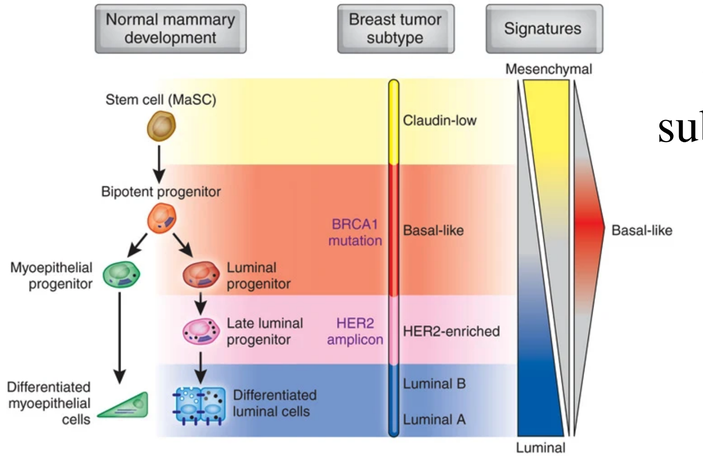
Prat, Perou, *Nat Med*. 2009,
Prat, Perou, *Mol Oncol*. 2011

Breast cancer heterogeneity is responsible for therapy failure

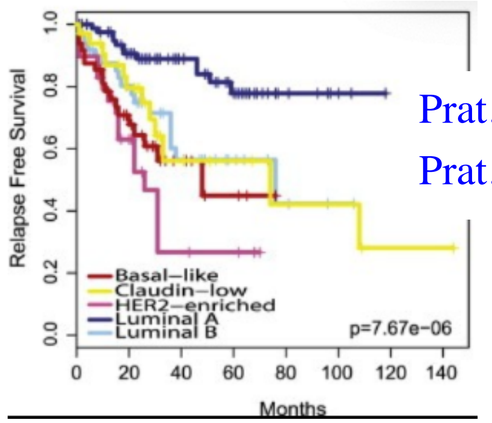
Cell of origin concept

inter-tumoral heterogeneity





Association between breast cancer (BC) molecular subtypes and differentiation status of healthy mammary cells based on gene expression profiling



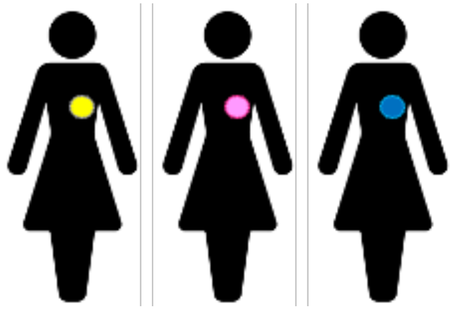
Prat, Perou, *Nat Med*. 2009,
Prat, Perou, *Mol Oncol*. 2011

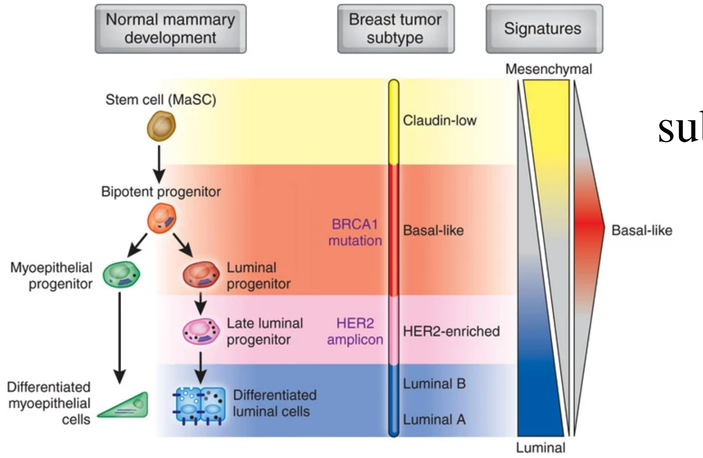
Endothelial protein C receptor (PROCR) is a marker of multiplotent mammary stem cells (MaSCs) in mouse Wang et al, *Nature*, 2015

Breast cancer heterogeneity is responsible for therapy failure

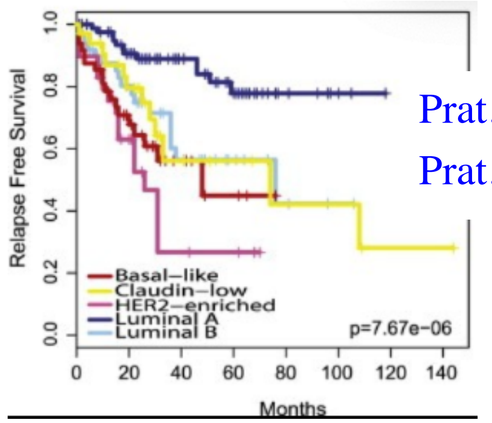
Cell of origin concept

inter-tumoral heterogeneity





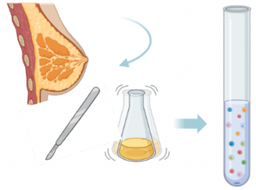
Association between breast cancer (BC) molecular subtypes and differentiation status of healthy mammary cells based on gene expression profiling



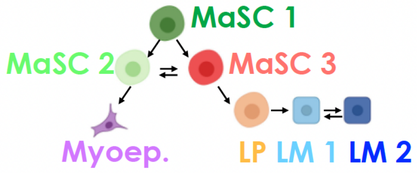
Prat, Perou, *Nat Med*. 2009,
Prat, Perou, *Mol Oncol*. 2011

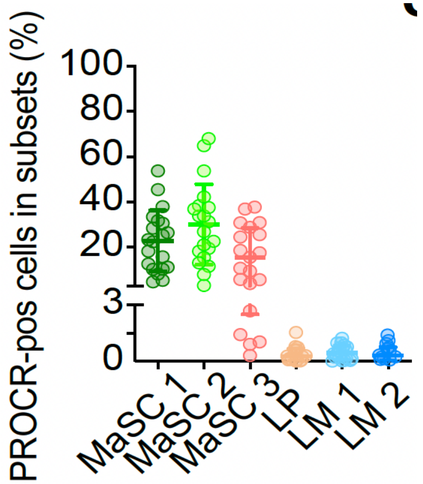
Endothelial protein C receptor (PROCR) is a marker of multiplotent mammary stem cells (MaSCs) in mouse Wang et al, *Nature*, 2015

PROCR+ cells are found in Mammary Stem Cells populations



MaSC subsets from
Morel, Ginestier et al., *Nat Med*., 2017

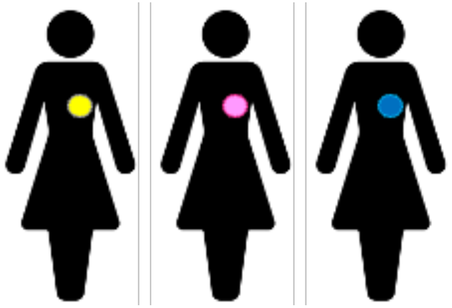


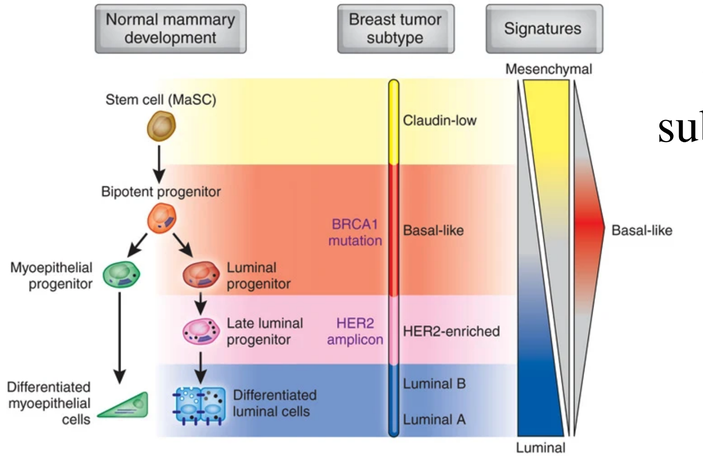


Breast cancer heterogeneity is responsible for therapy failure

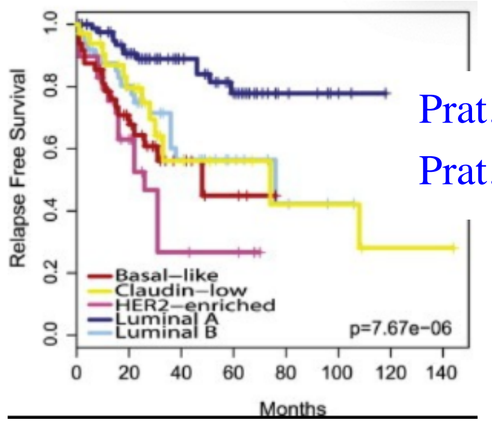
Cell of origin concept

inter-tumoral heterogeneity





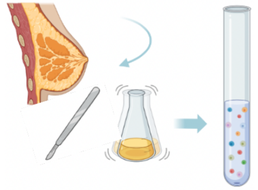
Association between breast cancer (BC) molecular subtypes and differentiation status of healthy mammary cells based on gene expression profiling



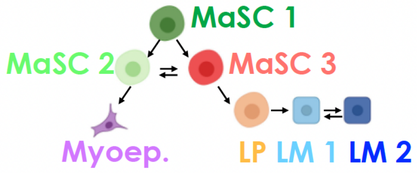
Prat, Perou, *Nat Med*. 2009,
Prat, Perou, *Mol Oncol*. 2011

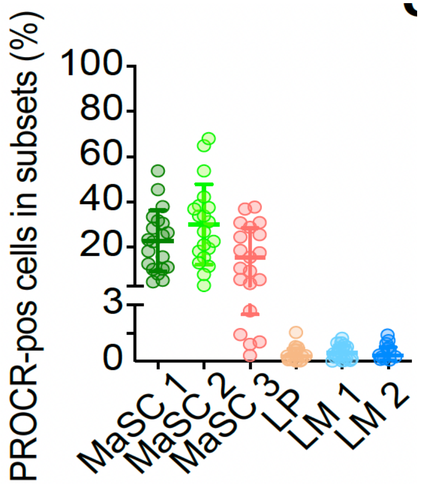
Endothelial protein C receptor (PROCR) is a marker of multiplotent mammary stem cells (MaSCs) in mouse Wang et al, *Nature*, 2015

PROCR+ cells are found in Mammary Stem Cells populations

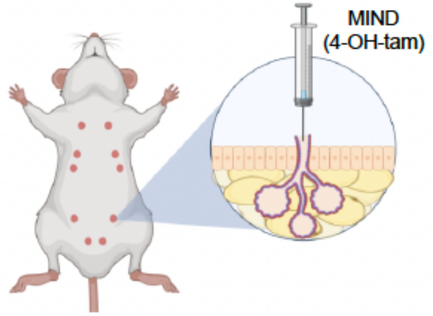


MaSC subsets from
Morel, Ginestier et al., *Nat Med*., 2017





in mouse models PROCR+ MaSCs give rise to tumors



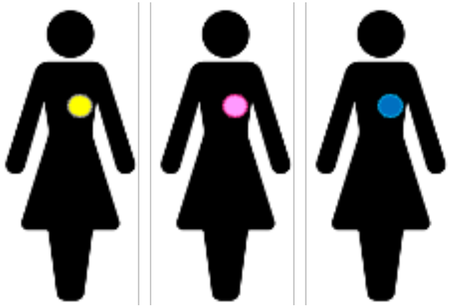
Ctrl: *Procr*-Cre; *EYFP*

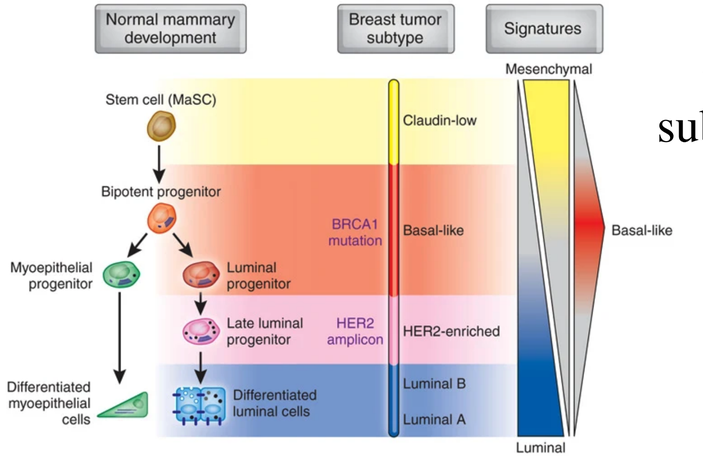
Mut: *Procr*-Cre; *PIK3CA-H1047R*; *KRAS-G12D*; *Tp53fl/fl*; *EYFP*

Breast cancer heterogeneity is responsible for therapy failure

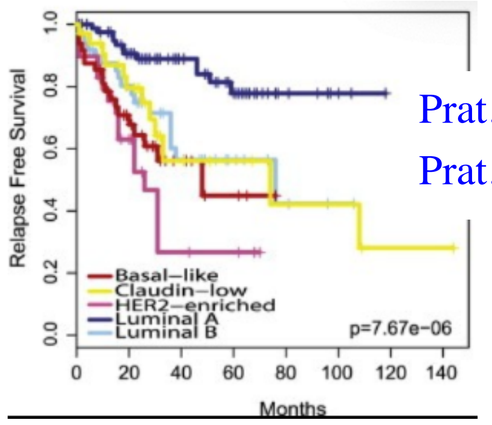
Cell of origin concept

inter-tumoral heterogeneity





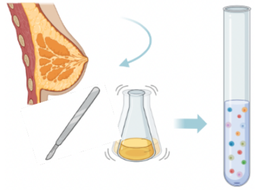
Association between breast cancer (BC) molecular subtypes and differentiation status of healthy mammary cells based on gene expression profiling



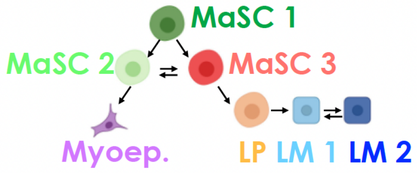
Prat, Perou, *Nat Med*. 2009,
Prat, Perou, *Mol Oncol*. 2011

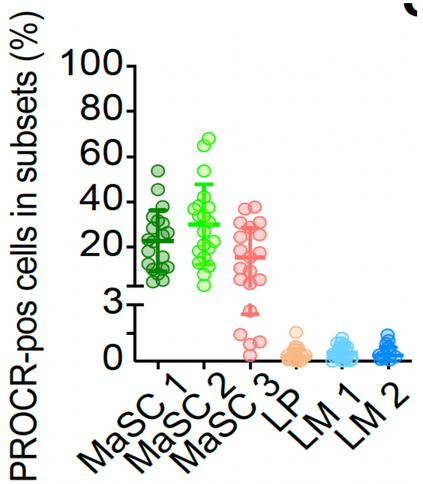
Endothelial protein C receptor (PROCR) is a marker of multiplotent mammary stem cells (MaSCs) in mouse Wang et al, *Nature*, 2015

PROCR+ cells are found in Mammary Stem Cells populations

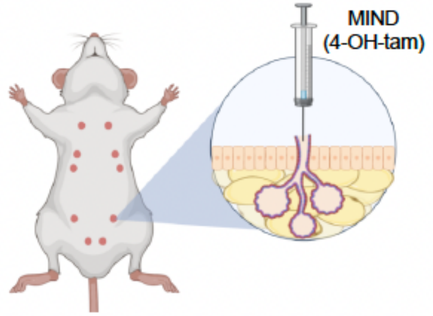


MaSC subsets from
Morel, Ginestier et al., *Nat Med*., 2017





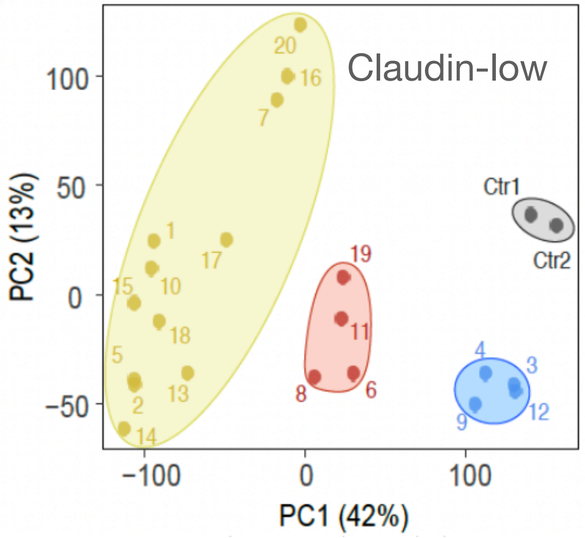
in mouse models PROCR+ MaSCs give rise to tumors



Ctrl: *Procr*-Cre; *EYFP*

Mut: *Procr*-Cre; *PIK3CA-H1047R*; *KRAS-G12D*; *Tp53fl/fl*; *EYFP*

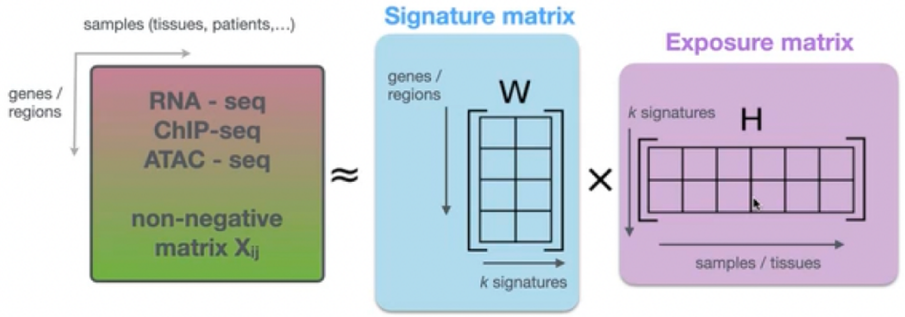
RNAseq on the tumors



Signature extraction

Quintero, Hübschmann, Kurzawa, Steinhauser et al, *Biol. Methods Protoc.*, 2020

Non-negative matrix factorization (NMF)

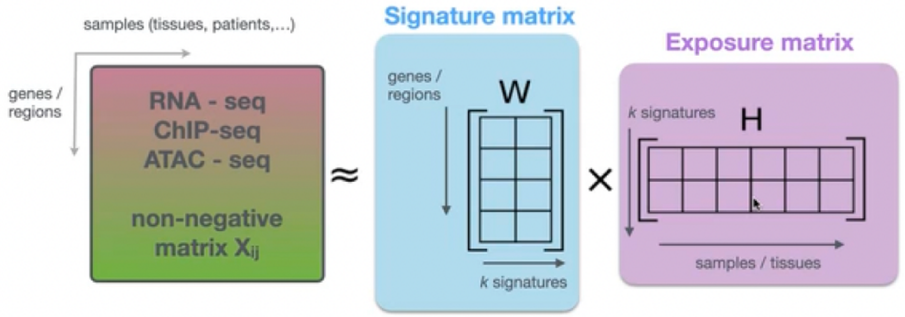


- unsupervised iterative algorithm with random intializations of $W, H \geq 0$
- *sparsity* in the decomposition, better *interpretability* of the features

Signature extraction

Quintero, Hübschmann, Kurzawa, Steinhauser et al, *Biol. Methods Protoc.*, 2020

Non-negative matrix factorization (NMF)

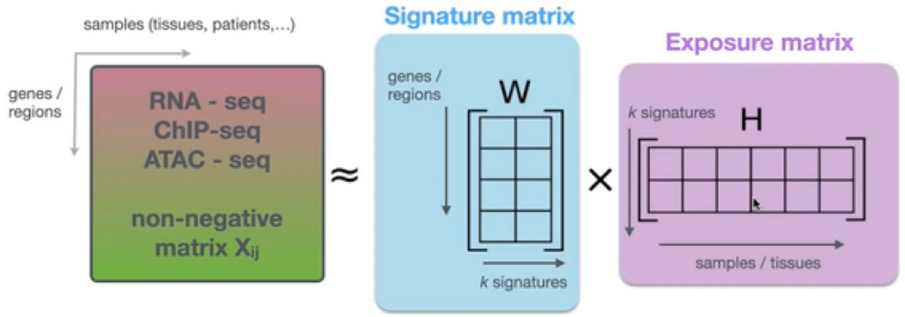


- unsupervised iterative algorithm with random intializations of $W, H \geq 0$
- *sparsity* in the decomposition, better *interpretability* of the features

Signature extraction

Quintero, Hübschmann, Kurzawa, Steinhauser et al, *Biol. Methods Protoc.*, 2020

Non-negative matrix factorization (NMF)



- unsupervised iterative algorithm with random intializations of $W, H \geq 0$
- *sparsity* in the decomposition, better *interpretability* of the features

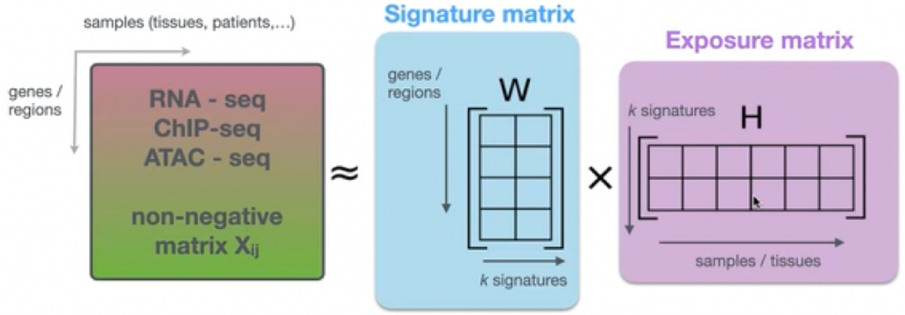
Signatures (ingredients)

Exposures (how much)

Signature extraction

Quintero, Hübschmann, Kurzawa, Steinhauser et al, *Biol. Methods Protoc.*, 2020

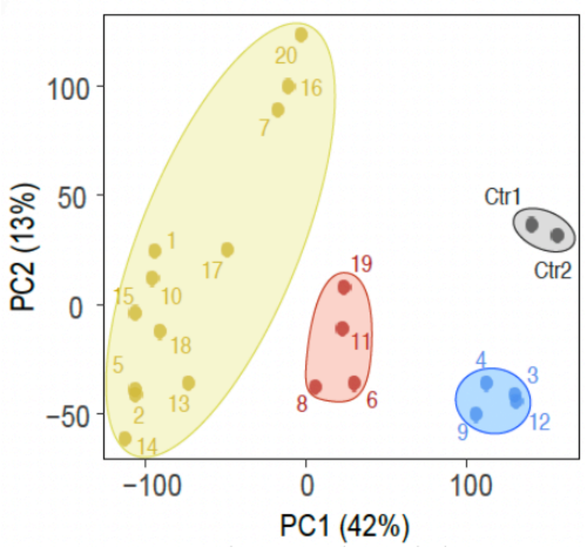
Non-negative matrix factorization (NMF)

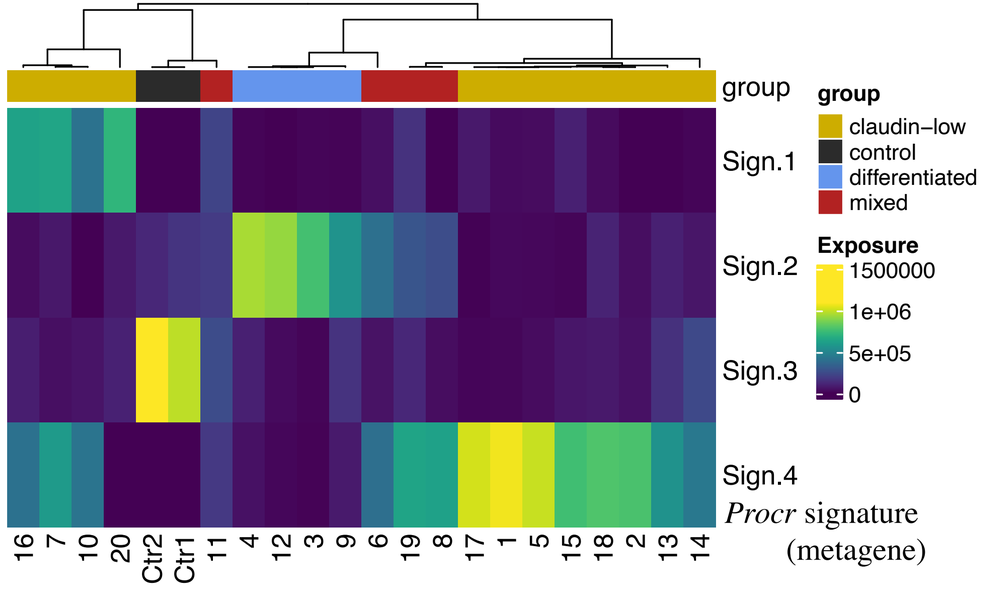


- unsupervised iterative algorithm with random intializations of $W, H \geq 0$
- *sparsity* in the decomposition, better *interpretability* of the features

Signatures (ingredients)

Exposures (how much)



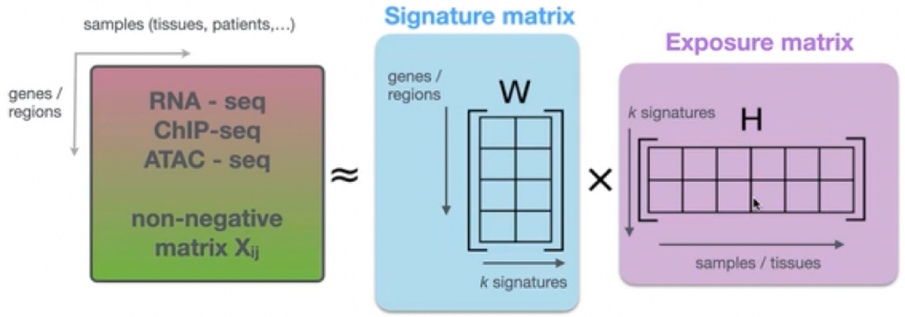


Procr signature (metagene)

Signature extraction

Quintero, Hübschmann, Kurzawa, Steinhauser et al, *Biol. Methods Protoc.*, 2020

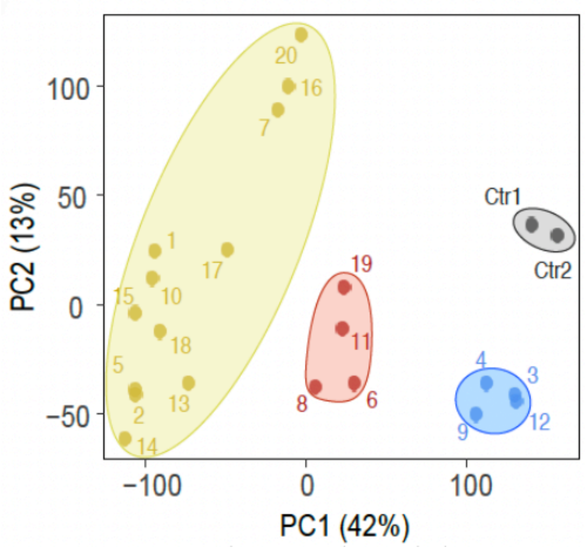
Non-negative matrix factorization (NMF)

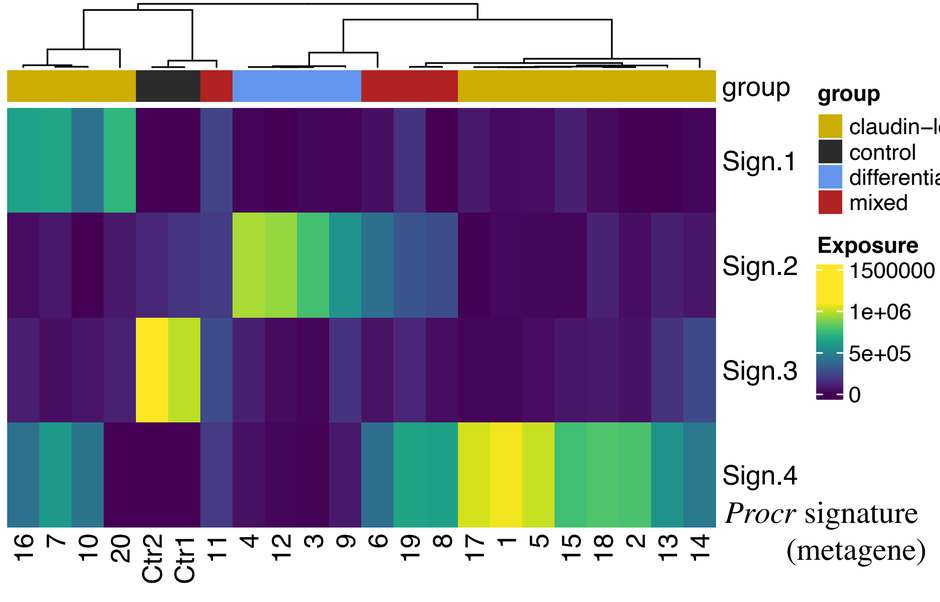


- unsupervised iterative algorithm with random intializations of $W, H \geq 0$
- *sparsity* in the decomposition, better *interpretability* of the features

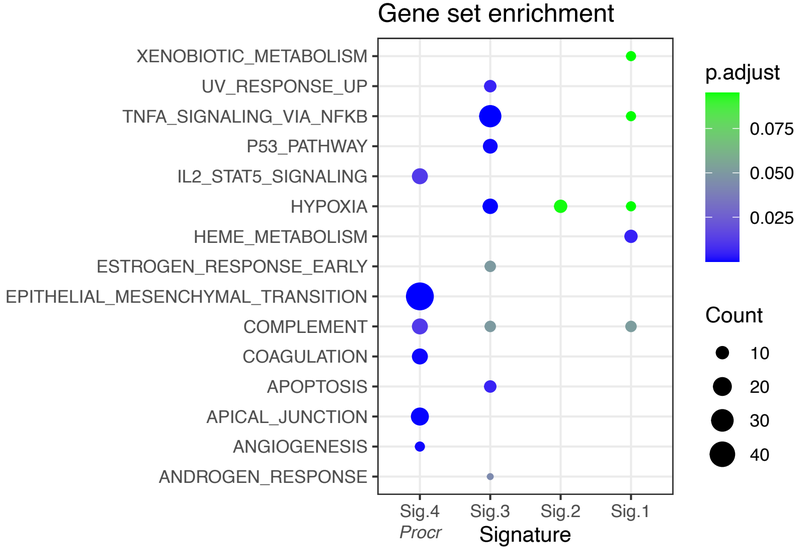
Signatures (ingredients)

Exposures (how much)





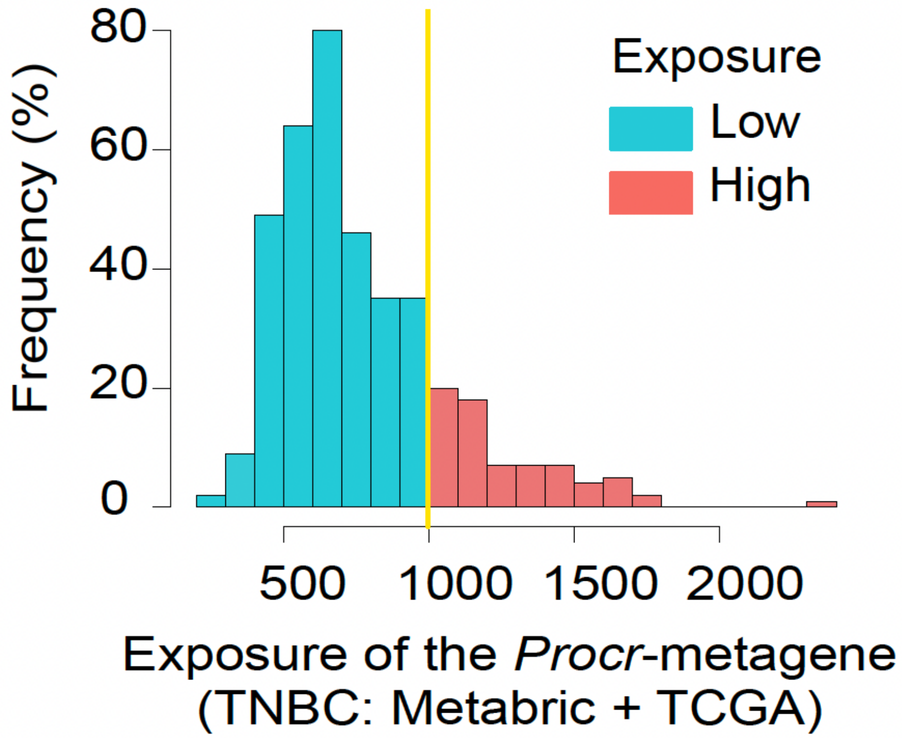
Procr signature (metagene)



High exposure to PROCR signature predicts worse outcome in triple-negative breast cancer patients

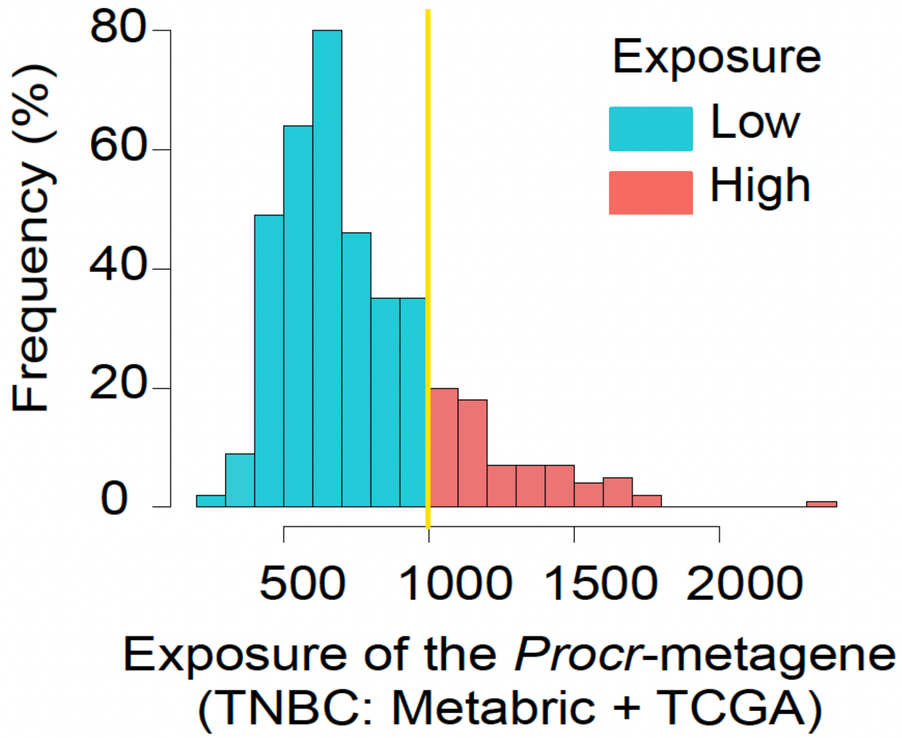
High exposure to PROCR signature predicts worse outcome in triple-negative breast cancer patients

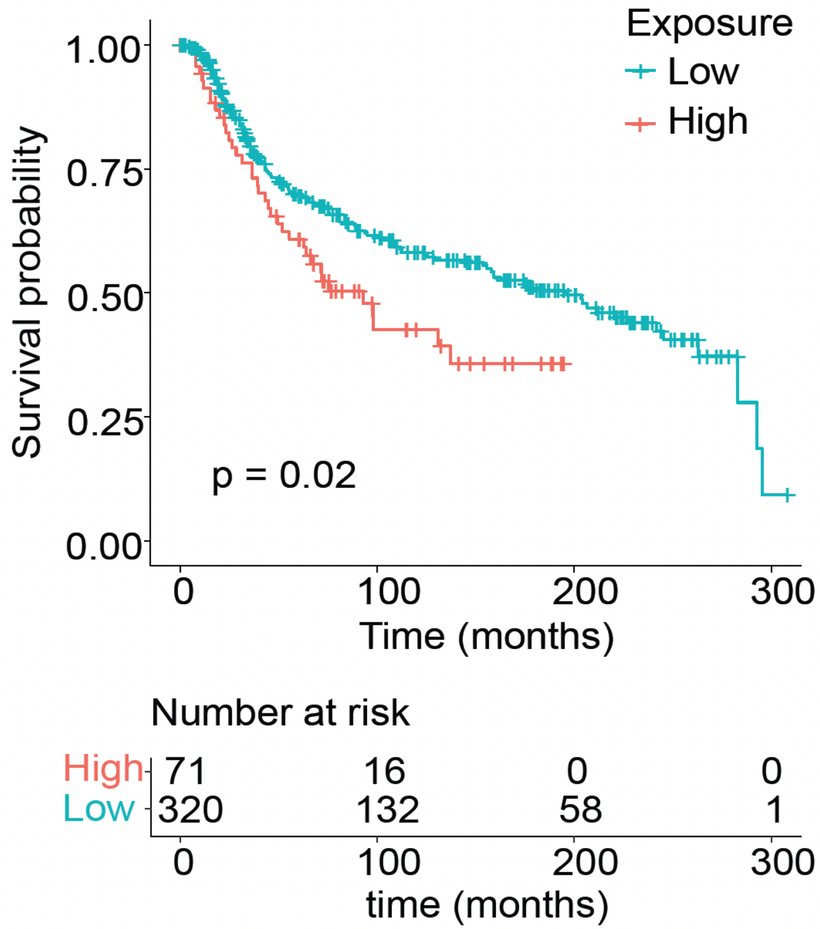
TCGA and Metabric patient cohorts



High exposure to PROCR signature predicts worse outcome in triple-negative breast cancer patients

TCGA and Metabric patient cohorts





Come and meet me at Poster 11!

michal.kloc@unibas.ch

Bentires-Alj lab