

Molecular response of the axillary lymph node microenvironment to metastatic colonization

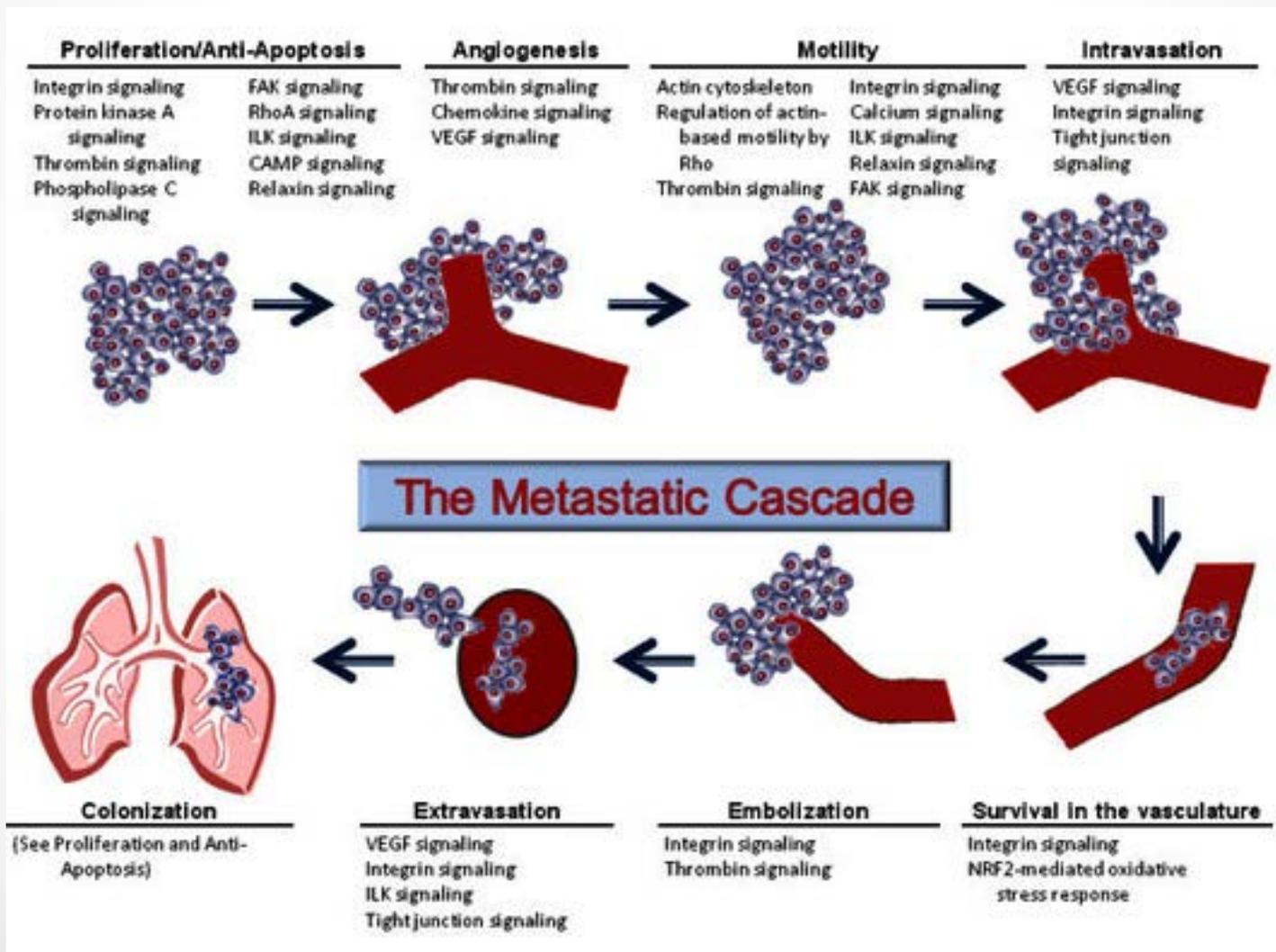
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Colonization

- To become established in a new environment



Metastatic cascade



What is the role of the foreign microenvironment in metastatic colonization?

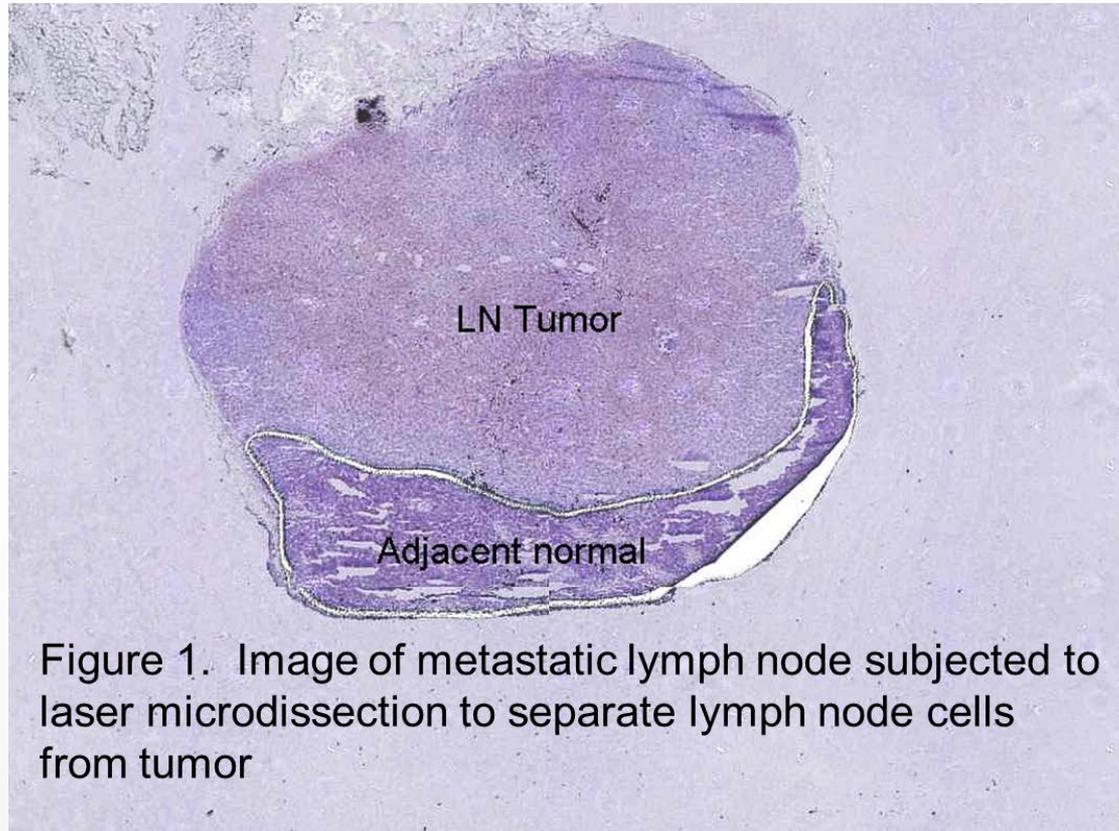


Figure 1. Image of metastatic lymph node subjected to laser microdissection to separate lymph node cells from tumor

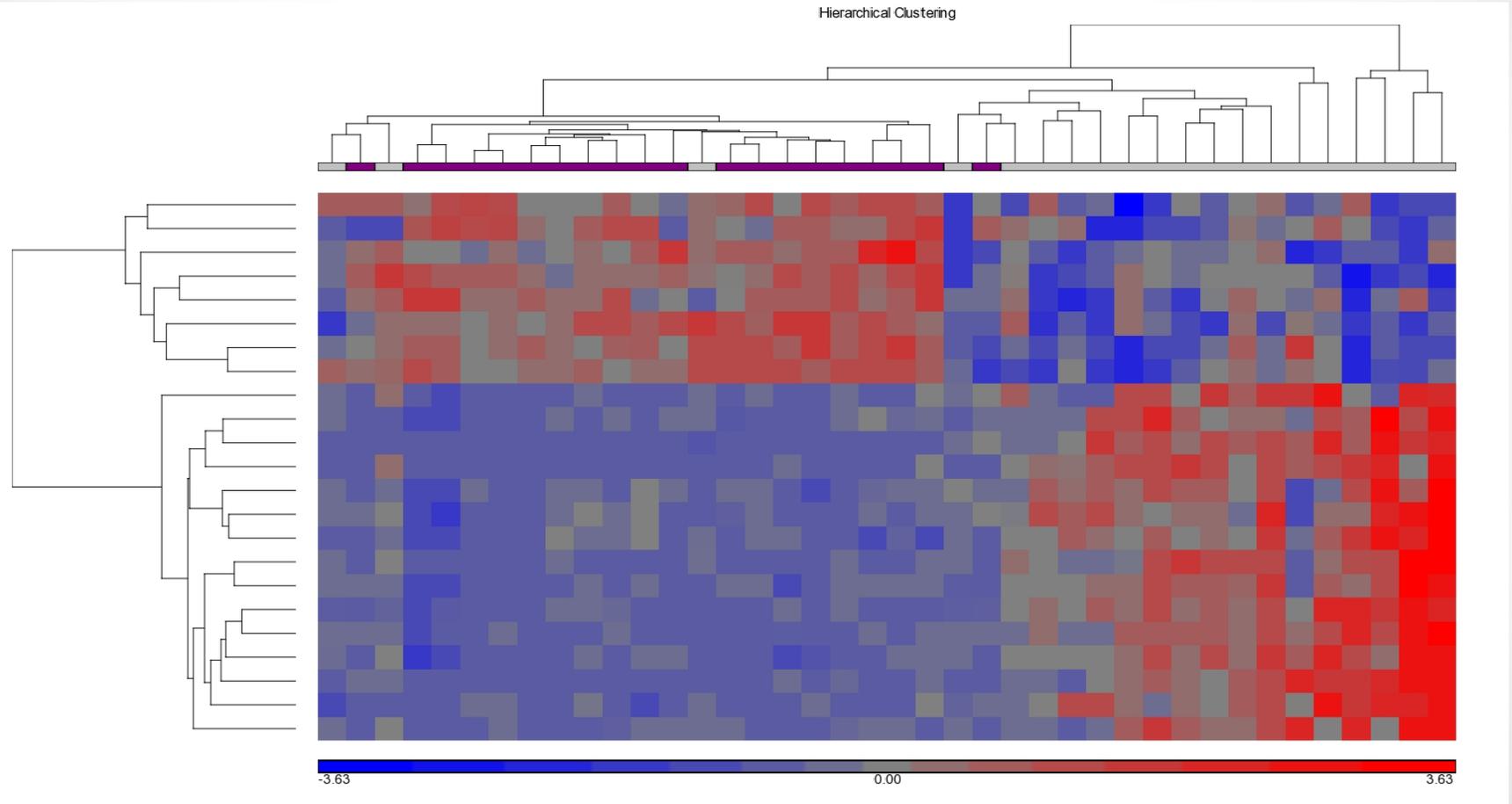
Study design

- 40 women with both positive LN (with sufficient residual lymph tissue) and negative LN available
- Gene expression using U133 2.0 arrays



Results

Hierarchical Clustering



Grey = colonized LN, purple = negative LN

Differentially expressed genes

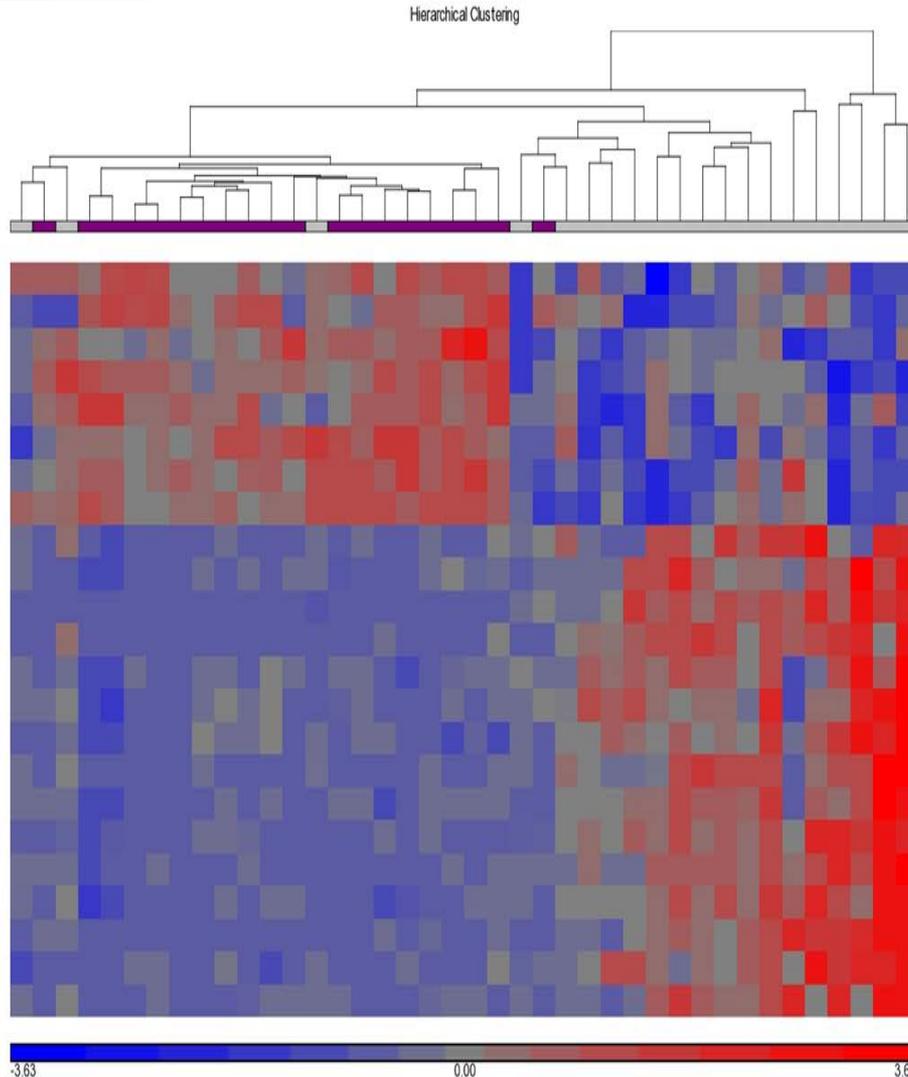
AMPD1
CLEC4M
CXCL2
CXCL5
HPGDS
PROS1
STAB2
TFPI

Lower expression

AGR2
AP1M2
AZGP1
CRABP2
EPCAM
FOXA1
FXYD3
KRT19
MUC1
PIP
S100A14
TFAP2A
TFAP2C

Higher expression

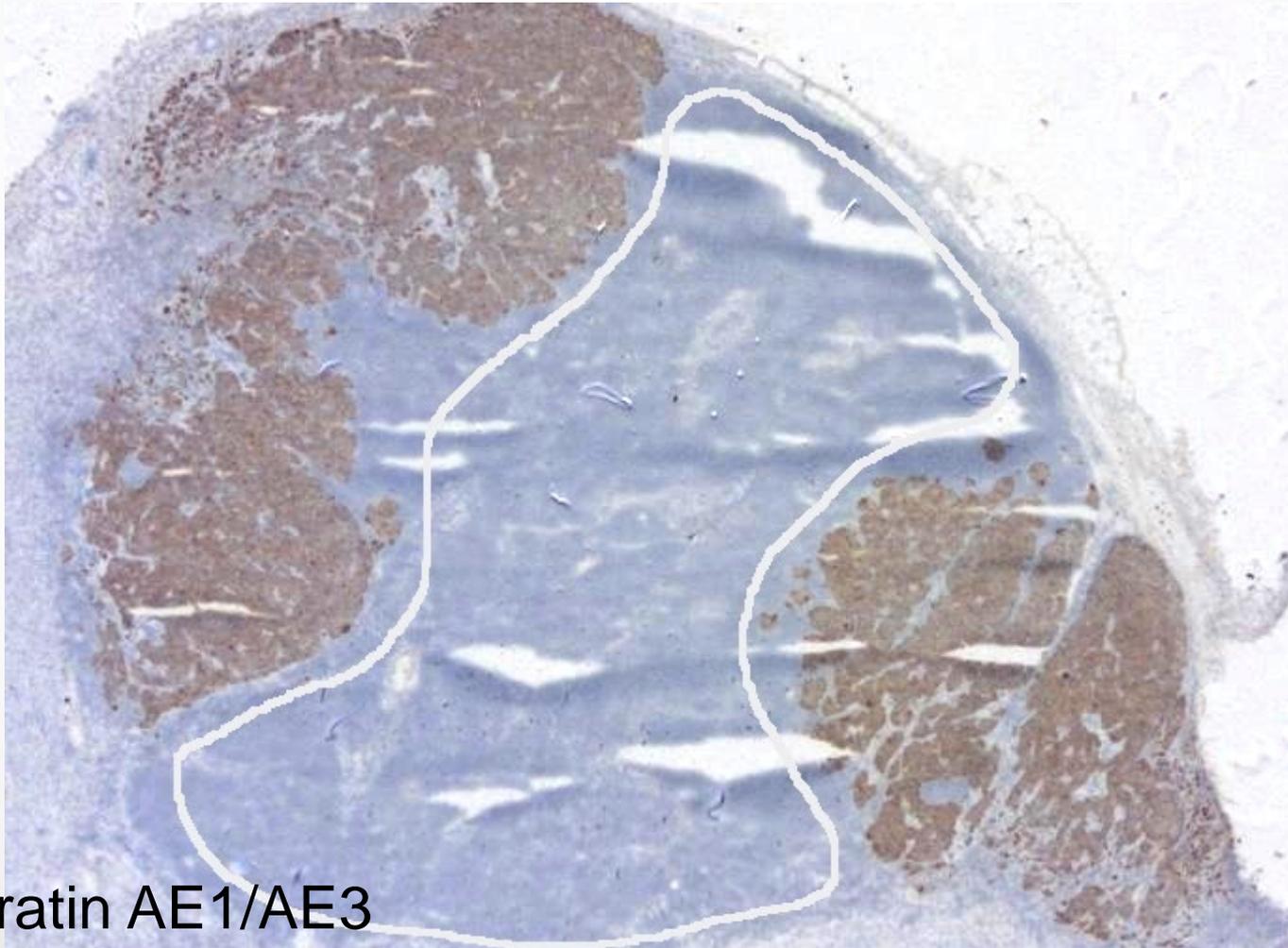
What are these genes?



Genes DOWN
in colonized
LN = immune
response

Genes UP in
colonized LN
= genes
involved MET,
proliferation

Is this the result of contamination by metastatic (epithelial) breast cells?



Pan Keratin AE1/AE3

Conclusion

- gene expression profiles in colonized lymph node tissues are significantly different from those in negative lymph nodes
- genetic changes involved in immune response, cellular proliferation and MET
- thus, lymph nodes not simply overrun with metastatic breast cells, but plays an active role in metastatic colonization.

Colonization (active)



Collaborators

- Windber Research Institute
 - Allyson L Valente
 - Jennifer L Kane
 - Darrell L Ellsworth
- WRNMMC
 - Craig D Shriver
- Patients who willingly donated to further breast cancer research

