

# ***Clinical utility of cancer biomarkers assessed by virtual microscopy***

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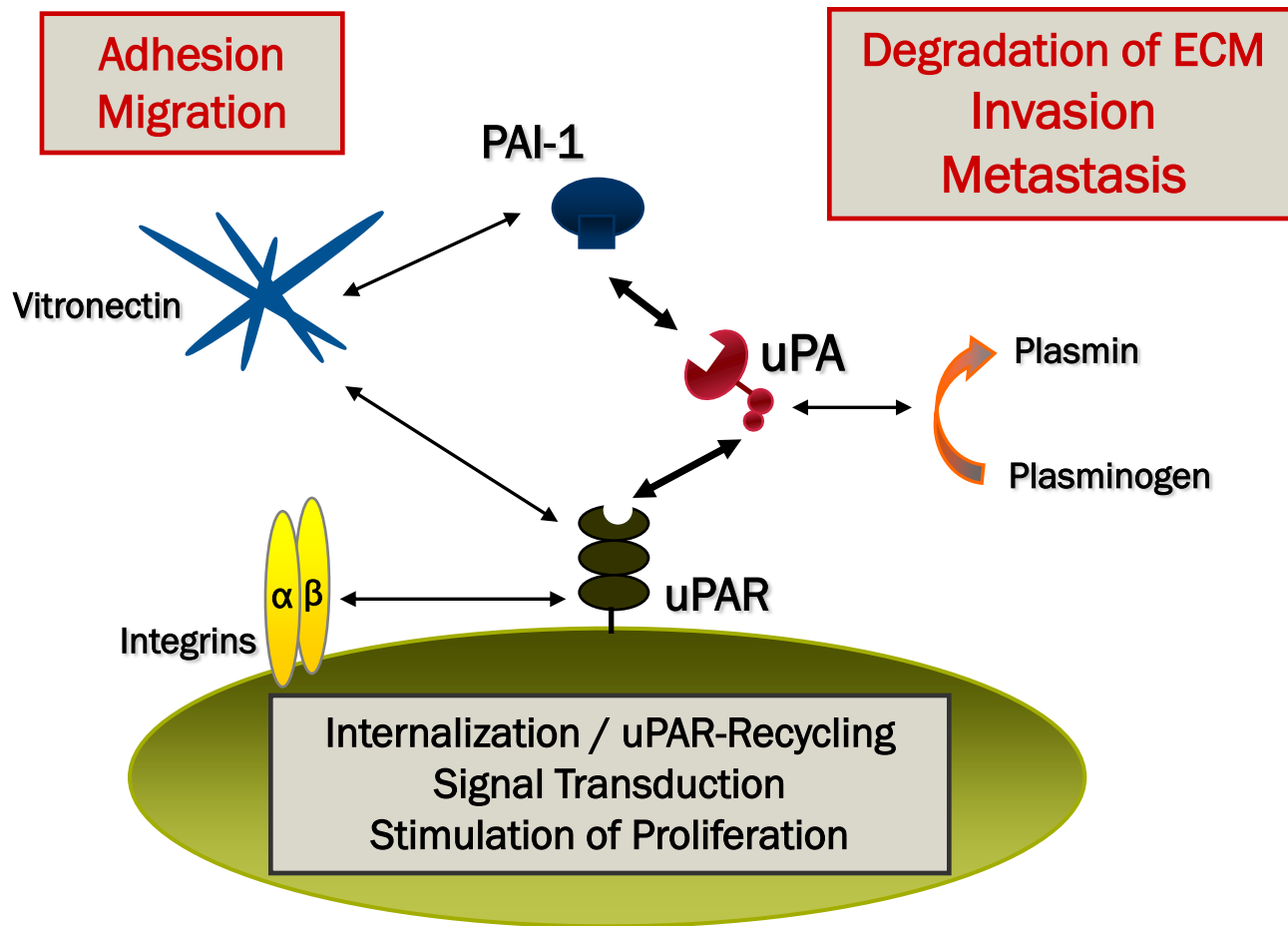




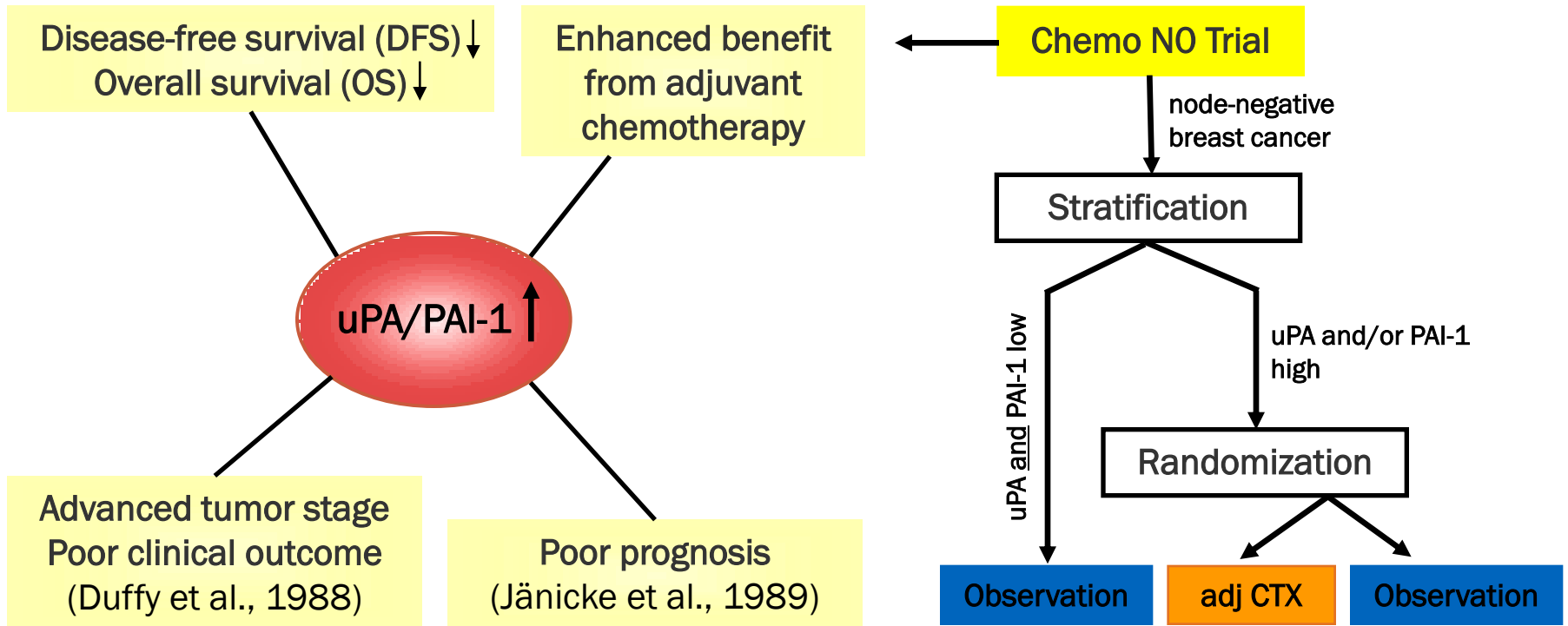
## *Established prognostic/predictive markers for breast cancer*

- **Steroid hormone receptors**
  - estrogen receptor (ER)
  - progesterone receptor (PR)
- **HER2**
- **uPA (urokinase-type plasminogen activator)**  
**PAI-1 (plasminogen activator inhibitor-type1)**
  - secreted serine protease and its inhibitor
  - degradation and remodeling of ECM
  - chemotaxis, migration/invasion, adhesion, proliferation, angiogenesis

# *uPA and PAI-1 are key factors in tumor invasion and metastasis*



# Clinical impact of uPA and PAI-1 in breast cancer

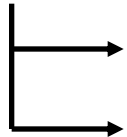


**➔** Prognostic and predictive impact of uPA and PAI-1 in node-negative breast cancer validated at the highest level of evidence (LOE-1)

# ***Clinical impact of uPA and PAI-1 in breast cancer***

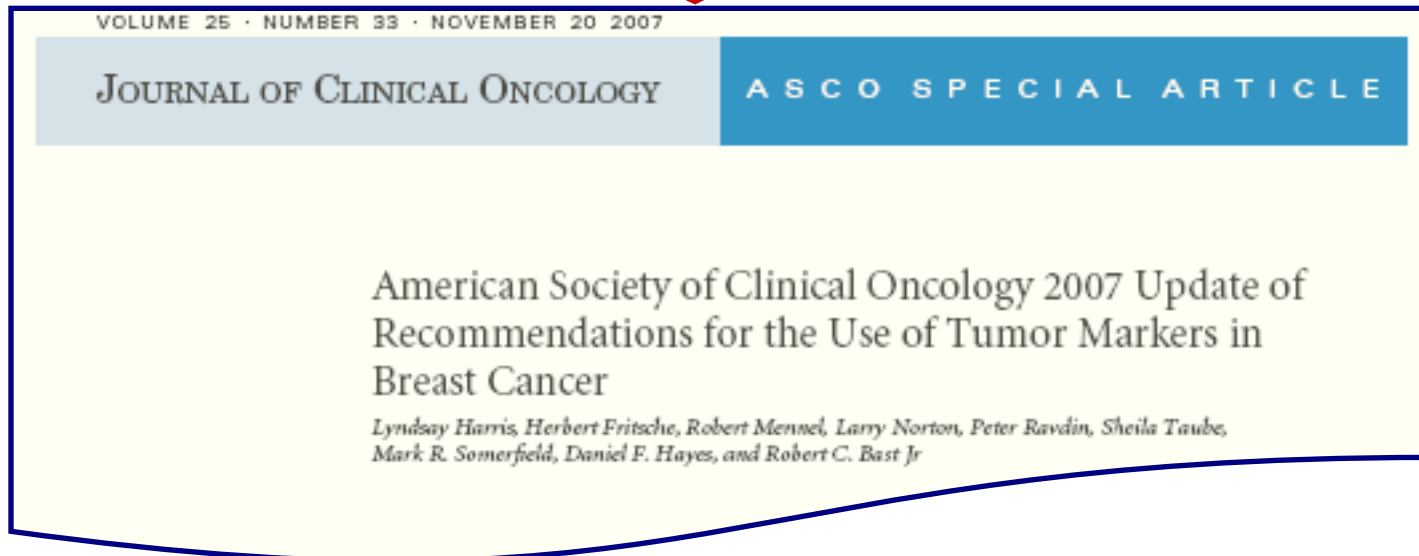


Look et al.; JNCI 2002 (meta-analysis of 8377 primary breast cancer patients)



uPA and PAI-1 are strong prognostic factors for DFS and OS

High uPA and/or PAI-1 double risk of disease recurrence or dying from breast cancer



## ***Techniques for the determination of uPA and PAI-1 in tumor tissues***

- **ELISA**

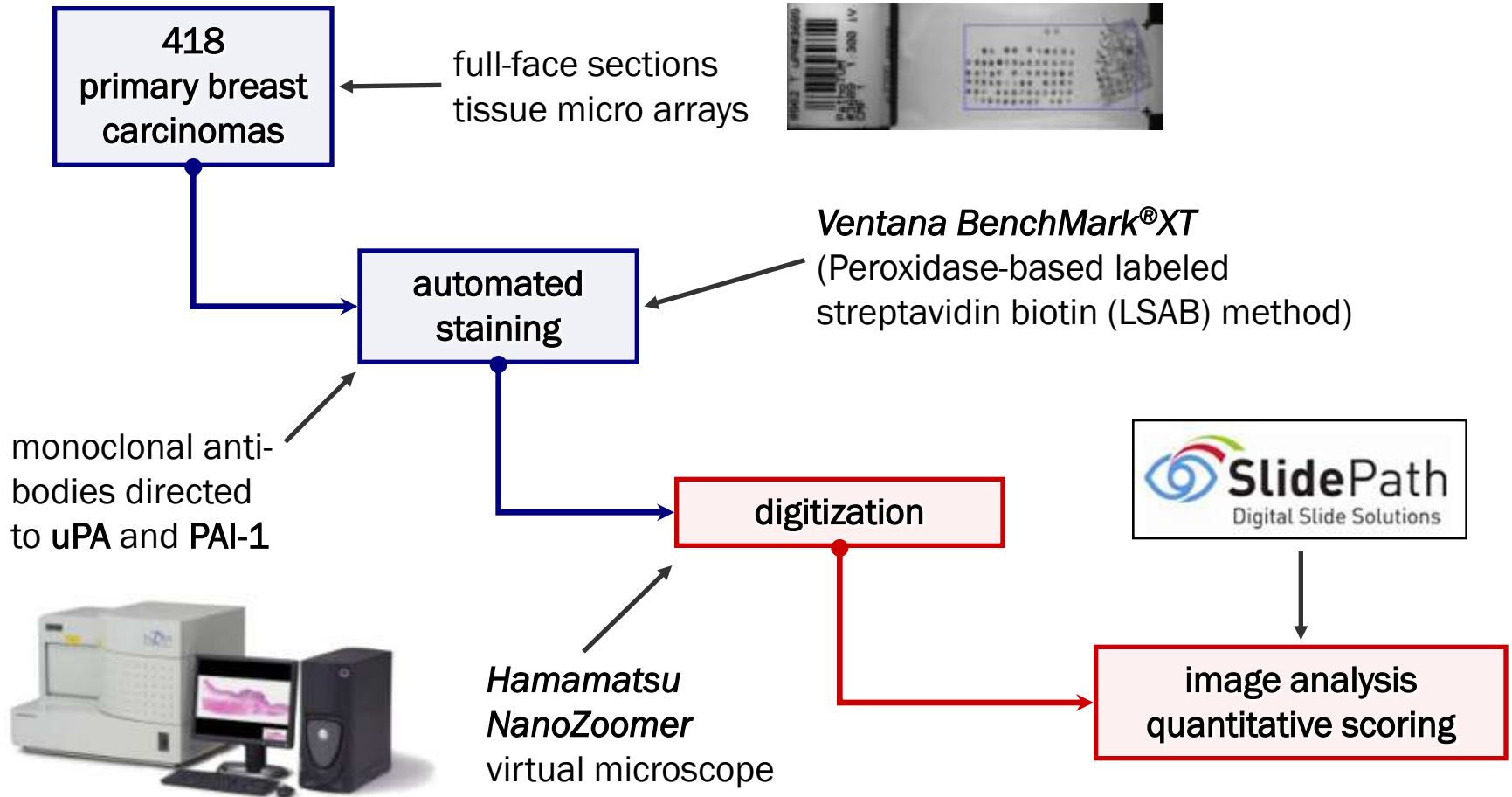
- commercially available  
(e.g. FEMTELLE®; American Diagnostica Inc., USA)
- international quality assurance
- fresh-frozen breast cancer tissue specimens (100-300 mg)
- cut-off values: 3 ng/mg (uPA), 14 ng/mg (PAI-1)
- **gold standard**



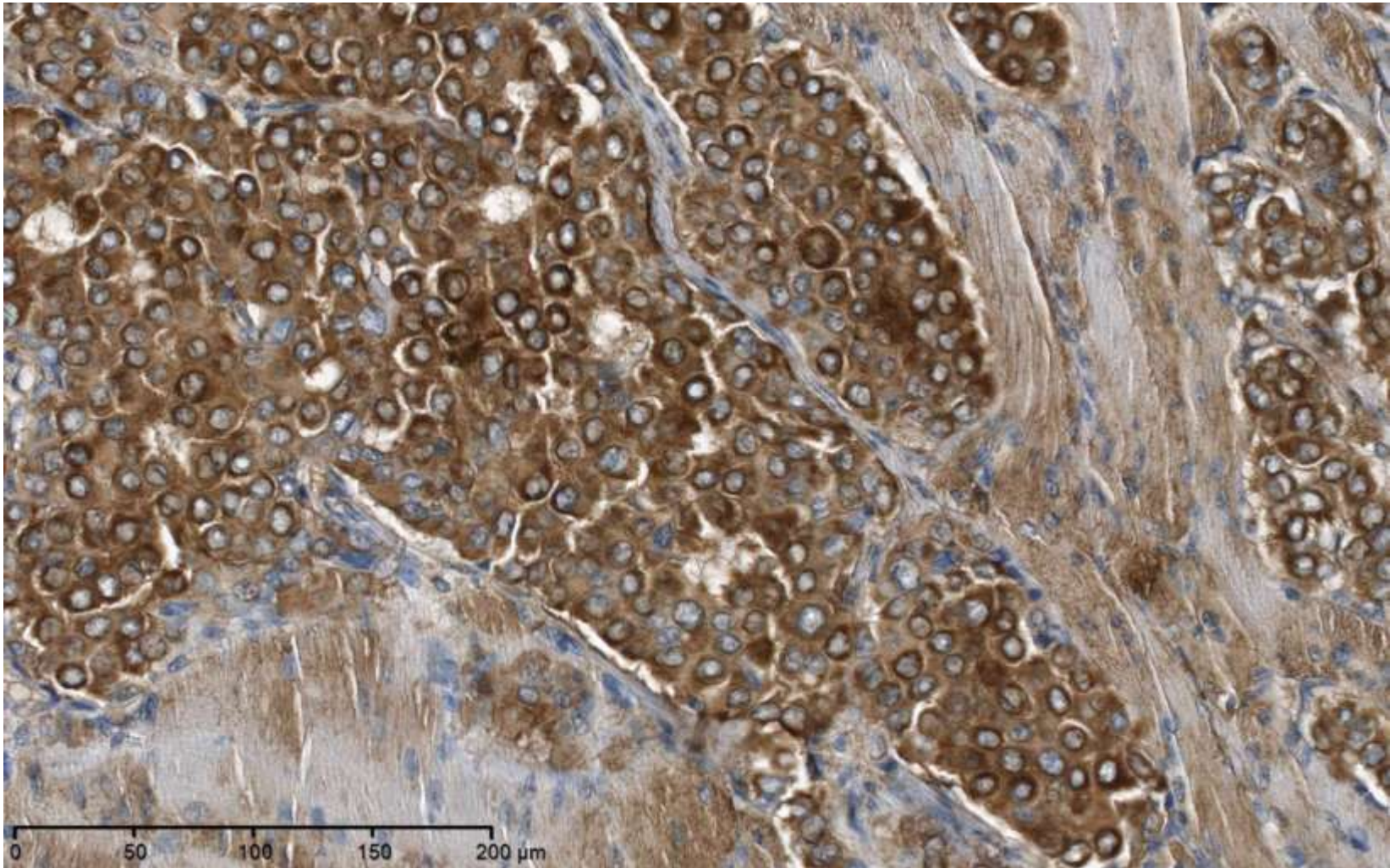
- **Immunohistochemistry (IHC)**

- fixed, paraffin-embedded tissue sections
- increase in uPA/PAI-1 values in ELISA leads to increasing staining intensity (Jänicke et al., 1990; Reilly et al., 1992)
- automated scanning of tumor tissue specimens

# Immunohistochemical evaluation of uPA and PAI-1 protein levels



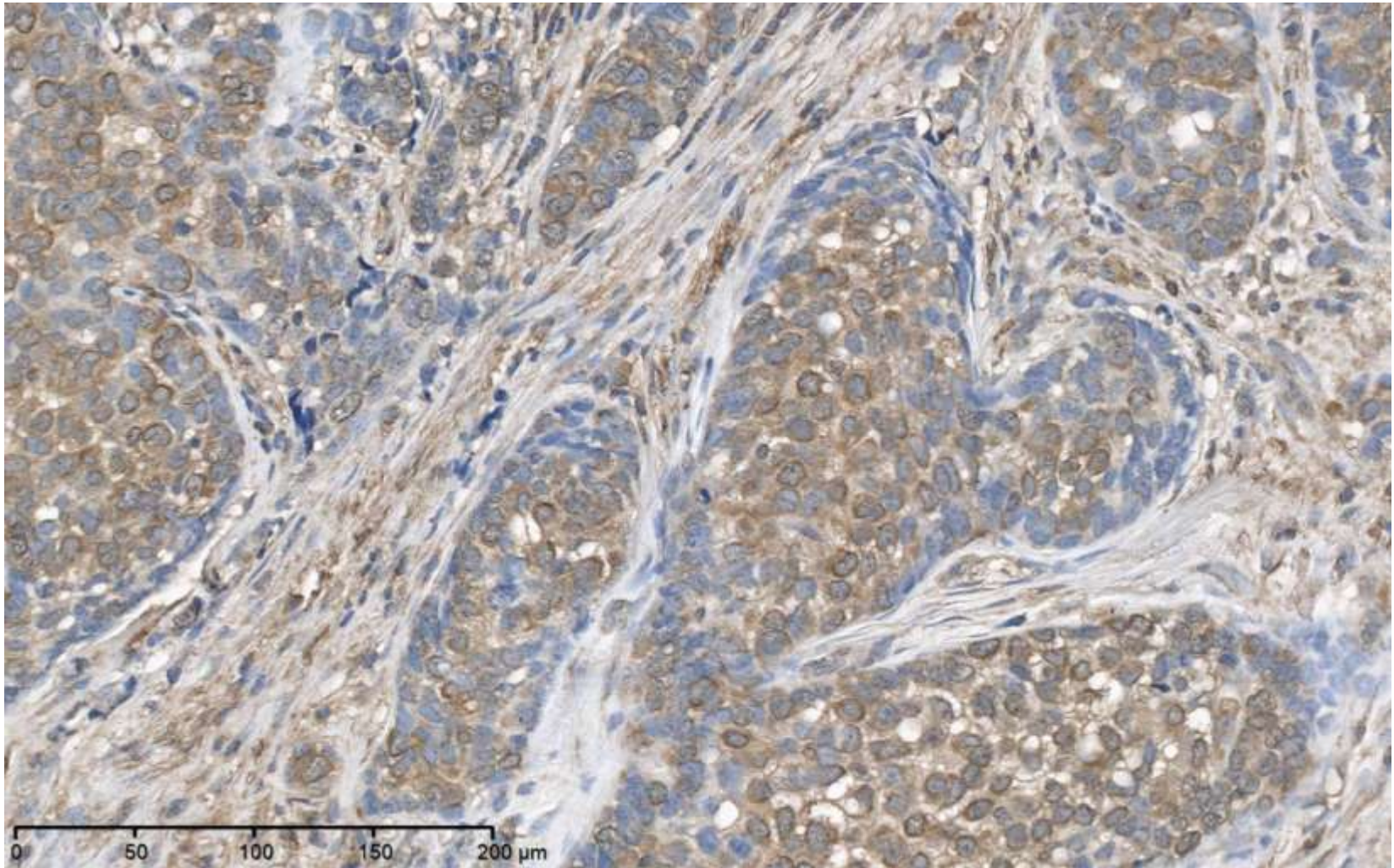




**uPA protein expression in ductal invasive breast cancer**  
(mouse monoclonal antibody directed to uPA, Ventana BenchMark®)

scanned with a Hamamatsu NanoZoomer virtual microscope (Hamamatsu Instruments, Herrsching, Germany)

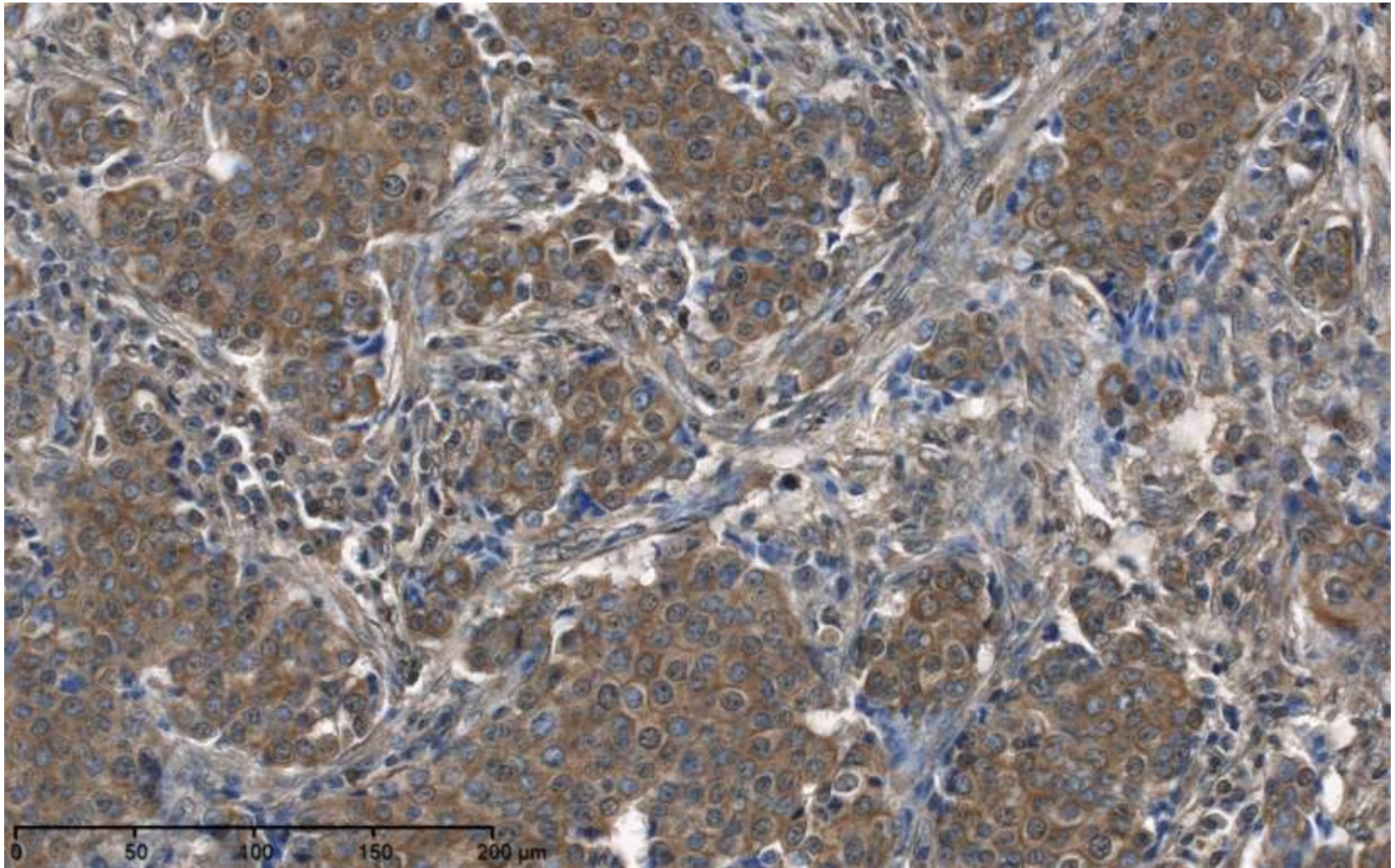




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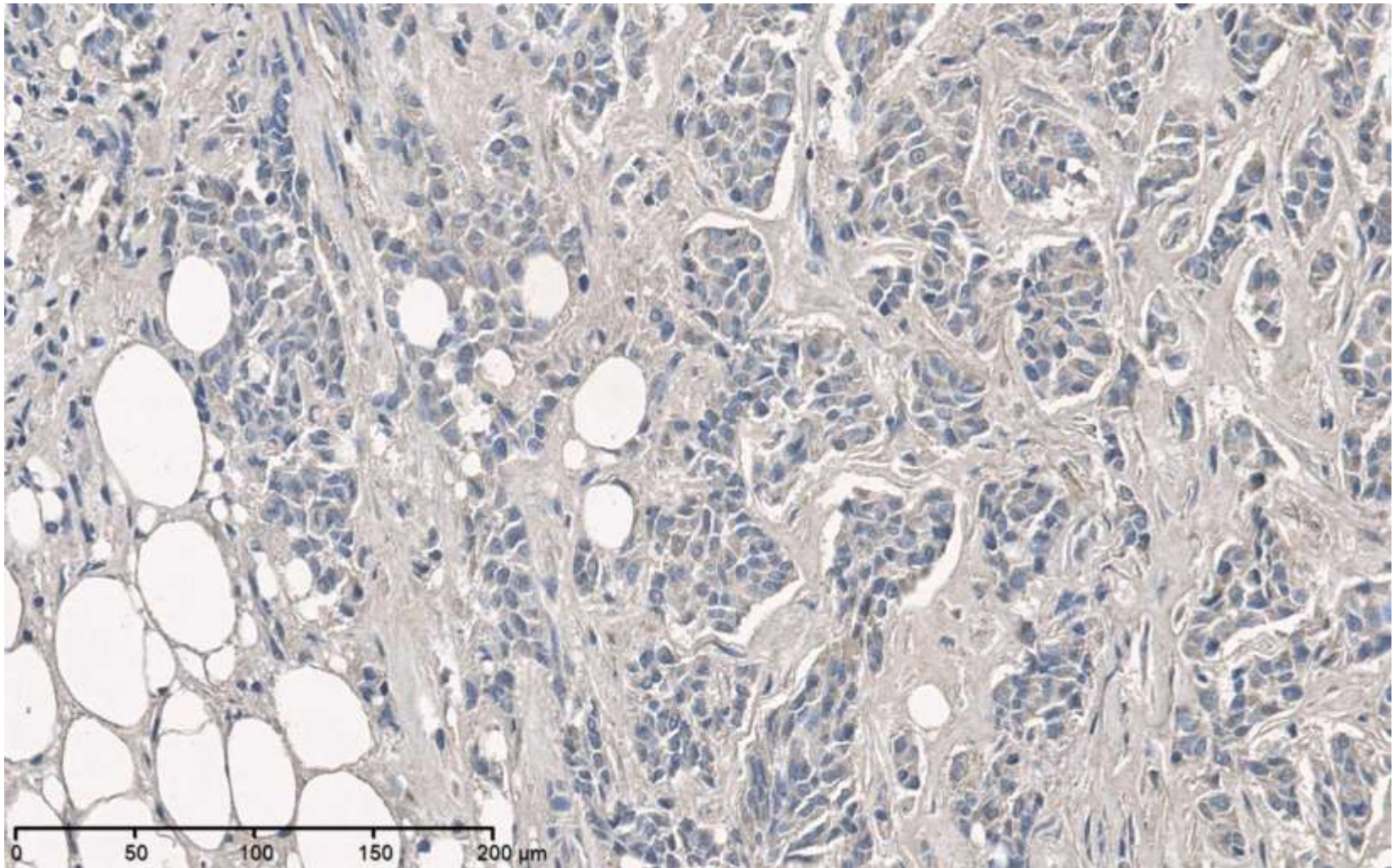




**PAI-1 protein expression in ductal invasive breast cancer**  
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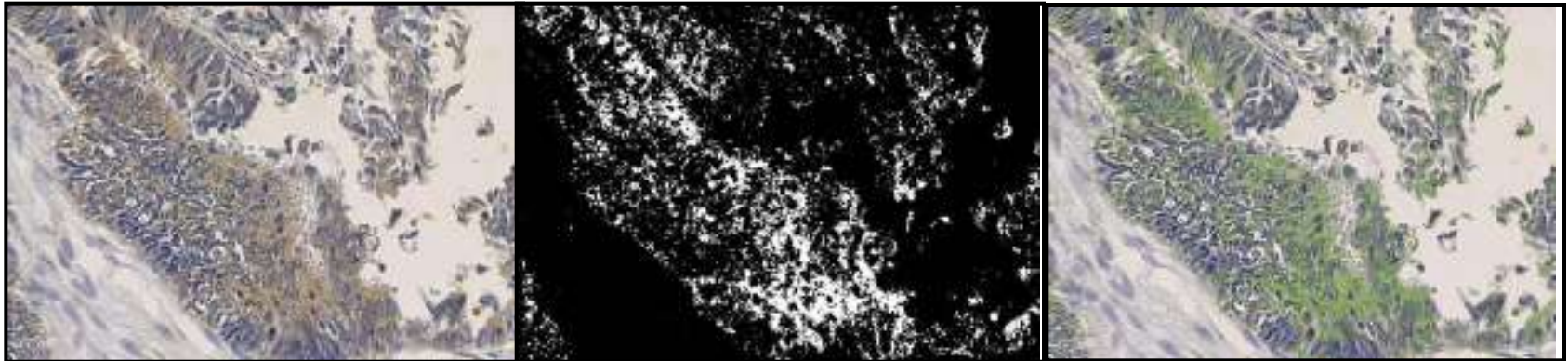




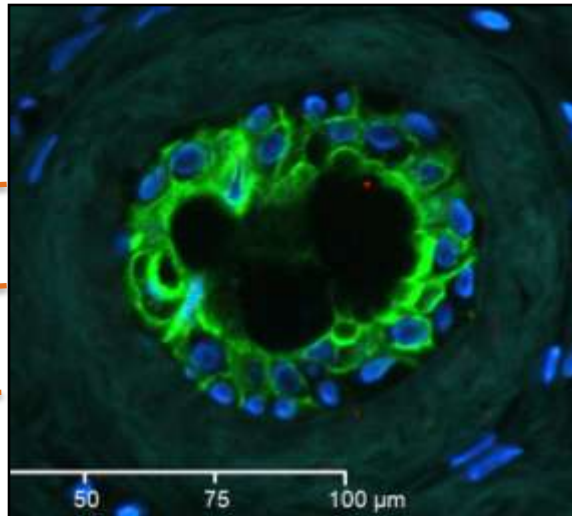
**PAI-1 protein expression in ductal invasive breast cancer**  
(mouse monoclonal antibody directed to PAI-1, Ventana BenchMark®)

scanned with a Hamamatsu NanoZoomer virtual microscope (Hamamatsu Instruments, Herrsching, Germany)

# Automated image analysis



SlidePath, Dublin



score



quantification

intensity

extent



## ***Correlation of uPA and PAI-1 values obtained by IHC score with***

- **ELISA values**
- **Clinical data**
  - **patient age**
  - **tumor size**
  - **nodal status**
  - **hormone receptors**
  - **HER2**
- **Prognosis**





## ***People involved...***

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