

Co-expression of p-HER2 and p-HER3 defines a novel subgroup among HER2-negative breast cancer patients



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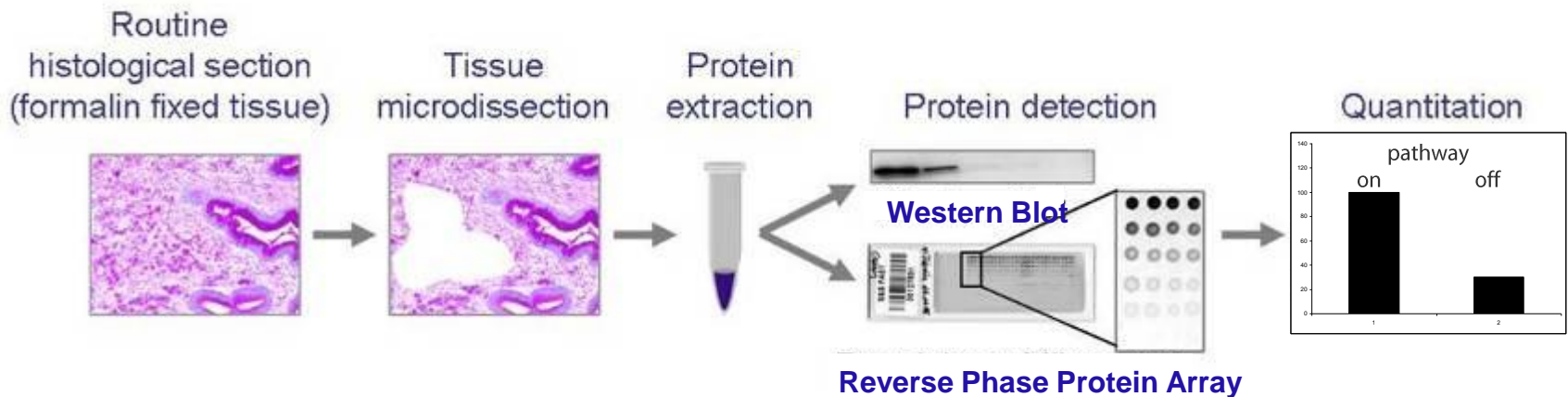


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Our approach:

“Liquid Morphology”



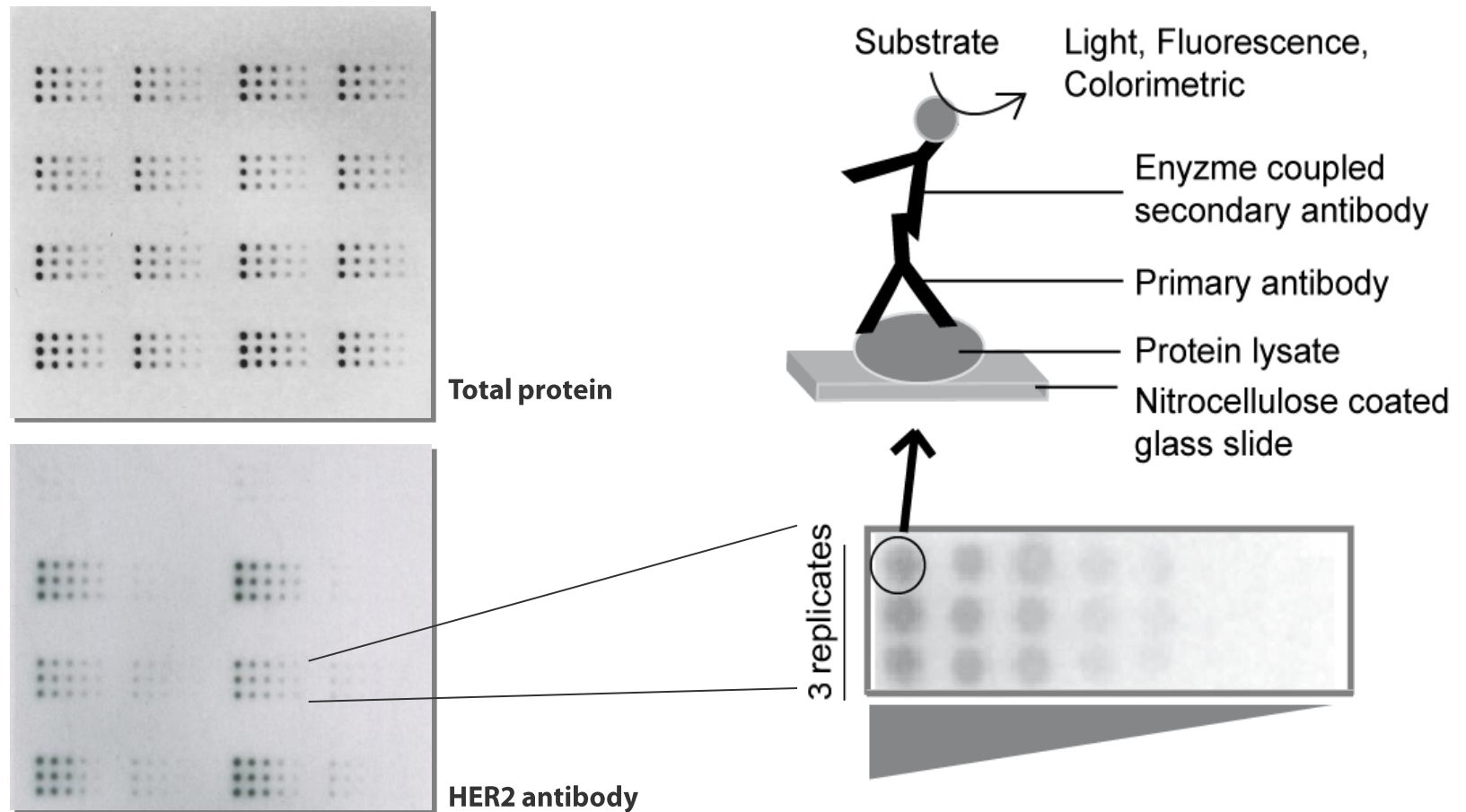
“Liquid Morphology”: Combining Proteomics With Immunohistochemistry.

Becker, Karl-Friedrich and Taylor, Clive R.
 Applied Immunohistochemistry & Molecular Morphology, 2011

Quantitative protein analysis from formalin-fixed tissues: implications for translational clinical research and nanoscale molecular diagnosis

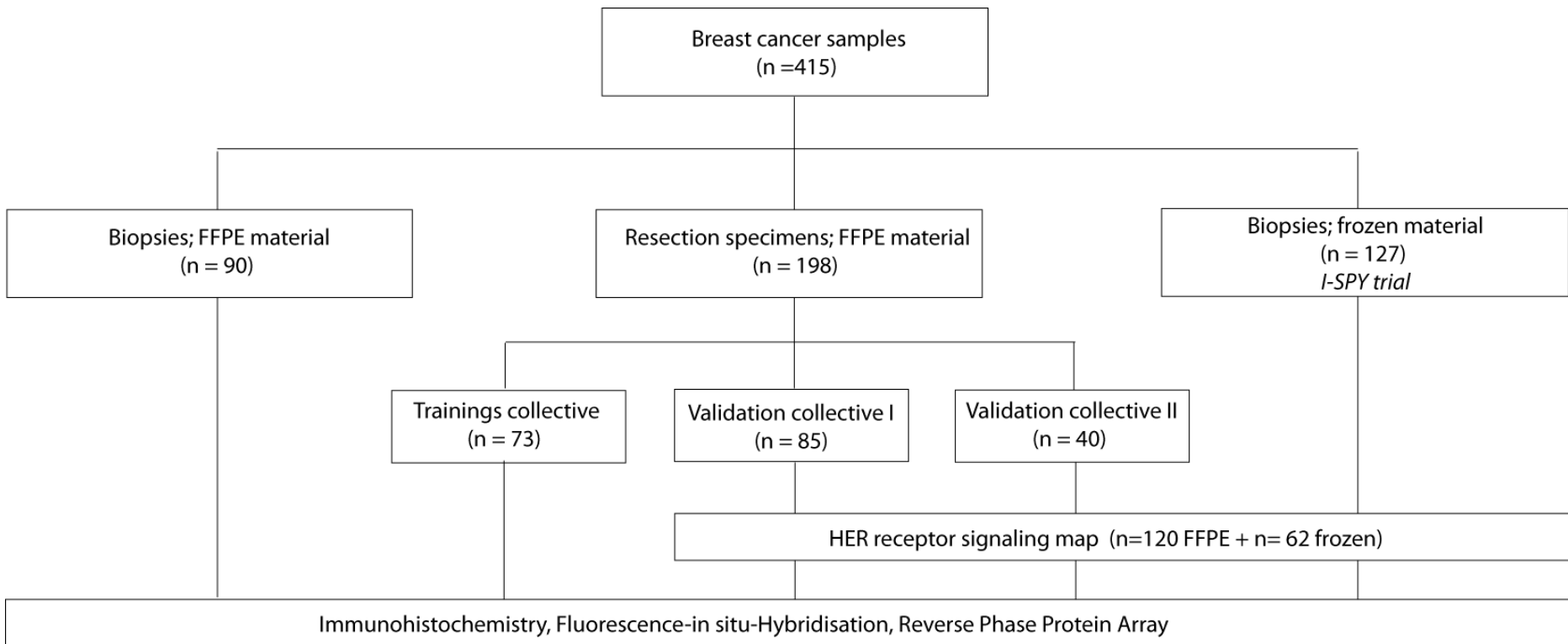
Becker *et al.* Journal of Pathology, 2007

The principle of Reverse Phase Protein Array

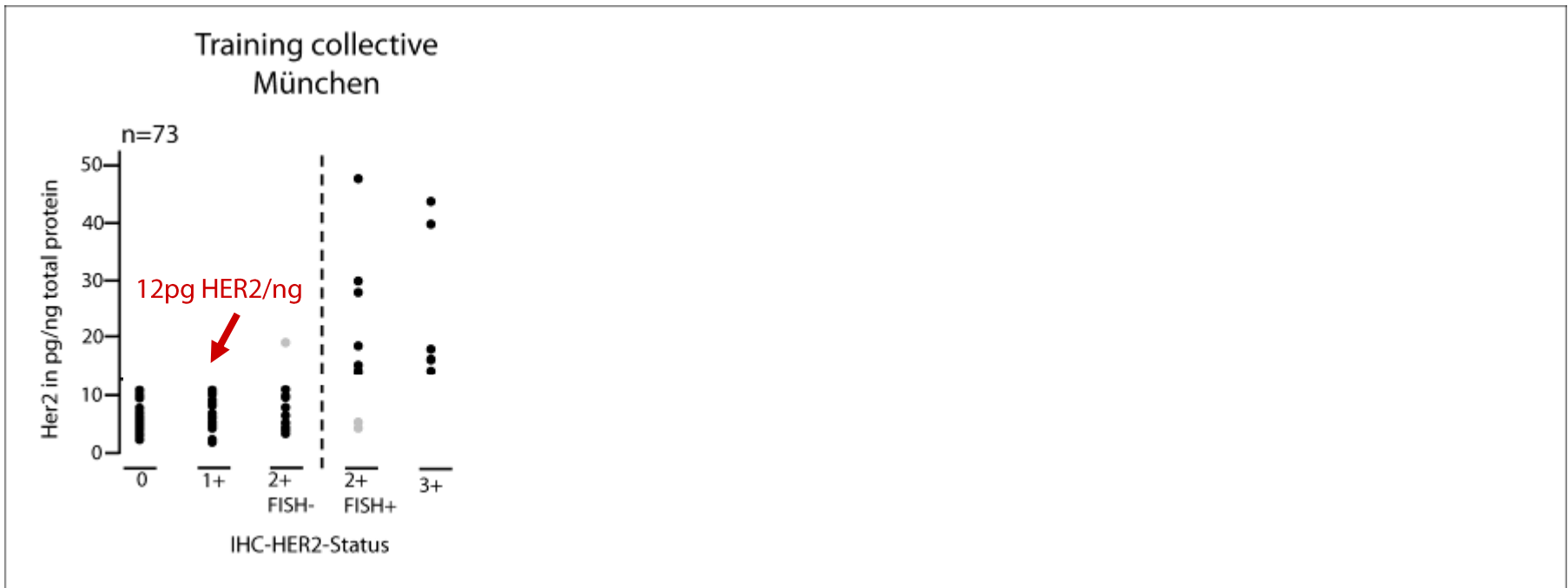


Example: HER2 in breast cancer

The patient cohort



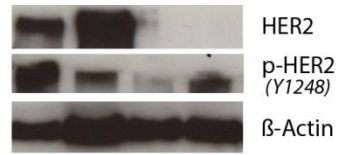
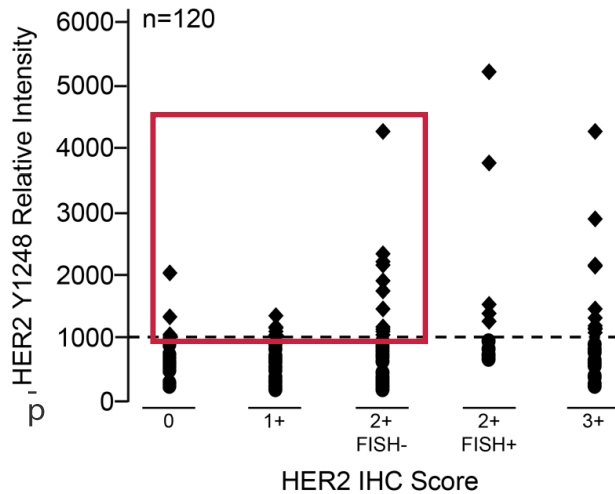
RPPA as a reliable method for HER2 determination



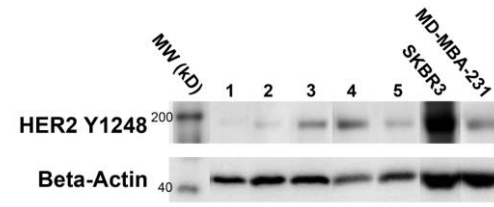
Concordance between RPPA and IHC/FISH: 93%

HER2 negative but p-HER2 positive cases

Germany/FFPE



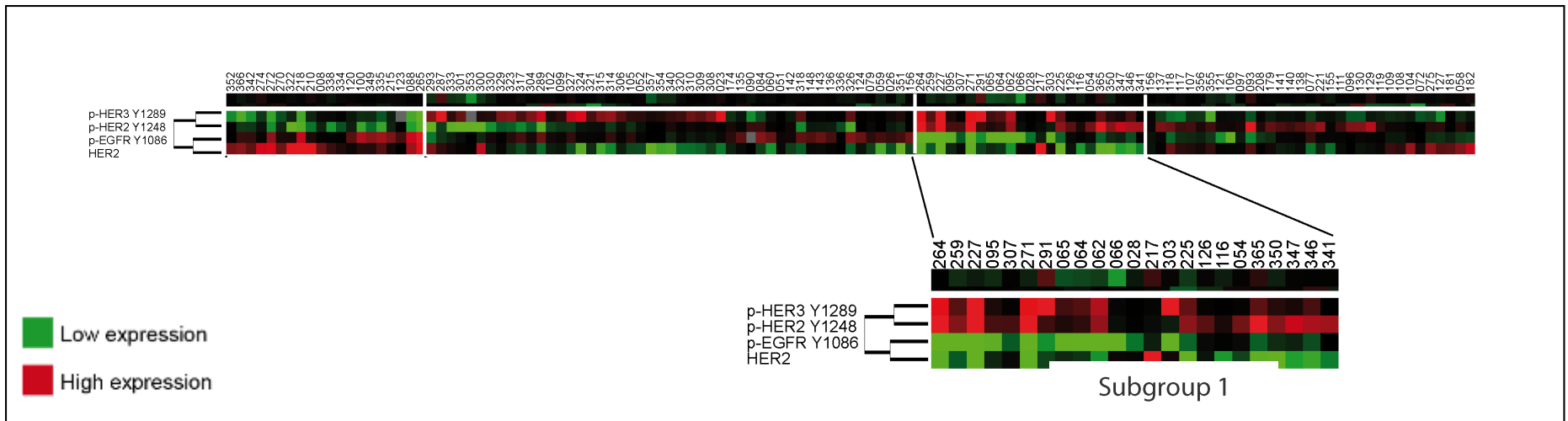
HER2 IHC/FISH	+	+	-	-
HER2 RPPA	+	+	-	-



Her2 FISH Status:	-	-	-	-	+
HER2 IHC Status:	-	-	-	-	+
HER2 RPPA Status:	-	-	-	-	+
pHER2 RPPA Status:	-	-	+	+	-

Example: HER2 in breast cancer

Identification of a novel subgroup



HER2 negative

but p-HER2 positive and p-HER3 positive

→ Candidates for trastuzumab and/or pertuzumab therapy

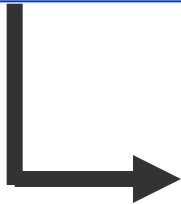
Molecular Analysis of HER2 Signaling in Human Breast Cancer by Functional Protein Pathway Activation Mapping.
Wulfkühle et al.; Journal of Clinical Oncology, submitted.

HER2 Status and Benefit from Adjuvant Trastuzumab in Breast Cancer

Paik S, Kim C, Wolmark N.

N Engl J Med. 2008 Mar 27;358(13):1409-11.

„Among the 1787 patients with follow-up data, 174 patients had breast cancers that were found to be central HER2-negative (9.7%), yet these patients also appeared to benefit from trastuzumab..“



Our hypothesis:
These patients may be phospho-HER2 positive!

(negotiation for collaboration is initiated)

Summary

- 1. Tumors will be categorized according to deregulated pathways/networks**
- 2. Precise quantification of (activated) proteins in clinical tissues using RPPA**
- 3. 117 signaling endpoints established so far**
- 4. p-HER2 detected in HER2-negative breast cancers (up to 25% of the HER2 negative cases) -> novel biomarker for trastuzumab/pertuzumab therapy?**
- 5. Clinical studies warranted**

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Example: HER2 in breast cancer

Absolute quantification

