

**EORTC-NCI-ASCO Meeting on Molecular Markers in Cancer 15-17th
November 2007, Brussels**

**Validation of Novel Breast Cancer
Biomarkers Arising from Re-Analysis
of Publicly Available DNA Microarray
Datasets via Tissue Microarray
Technology**

**Dr Cathy Kelly
Clinical Oncology Fellow**



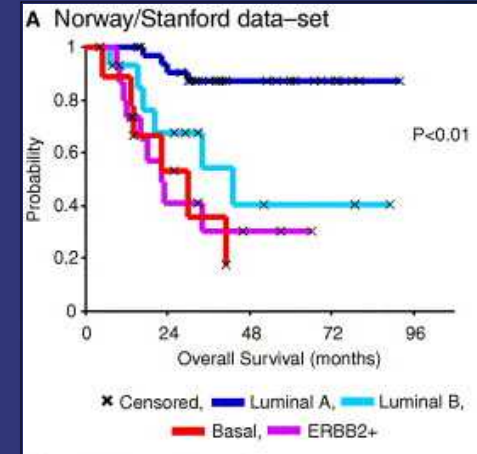
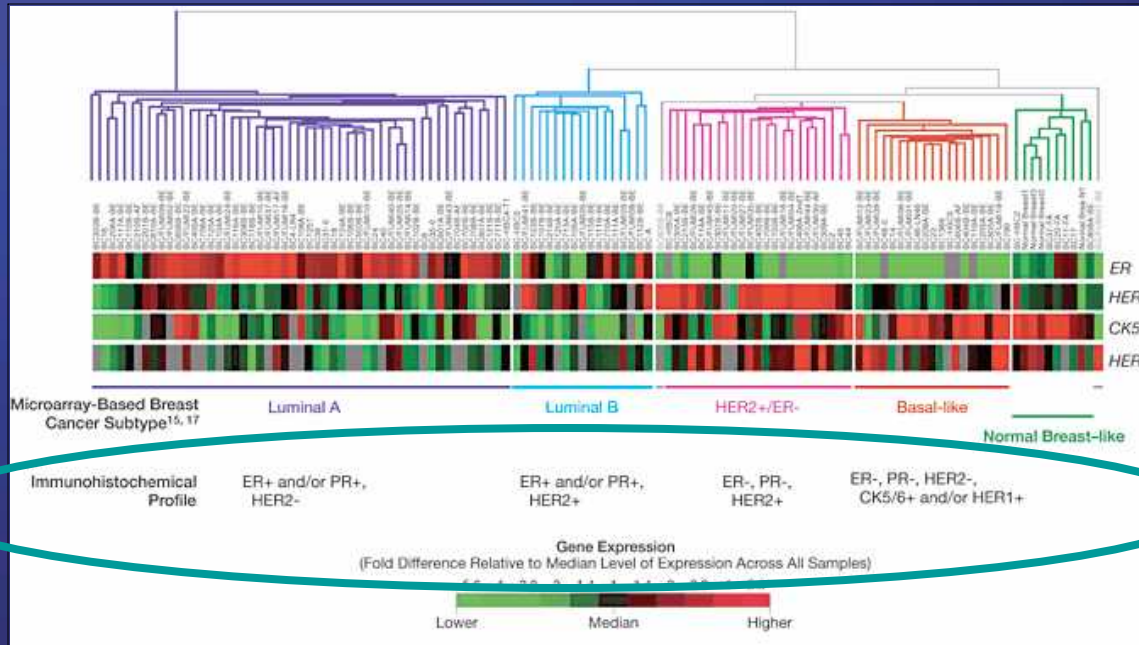
**UCD School of Biomolecular and Biomedical Science
UCD Conway Institute, University College Dublin**



Biomarkers in Breast Cancer

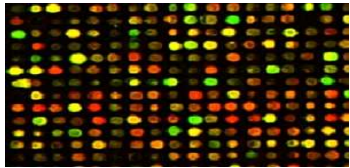
Biomarker	Type	Source	Assay	Clinical Use
ER and PR	Protein	Breast Tumour	IHC	Prognosis and selection of therapy
HER2/NEU	Glycoprotein	Breast Tumour	IHC	Prognosis and selection of therapy
HER2/NEU	Glycoprotein	Serum	ELISA	Monitoring
HER2/NEU	DNA	Breast Tumour	FISH	Prognosis and selection of therapy
Cytokeratins	Protein	Breast Tumour	IHC	Prognosis
CA15-3	Glycoprotein	Serum	ELISA	Monitoring
CA27-29	Glycoprotein	Serum	ELISA	Monitoring
MammaPrint	DNA microarray	Fresh frozen tissue	DNA microarray	Prognosis
Oncotype DX	DNA microarray	FFPE tissue	RT PCR	Prognosis

IHC Surrogate of Gene Expression Profiles



Sorlie *et al.* PNAS (2002)

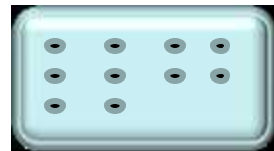
Nielsen *et al.* Clin. Cancer Res. (2004)
Carey *et al.* JAMA (2006)



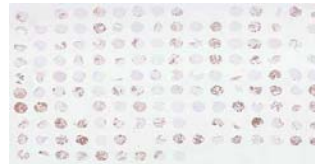
1. Biomarker discovery using DNA microarray datasets



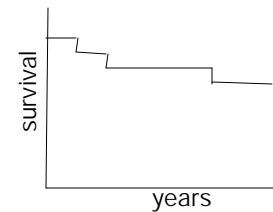
2. Specificity assessment



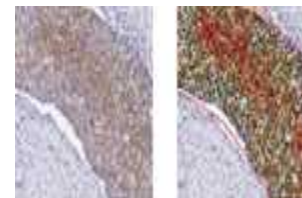
3. IHC optimization



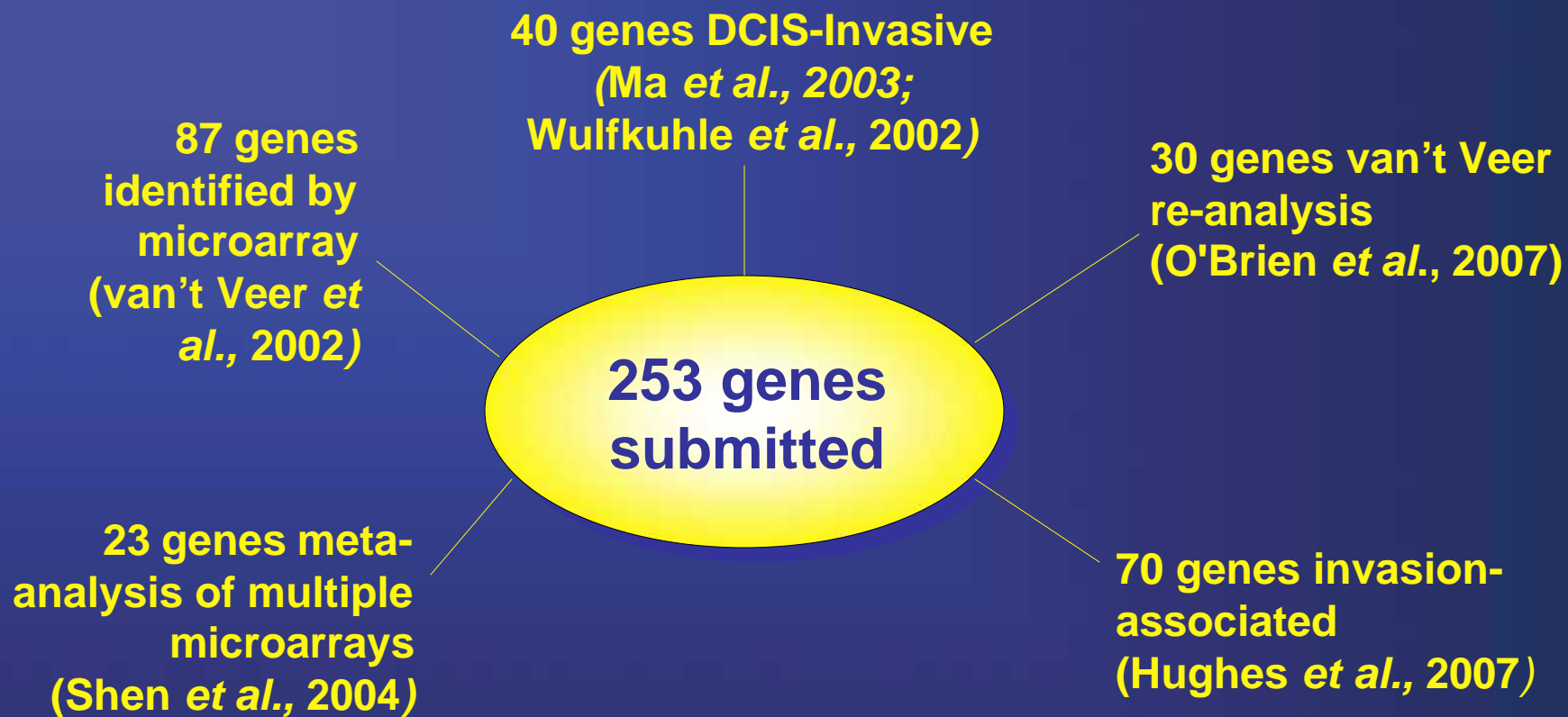
4. Optimisation on TMA



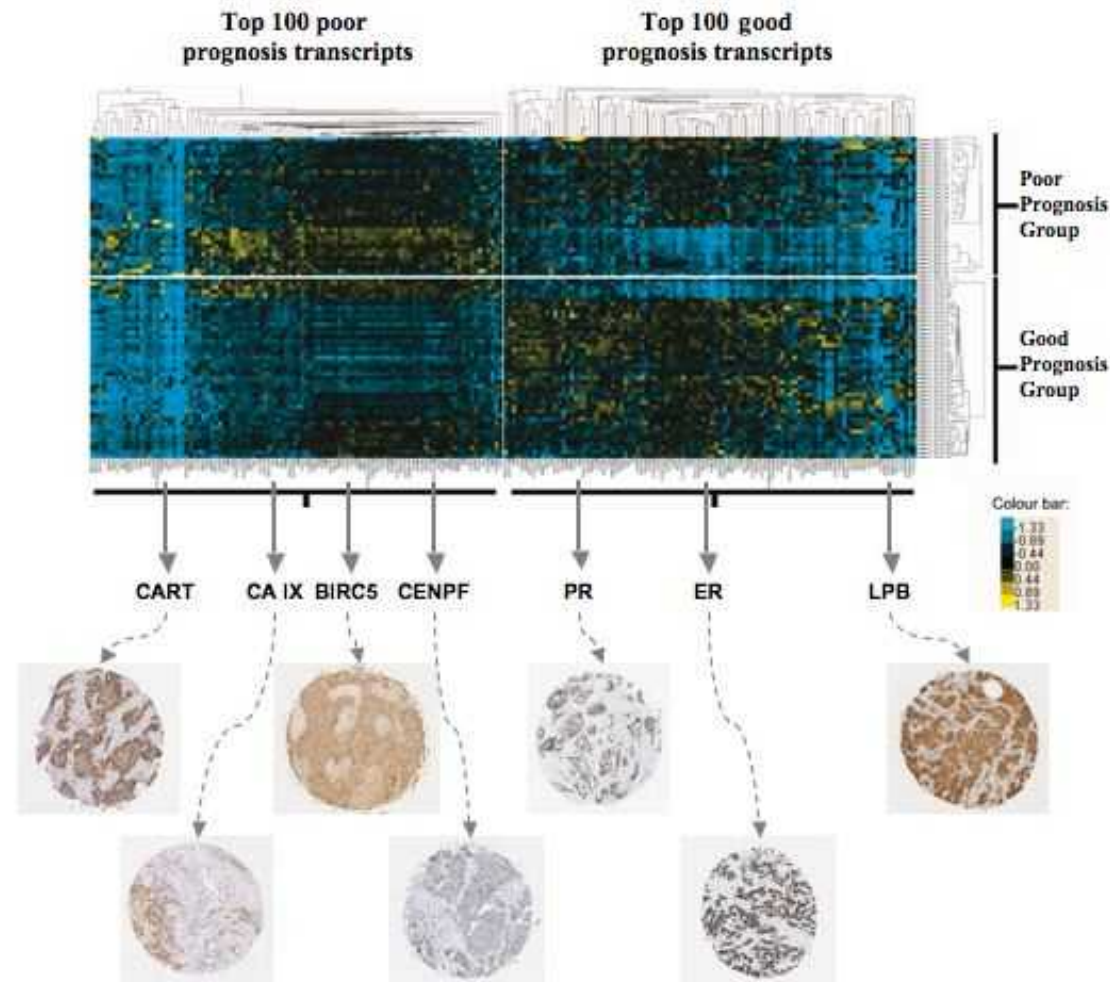
5. Validation



6. Image analysis



From DNA to Tissue Arrays



O'Brien SL *et al.* *Int J Cancer*, 120(7), 1426-1435 (2007)

Human Protein Atlas [COLLABORATOR VERSION] - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address <http://hpr-external.genpat.uu.se/>

hpa the project protein atlas dictionary disclaimer submission of antibodies

HUMAN PROTEIN ATLAS

The human protein atlas displays expression and localization of proteins in a large variety of normal human tissues and cancer cells. The data is publically available and presented as high resolution images of immunohistochemically stained tissues and cell lines. Available proteins can be reached through searches for specific genes or by browsing individual chromosomes. In addition, the [advanced search](#) includes the possibility to search for expression patterns in defined tissues and cells. The human protein atlas is periodically upgraded and new data is added to the database annually.

Enter search:

Or choose a chromosome:

1	5	9	13	17	21
2	6	10	14	18	22
3	7	11	15	19	X
4	8	12	16	20	Y

OTHER

2006-10-30
A new version of the Human Protein Atlas has been released. The new version contains more than 1 million images corresponding to more than 1500 antibodies. All HPA-antibodies in the Human Protein Atlas are now [available](#).

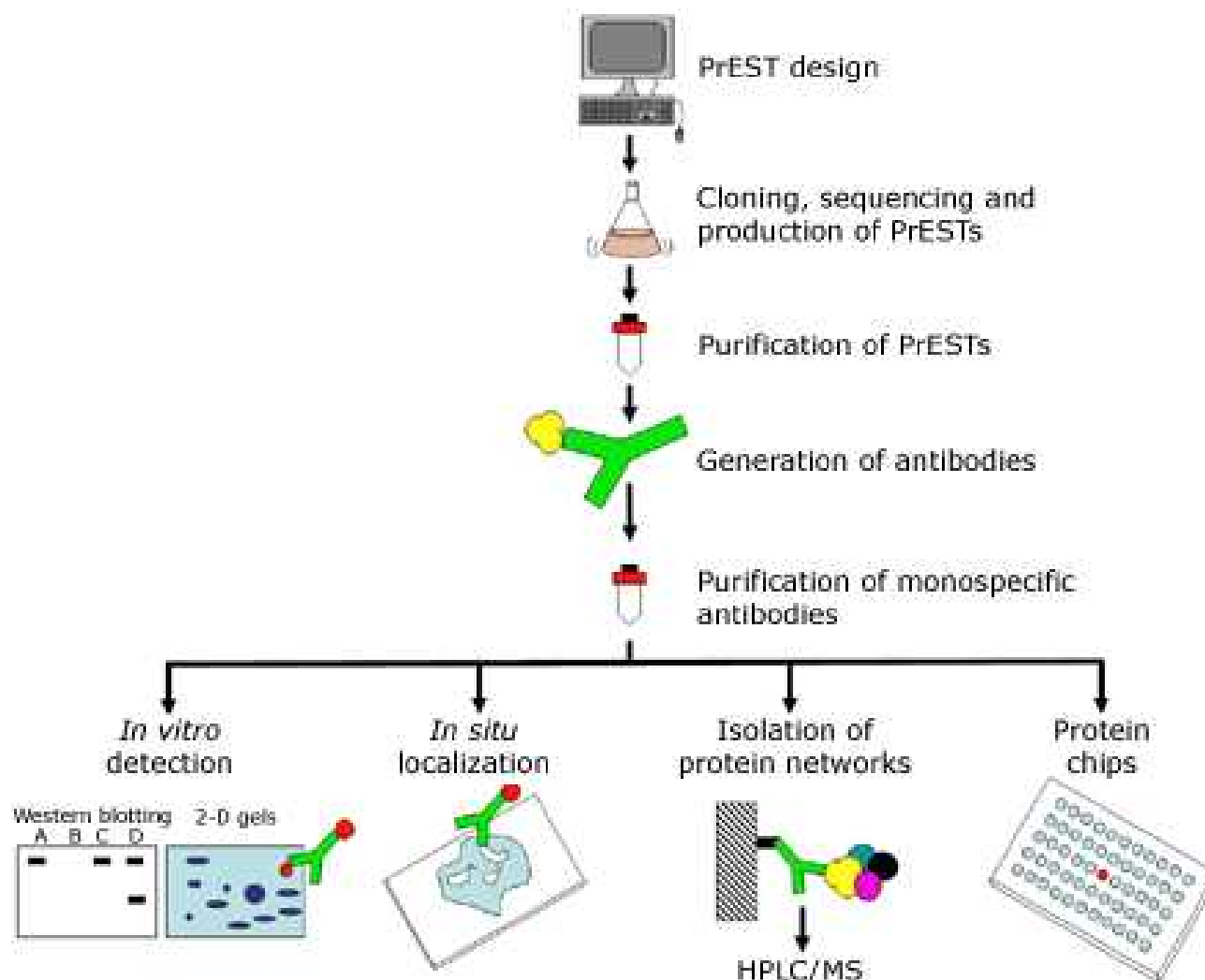
Collaborator access:
Username: Password:

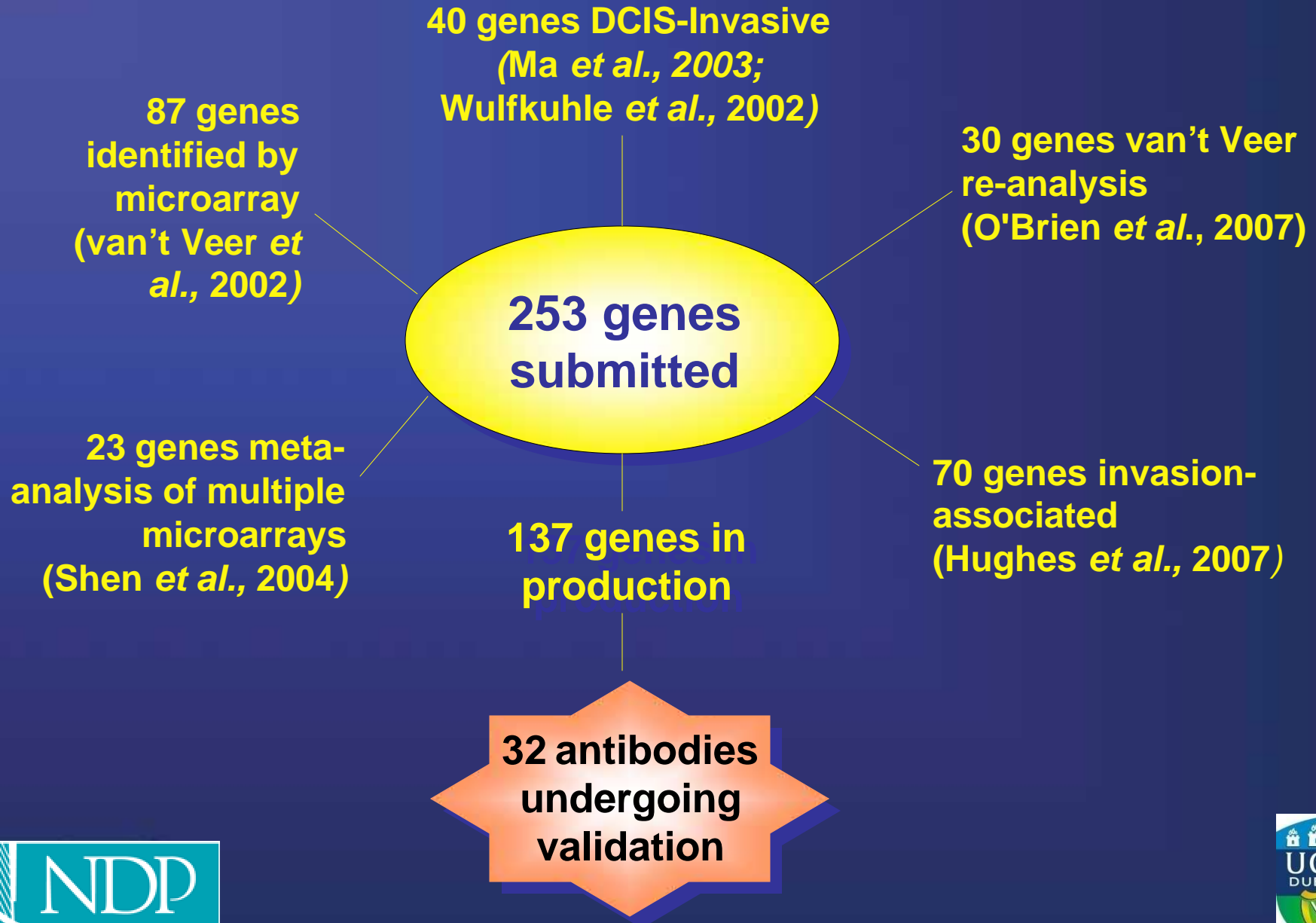
Knut och Alice Wallenbergs Stiftelse
The HPR project is funded by the Knut & Alice Wallenberg foundation. The atlas is part of the HUPO Human Antibody Initiative ([HAI](#)).

Start Entrez PubM... UCD Connect... https://imap... https://imap... https://imap... Human Prot... Microsoft Po... Wireless Net... Z Microsoft ... EN Norton 04:30

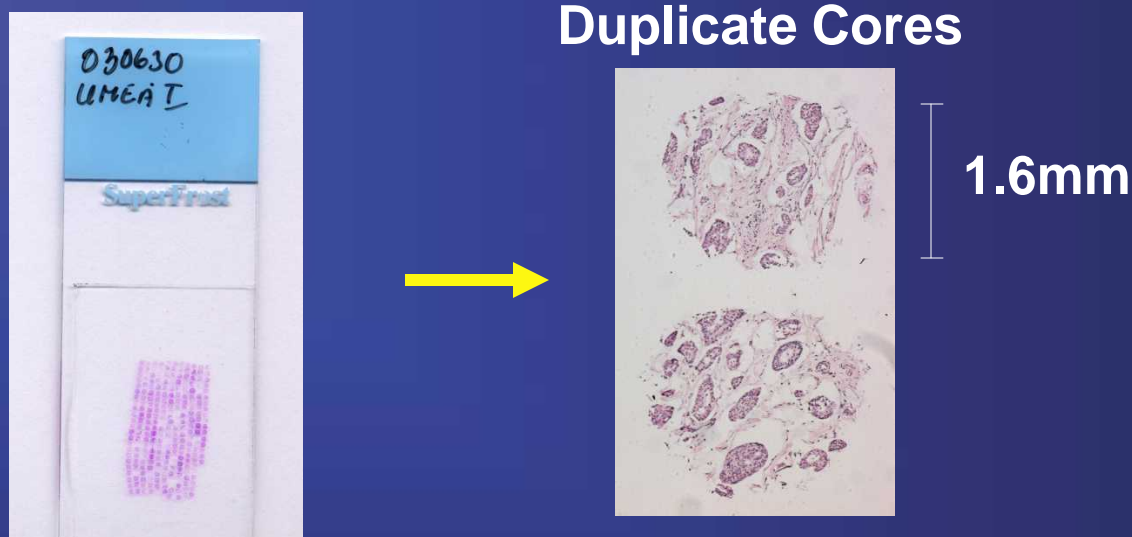


Swedish Human Proteome Resource Antibody Production



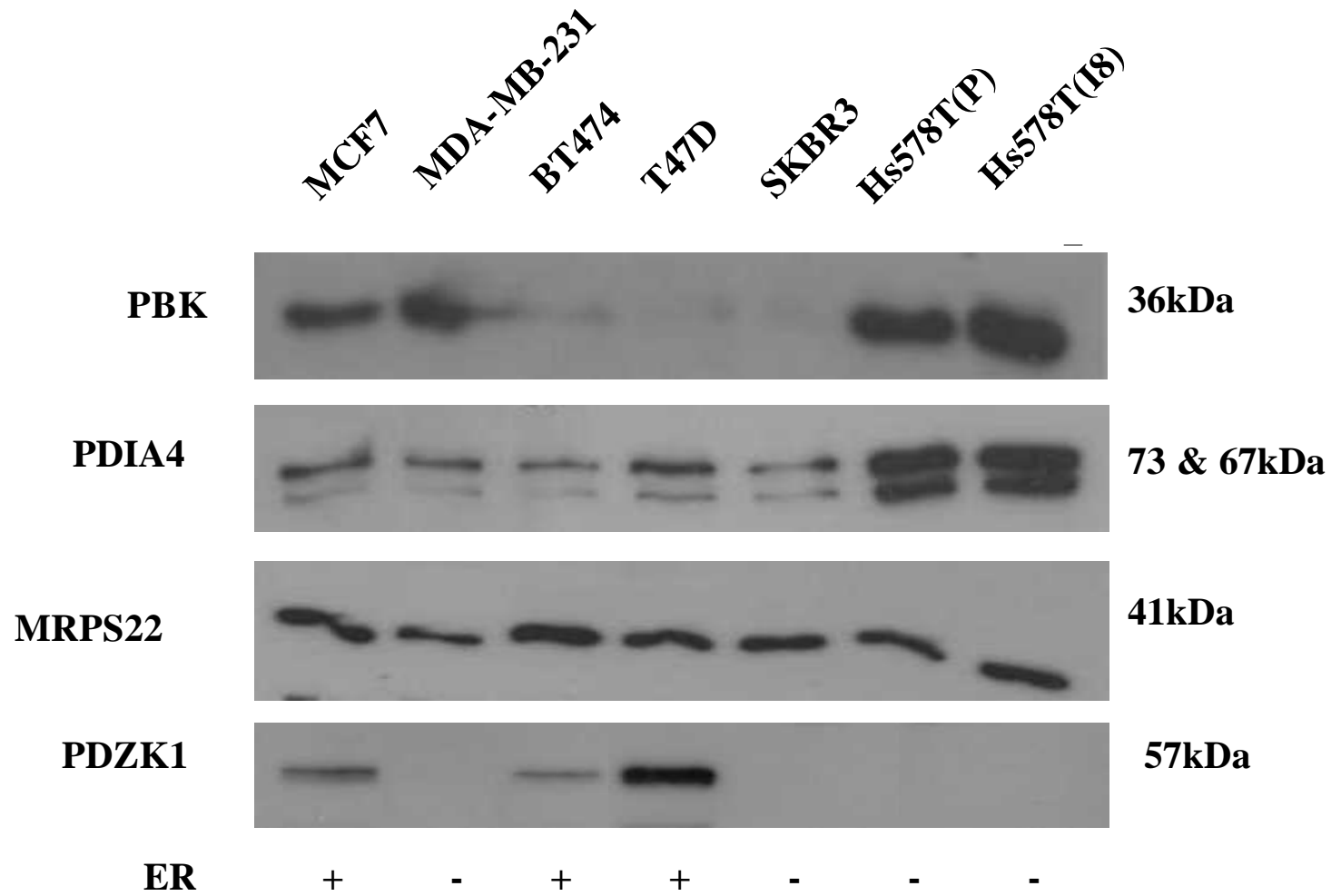


Breast Cancer TMAs



- Breast tumours were collected and the TMA generated at Malmo University Hospital, Sweden
- Tumours come with extensive clinicopathological data, e.g. response to tamoxifen treatment

Work in Progress

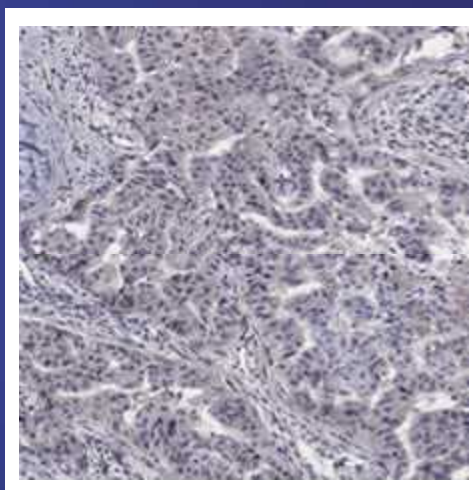
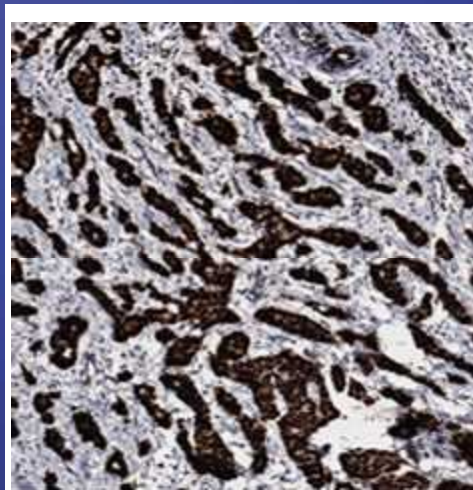


PDZK1 Staining Correlates with ER Positivity

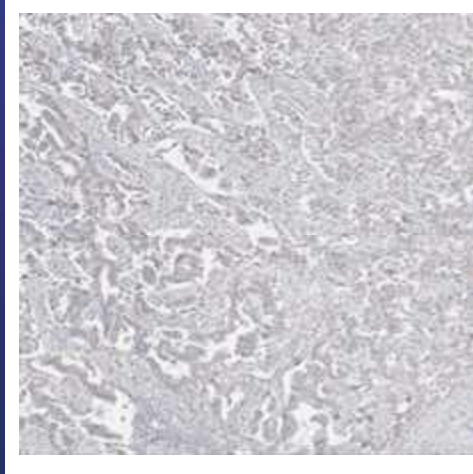
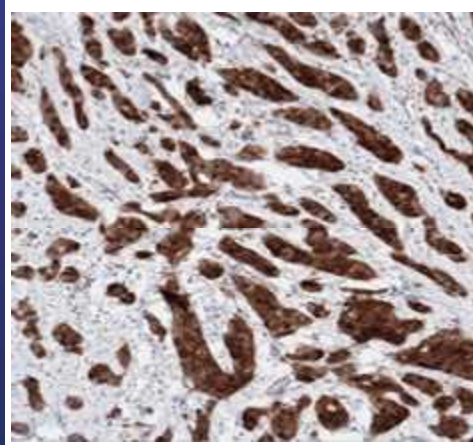
POSITIVE

NEGATIVE

ESTROGEN
RECEPTOR



PDZK1

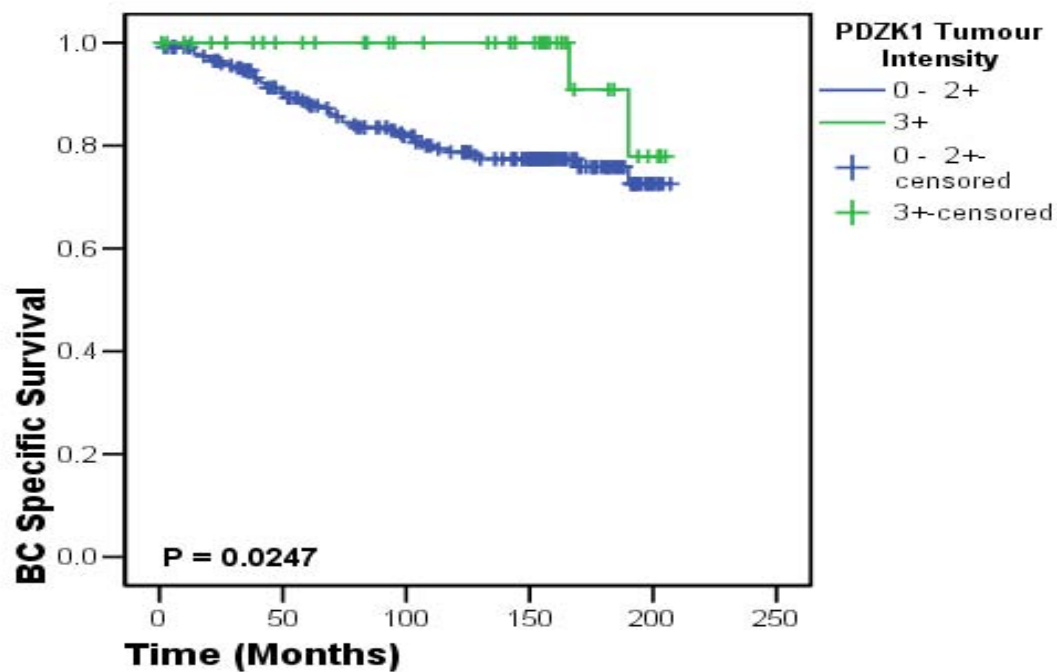


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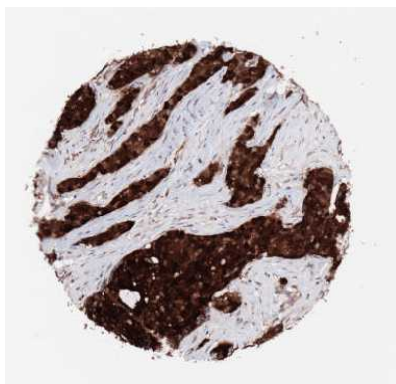
Biology of PDZK1

- Estrogen-responsive gene
- BGA “Good Prognosis” list
- Signal transduction, cell polarity, ion channel gating
- Role in breast cancer?
- Physiological response to estrogen

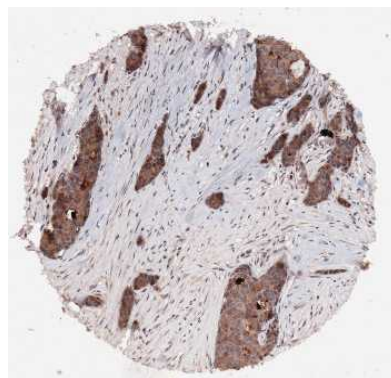
PDZK1 Expression Associated with improved breast cancer specific survival



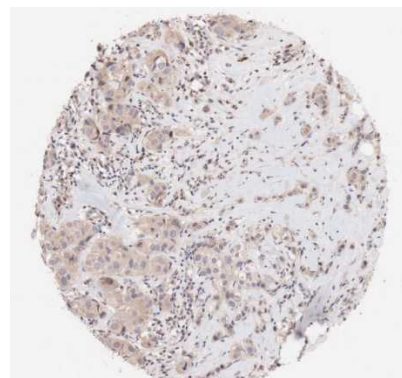
3+



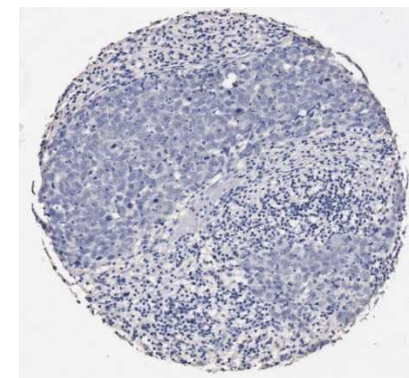
2+



1+



0



Summary

- Biomarker validation continues to lag behind discovery
- Re-analysis of publicly available DNA microarray datasets can be cost-effective method for candidate biomarker selection/prioritisation
- Good quality TMAs can be used to validate both prognostic and predictive biomarkers
- Digital slide scanning/TMA technology will help to accelerate the validation process

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The European Commission
IRCSET
European Molecular Biology Organization



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