A Day in the Life of a Breast Cancer Doctor: Integrating Omics to Optimize Patient Outcomes

CANCER PROGRESS by Defined Health

March 17-18, 2015
New York, NY

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Moderator:

Otis Webb Brawley, MD, FACP, Chief Medical and Scientific Officer, Executive Vice President, Research, American Cancer Society

Panelists:

- *Brad Gray*, President & CEO, NanoString Technologies, Inc.
- *Amy Krie, MD*, Medical Oncology and Hematology, Avera Cancer Institute
- *Manfred Lehnert, MD*, VP and Head, Innovation, Oncology Therapeutic Area Unit, Takeda Pharmaceuticals International Co.
- *Brian Leyland-Jones, MB BS, PhD*, VP, Molecular and Experimental Medicine, Avera Cancer Institute
- *John J. Sninsky, PhD*, Chief Scientific Officer, CareDX

Integrating Omics to Optimize Patient Outcomes

The Power of Molecular Subtype

Brad Gray
President & CEO
NanoString Technologies

Cancer Progress by Defined Health
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TCGA Breast Study: Thorough Study of Breast Cancer Genomics and Proteomics

4 OCTOBER 2012 | VOL 490 | NATURE | 61

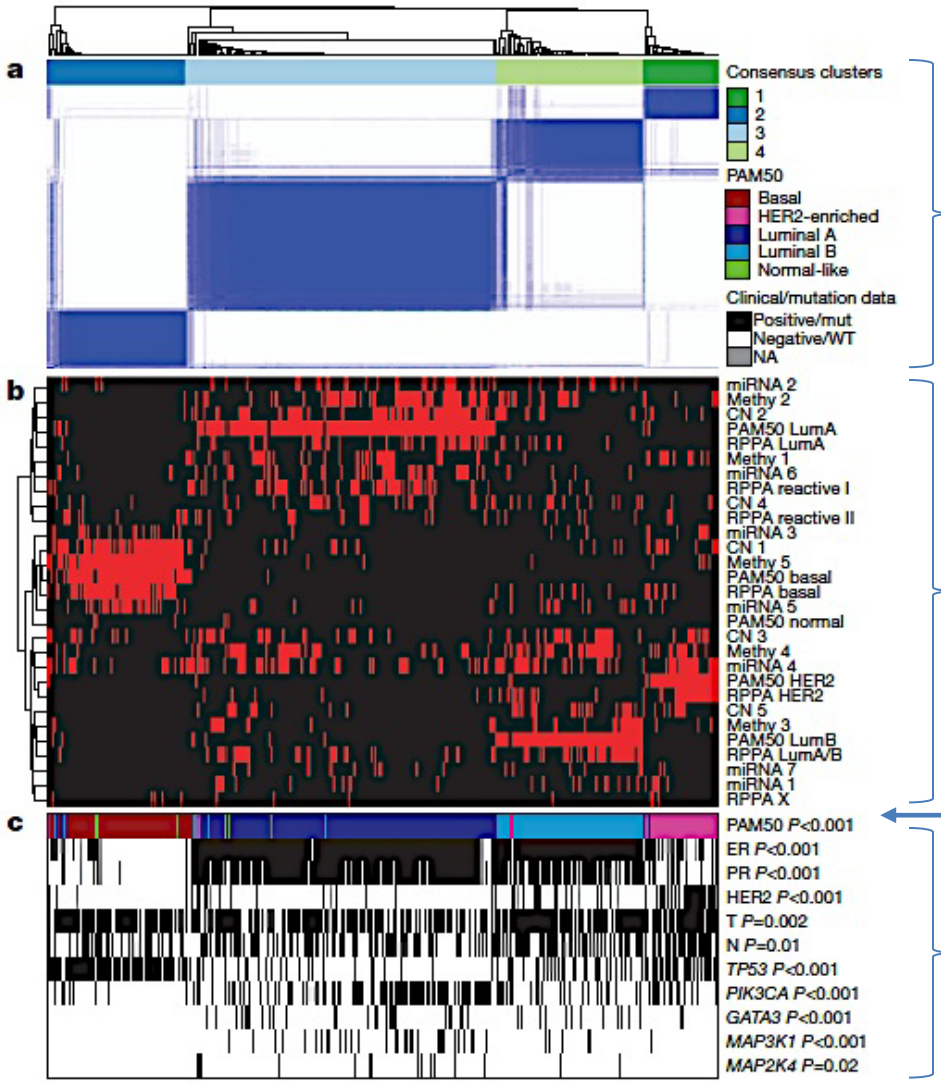
Comprehensive molecular portraits of human breast tumours

The Cancer Genome Atlas Network*

- Profiled tumor and germline from 825 cancer patients
- 466 tumors with sufficient material to profile across all 5 platforms
  - Agilent mRNA expression microarrays
  - Illumina Infinium DNA methylation chips
  - Affymetrix 6.0 SNP arrays
  - miRNA sequencing
  - Whole-exome sequencing
- 348 of the 466 profiled on reverse-phase protein array (RPPA)

Source: *Comprehensive molecular portraits of breast cancer.* Nature. 2012 Oct 4;490(7418):61-70.

TCGA Breast Study: Gene & Protein Alterations Correlated with Molecular Subtypes defined by PAM50 Gene Signature



TCGA consensus clustering generates four breast cancer subtypes

Heat-map of subtypes defined independently by:

- miRNAs
- DNA methylation
- copy number
- RPPA expression

Molecular subtype defined by PAM50 (LumA, LumB, HER2-enriched, Basal)

Associations with molecular and clinical features (e.g., mutations)

Source: *Comprehensive molecular portraits of breast cancer.* Nature. 2012 Oct 4;490(7418):61-70.

Molecular Subtypes: Guide Therapy per St. Gallen Guidelines

Luminal A	• Endocrine therapy alone
Luminal B	• If HER2^{-}, endocrine +/- cytotoxic therapy • If HER2^{+}, cytotoxics + anti-HER2 + endocrine • Could include anthracyclines and taxanes
HER 2 enriched	• Cytotoxics + anti-HER2 • Could include anthracyclines and taxanes
Basal-like	• Cytotoxics therapy alone, potentially including anthracyclines, taxanes and analkylating agent • Do not routinely use cisplatin or carboplatin

Strategies for subtypes—dealing with the diversity of breast cancer: Highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Annals of Oncology. Advance Access published on line June 27, 2011.

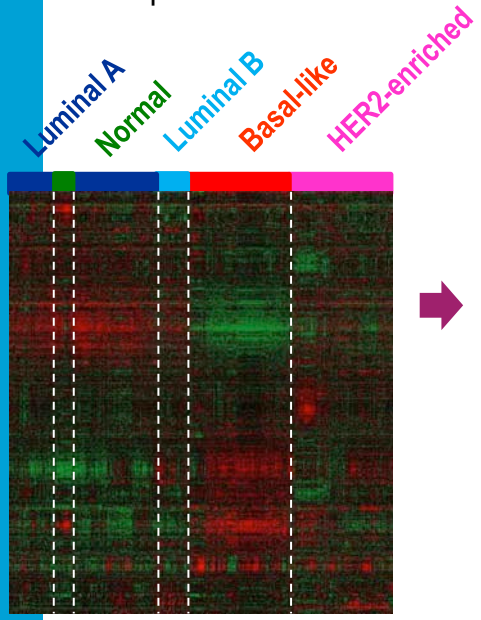
Prosigna: Delivering Molecular Subtype to the Clinic

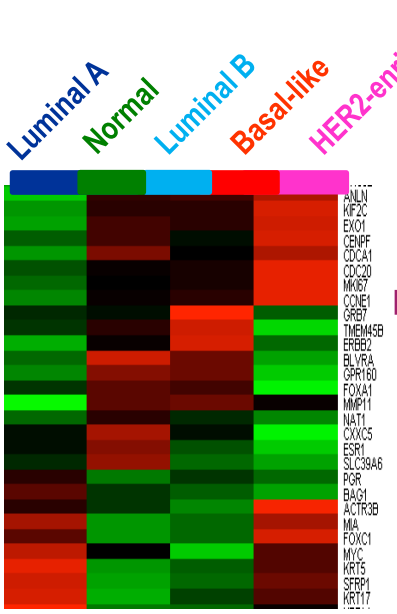
2000
Researchers first describe breast cancer intrinsic subtypes based on microarray experiments

2009
Researchers first describe "PAM50" gene expression signature

2010
NanoString exclusively licenses PAM50 gene expression signature

2013
NanoString began marketing Prosigna after receipt of CE Mark & FDA 510(k)





prosigna™
Breast cancer
prognostic gene signature assay

nanoString®
TECHNOLOGIES

Prosigna: Decentralized *In Vitro* Diagnostic based on PAM50

Hardware
nCounter Dx Analysis System

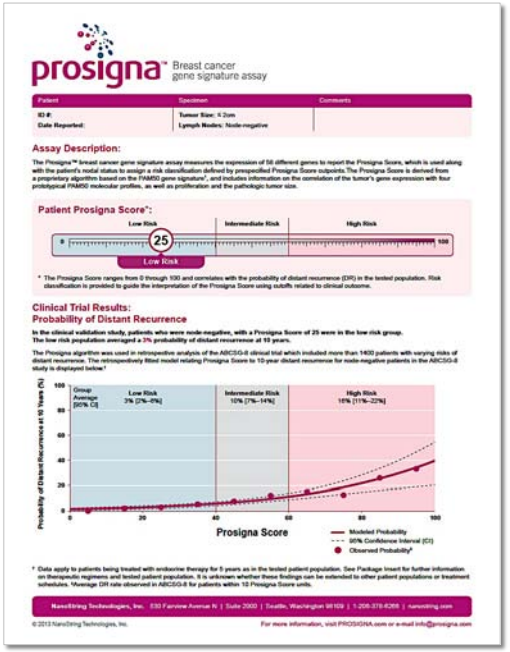
nCounter Dx Prep Station

nCounter Dx Digital Analyzer

Consumable
Prosigna Kits

- 50 gene-based CodeSet with 8 controls
- RNA isolation kit
- Other consumables required for assay

Software
Prosigna Report



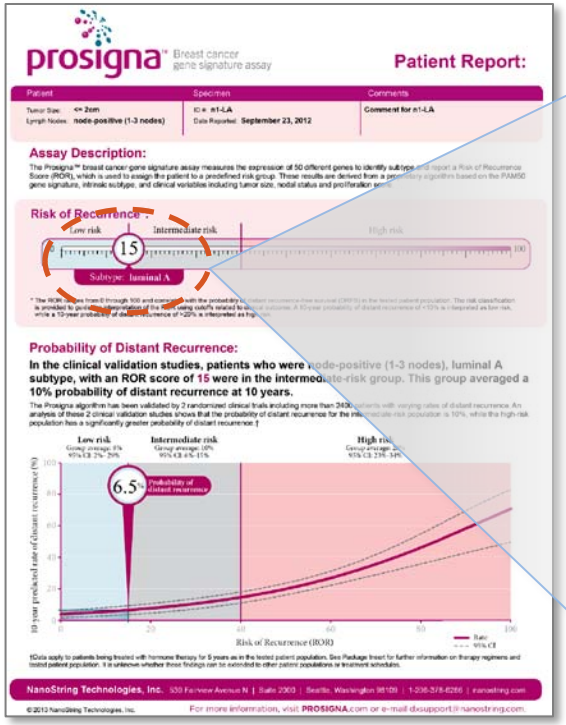
FDA Cleared & CE-IVD Marked

Adopted by 37 Clinical Labs across 12 Countries

The nCounter Dx Analysis System is FDA 510(k) cleared for use with the Prosigna Breast Cancer Prognostic Gene Signature Assay. To date, it has not been cleared by the FDA for other indications or for use with other assays.

Prosigna: Provides Information that Helps Guide Treatment

Prosigna Patient Report[1]



Risk of Recurrence (ROR) Score

- Zero to 100
- Relates to recurrence rate on endocrine therapy alone

Risk Group

- Low, Intermediate, or High risk
- Based on ROR Score and nodal status

Molecular Subtype[1]

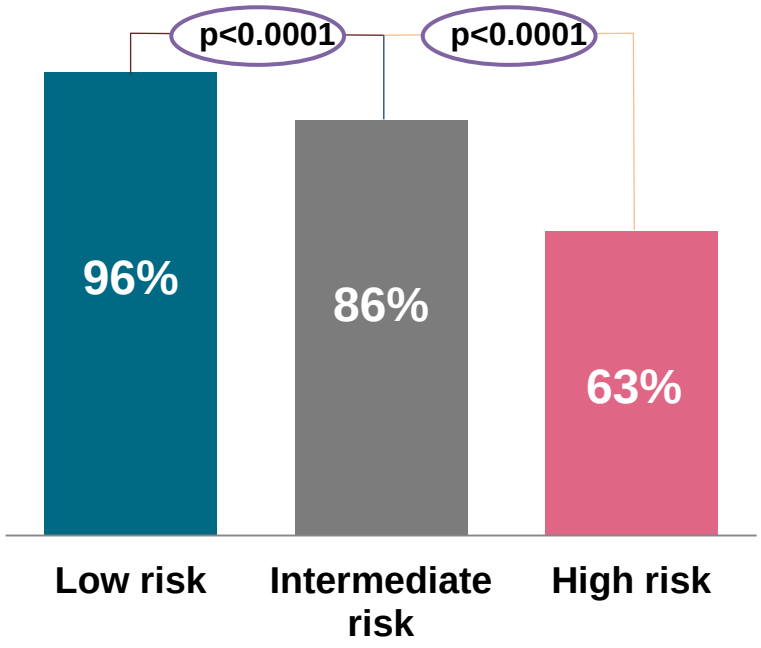
- One of four categories
- Describes underlying biology of breast cancer

1 The Prosigna report shown is the version available in markets which recognize the CE Mark. The FDA cleared version of Prosigna does not report intrinsic subtype.

Prosigna: Prognosis Informs Use of Chemotherapy Today

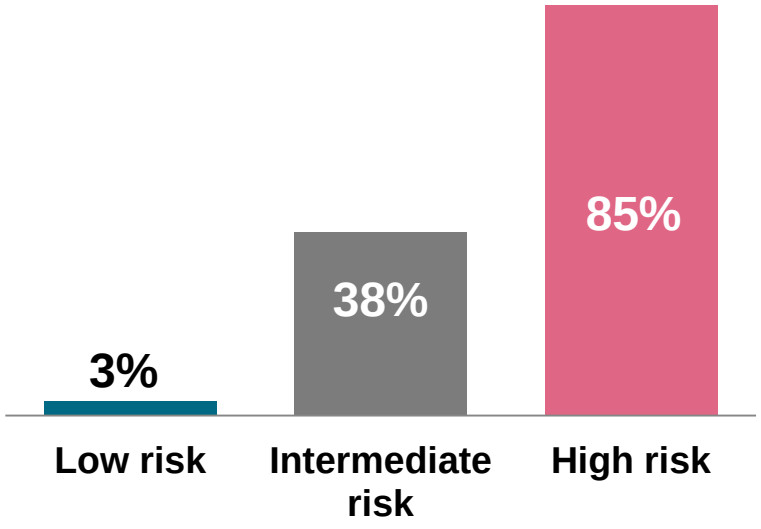
Clinical Validation
TransATAC Study (N = 1,007)

10 year Distant Recurrence Free Survival



Treatment Decisions
Decision Impact Study (N = 200)

Percent patients receiving chemotherapy



1 DRFS = Distant Recurrence Free Survival
2 P-value calculated based on comparison to intermediate risk group
Source: Prosigna CE-IVD Package Insert. Based on based on Dowsett M. et al., Journal of Clinical Oncology, August 1, 2013 vol. 31 no. 22 2783-2790.

Prosigna: Potential Future Indications and CDx Opportunities

	Clinical Decision	Information Needed	Prosigna Studies Published
Today	**Chemotherapy** *Yes or No*	Risk of **recurrence over 10 years** if spared adjuvant chemotherapy	✓
Future	**Chemotherapy** *Selection of agent*	**Differential benefit** between specific agents or regimens	✓
	Endocrine Therapy *Duration*	Risk of **late recurrence** if treated with 5 years of endocrine therapy alone	✓
	Radiation Therapy *Yes or No*	Risk of **recurrence over 10 years** if spared adjuvant radiation therapy	**In planning**
	Novel Therapeutics *Selection of agent*	Correlation of **molecular subtype** and response to novel therapeutics	**In progress**

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