

Molecular Management of Cancer Genetics

Kourtney Puckett

April 30, 2015

Undergraduate Research Day

Outline

- ⊗ Motivation for Molecular Data Collection
- ⊗ Examples of Specific Genes Correlating with Cancer Development
- ⊗ Usefulness of Cancer Panels

Clinical Genomics to Improve Treatment

- ⊗ Traditional Tumor Markers
- ⊗ Expression Profiling
- ⊗ Targeted Breast Cancer Treatments

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Motivation for Molecular Data Collection

Motivating Reasons:

- Familial Inherited Disorders
- Family Ancestry
- Family Planning
- Personal Curiosity
- Cultural Susceptibility

Considerations on the effects of these genetic test results.

- ✧ **Prophylactic treatments (ex: PBM-prophylactic bilateral mastectomy)**
- ✧ **Earlier screenings (ex: mammogram)**
- ✧ **Increased blood work and physicals**

Specific Genes and Cancer Development

Examples of high-penetrance genes that a single-gene test may detect:

❁ BRCA 1 and BRCA 2

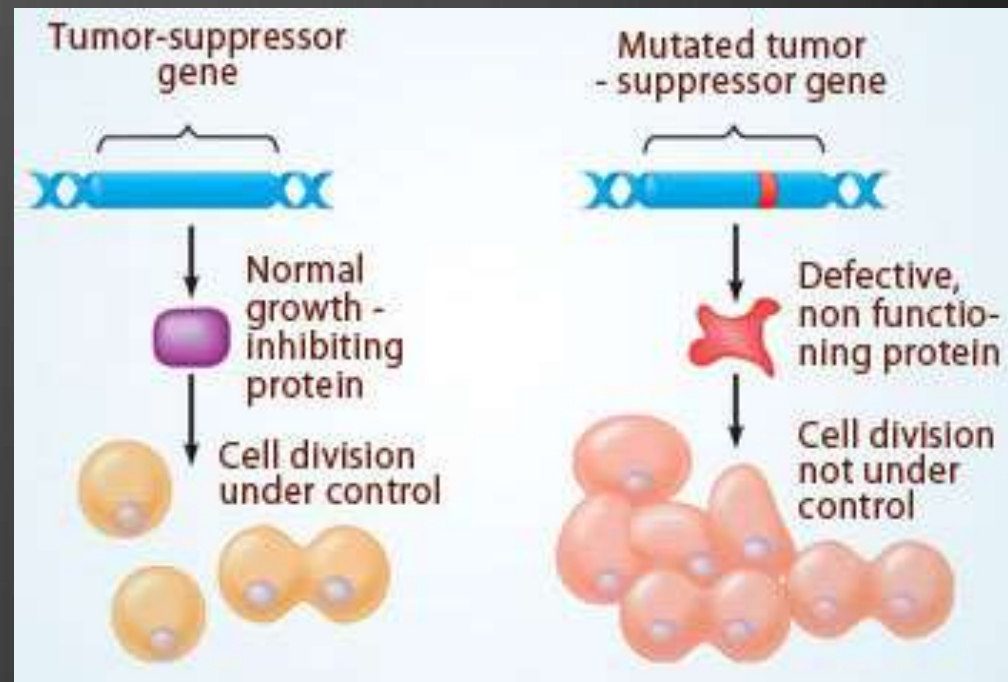
- ❁ 12% population risk
- ❁ 55-65% risk if mutant BRCA
- ❁ 39% ovarian cancer risk (BRCA 1)

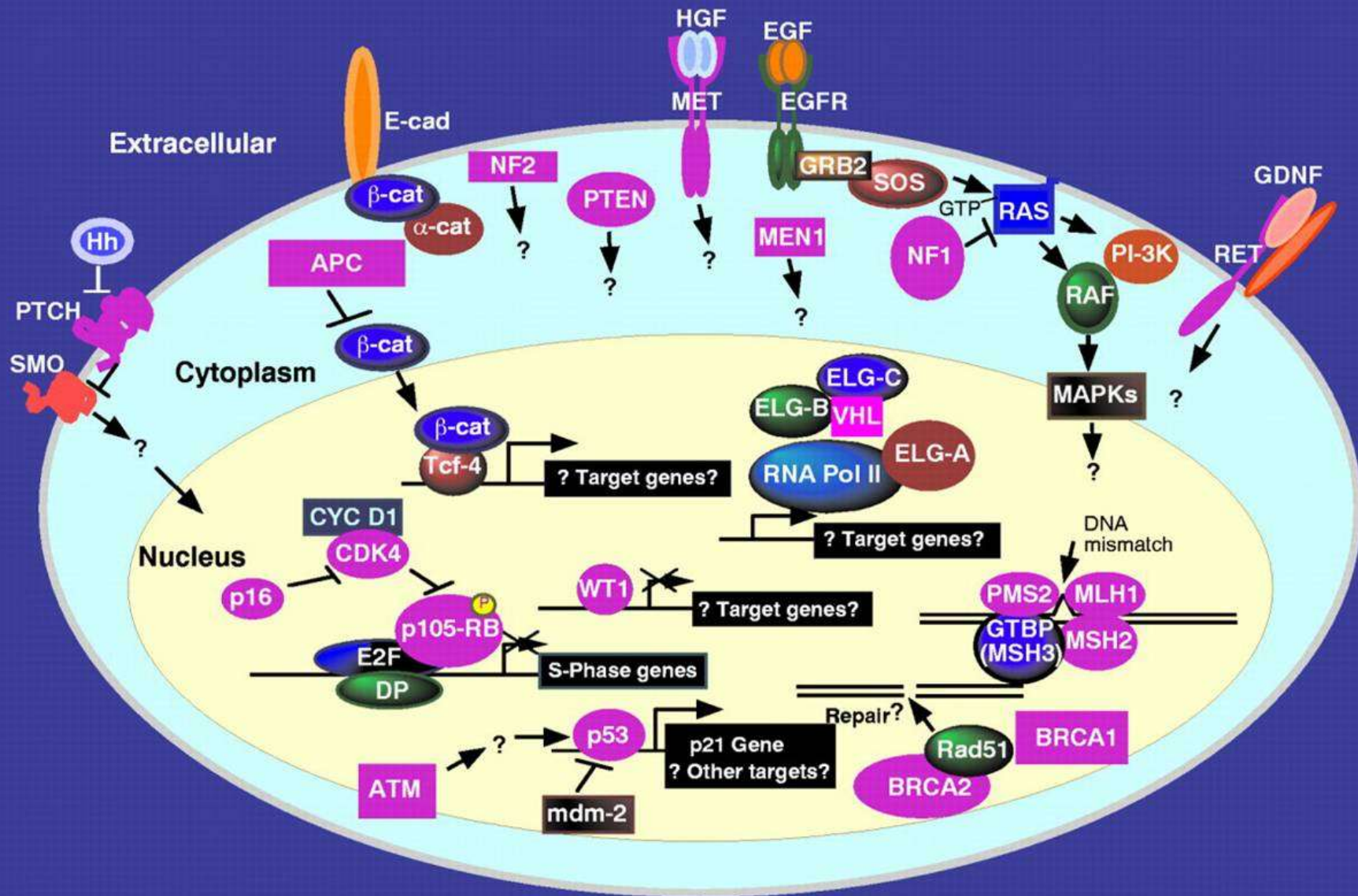
❁ P53

- ❁ “Guardian of the genome”
- ❁ 50% of all cancers
- ❁ Li-Fraumeni Syndrome

❁ APC

- ❁ Familial Adenomatous Polyposis





Cancer Panels

Benefits:

- Increased sensitivity
- Increased target audiences
- Better risk assessment
- Improved clinical decisions

Challenges:

- Increased complexity of test results
 - VUS
- Estimating risk
- Effective patient communication



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Breast Cancer Gene Panels and Assays

Test:	Company	Who is eligible?	Number of genes tested:	Goal of Test:	FDA Approved:
<u>OncoType DX - Breast</u>	<u>Oncotype DX</u>	-Stage I or II breast cancer -Invasive -Estrogen-receptor positive -Node-negative -Diagnosed with DCIS (ductal carcinoma in situ)	21	-Recurrence risk -Benefit from chemotherapy -Benefit from radiation therapy if treated for DCIS	Approved
<u>MammaPrint</u>	<u>Agendia</u>	-Stage I or II breast cancer -Invasive -<5cm tumor -estrogen receptor positive or negative	70	-Recurrence after 10 years	Approved
<u>Mammostrat</u>	<u>Clariant Diagnostic Services</u>	-Stage I or II breast cancer -hormone-receptor positive	5	-Recurrent risk	Not Approved

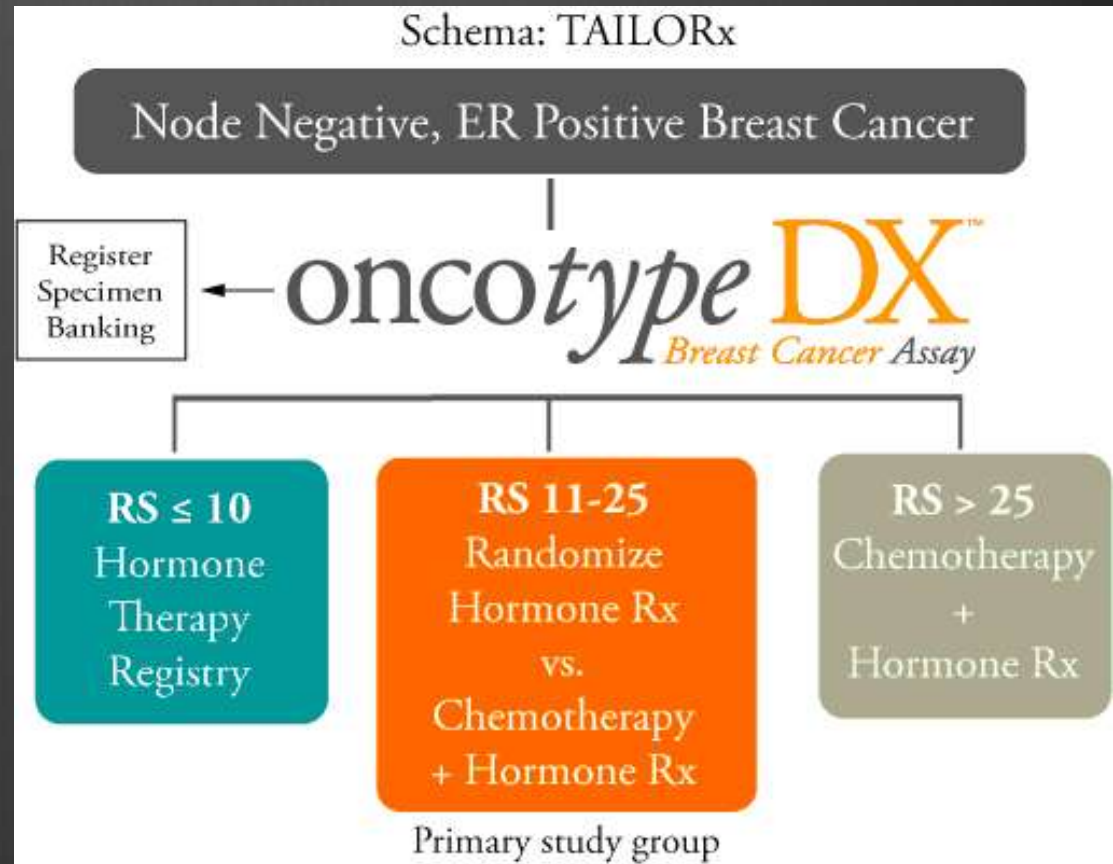
Breast Cancer Prognostic Gene Signature Assay (PAM50)		<ul style="list-style-type: none"> cancer with node-negative -Stage II with 1-3 nodes-positive -Hormone-receptor positive -Invasive -Post-surgery and hormone therapy patient 		<ul style="list-style-type: none"> 5-10 years -Benefits of hormone therapy after 5 additional years in postmenopausal women 	
<u>EndoPredict</u>	<u>Sividon Diagnostics</u> (distributed by Myriad)	<ul style="list-style-type: none"> -Stage I or II breast cancer -Hormone-receptor positive -HER-2 negative -Node-negative -3 or more nodes-positive 	12	<ul style="list-style-type: none"> -Chance of metastasis after 10 years of diagnosis 	Not approved
Breast Cancer Index	<u>bioTheranostics</u>	<ul style="list-style-type: none"> -Early-stage breast cancer (stage I-III) -Node-Negative -Hormone-receptor positive 	7	<ul style="list-style-type: none"> -Recurrence after 5-10 years -Benefits of hormone therapy 	Not approved

Clinical Genomics

- ❁ Traditional Tumor Markers
 - ❁ Antigens, hormones, glycoproteins, immunoglobulins, gene expression changes
 - ❁ Example: Prostate Specific Antigen (PSA)
 - ❁ CANNOT solely be diagnostic
- ❁ Expression Profiling
 - ❁ Identifying cell RNA activity
 - ❁ RT-PCR, microarray technology, FISH, etc.

Clinical Genomics in Breast Cancer

- ❁ Oncotype Dx Breast
 - ❁ TAILORx Trial
 - ❁ qRT-PCR
 - ❁ 21 genes tested
- ❁ Mammaprint
 - ❁ MINDACT Trial
 - ❁ Microarray
 - ❁ 70 genes tested



Targeted Breast Cancer Treatments



- ❁ HER2 receptor status
- ❁ Estrogen and progesterone receptor status
- ❁ Results of Breast Cancer Assay
 - ❁ Chemotherapy versus hormone therapy only
- ❁ CYP2D6 enzyme expression
 - ❁ Major enzyme in Tamoxifen catabolism