A Case of Mistaken Identity: Biomarkers for High Risk Premalignant Breast Lesions

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A case of mistaken identity --- Biomarkers for high risk premalignant breast lesions

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Estimated costs: $20,000 to $100,000/patient.

Campbell JD, Ramsey SD. Pharmacoeconomics. 2009;27(3):199-209. PMID: 19354340
Atypical hyperplasias

Progression to invasive cancer

50,000 new cases annually

Expect 10,000 new cases annually

Up to $1B to treat

Atypical hyperplasias

Progression to invasive cancer
Developing biomarkers of high risk premalignant breast lesions

Subtypes of Atypical Hyperplasias

Subtypes of lesions with malignant potential
Bioanalyzer electropherograms

Intact RNA

FFPE RNA
Log2 expression values

Normal  Ductal AH  Lobular AH

-1.0  0.0  1.0

Genes:
- Cl0orf81
- KIT
- PROM1
- EDN3
- CCL28
- ANXA1
- MMP16
- SNORD116-21
- SCARNA17
- RBMS1
- CNTNAP3
- ACTA2
- GK3P
- CRYAB
- ARRD3
- MAML2
- NDRG2
- SFRP1
- AK05
- Lrig3
- NAT1
- POTEG
- UGDH
- EEF1A2
- SGK3
- MCM3
- PSPH
- GPRC5A

Cluster analysis of differentially expressed genes in normal, ductal, and lobular breast tissues.
Patient Population: Diagnosis of Breast Cancer or Benign Breast Disease

IRB-approved Registry
Patient consent
Assign study ID

Patient Registry
Survey data
Clinical data
Archived tissues

Data Manager
- Collate data
- Provides summary data
- Extract data from clinical records
- Coded data for IRB-approved projects

IRB-approved projects

Project 1
Project 2
Project 3
Project 4

Data/Tissue With Study ID
Atypical hyperplasia (UMMS 1999-2003)

Upstaging upon re-excision

2833 breast core biopsies
120 with primary diagnosis of ADH
Summary

• Value of diagnostic test
  – Large interobserver variability in diagnosing premalignant lesions (Jain et al., 2011. PMID 21532546)
  – Identify subgroups to benefit from preventive therapies.
  – Identify molecular pathways to provide appropriate preventive treatments

• Technical challenges
  – Minute amounts of tissue
  – Fragmentation of RNA in FFPE tissues
  – Amplification and labeling for robust detection
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