# Biomarkers

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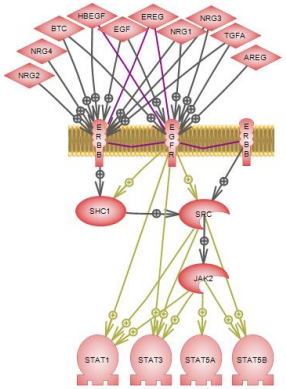
# What is a biomarker?

A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.

(De Gruttola et al., 2001, Control Clin. Trials)

- Examples:

  BP and Hb levels



# A Useful Biomarker

- Informs risk/benefit ratio when there is a decision to be made
- Does so in a better/faster/earlier/cheaper way than existing approaches
- Generally applicable: sample and technology must be available/accessible

(Hodegson et al., 2009, Molecular Oncology)

# What about biomarkers for complex diseases and why are they needed?

# Percentage of patient population for which a particular drug in a class is ineffective

| | | |
|---|---|---|
| Anti-depressants (SSRI's) | 38% |  |
| Asthma | 40% |  |
| Diabetes | 43% |  |
| Rheumatoid arthritis | 50% |  |
| Alzheimer's disease | 70% |  |
| Cancer | 75% |  |

*Data Source: "Clinical Trends in Molecular Medicine, Volume 7, Issue 5, 1 May 2001, Pages 201-204.*

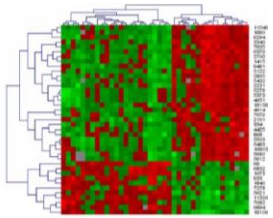
# Questions from patients that can be addressed by using biomarkers

- Have I got cancer? Early detection of the disease
- What type of cancer have I got and what is my prognosis? Testing- ER+ or Triple-negative (ER-, PR- and HER2-)
- What treatment is best for me? (Tamoxifen?)
- Is my treatment working? (Monitoring????????)
- Will my cancer come back? (Recurrence and possibility of other cancer)

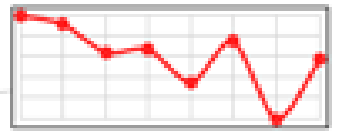
Personalized medicine- spare patients futile and potentially toxic treatments

# Key advantages of biomarkers

Early detection of disease



Drug development



# Biomarkers in early detection

# How Can We Save More Lives from Cancer?

- Most cancers are diagnosed when they are 1–4 cm in size
- By this time many have already metastasized
- To reduce cancer-specific mortality, we need effective Biomarkers and Methods for:
  - » Risk Assessment
  - » Early Detection
  - » Therapy

**"It costs $1 billion to funnel a single cancer medication through the regulatory pipeline. For a fraction of that, new diagnostics to spot cancers in their earliest stages ultimately could save more lives."** ***Dr. Lee Hartwell, President, Fred Hutchinson Cancer Research Center***

# From Biomarkers to In Vitro Diagnostics (IVD)

- Development of a diagnostic kit, that is-
  - Easy to use in clinical settings
  - Cost effective
  - Proven results
  - Samples- blood, serum, urine etc.

# Five FDA Approved Diagnostic Tests

| Biomarker | Clinical Utility | Year of Approval | EDRN Principal Investigator/ Industrial Partner |
|---|---|---|---|
| %[-2]proPSA | Reduce the number of unnecessary initial biopsies during prostate cancer screening. Also, appears to be highly associated with increased risk of aggressive disease. | 2012 | Dan Chan, Ph.D. Beckman Coulter |
| PCA3 (in urine) | Biopsy or re-biopsy decisions in patients at risk for prostate cancer. | 2012 | John Wei, M.D. Gen-Probe |
| OVA1™ (5 analytes: CA 125, prealbumin, apolipoprotein A-1, beta2 microglobulin, transferrin) | Prediction of ovarian cancer risk in women with adnexal mass. | 2010 | Dan Chan, Ph.D. Vermillion |
| Risk of Ovarian Malignancy (ROMA) algorithm with CA125 and HE4 blood tests for pelvic mass malignancies | Prediction of ovarian cancer risk in women with pelvic mass. | 2011 | Steve Skates, Ph.D. Fujirebio Diagnostics |
| DCP and AFP-L3 combined panel of markers | Risk assessment for development of hepatocellular carcinoma. | 2011 | Jorge Marrero, M.D. Wako Diagnostics |

# Biomarkers in drug development

Examples…

| Biomarker | Disease | Drug |
|---|---|---|
| HER2 | Breast Cancer | Herceptin |
| Estrogen or progesteron receptors | Breast Cancer | Tamoxifen |

HER2 = Human Epidermal growth factor Receptor 2

# Major function of biomarkers in clinical trials

- Is the therapy hitting the target?
  - Pharmacodynamic (PD) biomarkers
- Is there a response to the therapy?
  - Efficacy biomarkers
- Will there be a response to the therapy?
  - Patient stratification, patient selection biomarkers
- Is there or will there be toxicity for the therapy?
  - Toxicity biomarkers

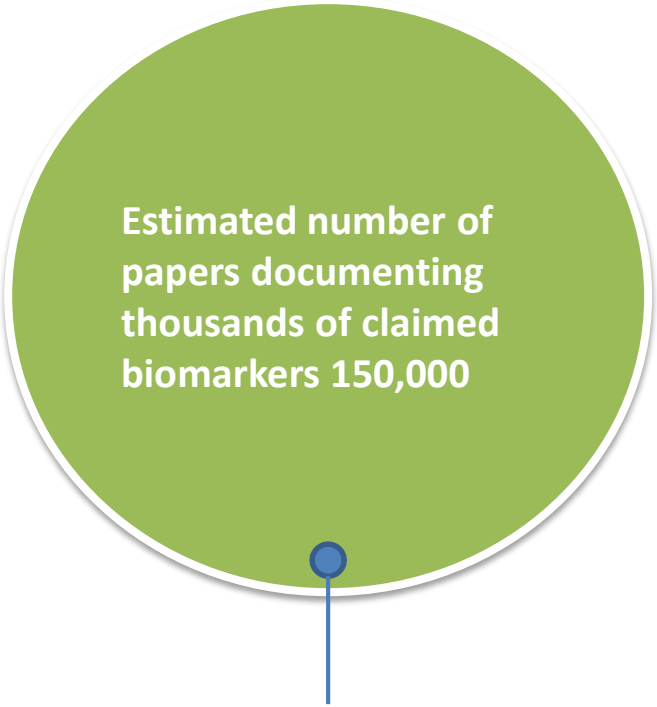
# Why new biomarkers are needed?

- False positive results
- Cannot differentiate between stages of disease
- Not universal

  For example- CA 125 is expressed in 50-60% of patients during early stages of Ovarian Cancer.

# Bottle-neck in biomarker development

- Quality samples
- Validation




Estimated number of biomarkers routinely used in the clinic= 100

(Poste, 2011, Nature)

# Why is Discovery of Clinically Useful Biomarkers Difficult?

- Biology
- Need for Infrastructural Support
- Need for Collaborations Among Stakeholders
  - Basic scientists
  - Clinicians
  - Public Health Professionals
  - Informaticians and Bioinformaticians
  - Advocates
  - Funding organizations
  - Regulatory authorities

# What is needed?

- Collaborations between Academic institutions and industries (Both pharma and diagnostic)
- With input from regulation experts
- Repositories of quality samples
- More funds to promote biomarker research at academic level

# All around benefits of biomarker based drug development

| Stakeholder | Benefit |
|---|---|
| Patients | Increased effectiveness of therapies |
| Doctors | Increased safety in treatment decisions |
| Healthcare providers | Better outcomes for less cost |
| Pharma companies | Regulatory approval and competitive advantage |
| Diagnostic companies | New market opportunities |

Adapted from: http://www.bioscience alliance.net/documents/qiagen_copenhagen2240310.pdf

# Global market for biomarkers

Total global estimates-

2010 = $13.5 billion

2015 = $33.3 billion

2021 = $ 53.3 billion

(http://www.bccresearch.com/report/biomakers-technologies-markets-bio061b.html)

http://www.marketsandmarkets.com/Market-Reports/biomarkers-advanced-technologies-and-global-market-43.html