



Non-Invasive Array Based Screening for Cancer

Dr. Amit Kumar
President and CEO
CombiMatrix Corporation
www.CombiMatrix.com
May 13, 2009



This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of various factors and uncertainties, including the recent economic slowdown affecting technology companies, our ability to successfully develop products, rapid technological change in our markets, changes in demand for our future products, legislative, regulatory and competitive developments and general economic conditions. Acacia Research: CombiMatrix Annual Report on Form 10-K, recent and forthcoming Quarterly Reports on Form 10-Q, recent Current Reports on Forms 8-K and 8-K/A, and other SEC filings discuss some of the important risk factors that may affect our business, results of operations and financial condition. We undertake no obligation to revise or update publicly any forward-looking statements for any reason.



Outline of Presentation

- Background on Company
- Background on Cancer
- Technology
- Comprehensive Cancer Array (CCA)
- Data
- Next Steps and Conclusions



Company Background

- **NASDAQ: CBMX**
 - Corporate Headquarters near Seattle, WA
 - CLIA Laboratory in Irvine, CA
- **Two DNA Array Platforms**
 - **Bacterial Artificial Chromosome Arrays (BAC-Arrays)**
 - **Oligonucleotide Arrays**
- **Leader in DNA Array Diagnostics and Personalized Medicine**
 - More diagnostic products than all array companies combined
 - Favorable FDA opinion
- **Non-Invasive Cancer Screen In Development**

Background on Cancer

- **Most cancers (especially solid tumors) can be treated if caught early.**
 - 5-year survivability is highest for early diagnosis and intervention
 - Poor survivability for late stage and metastasis
- **Cancers with poor 5-year survivability are diagnosed at late stage because symptoms occur at later stages.**
 - Ovarian (Only 1 out of 5 alive, in 5 years)
 - Pancreatic
 - Even other cancers if missed at early stage (breast, colon)
- **Diagnosing Cancer Early is Challenging-Good Screening Approaches Are Few**
 - Breast Cancer - self exams, mammograms
 - Prostate Cancer - Prostate Specific Antigen (PSA) - non-invasive
- **Other Screening Processes are Invasive, Unpleasant or Expensive**
 - Sigmoidoscopy, Colonoscopy
 - Biopsies

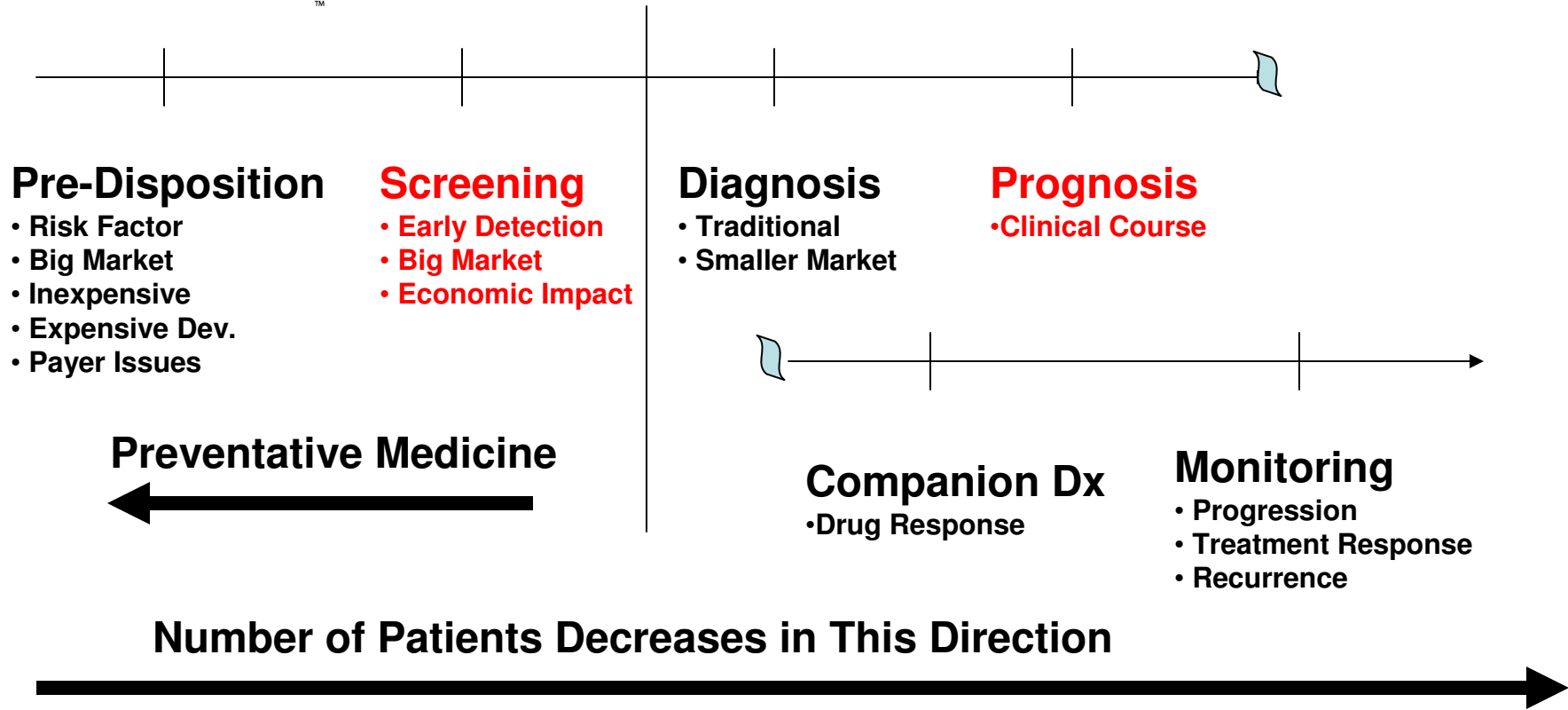


“Holy Grail” of Cancer Screening

- Broad, Comprehensive Cancer Screen
- **Non-Invasive- Blood Test**
- Screens for Multiple Spurious Growths Simultaneously
- Specify organ/tissue
- Early Indication
 - Confirm with other Invasive Method
 - Not a guaranteed diagnosis, but an indicator of concern - verify with other method (like PSA-Prostate Specific Antigen test)
- This would be a revolutionary test with massive public health impact and tremendous market potential.



Categories of Tests



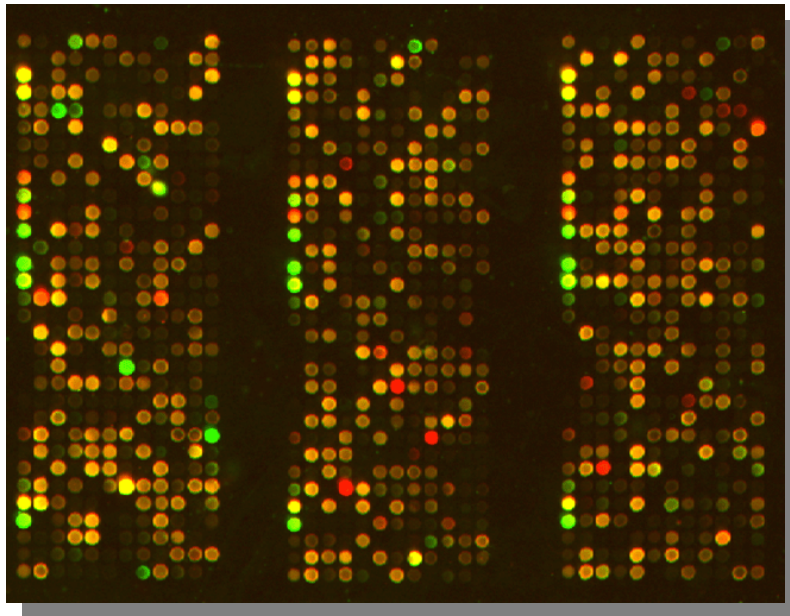
**CBMX has tests on Market in Prognosis, and is Developing Screening Test
Today's Presentation Focuses on **Screening** Test**



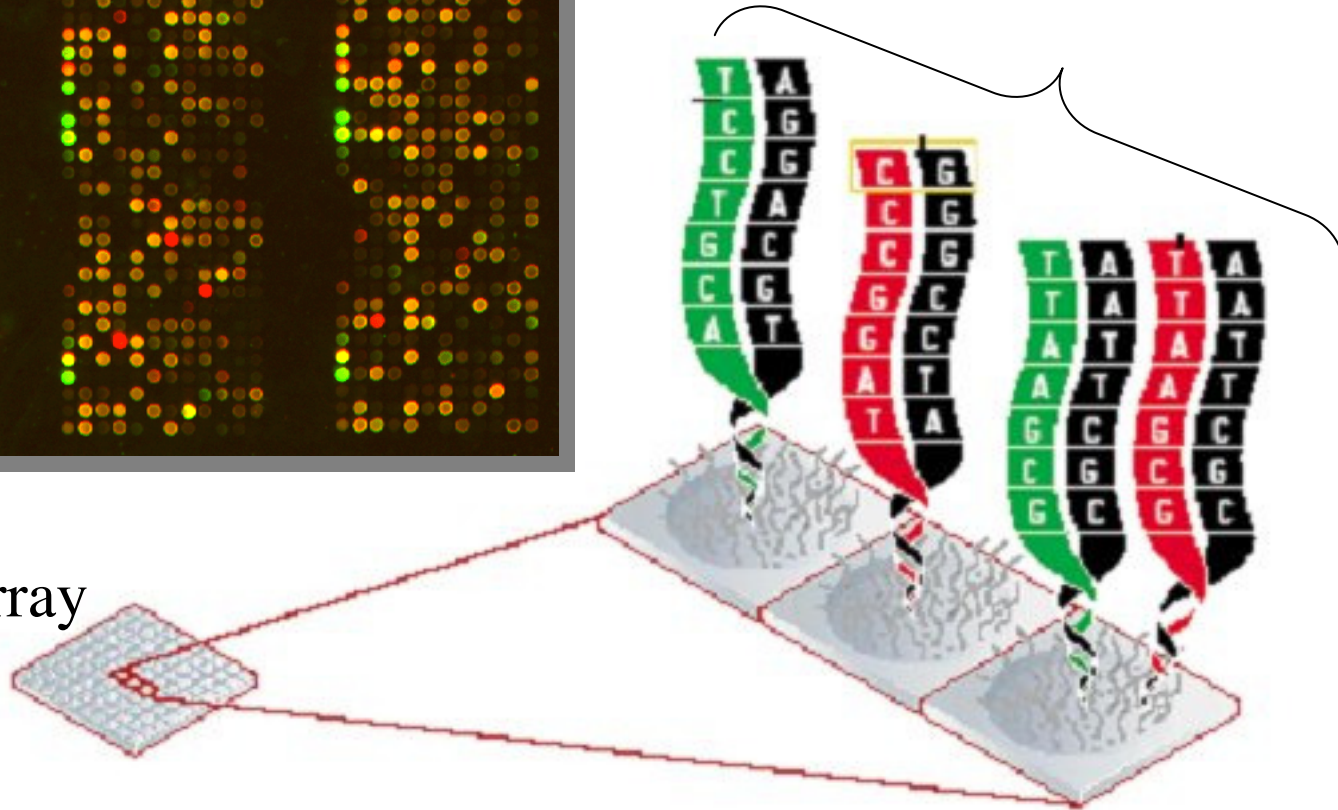
CBMX Oligonucleotide Array Technology

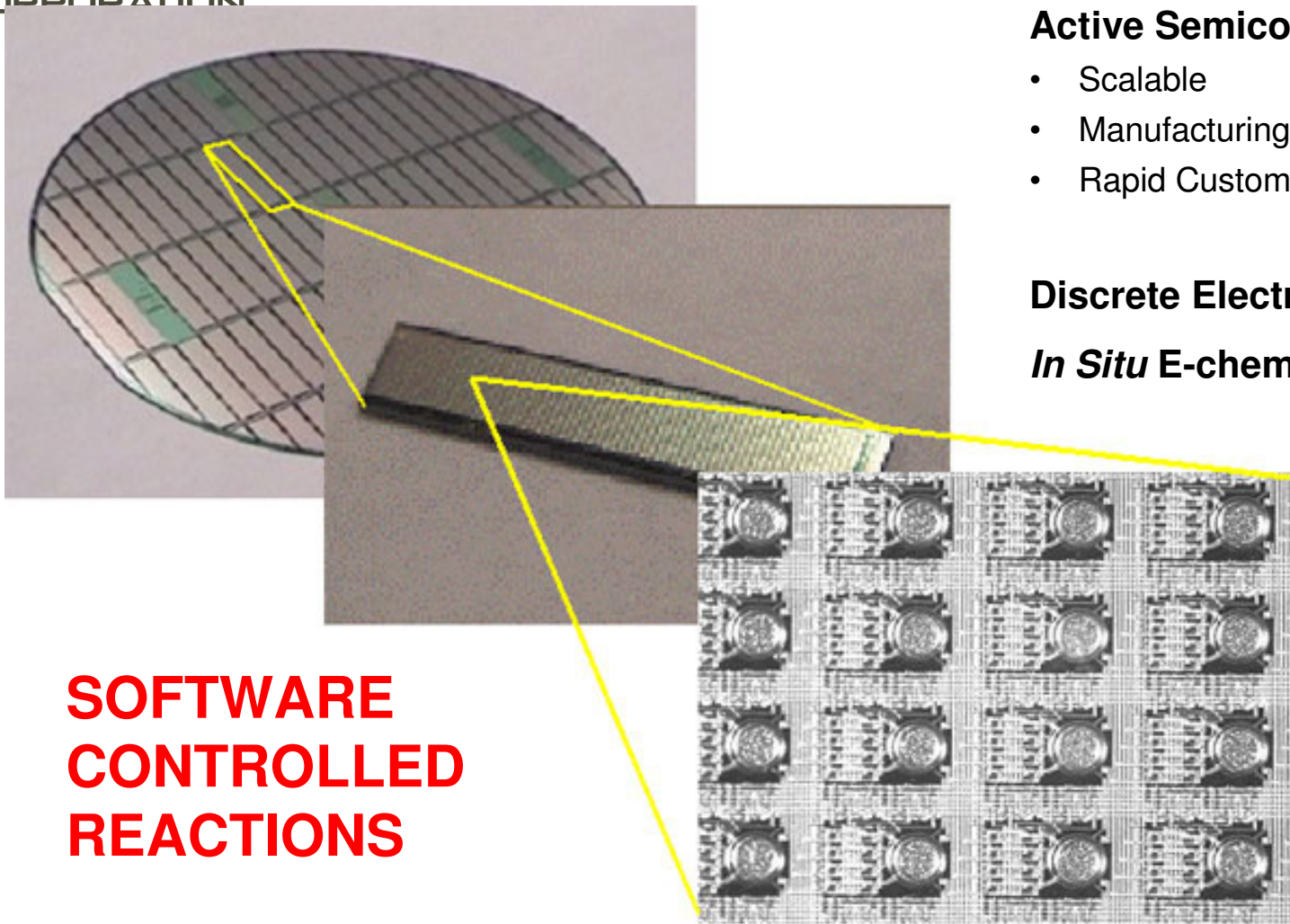
DNA MicroArrays

Analyze multiple
biomarkers simultaneously



Microarray





Active Semiconductor

- Scalable
- Manufacturing Costs
- Rapid Customization

Discrete Electrodes

***In Situ* E-chem Synthesis**

**SOFTWARE
CONTROLLED
REACTIONS**

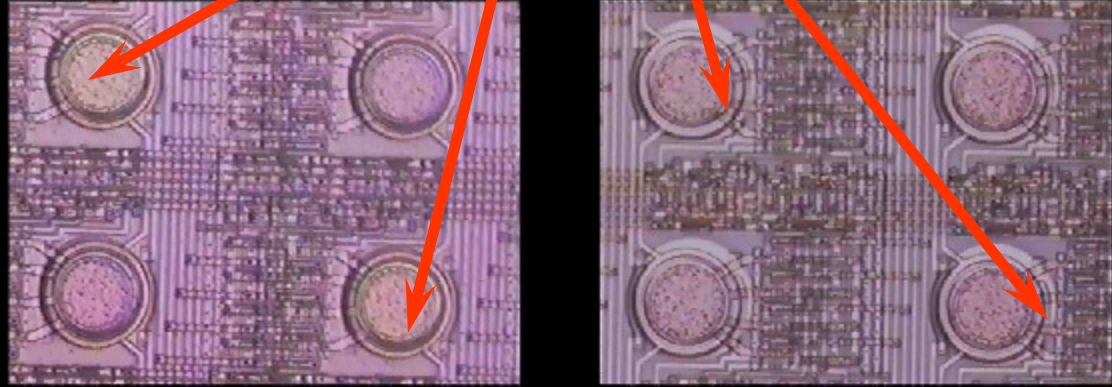
Virtual Flask Technology

Dye = Acid pH

Dye = Neutral pH

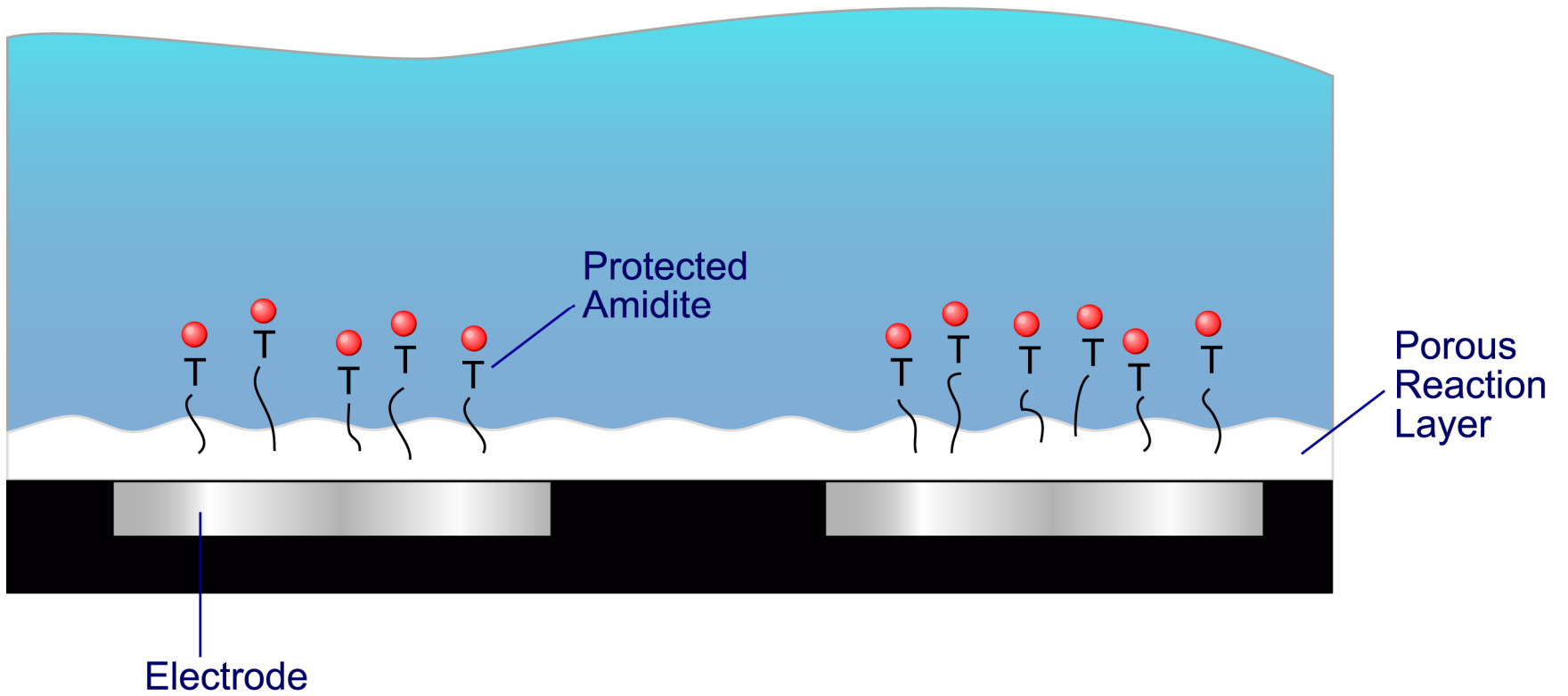
**Electrochemically
Generated Acid**

Virtual Flasks **Unconfined**

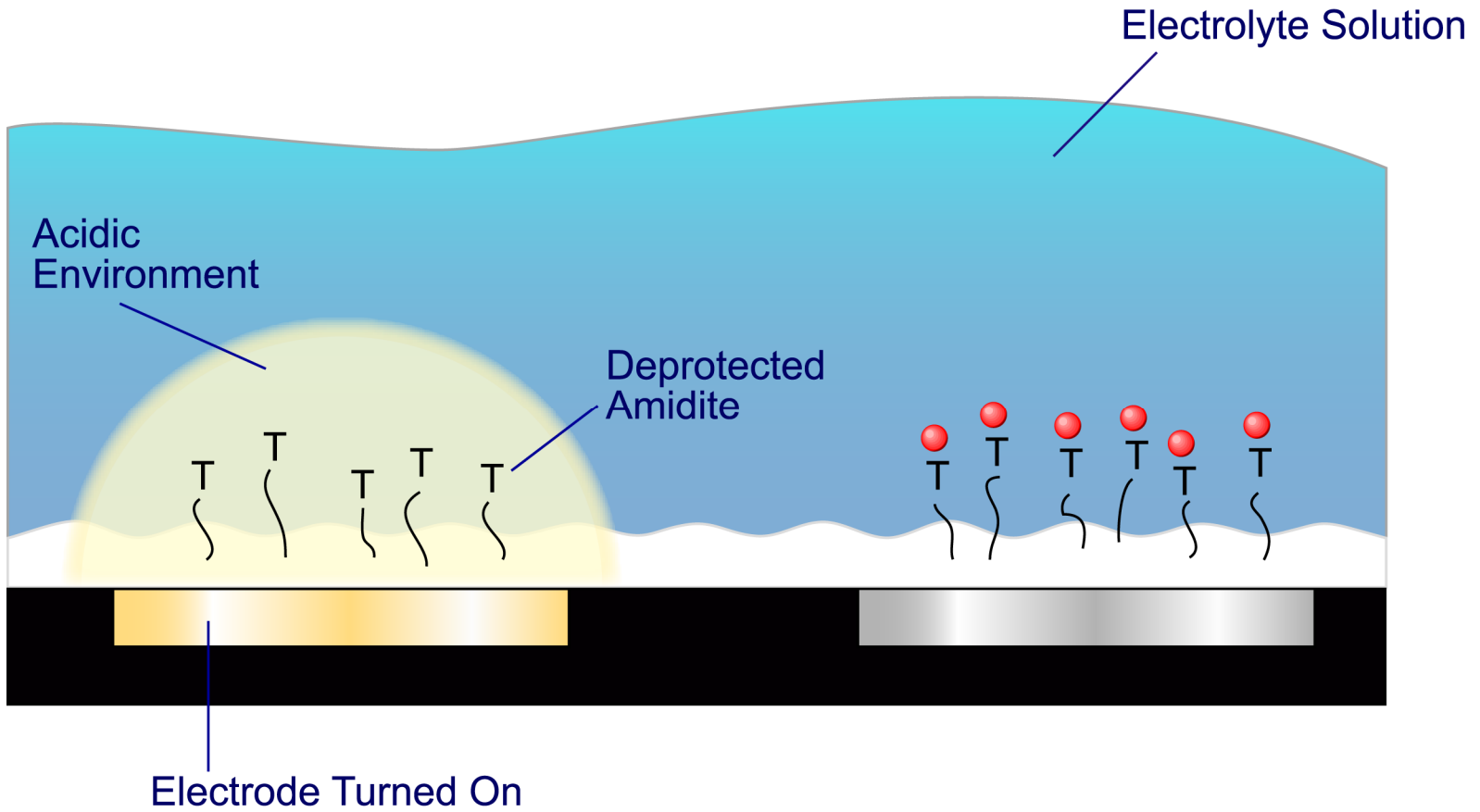


- **Porous Reaction Layer on Chips**
- **Conditions Identical on Both Chips**

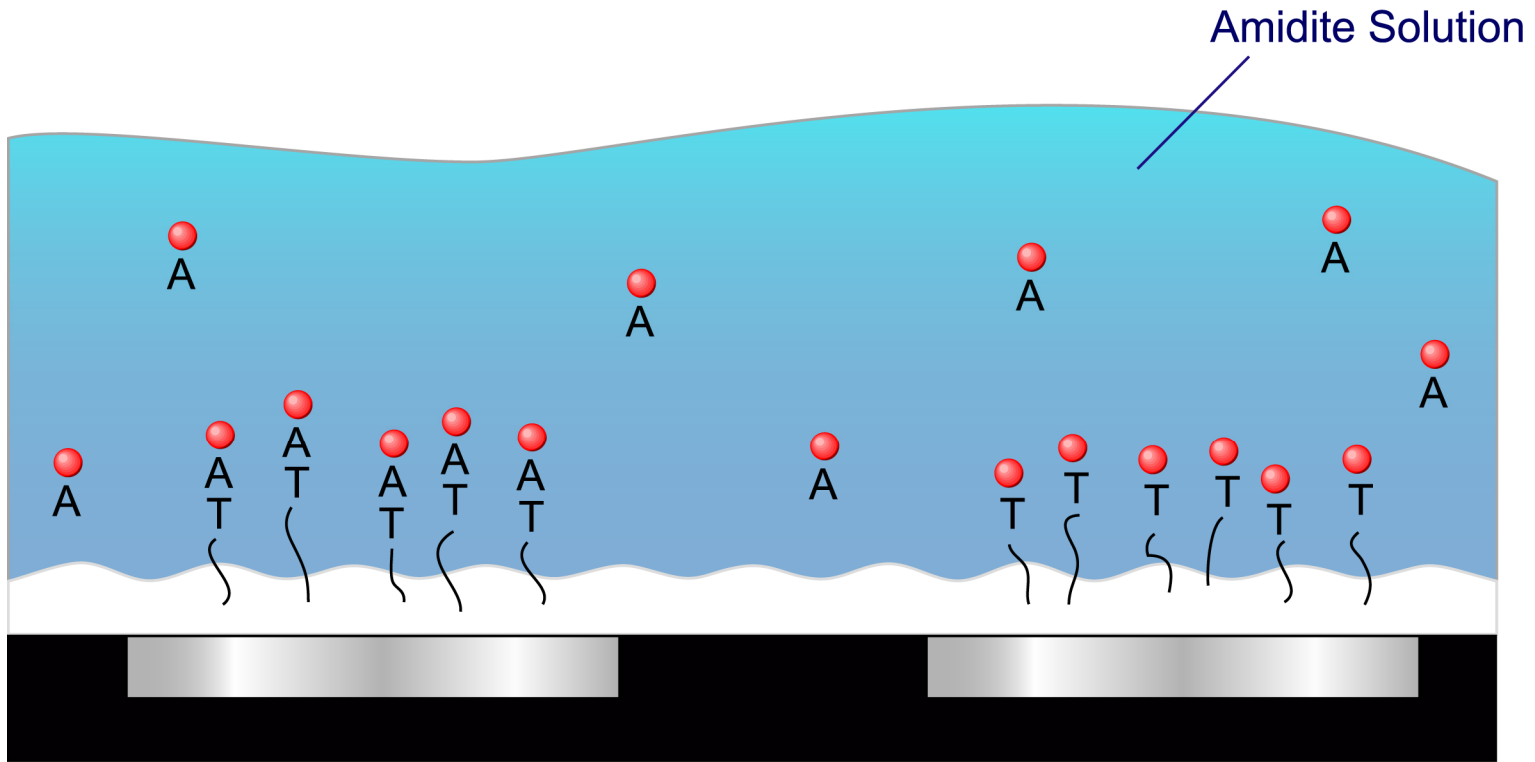
START



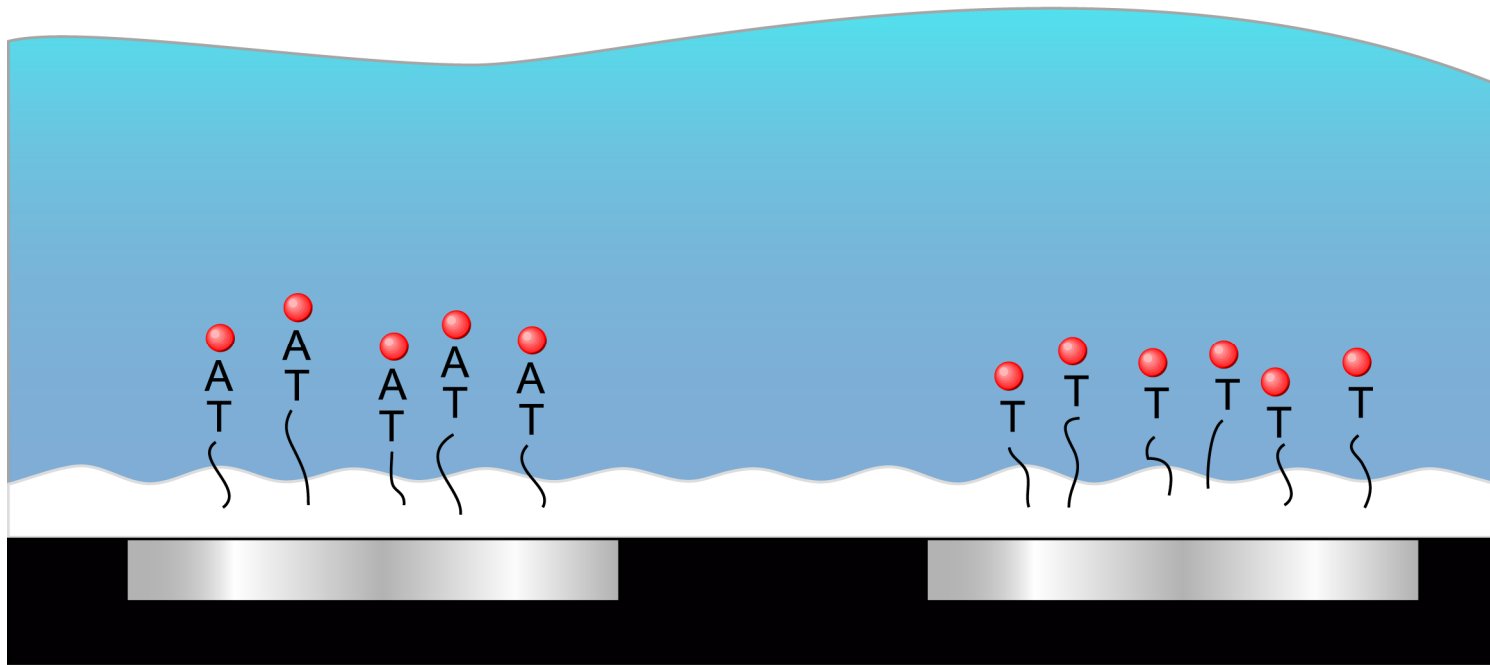
DEPROTECT



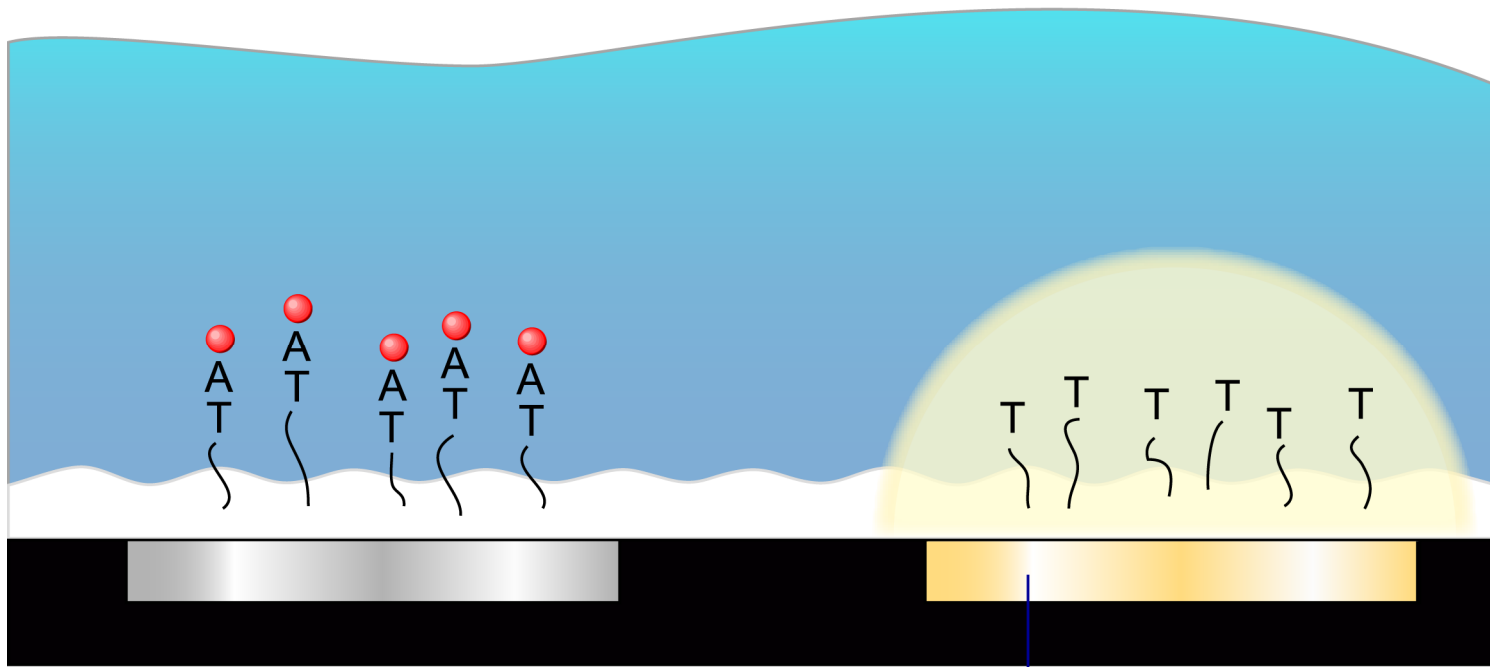
COUPLE



WASH

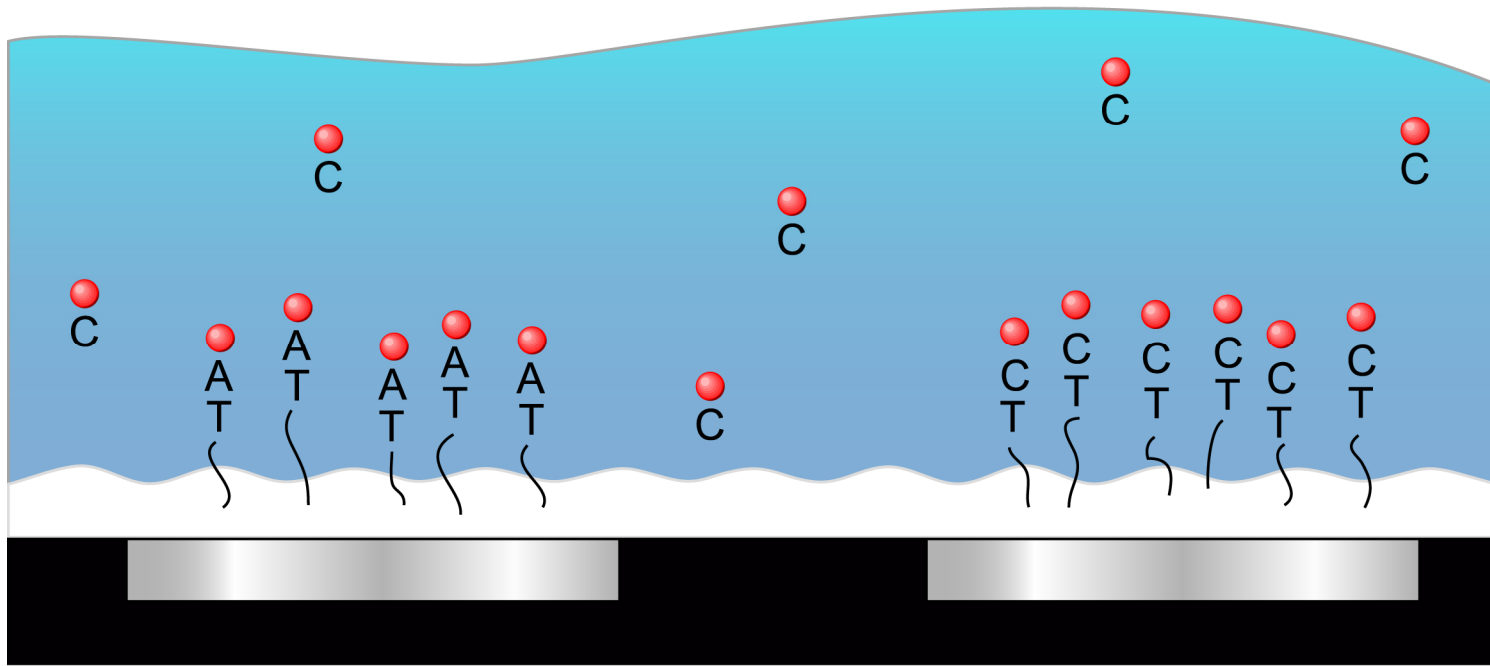


DEPROTECT

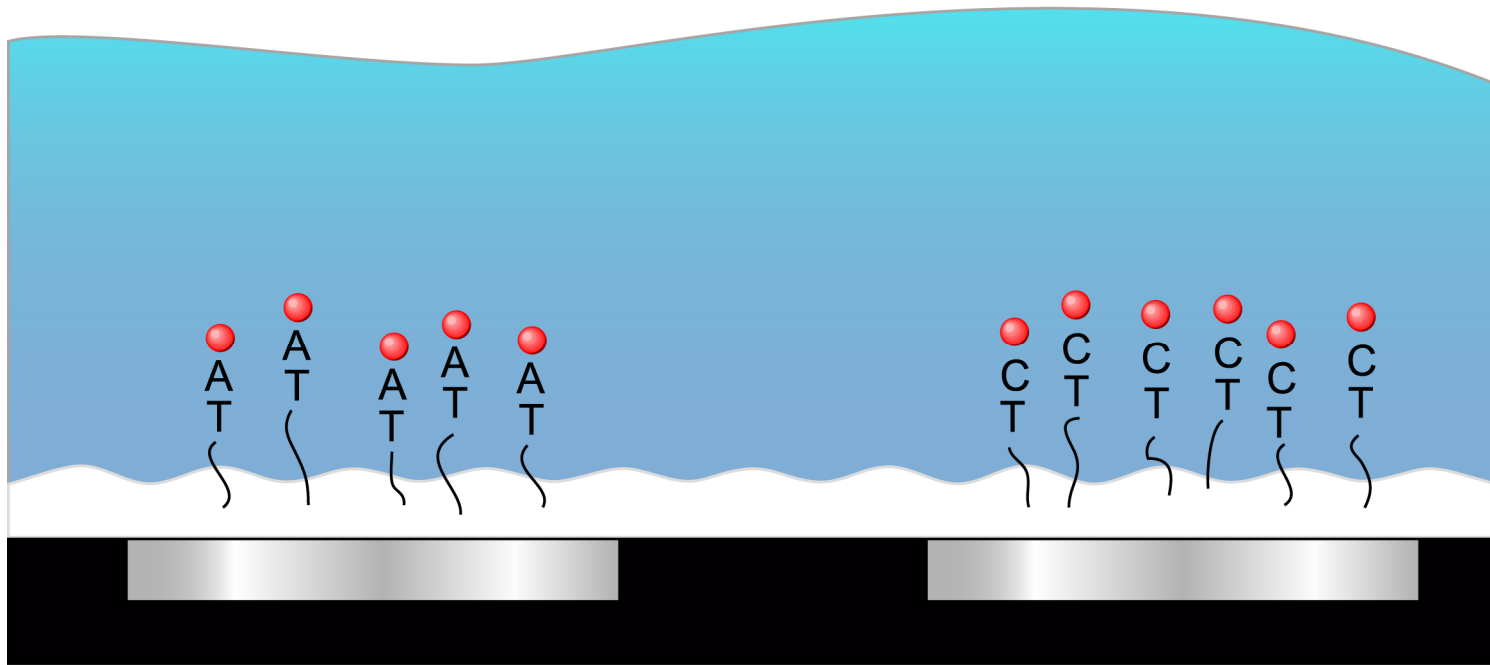


Electrode Turned On

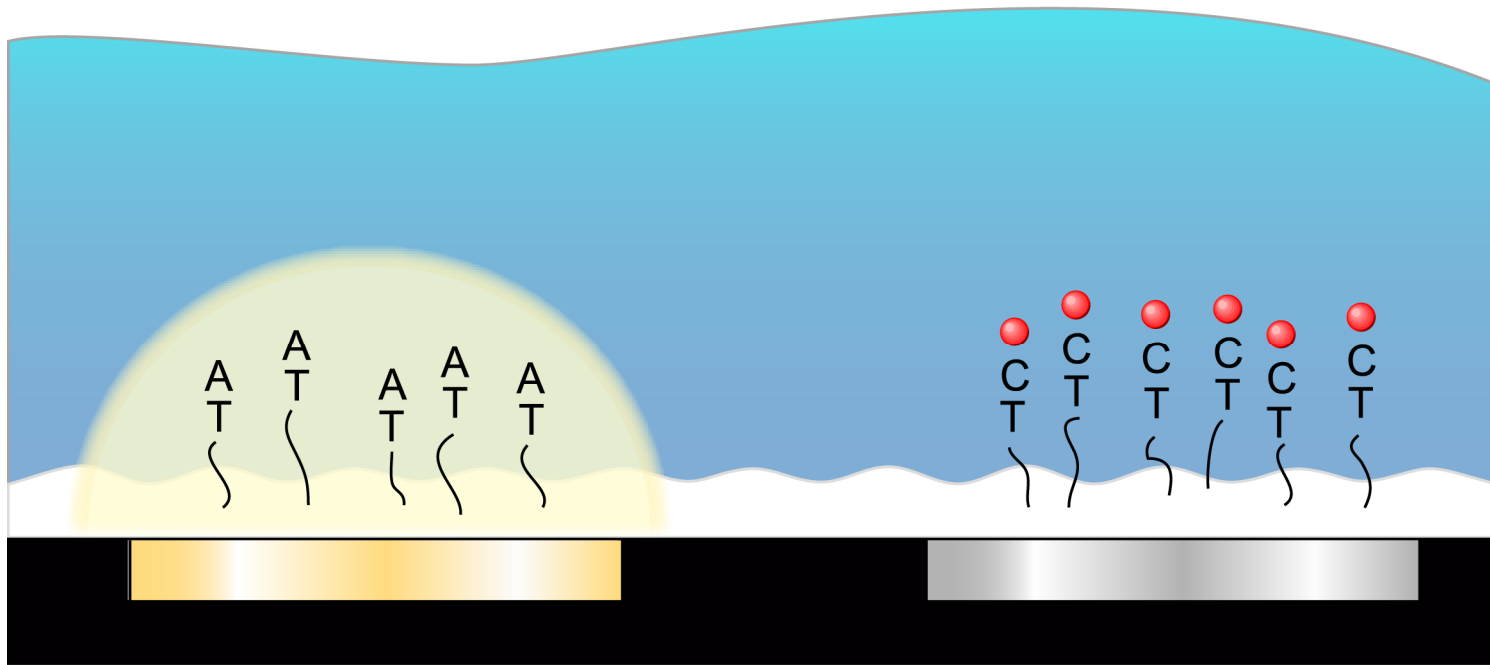
COUPLE



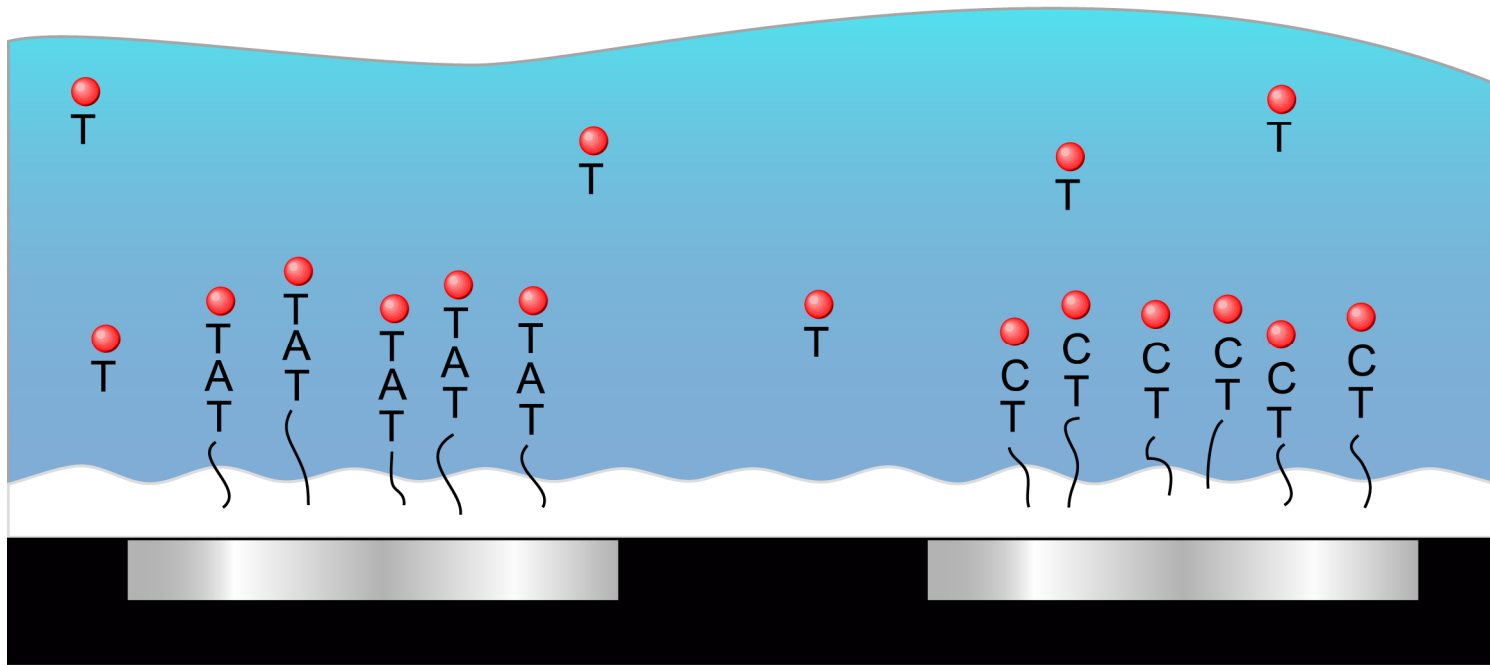
WASH



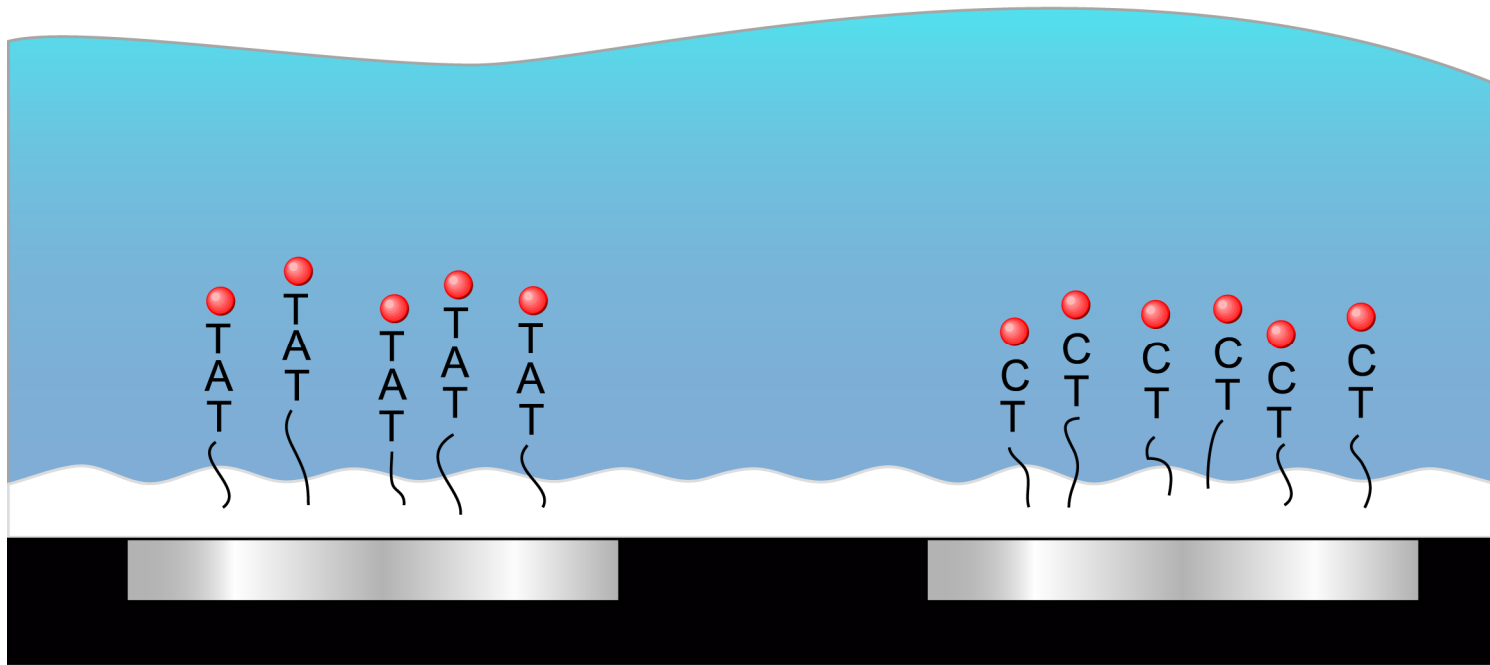
DEPROTECT



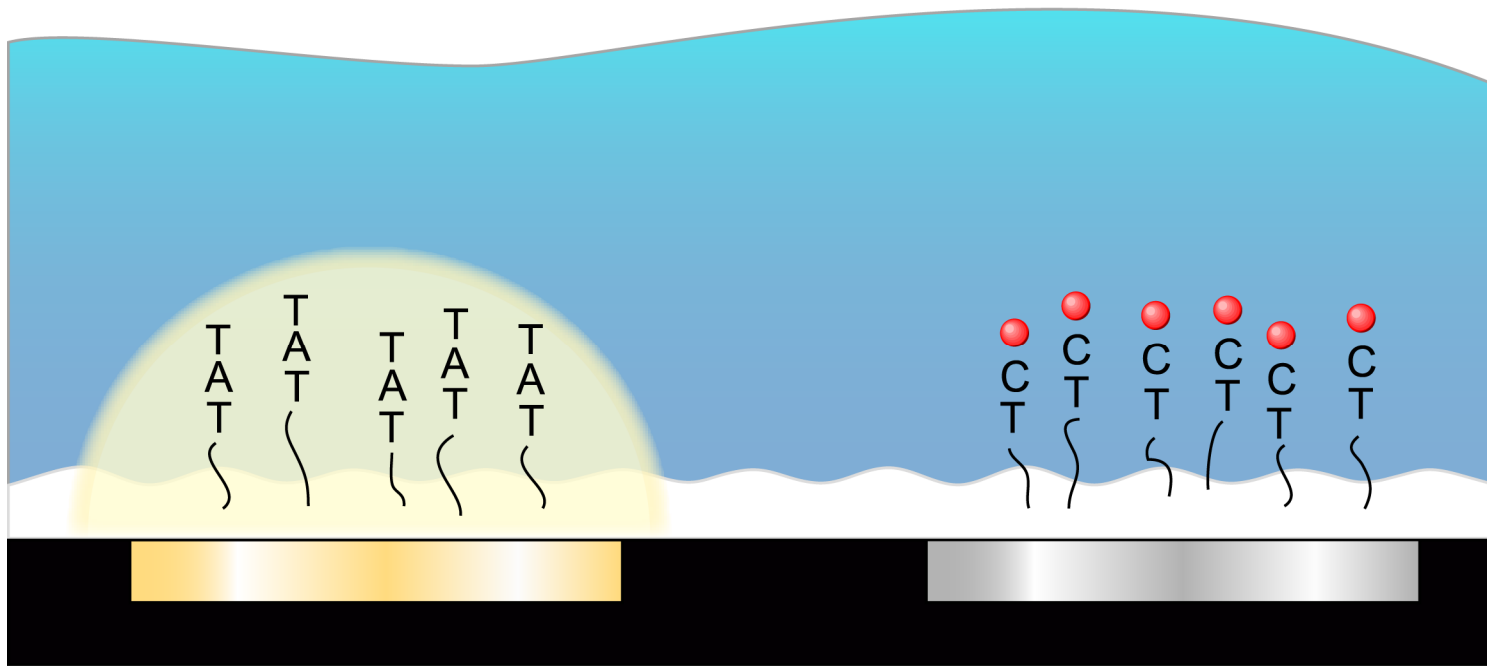
COUPLE



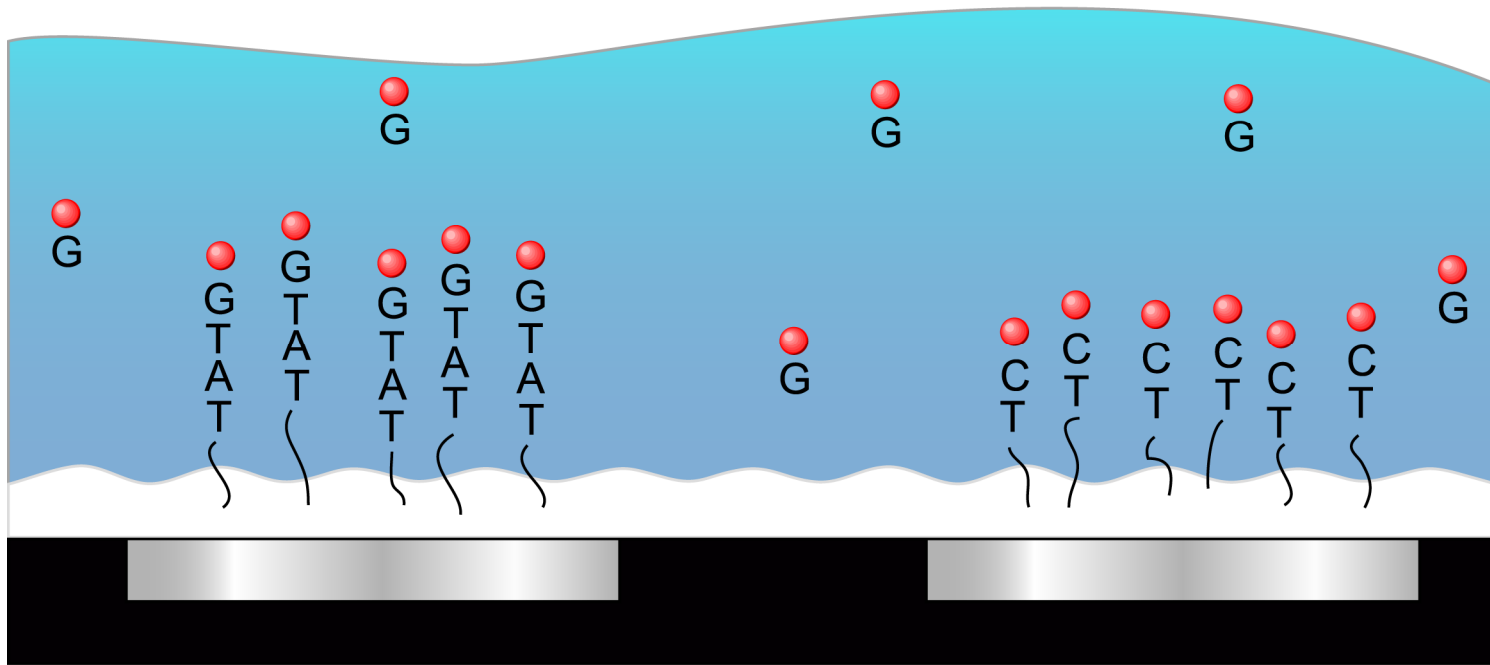
WASH



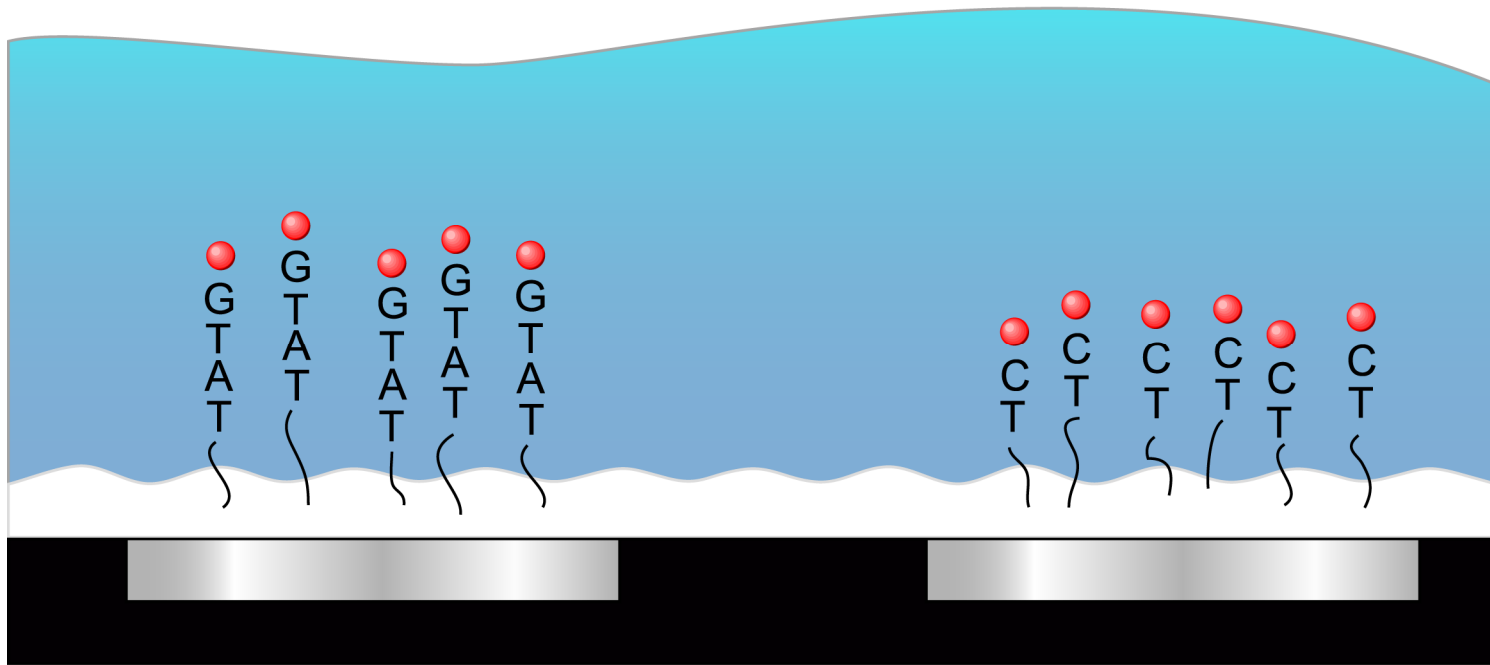
DEPROTECT



COUPLE



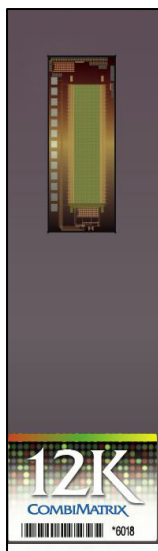
WASH



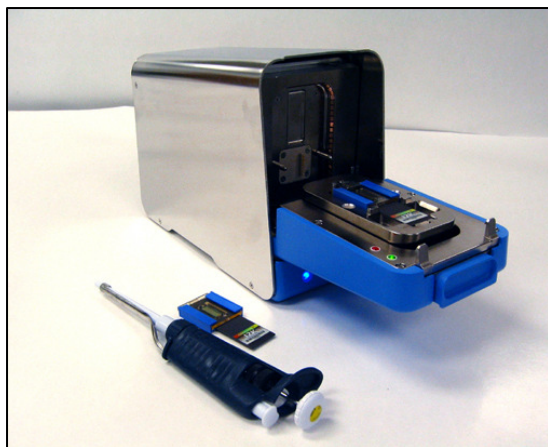


Three Major Differentiating Characteristics of CBMX Array Technology

Arrays
Quick, Inexpensive Fabrication



**Electro-Chemical
Detection (ECD)
Enables Revolutionary
Inexpensive, Compact
Instruments**



Bench Top Synthesizer
In-house Array Fabrication





How Can We Screen for Growths Early and Identify Organ of Interest?

- We know that tumors are constantly spilling cellular contents into blood.
 - Cells that break up
 - Organelles
 - Proteins
 - Nucleic Acids
- We also know that some of these contents are unique to the tumor.
- However, when tumor is small, the amount of these components in blood is very low and difficult to detect.

Past Attempts

- Previous attempts have focused on measuring contents, but often they are too low in abundance to detect, or are broken down rapidly, or both.
- Circulating Tumor Cells - usually can be identified once the tumor is relatively large.
- Organelles - Broken down quickly.
- Proteins - Low concentrations, broken down quickly.
 - Some notable successes - PSA for Prostate Cancer
- Nucleic Acids - Low concentration, broken down quickly.
 - DNA
 - mRNA- messenger RNA

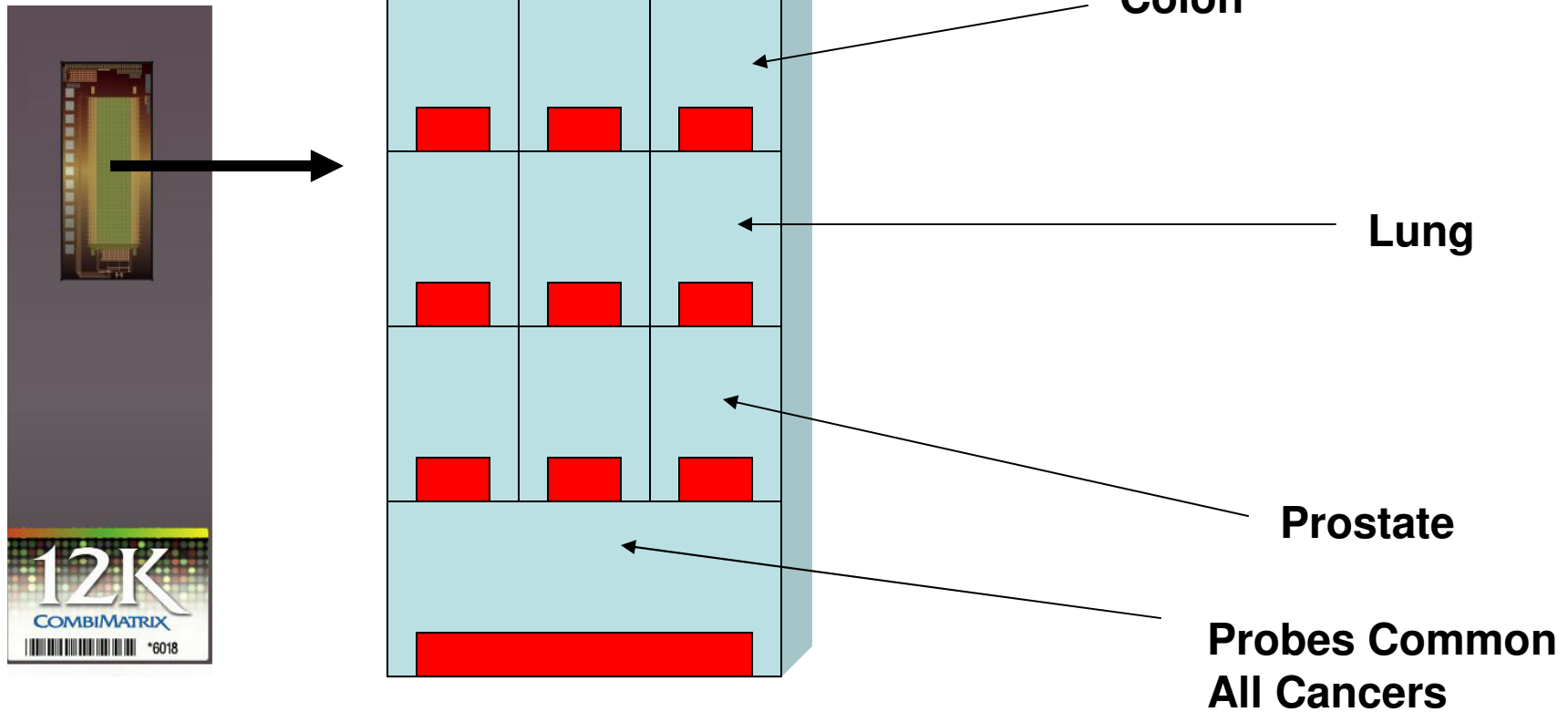
Great focus on nucleic acids --- they can be amplified

- New Type of Nucleic Acid Discovered
 - miRNA - microRNA
 - Small sequence of regulatory RNA
 - CBMX has made miRNA arrays for 3 years
 - **Two Characteristics of miRNA**
 - miRNA Patterns are unique for each cancer
 - Much more stable in blood than DNA or mRNA

Hypothesis: We can identify miRNAs in Blood that indicate a spurious growth somewhere else in the body



Comprehensive Cancer Array



Each segment carries specific probes that bind to miRNAs from blood that are characteristic of different tumor growths with appropriate controls (red).



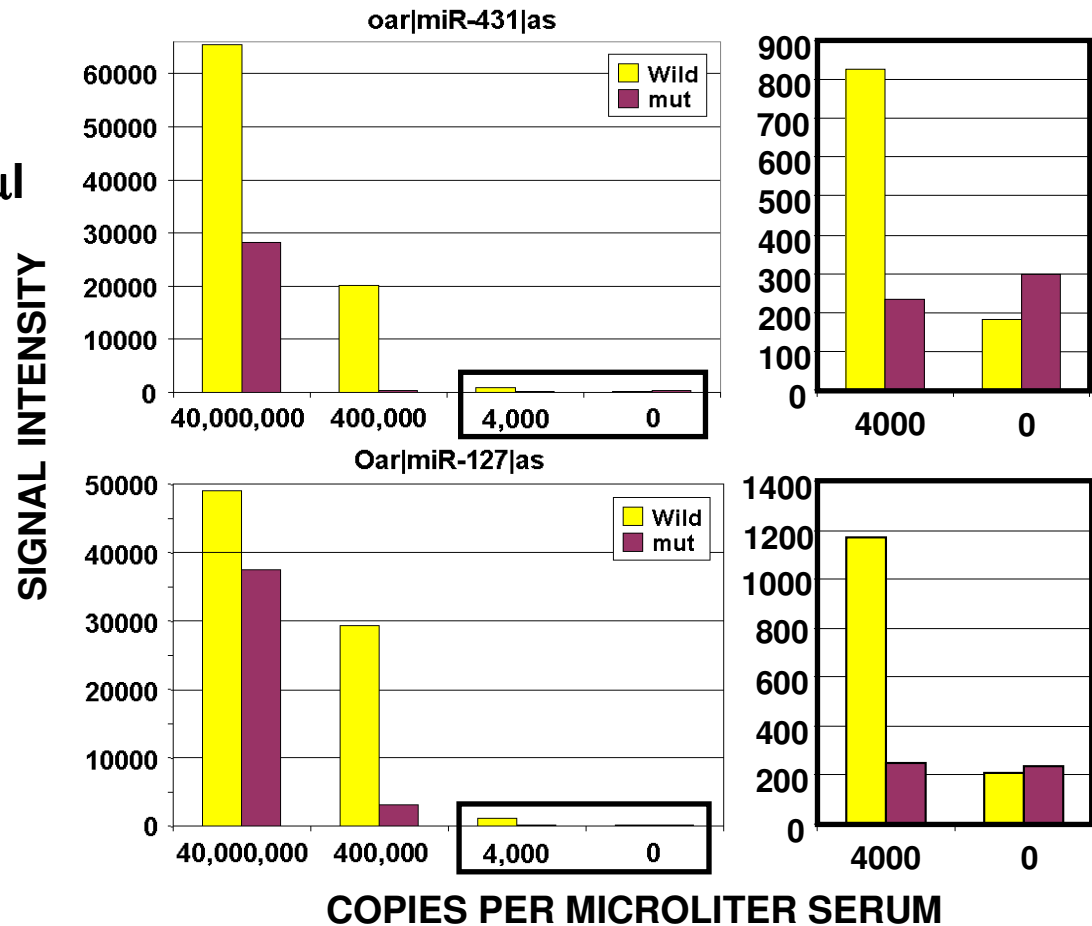
DATA



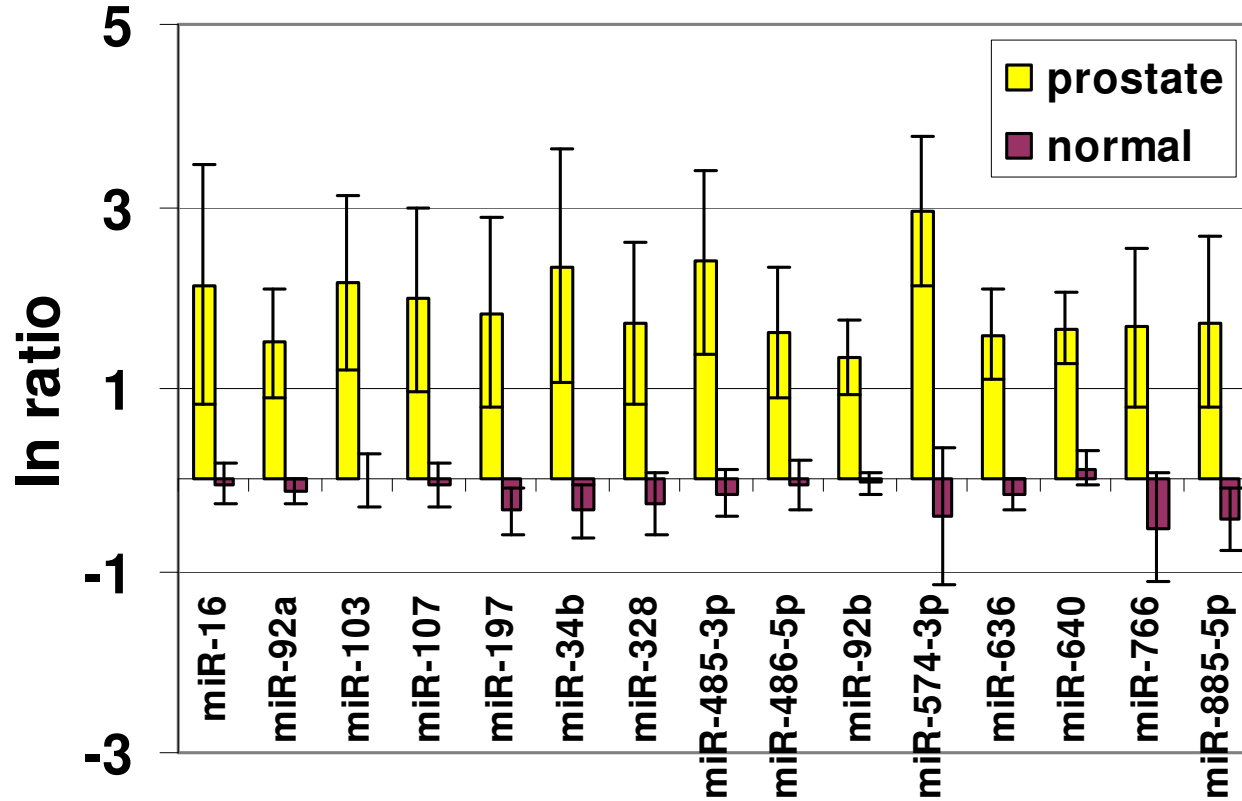
CBMX Arrays Are Very Sensitive

CBMX Microarrays can see signal down to 4,000 copies/ μ l of serum

This level of sensitivity is sufficient to perform this assay in blood

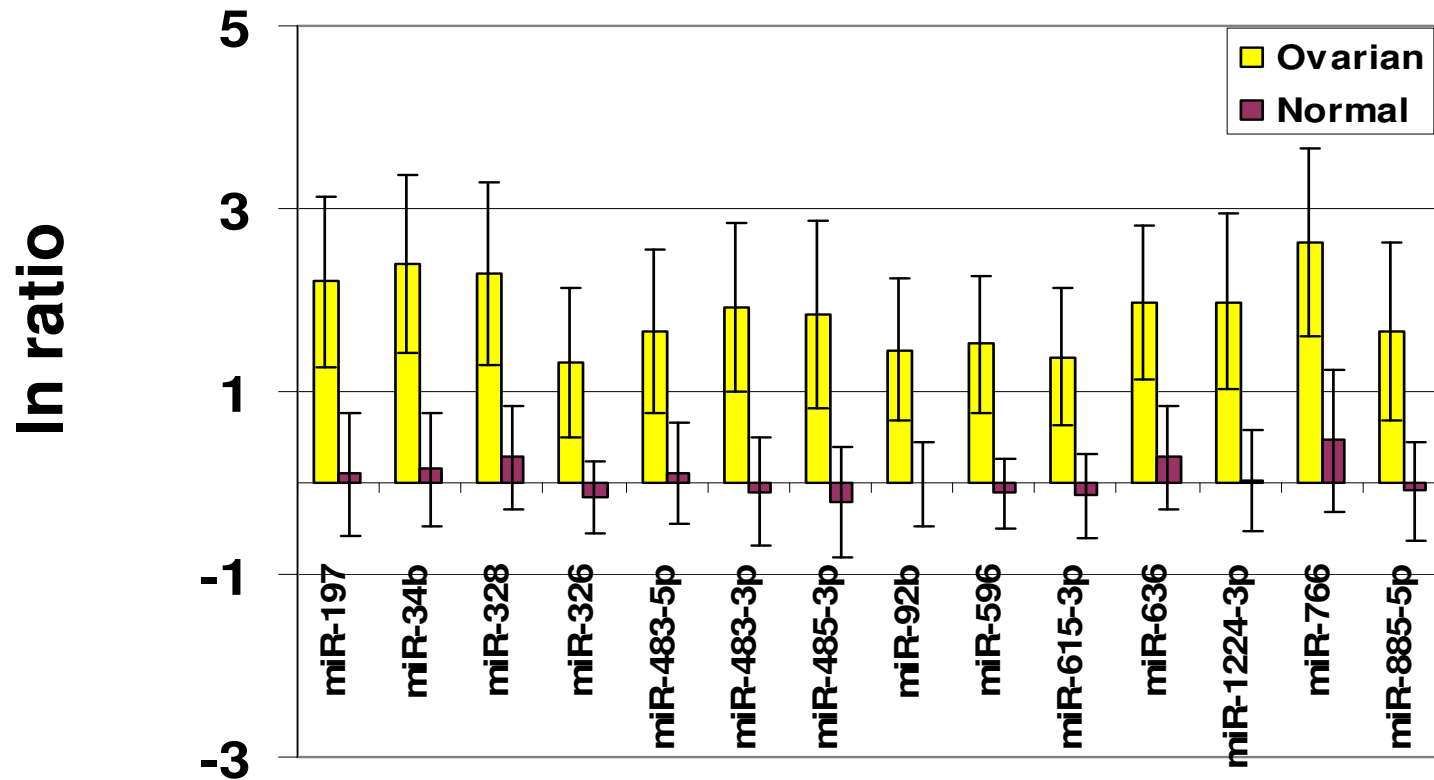


Blood Based Profile: Prostate vs. Normal (male)



We can distinguish Prostate Cancer form Normal

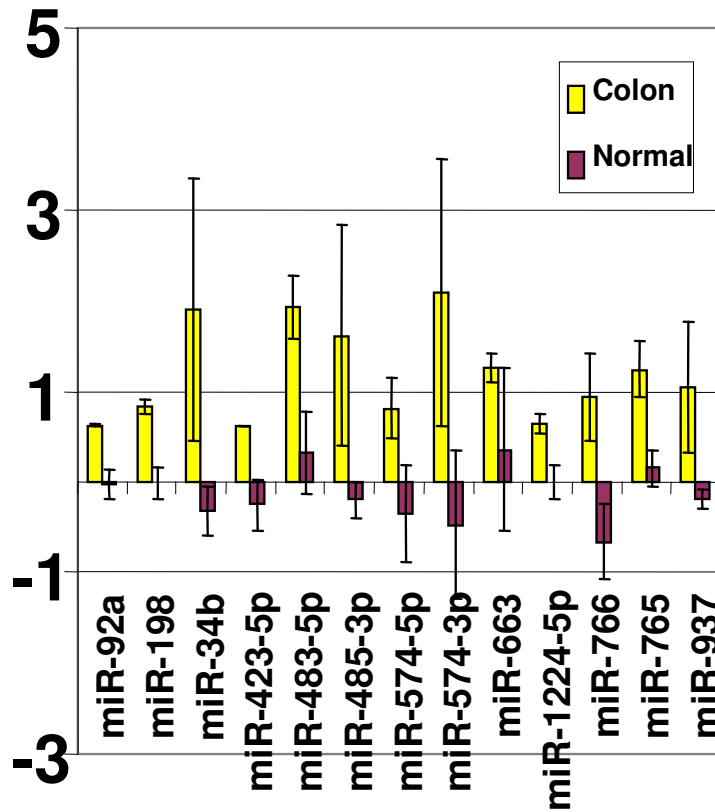
Blood Based Profile: Ovarian vs. Normal (female)



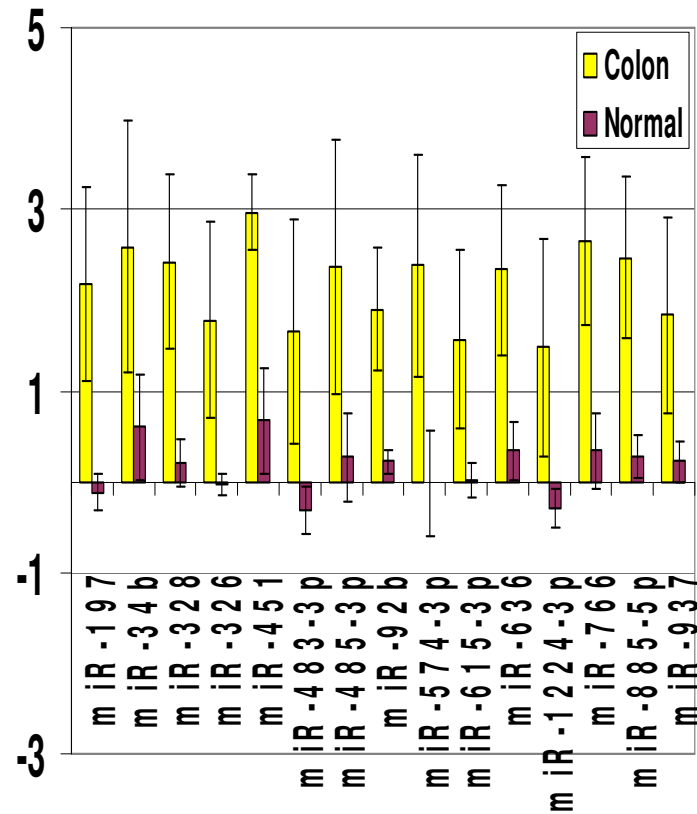
We can distinguish Ovarian Cancer form Normal

Blood Based Profile: Colon vs. Normal (male and female)

Male

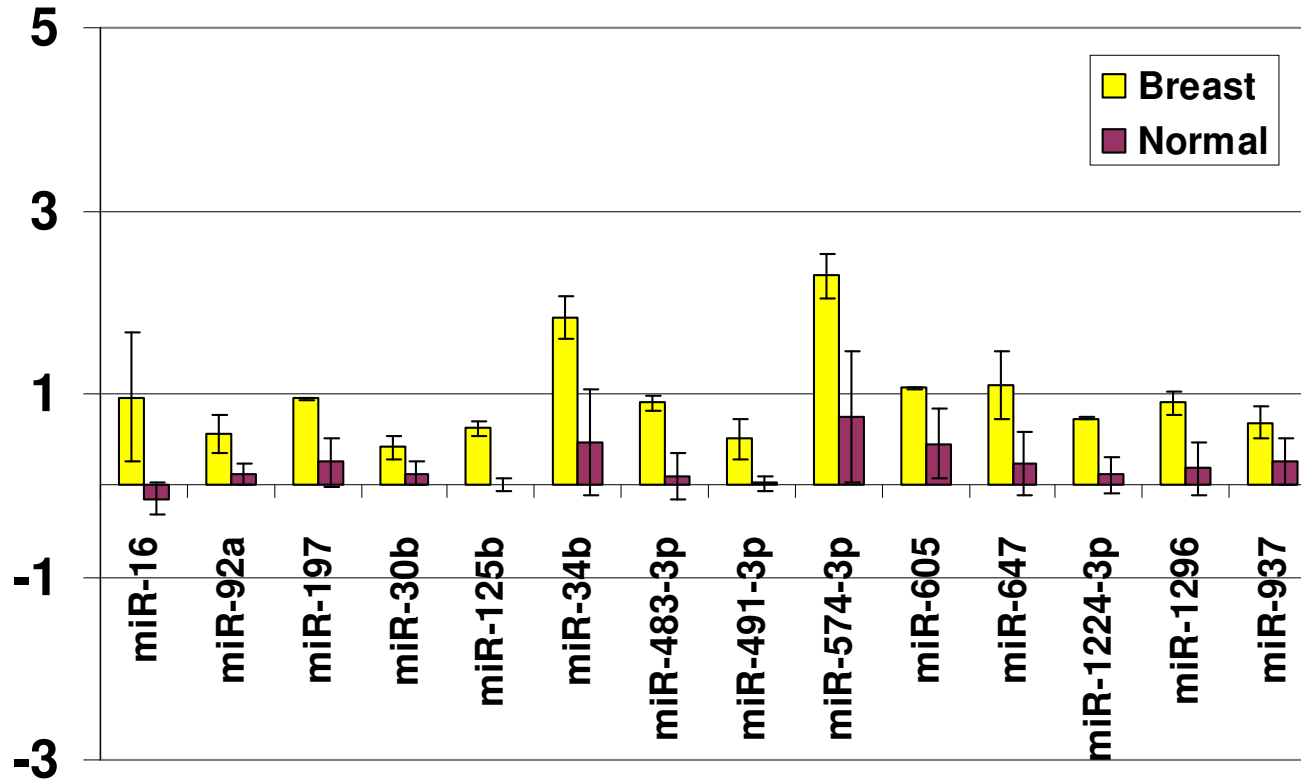


Female



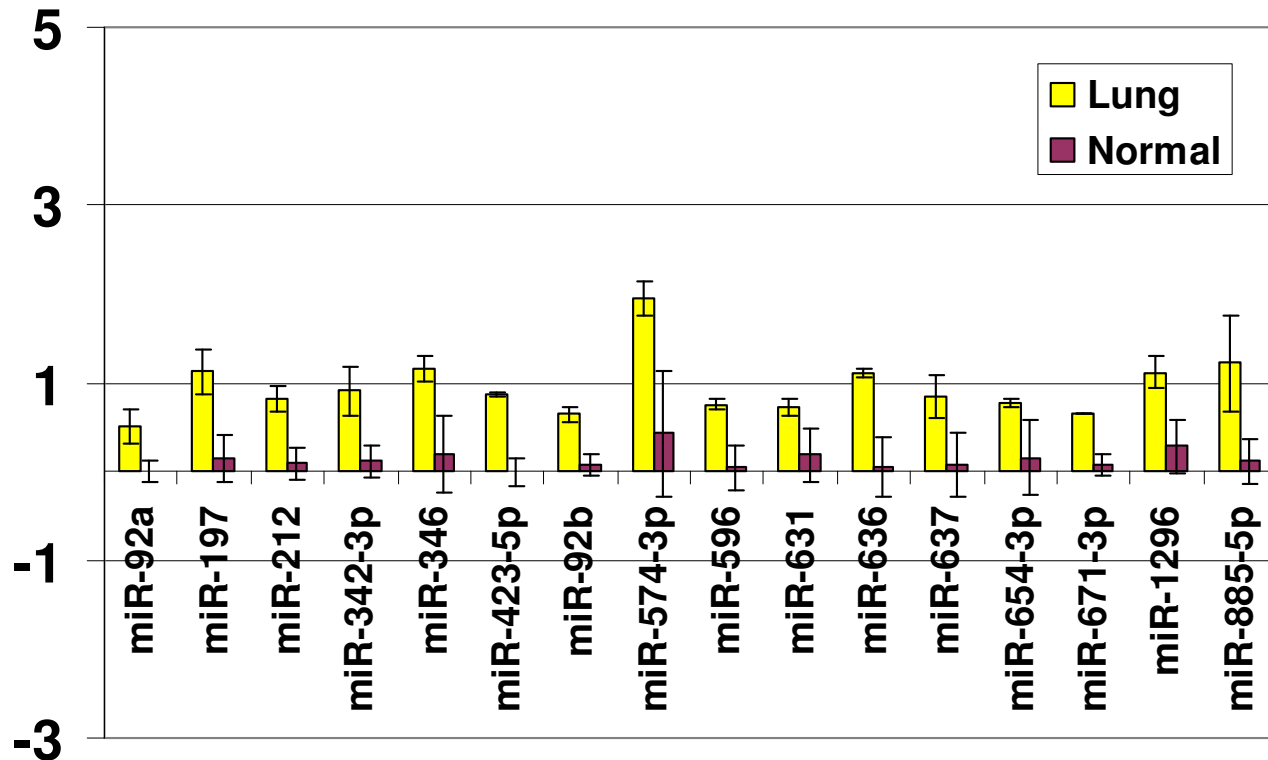
We can distinguish Colon Cancer form Normal

Blood Based Profile: Breast vs. Normal (female)



We can distinguish Breast Cancer form Normal

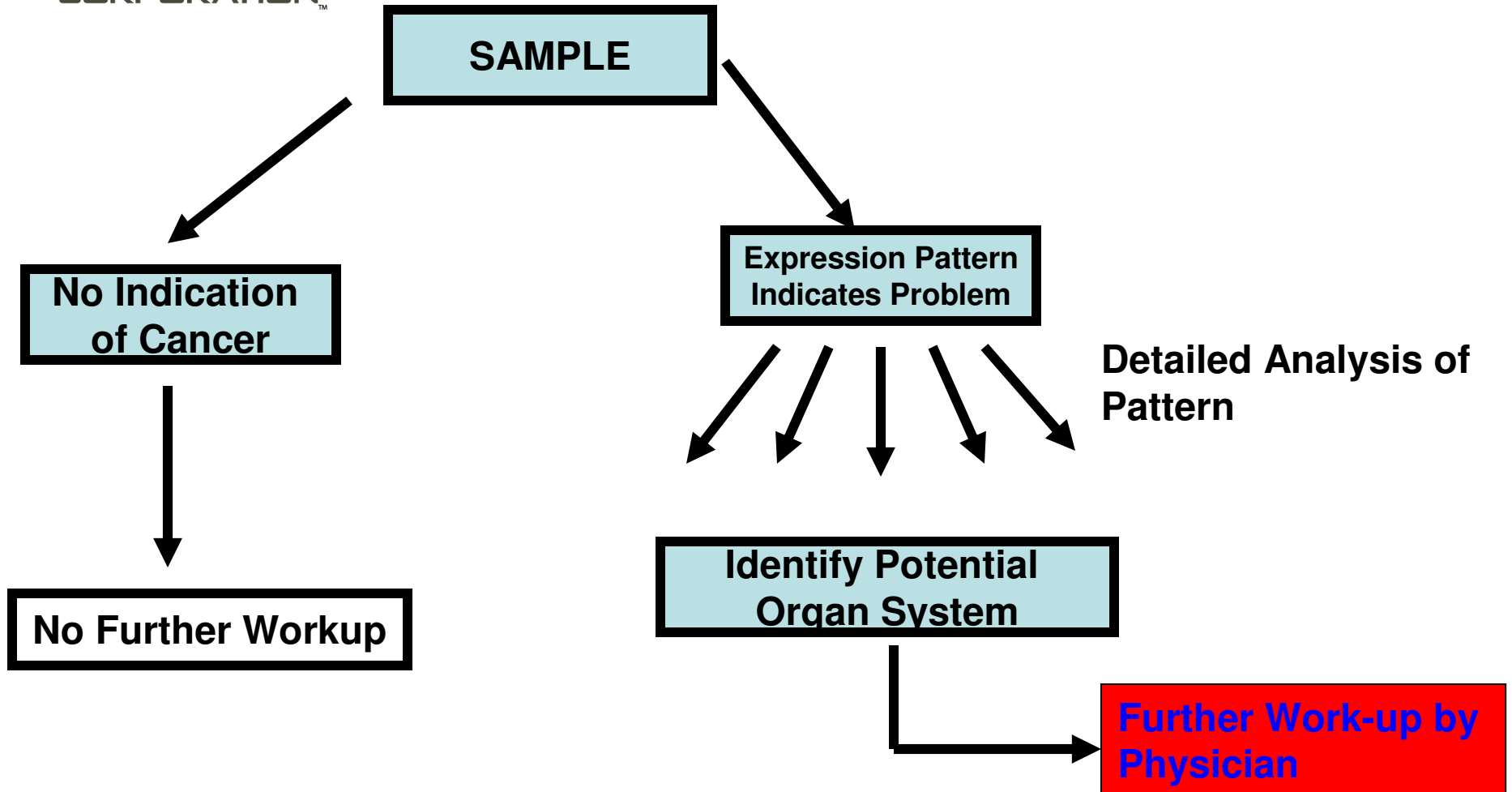
Blood Based Profile: Lung vs. Normal (small cell and NSC)



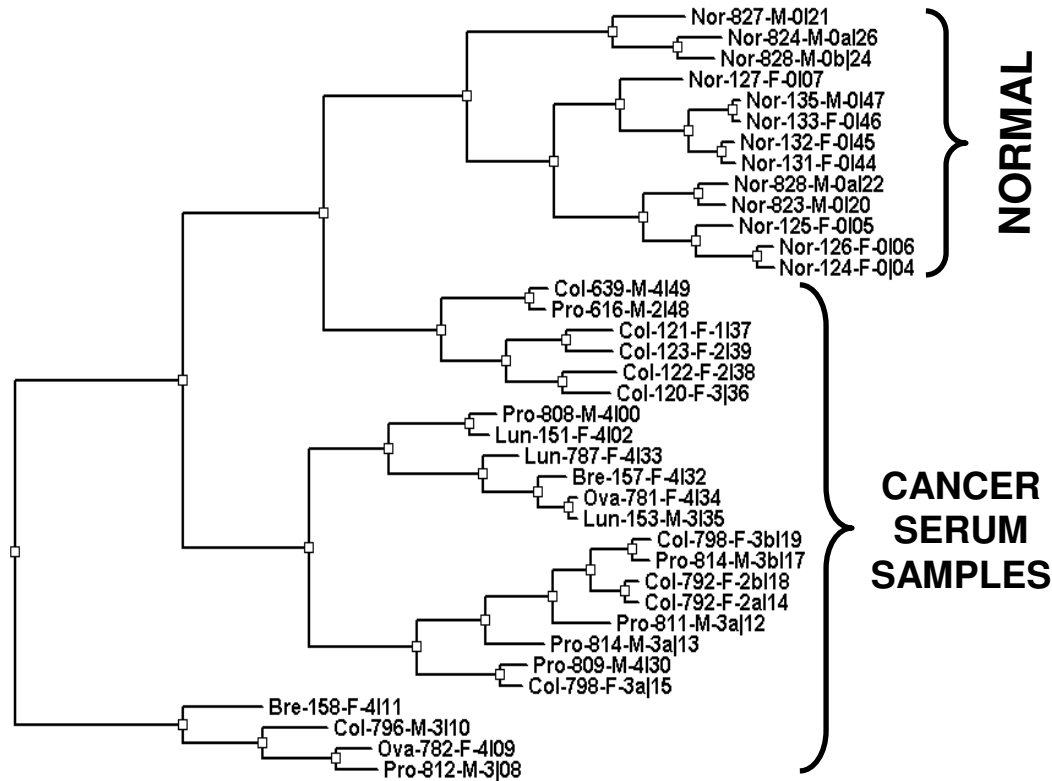
We can distinguish Lung Cancer form Normal



Decision Process



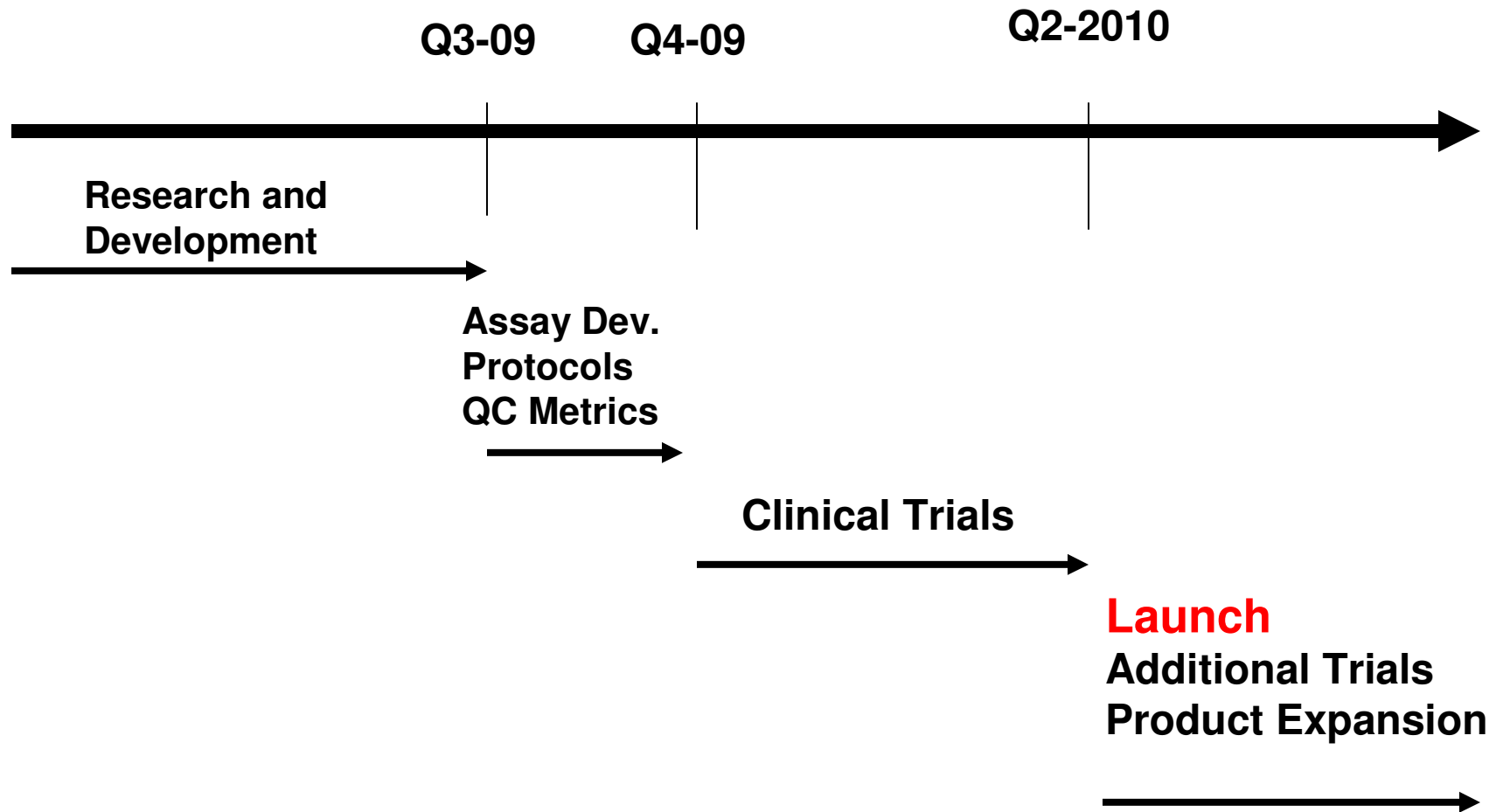
Clustering Analysis



Normals cluster together, Cancers cluster away from normals
Types of cancer cluster together, in general, but more distinction is needed



CCA-Timeline



Conclusions

- Array is Sensitive Enough
- Can Distinguish Cancer vs. Normal for 5 cancers
- Initial Focus
 - Breast, Lung, Colon, Ovarian, Prostate
 - 85% of all solid tumors in these categories
- Evaluated over 100 normal and cancer patients
- Stage 1-4
- Focused on Distinguishing Specific Cancers
- Decision Tree Approach