

# Catching More Fish from the Stream

## Metabolomic Biomarkers Using Preservation by Extraction and Fixation (PREF)

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# WHY DO PATIENTS AND DOCS NEED BIOMARKERS?

## People Differ - Diseases Differ

“...we knew that there were... cancer patients ..

Letter to the editor WSJ  
Dec 2, 2009  
Joseph R. Barrie, MD

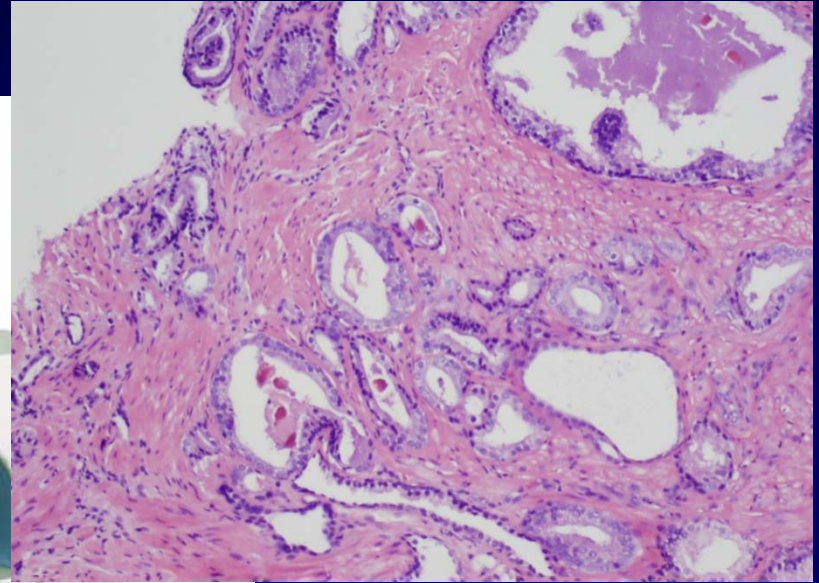
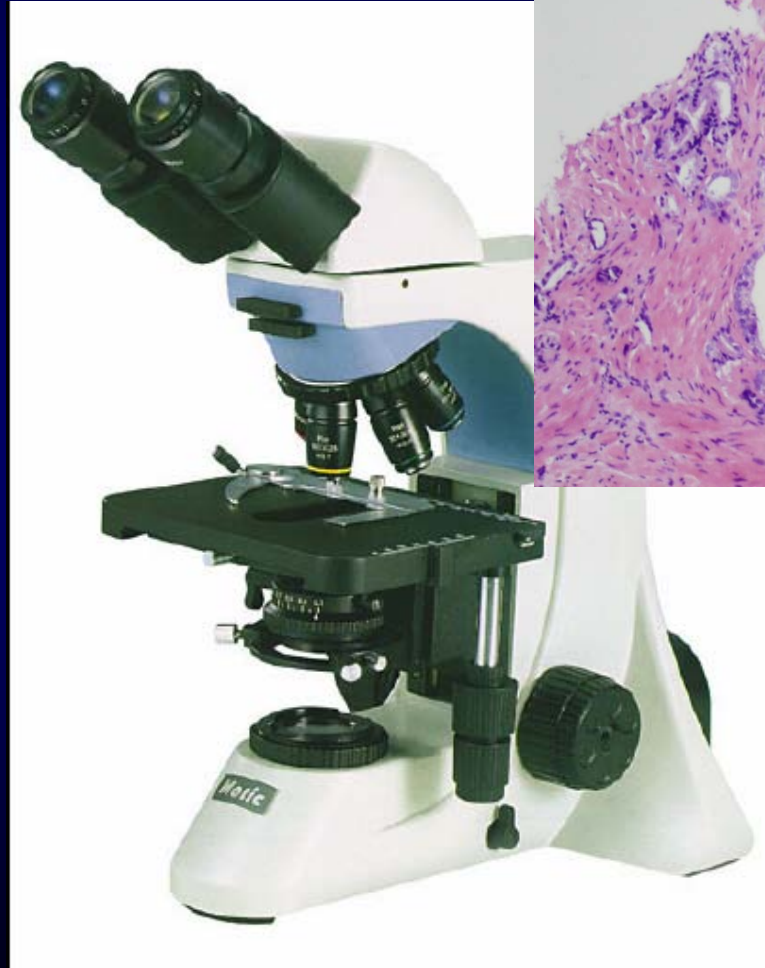
who did well no matter how little we did

who did poorly no matter how much we did

and that there were  
some for whom our interventions were of value...”



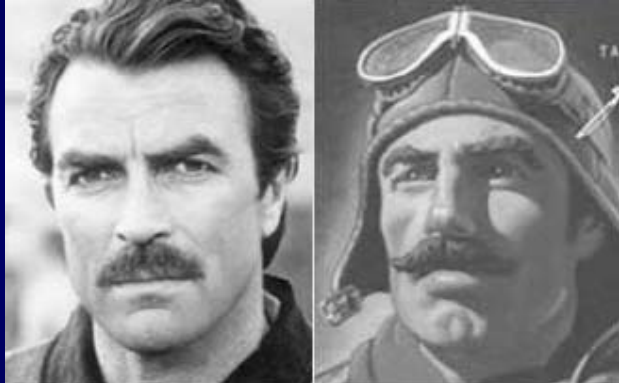
# Diagnosis by Pathologist Using Microscope



# BIOMARKERS BY HISTOLOGY – Some are Easier than Others



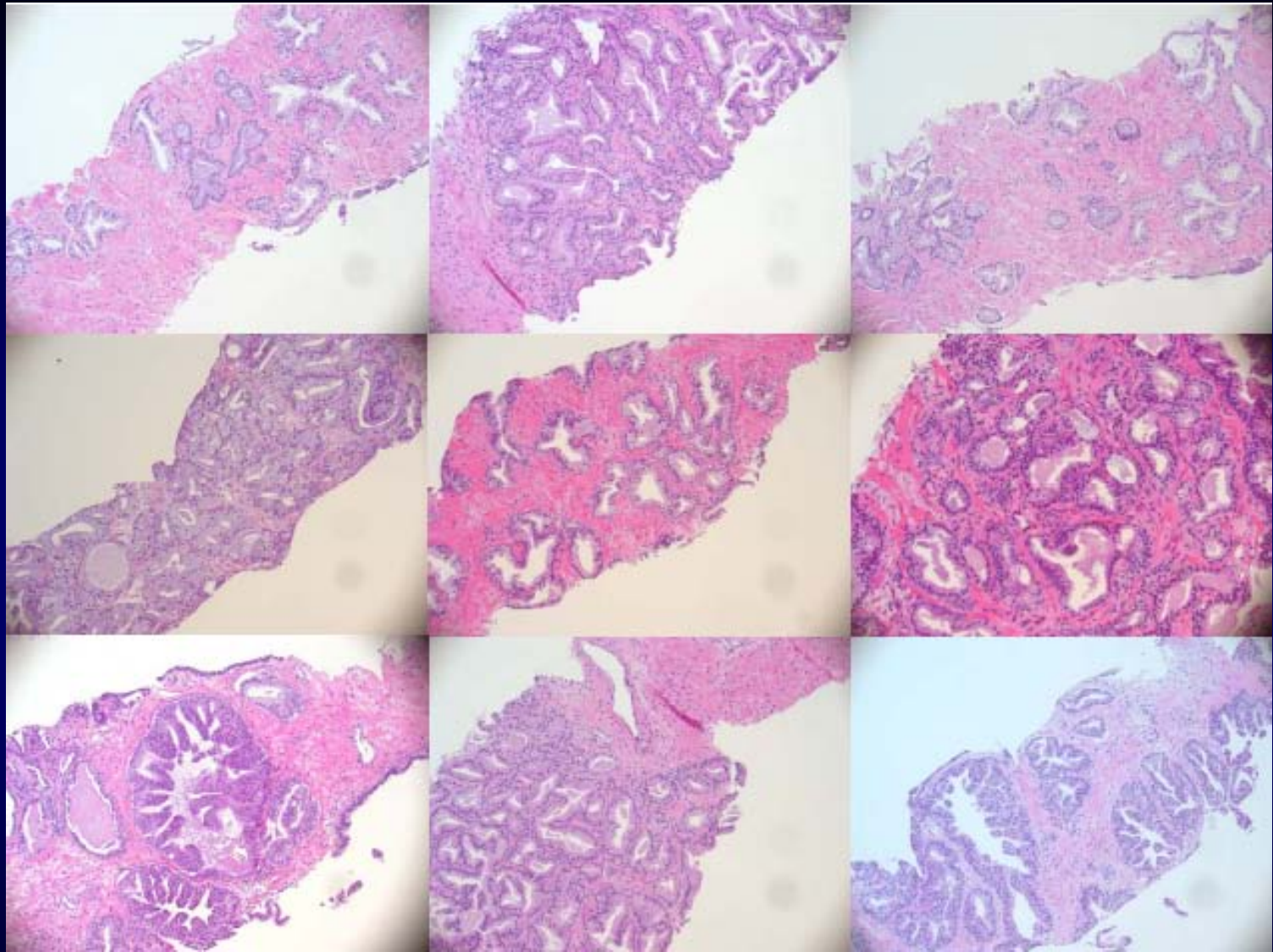
Jamie Hyneman or the Walrus?



Tom Selleck or The Red Baron?

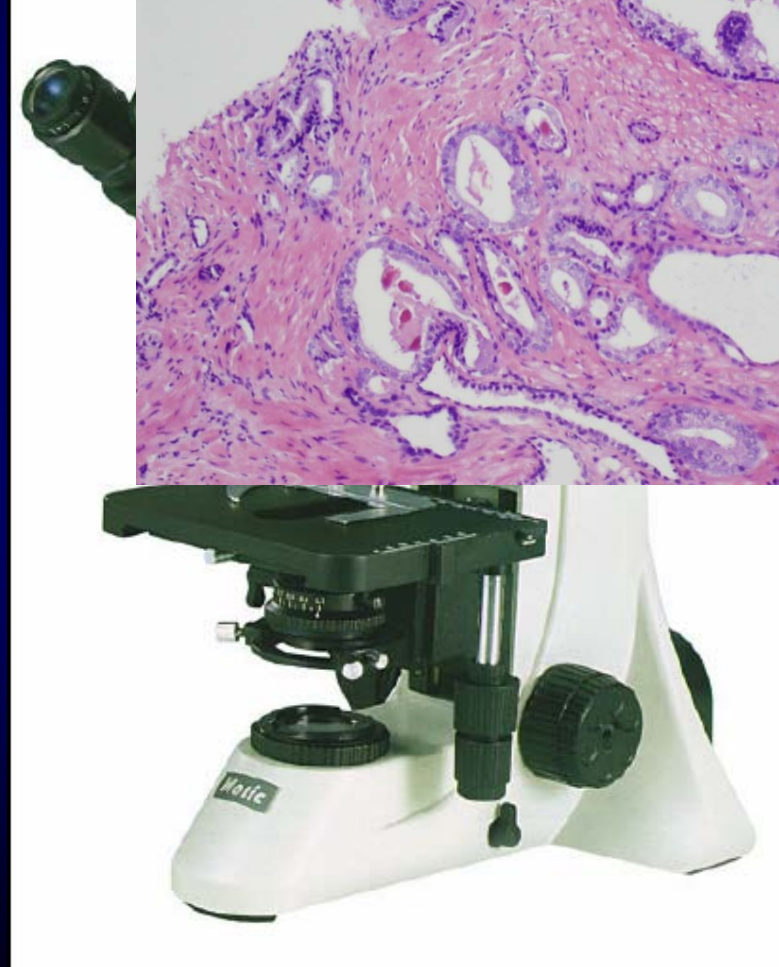
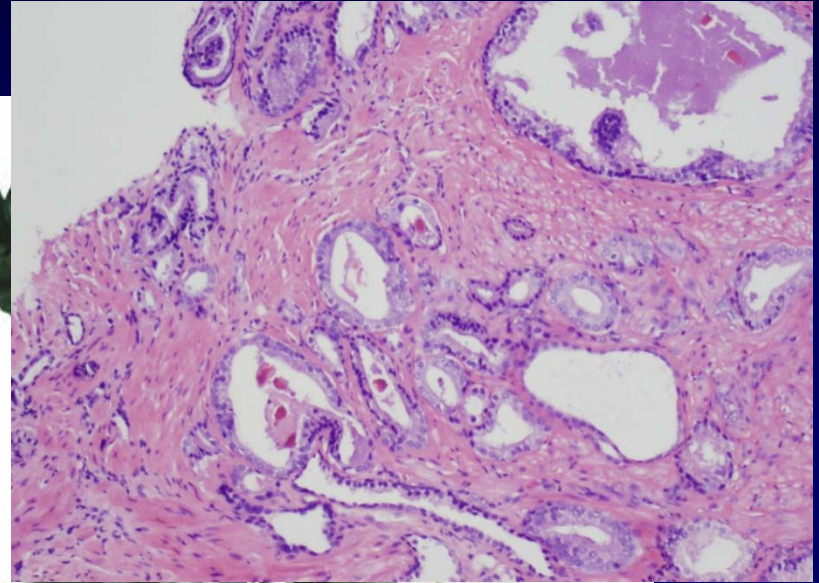


Where's the Governor?



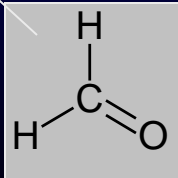
# How Diagnosis Works

## Tissue is Fixed to Prepare Slide

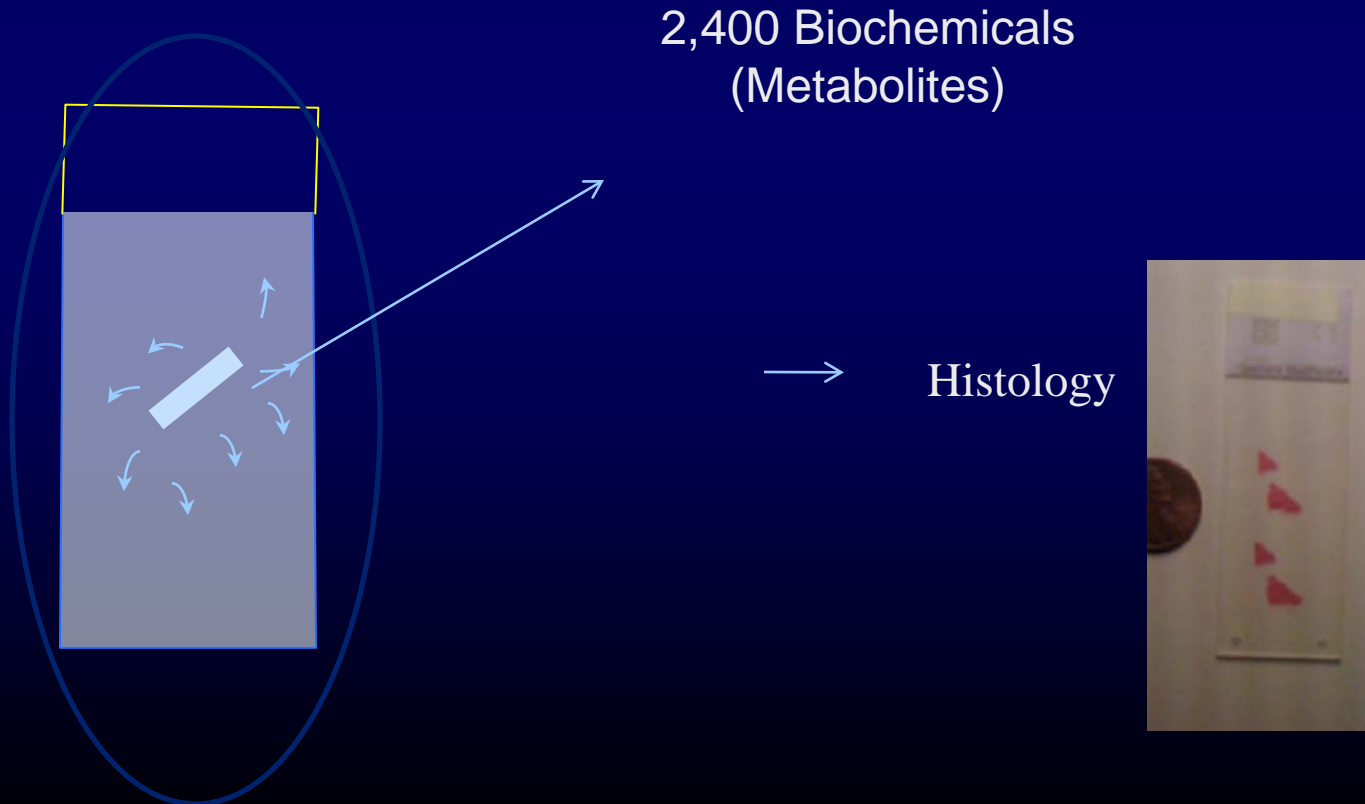


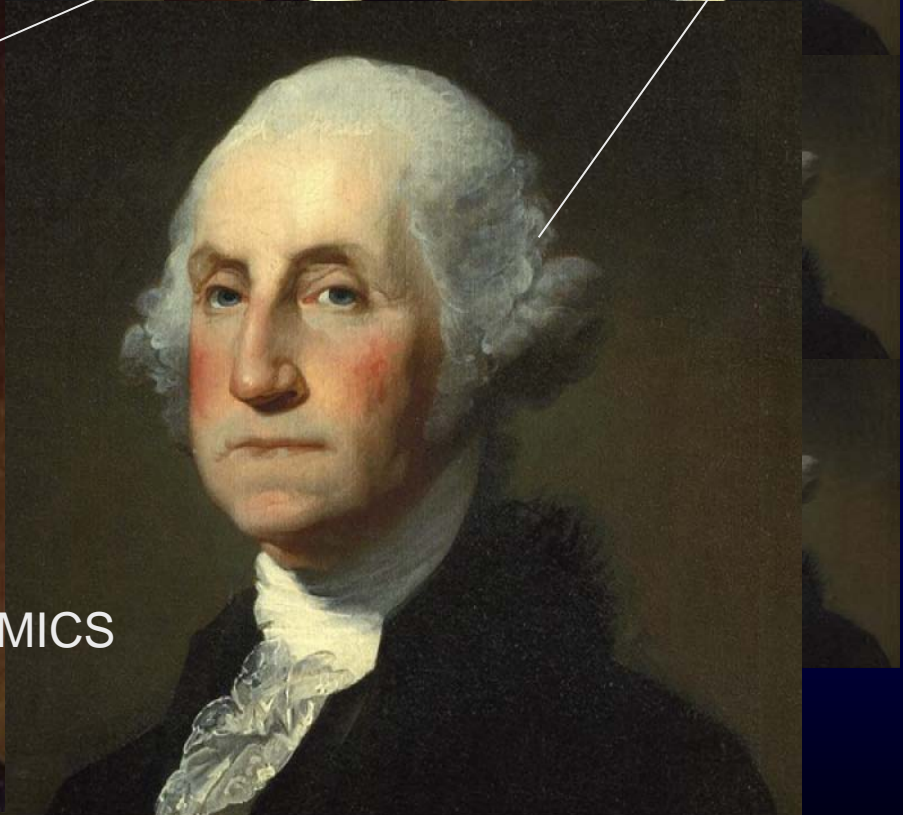
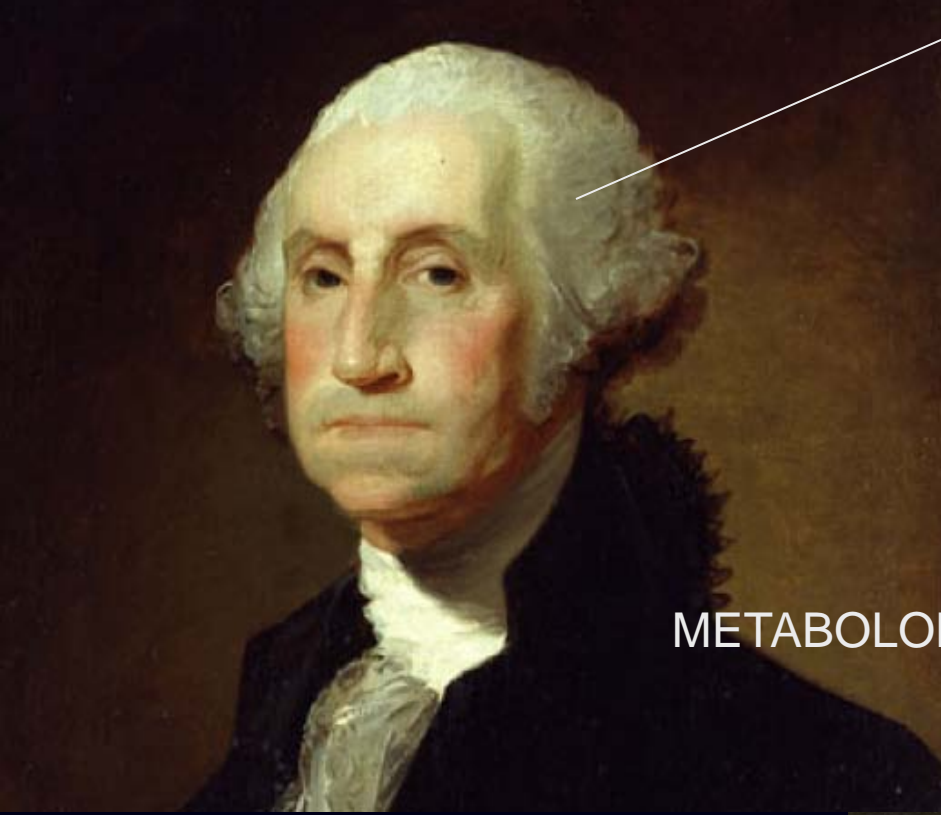
Tissue Biopsy  
From Patient

Fixative  
(Formaldehyde)

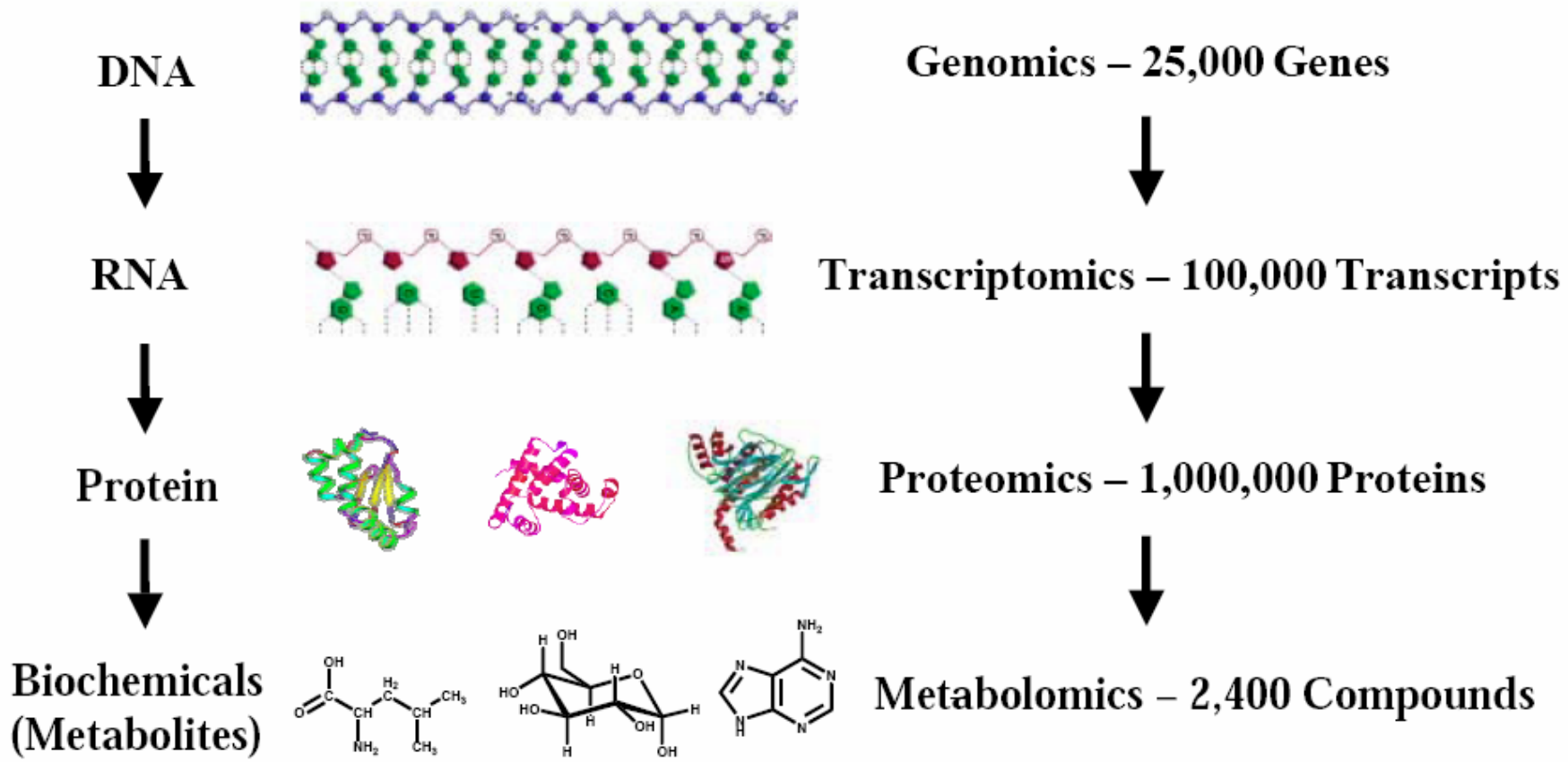


# Preservation by Extraction and Fixation

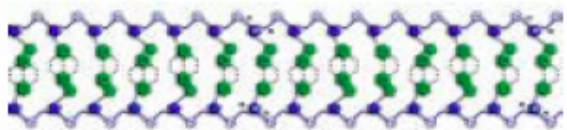




METABOLOMICS



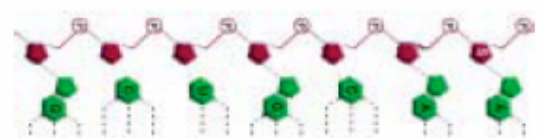
**DNA**



**Genomics – 25,000 Genes**



**RNA**



**Transcriptomics – 100,000 Transcripts**



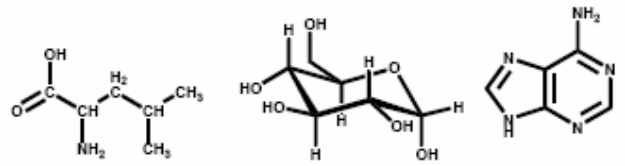
**Protein**



**Proteomics – 1,000,000 Proteins**

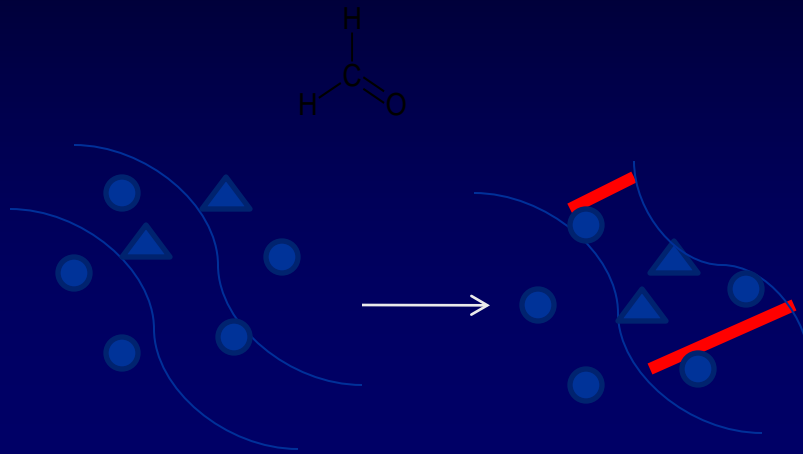


**Biochemicals  
(Metabolites)**



**Metabolomics – 2,400 Compounds**

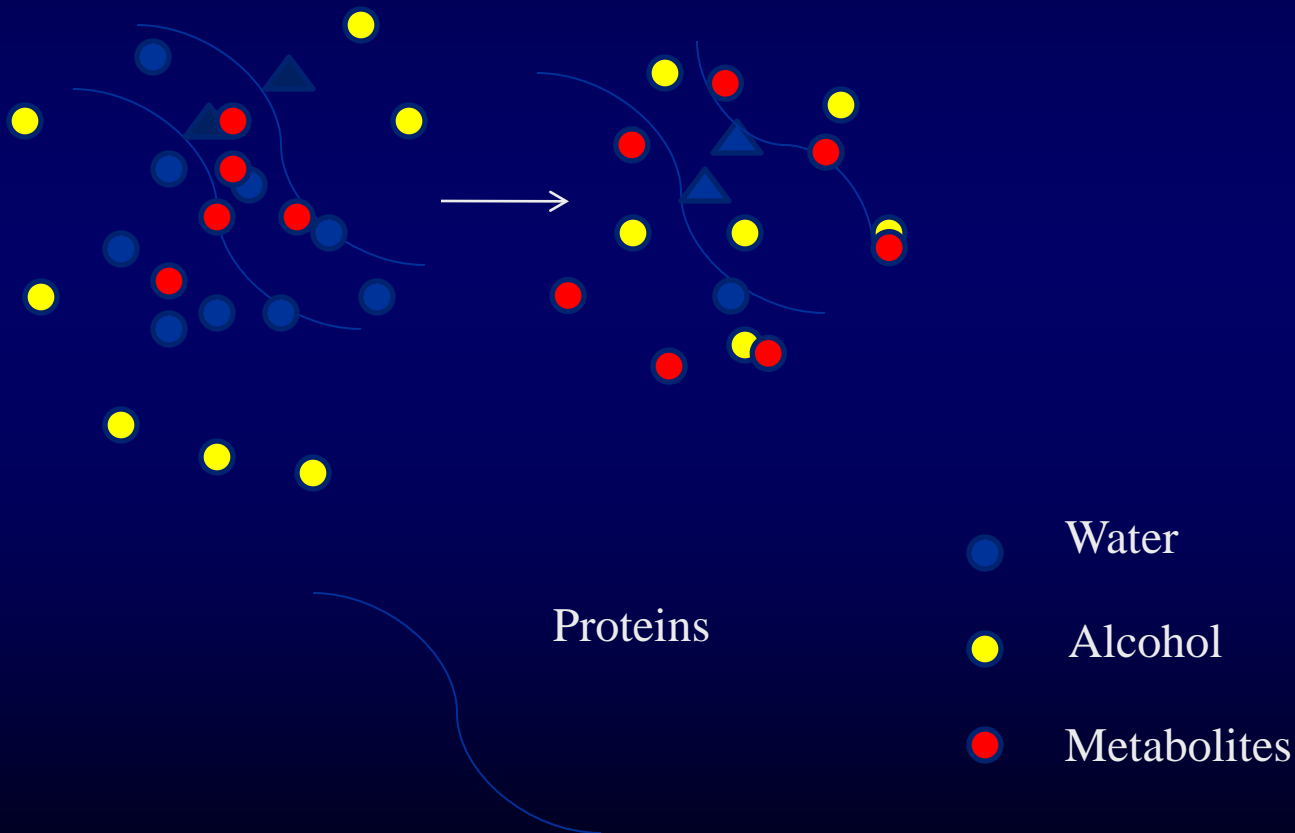
# Proteins cross-linked by formaldehyde



Epitopes for antibodies “covered” by cross-linking  
Water and Metabolites remain in place

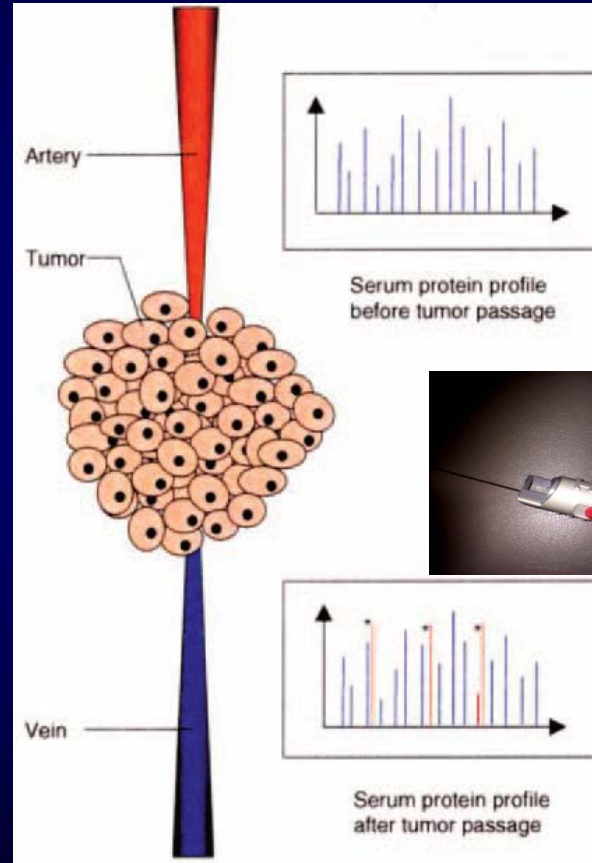
# Alcohol Fixatives

## “Coagulants” vs. Cross linking



# TISSUE IS STILL THE ISSUE

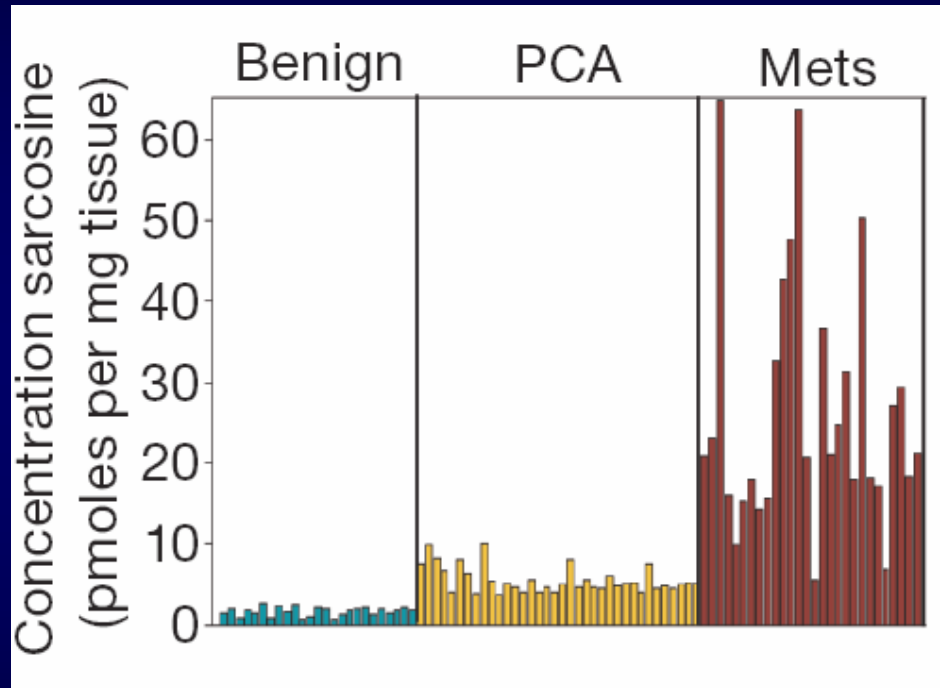
Tumor  
Undiluted by Blood or Urine





# Are Metabolites Prognostic?

## Sarcosine in pCa Tissues



Sreekumar, S. Nature, 457, 910-915

# What Collaborations?

- **Diabetes**
- **Transplantation/allografts**
- **Animal Models**
- **Food processing**
- **Materials Sciences?!**

**Anything that can be sectioned and  
examined under a microscope**