About OMICS Group

OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 400 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 300 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS Group Conferences

OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Phrama scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Changes in blood, detected in urine

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Chinese Academy of Medical Sciences

University of Oxford 2014-4-15

What is biomarker?

My Definition

- **Biomarker is the measurable change associated with a physiological or pathophysiological process.**

blog.sciencenet.cn/home.php?mod=space&uid=244733&do=blog&id=725226


Biomarker=Change

In Blood

Homeostasis mechanisms
=minimal changes
=less biomarkers

In Urine

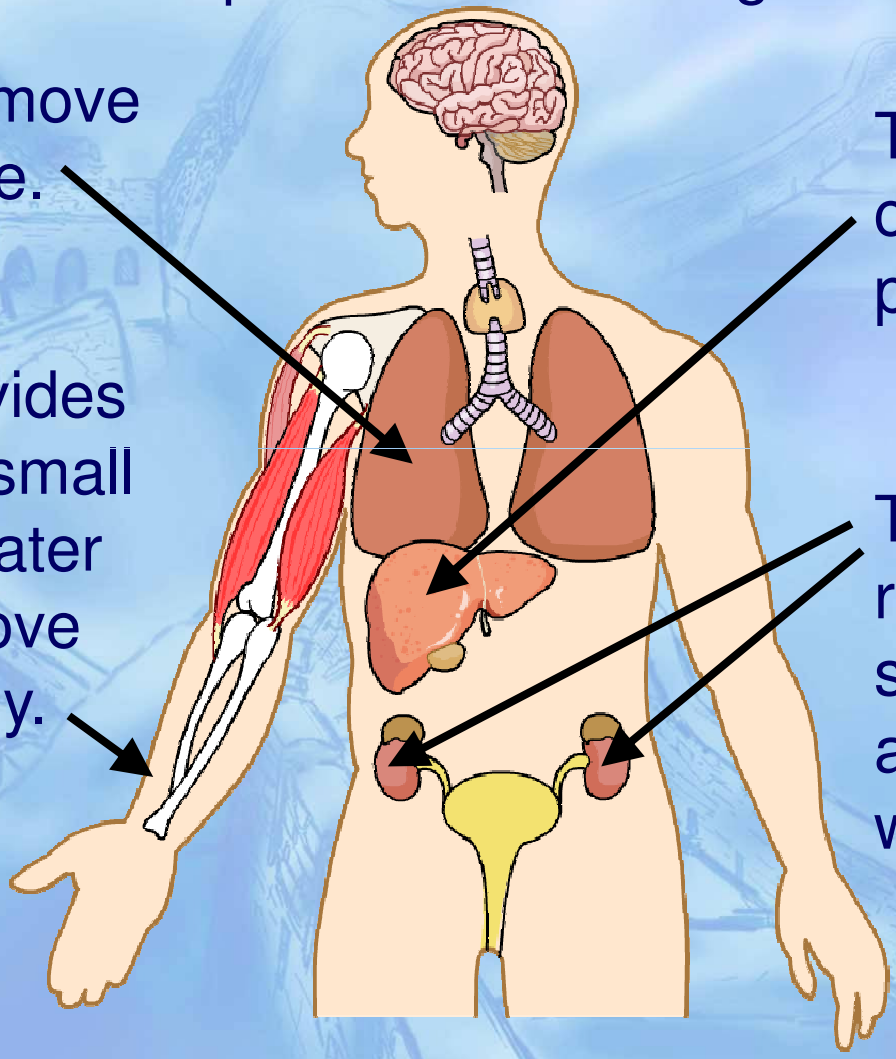
Accumulate all the changes =
Lots of biomarkers

Change removal

Several organs are important in removing waste from the body.

The **lungs** remove carbon dioxide.

The **skin** provides a surface for small amounts of water and salt to move out of the body.

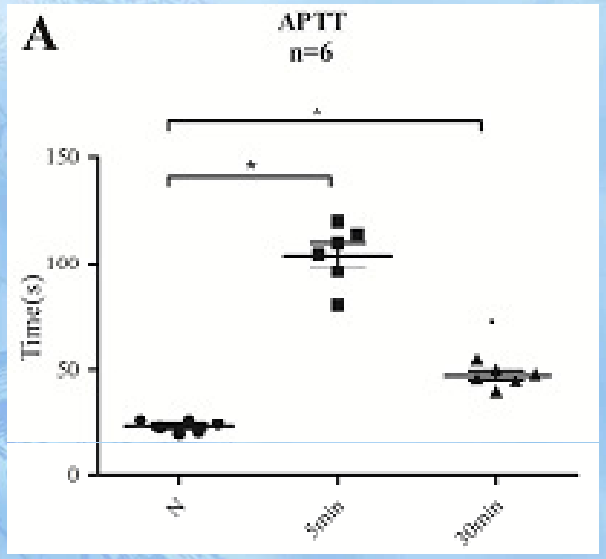


The **liver** converts excess protein into **urea**.

The **kidneys** remove unwanted substances such as urea, excess water and salt.

Changes of proteins induced by anticoagulants can be more sensitively detected in urine rather than plasma

Changes of protein induced by anticoagulants

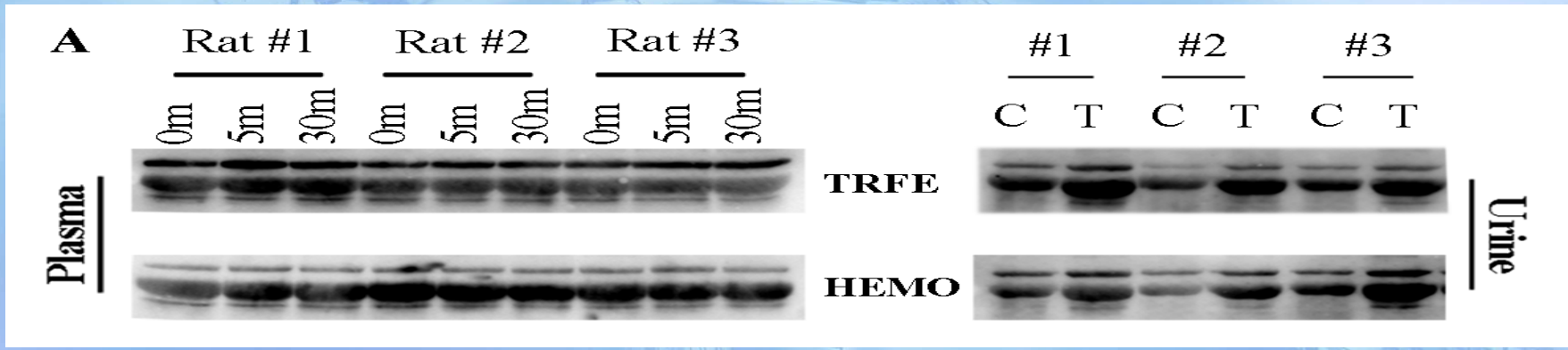


Clotting times increased

Changes

- Heparin
- 27 proteins in urine
- 3 proteins in plasma

- Argatrabon
- 61 proteins in urine
- 1 proteins in plasma



Validation of changes in protein levels

Advantages of Urine Proteome

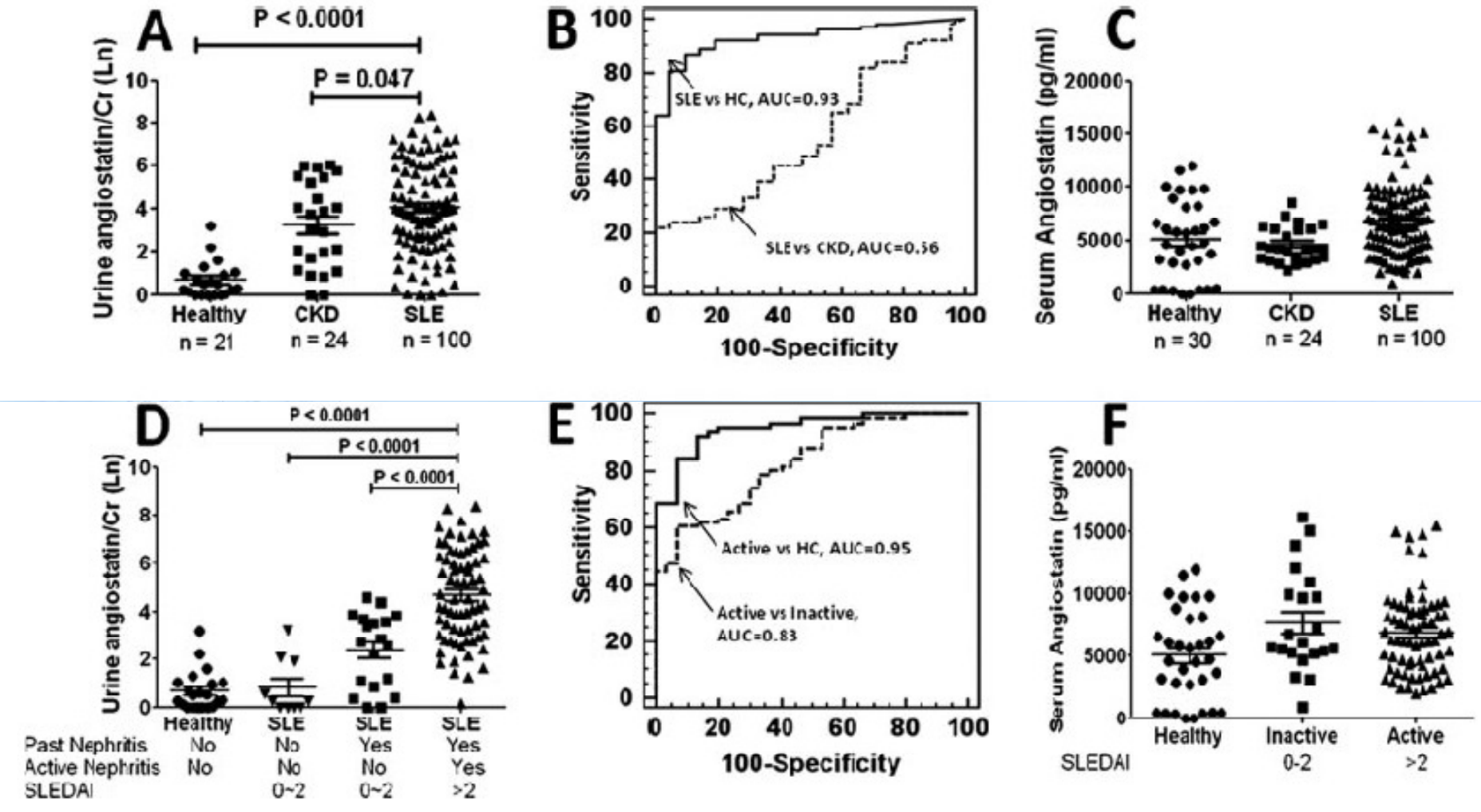
- Non-invasive
- Simpler than plasma
- Reflects changes of plasma
- Close to kidney and prostate

Urine Proteome is Informative

- Up to published result in 2011, 2300 proteins identified totally
- 4000-5000 with current technology

Low Background

- Actually low protein concentration is better for biomarker discovery
- Low constitutional component is better for revealing the changes



Molecular & Cellular Proteomics 12:
10.1074/mcp.M112.021667, 1170–1179, 2013.

TABLE III. Frequency of Aberrant Methylation in Urine and Plasma DNA

	GSTP1		RASSF2	
	Urine	Plasma	Urine	Plasma
Positives (%)				
Young asymptomatic males	6%	20%	37%	2%
Biopsy negative	59%	31%	82%	16%
All stages PCa	81%	39%	59%	31%
T1 (n = 47 U, 46 P)	83%	37%	96%	35%
T2 (n = 28 U, 25 P)	71%	32%	82%	16%
T3 (n = 7)	100%	71%	100%	57%
T4 (n = 2)	100%	50%	100%	50%
Median DNA (range), ng/ml				
Young asymptomatic males	0 (0–0.07)	0 (0–0.00[a])	0 (0–0.09)	0 (0–0.00[a])
Biopsy negative	0.001 (0–0.15)	0 (0–0.02)	0.007 (0–0.70)	0 (0–0.04)
All stages PCa	0.008 (0–91.18)	0 (0–0.27)	0.025 (0–112.45)	0 (0–0.19)
T1 (n = 47 U, 46 P)	0.006 (0–91.80)	0 (0–0.18)	0.024 (0–112.45)	0 (0–0.19)
T2 (n = 28 U, 25 P)	0.008 (0–0.88)	0 (0–0.05)	0.022 (0–0.91)	0 (0–0.00[a])
T3 (n = 7)	0.029 (0.001–14.37)	0.001 (0–0.27)	0.042 (0–19.08)	0.0005 (0–0.02)
T4 (n = 2)	n.a. (0.014–0.14)	n.a. (0–0.00[a])	n.a. (0.07–0.08)	n.a. (0–0.00[a])
	HIST1H4K		TFAP2E	
	Urine	Plasma	Urine	Plasma
Positives (%)				
Young asymptomatic males	14%	8%	82%	2%
Biopsy negative	84%	31%	100%	6%
All stages PCa	92%	31%	100%	18%
T1 (n = 47 U, 46 P)	96%	28%	100%	24%
T2 (n = 28 U, 25 P)	82%	28%	100%	4%
T3 (n = 7)	100%	71%	100%	29%
T4 (n = 2)	100%	0%	100%	0%
Median DNA (range), ng/ml				
Young asymptomatic males	0 (0–0.02)	0 (0–0.01)	0 (0–0.24)	0.013 (0–0.00[a])
Biopsy negative	0.004 (0–0.16)	0 (0–0.00[a])	0.052 (0.001–0.94)	0 (0–0.00[a])
All stages PCa	0.008 (0–47.94)	0 (0–0.18)	0.096 (0.004–27.80)	0 (0–0.14)
T1 (n = 47 U, 46 P)	0.008 (0–47.94)	0 (0–0.18)	0.106 (0.01–27.80)	0 (0–0.14)
T2 (n = 28 U, 25 P)	0.008 (0–0.72)	0 (0–0.01)	0.096 (0.01–4.42)	0 (0–0.00[a])
T3 (n = 7)	0.024 (0.00–4.04)	0.0007 (0–0.02)	0.377 (0.01–6.81)	0 (0–0.01)
T4 (n = 2)	0 (0.01–0.06)	0	n.a. (0.08–0.09)	0

The Prostate 69:1257^1269 (2009)

Not just within urinary tract

- This is the first study to demonstrate that analysis of urinary MMPs may be useful in determining disease status in a variety of human cancers, both within and outside of the urinary tract.
- MMP:
  - 72KD
  - 92KD
  - >150KD

(CANCER RESEARCH 58, 1395-1399. 1998)

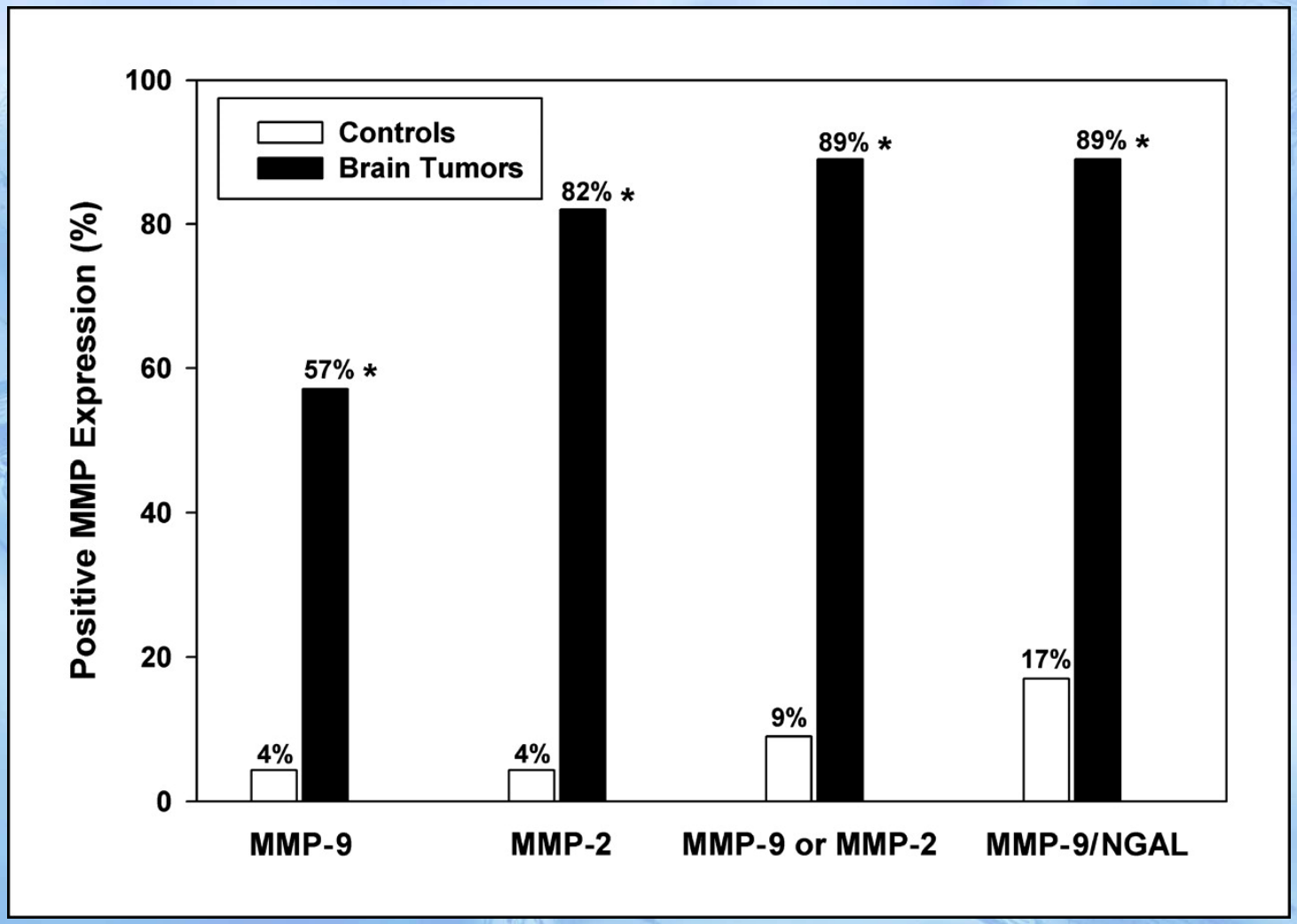
Plasma and Urinary Desmosine as biomarkers for COPD

Table 2 Demographic and desmosine data for group 2 consisting of healthy volunteers and patients with an exacerbation of chronic obstructive pulmonary disease (COPD)

	Group 2			
Sample type	Urine and sputum		Blood	
Group	Healthy volunteers (HV2a)	Patients with 'during an exacerbation' COPD	Healthy volunteers (HV2b)	Patients with 'during an exacerbation' COPD
Number of participants	62	50*	19	102*
Gender (M/F)	24/38	24/26	18/1	43/59
Smoking status (smokers/e-smokers/non-smokers/unknown)	13/41/8/0	31/2/15/2	10/0/9/0	55/33/0/14
Age (years)	22 (21–45)	69 (60–74)†	68 (65–73)	72 (66–79)
Body mass index	25±4	26±7	NA	26±7
FEV_1 (% predicted)	103±13	39±16†	NA	47±18
uDES (ng/mg creatinine)	8 (6–10)	16 (14–22)†	–	–
bDES (ng/ml)	–	–	0.17 (0.12–0.23)	0.30 (0.21–0.37)†

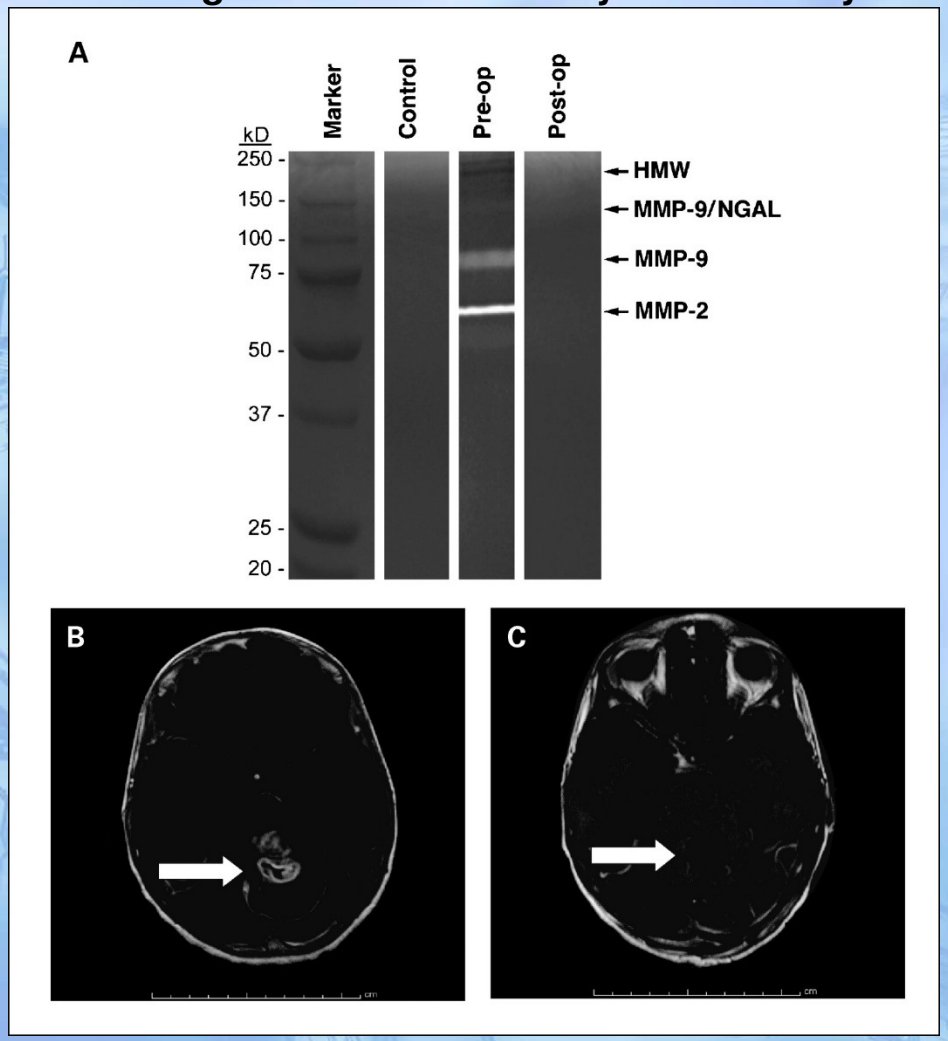
Thorax 2012 67: 502-508

Urine of brain tumor patients contains significantly higher levels of MMP-2, MMP-9, and MMP-9/NGAL compared with control samples.



Smith E R et al. Clin Cancer Res 2008;14:2378-2386

The loss of urinary MMPs after resection of a brain tumor, demonstrating that tumor presence is related to increased urinary MMP activity and removal of that tumor correlates with subsequent clearing of detectable urinary MMP activity.



Smith E R et al. Clin Cancer Res 2008;14:2378-2386

Urine/Blood in Biomarker Studies

Up to 2013-5-29

pubmed - (((blood) OR serum) OR plasma) AND biomarker		pubmed - (urine) AND biomarker		
year	count	year	count	**urine/blood**
2013	3436	2013	302	**8.79%**
2012	20759	2012	1401	**6.75%**
2011	19996	2011	1369	**6.85%**
2010	19097	2010	1288	**6.74%**
2009	17733	2009	1056	**5.95%**
2008	16993	2008	1057	**6.22%**
2007	16509	2007	952	**5.77%**
2006	15186	2006	918	**6.05%**
2005	15389	2005	860	**5.59%**
2004	14208	2004	767	**5.40%**
2003	13417	2003	696	**5.19%**

Urinary Protein Biomarker Database

- http://122.70.220.102/biomarker
- **Manually curated in the lab**
- **Around 450 papers at mid 2013**

Mol Cell Proteomics 2011 10: M111.010975

Disadvantages as Biomarker Source

- Big variation
- Need more cases to validate

Way to solve the problem

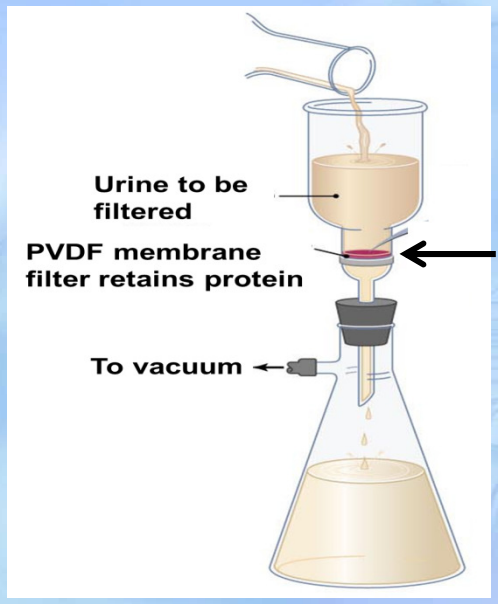
- More sample
- Higher throughput MS
- More analyzing power

Problem with samples

- Very diluted
- Protein degradation

Possible ways to save

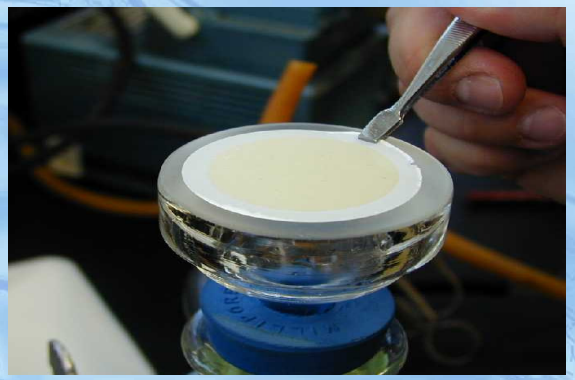
- Precipitate: organic solvent consuming
- Freeze dry: energy and labor consuming
- Extraction: cost
- Not suitable for large numbers of samples


Urine to be filtered
PVDF membrane filter retains protein
To vacuum


Membrane Solutions

Urimem

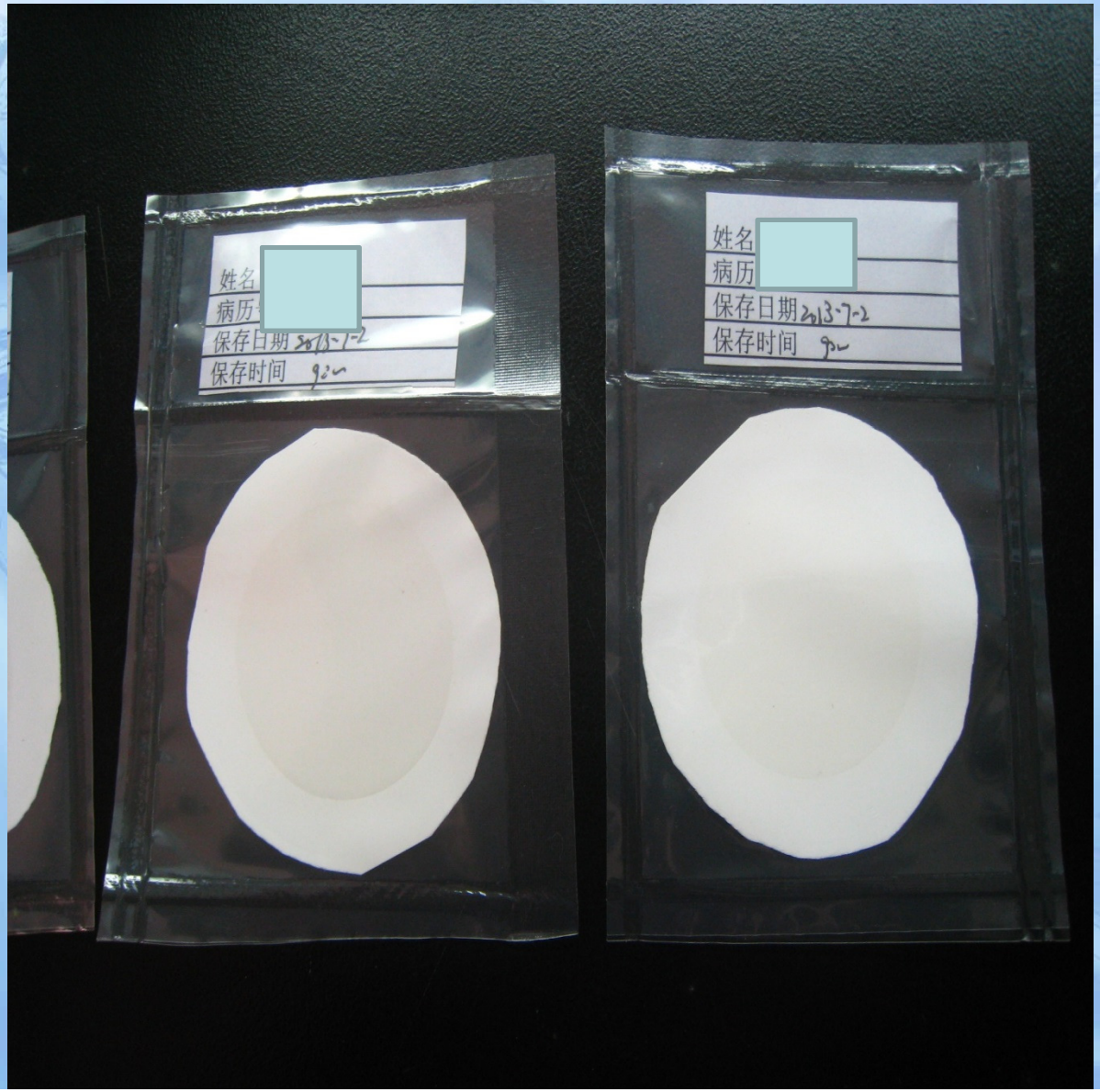

10/10/2012 23:43



Urimem

Urinary proteins dried on a filter and stored in vacuum

Urinary Proteins on Membrane



Why is that important?

Changed the face of medicine

- "Hard as it is to believe today, a single concept developed by Dr. Henry Plummer (1874 – 1936) at the beginning of the 20th century changed the face of medicine."

http://www.mayoclinic.org/tradition-heritage/medical-records.html

Changed the face of medicine

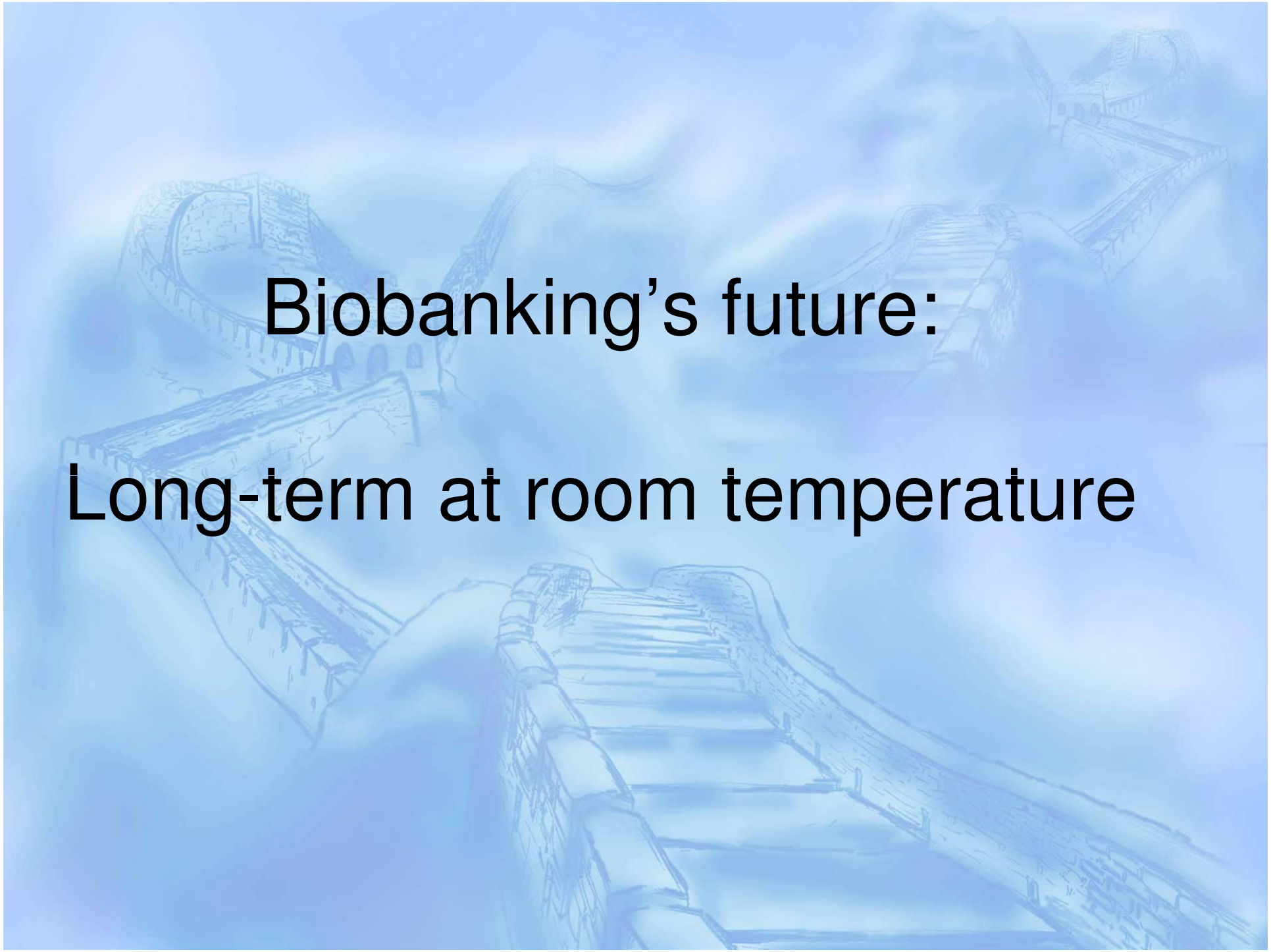
- The concept was a centralized medical record, stored in a single repository, and capable of traveling with the patient. (1907)
- Now
  - paperless
  - filmless
  - chartless

http://www.mayoclinic.org/tradition-heritage/medical-

Biobanking: foundation of personalized medicine

- Blood
- Urine
- Skin cells
- Organ
- Tissue
- other things taken from a body

Hewitt RE. Curr Opin Oncol. 2011 23(1):112-9


Biobanking's future:
Long-term at room temperature

Can we decode urine proteome?

- Not yet, especially in population
- But having large number of samples will help
- Need more researchers

We need control

- What is the normal variation of healthy human urine proteome?

Risk You Don’t Want to Take

You

- Discovery and validation in Blood
- Hard and expensive
- Patent

Others

- Take your clue, validate in urine
- Easy and Cheap
- New patent

Urine smells good!


It tastes even better!

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