生物信息中的生物学

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内容

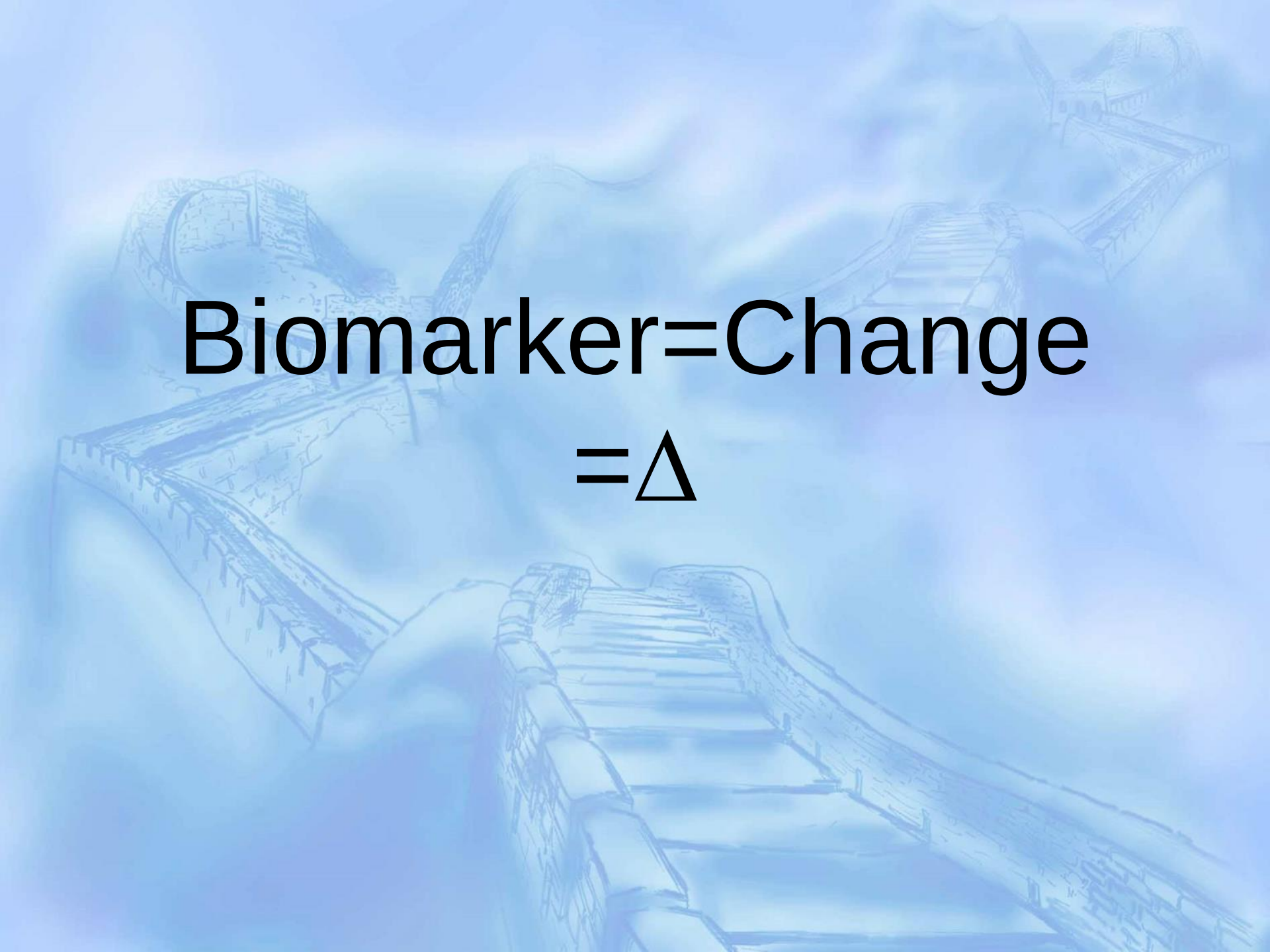
- 生物学中物质和信息的流动
  - –生物标志物
- 生物学中流动信息的使用
  - –经验保留时间
- 生物学中变化信息的利用
  - –蛋白质相互作用4Facts

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
Sci China Life Sci, 2013, 56: 1145–1146


Biomarker=Change
=Δ

In Blood

Homeostasis mechanisms

≈Constant

=minimal changes

=less biomarkers

In Urine

Accumulate all the changes

$=\Delta+\Delta+\Delta+\Delta+\Delta\ldots\ldots$

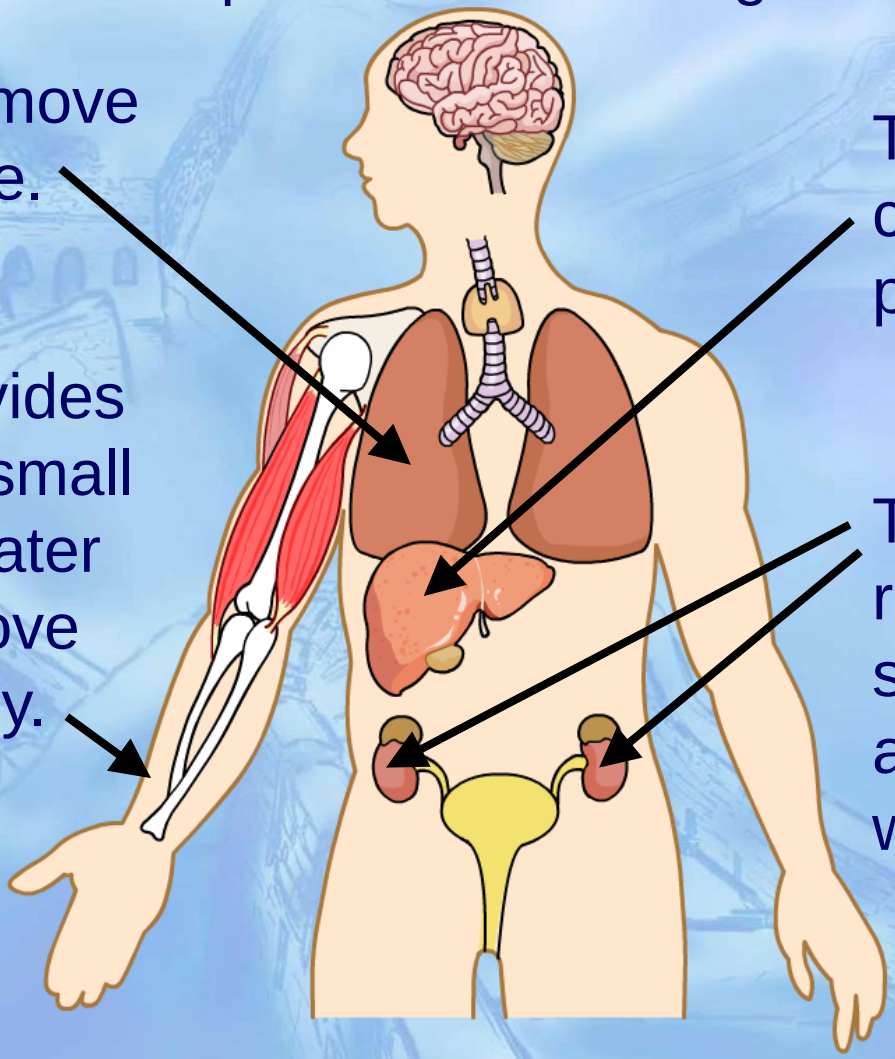
= Lots of biomarkers

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.

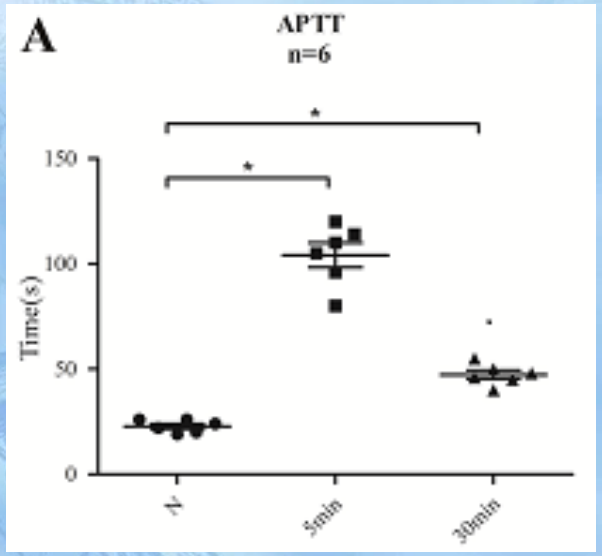


The **liver** converts excess protein into **urea**.

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

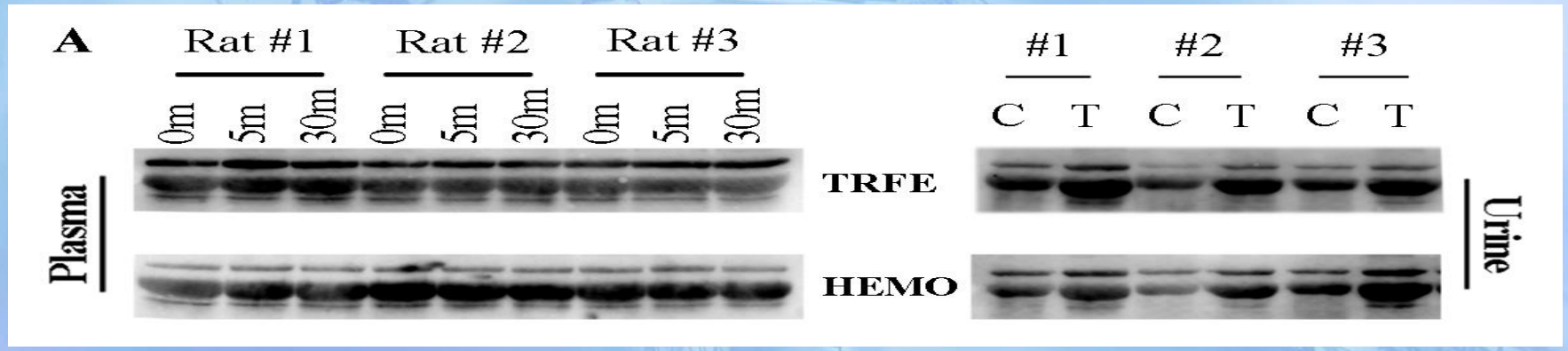


Clotting times increased

Changes

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

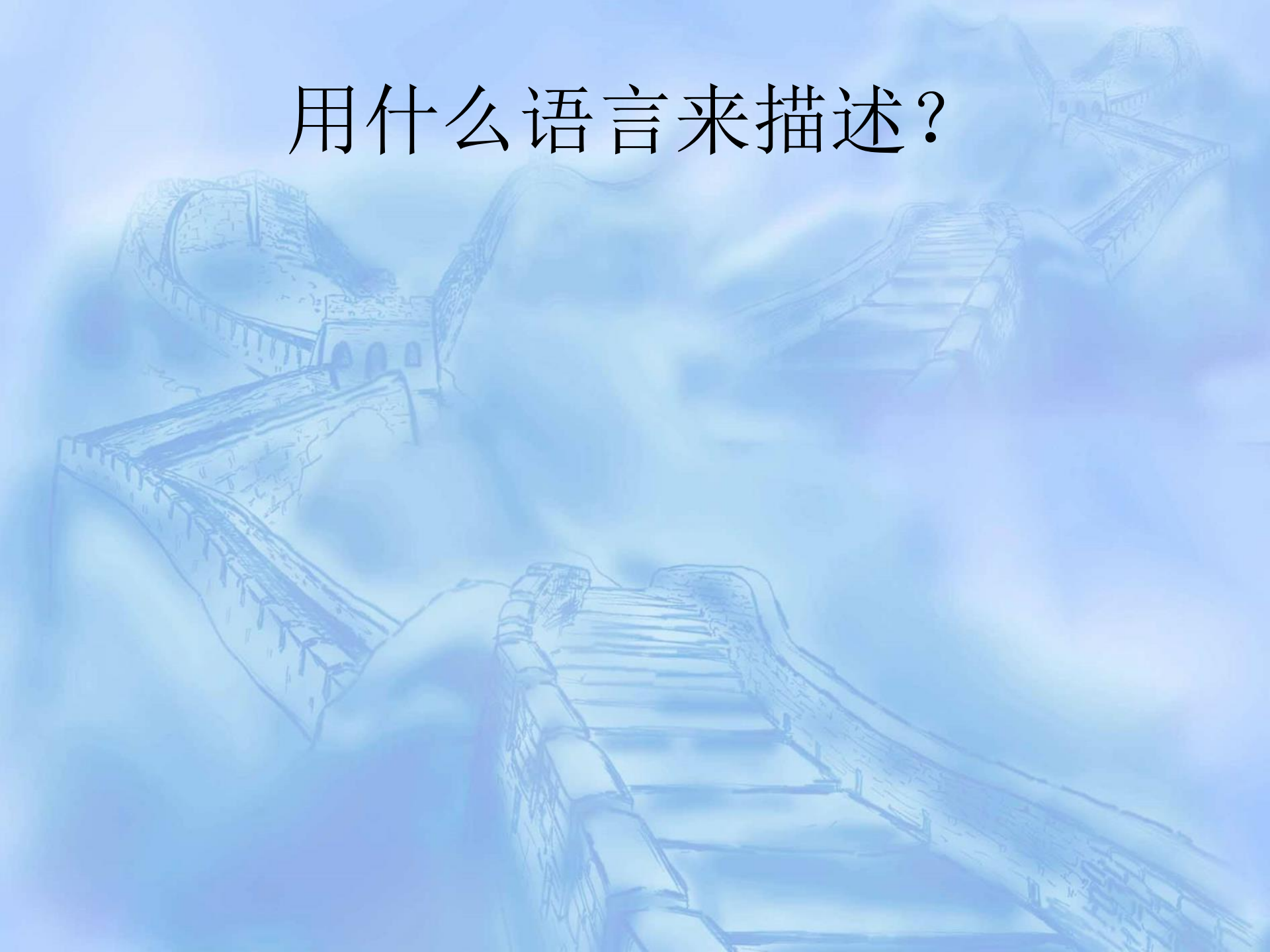
- Argatrabon
- 61 proteins in urine
- 1 proteins in plasma



Validation of changes in protein levels

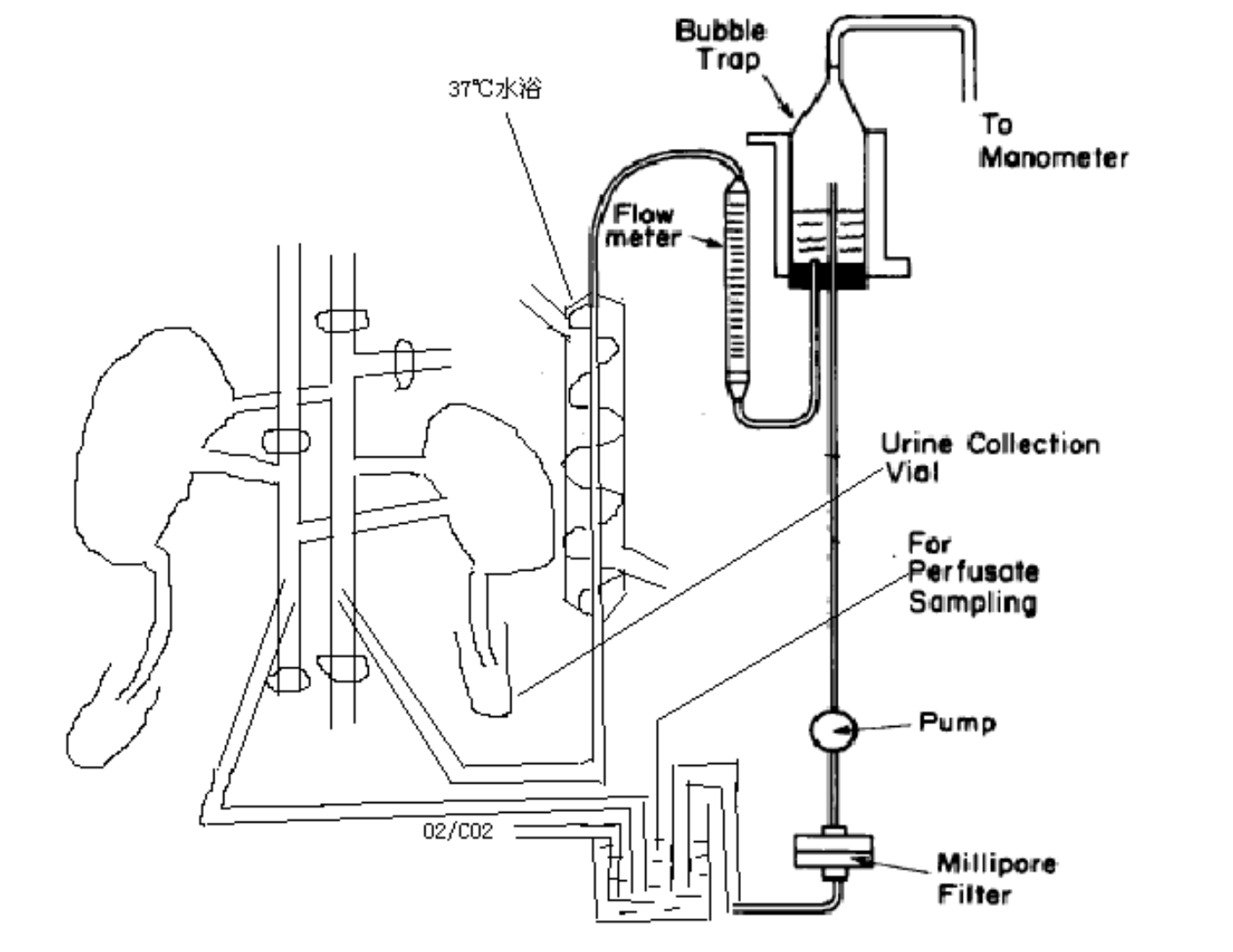
黑箱的方法研究肾脏功能

用什么语言来描述？

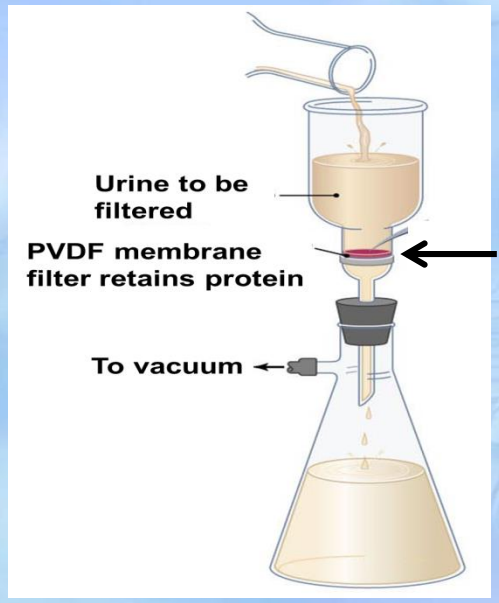


信息的分离-肾脏灌流

离体大鼠肾脏灌流示意图



尿蛋白信息的保存



Urimem

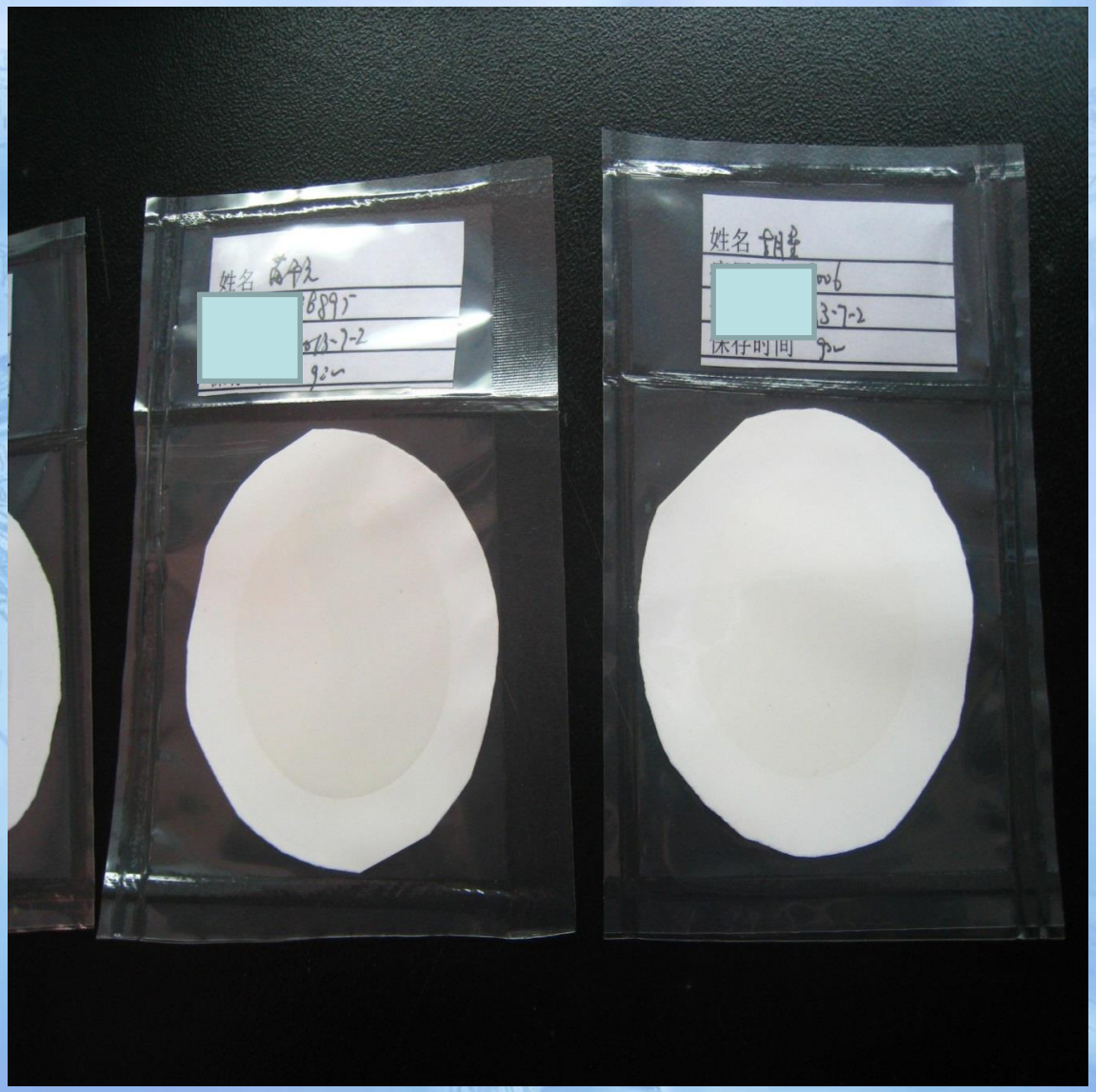
Sci China Life Sci, 2014 ,57(3): 336–339

Urimem

Urinary proteins dried on a filter and stored in vacuum

Sci China Life Sci, 2014 ,57(3): 336–339

Urinary Proteins on Membrane



Sci China Life Sci, 2014 ,57(3): 336–339

Roadmap

- Minimizing confounding factors
- Using animal models (of disease) to study the effects in urine
- Validate in human samples

直接相关性

- 临床样品如何区分疾病和药物的作用
- 动物模型可能是唯一的办法

Affected by Diuretics

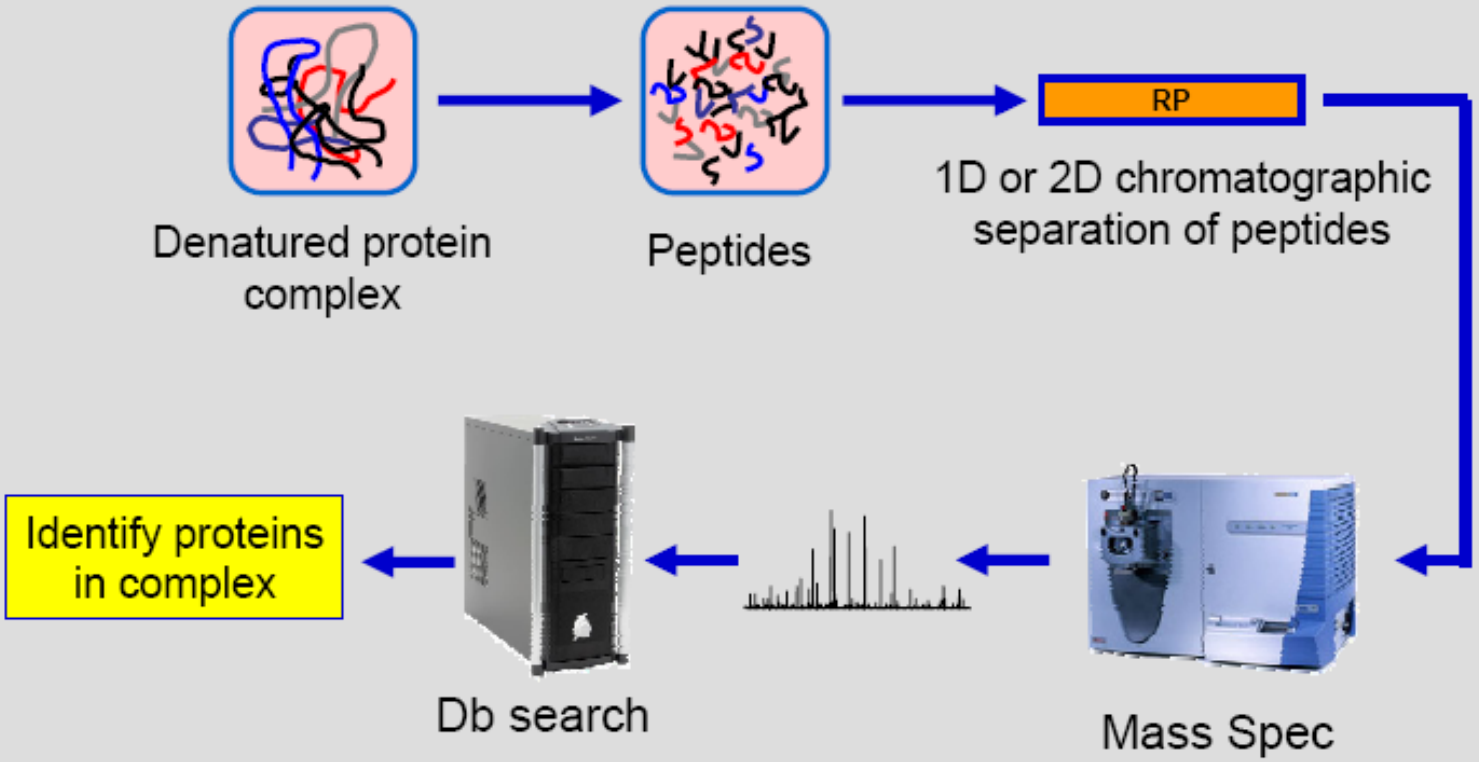
- 331, 302, 325 proteins with at least two peptides identified in furosemide, spirolactone and hydrochlorothiazide group
- 7, 5 and 2 proteins significantly changed
- 10 of the 14 proteins have been reported as disease biomarkers
- The effects of diuretics should be given more attention in future urinary protein biomarkers studies.

Proteome. Genomics Proteomics Bioinformatics. 2014 Jun;12(3):120-6

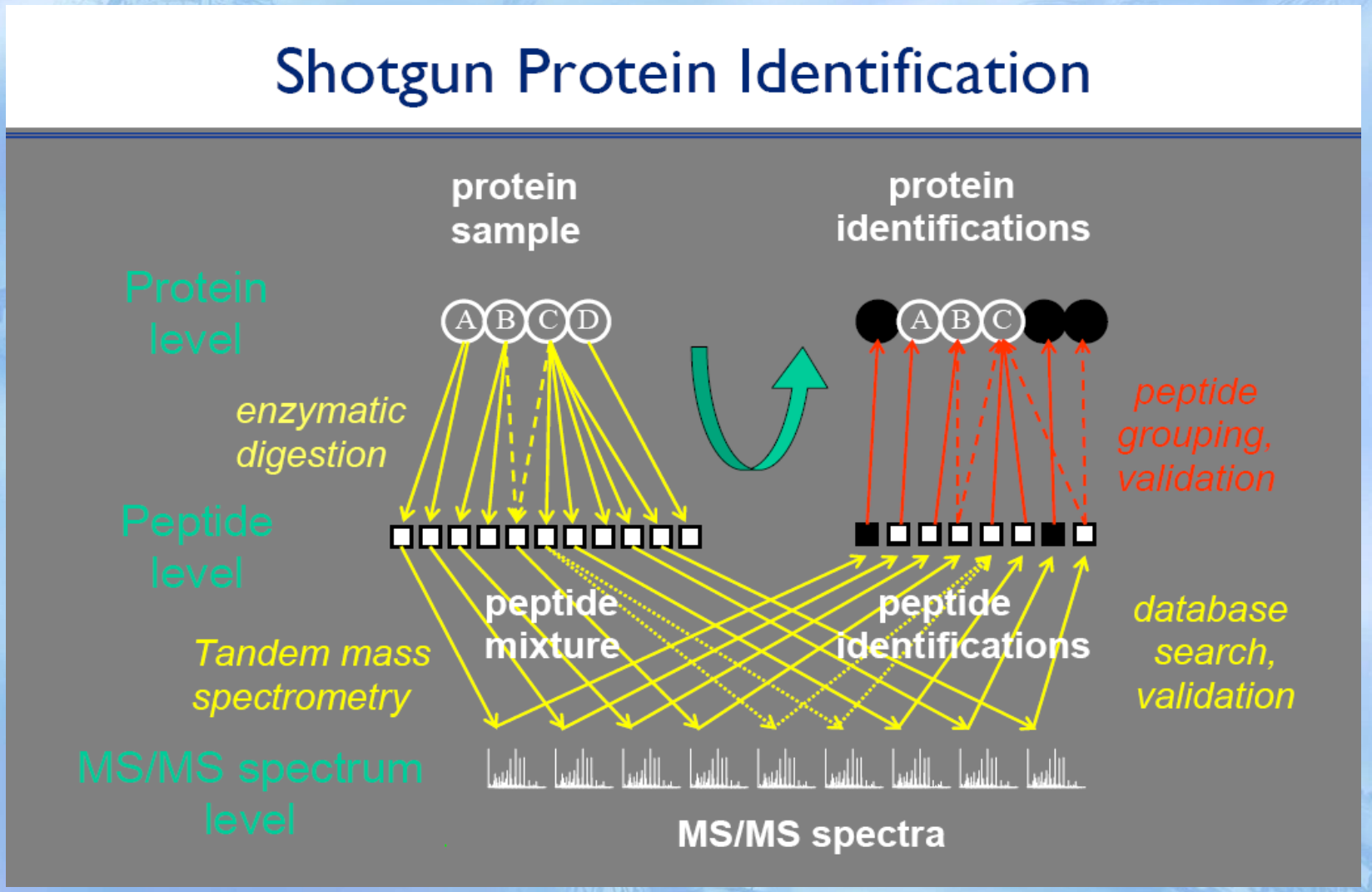
信息的利用

- 多肽保留时间的利用
- 样品在多肽水平的比较
- 蛋白质分子量信息的利用

多肽保留时间的利用


Denatured protein complex
Peptides
RP
1D or 2D chromatographic separation of peptides
Mass Spec
Db search
Identify proteins in complex

样品在多肽水平的比较


Shotgun Protein Identification
protein sample
protein identifications
Protein level
A B C D
A B C
enzymatic digestion
peptide grouping, validation
Peptide level
peptide mixture
peptide identifications
Tandem mass spectrometry
database search, validation
MS/MS spectrum level
MS/MS spectra

蛋白质分子量信息的利用

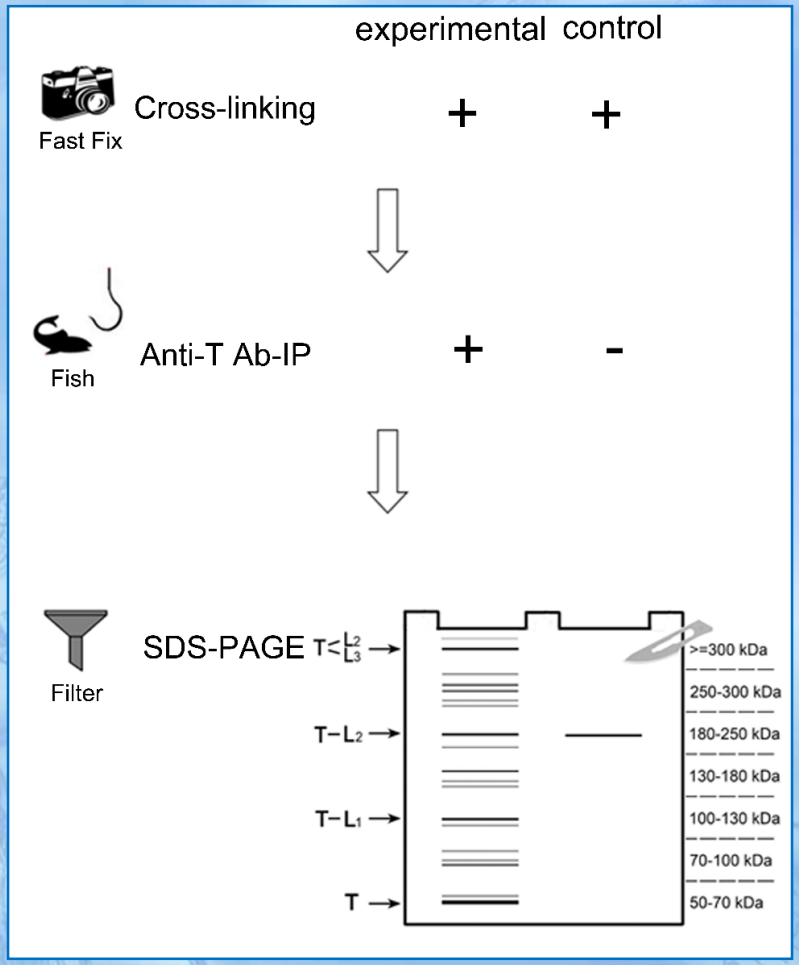
快速交联

对照去除
交联复合物与抗体
非特异结合

SDS下共价复合物

分子量筛选

全面切胶，灵敏



Thanks!

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