

北京蛋白质组研究中心贺福初团队  
北京生命科学研究所董梦秋陈涉团队  
华大基因研究院刘斯奇团队  
上海生物信息中心李亦学团队  
协和医科大学高友鹤团队  
中科院大化所邹汉法团队  
暨南大学何庆瑜团队  
复旦大学杨芃原团队  
上海生科院曾嵘团队  
清华大学张学工团队

系统生物学的高通量分析

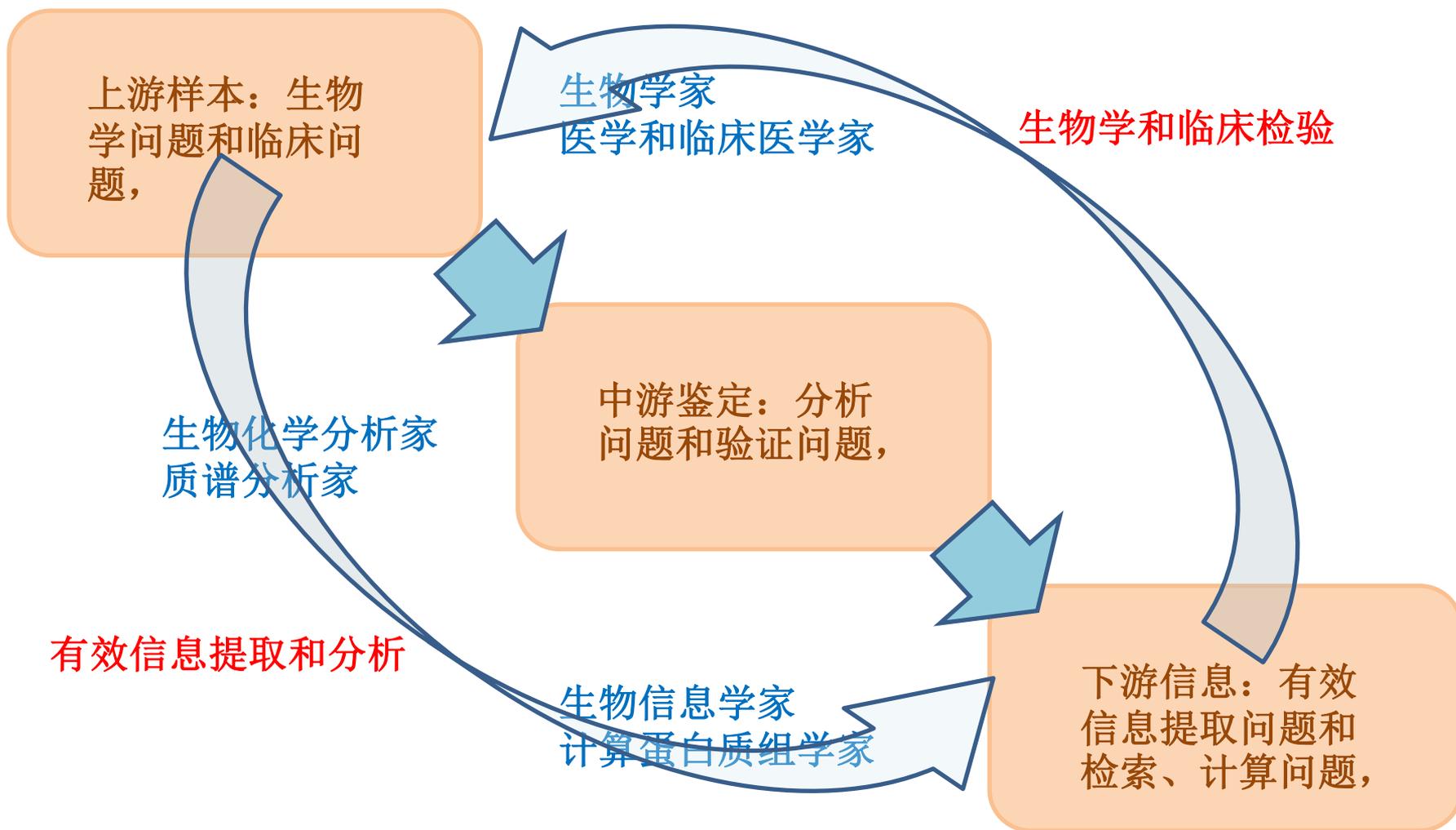
蛋白质表达-结构-功能的高通量分析

基于质谱技术的规模化蛋白质表达  
分析



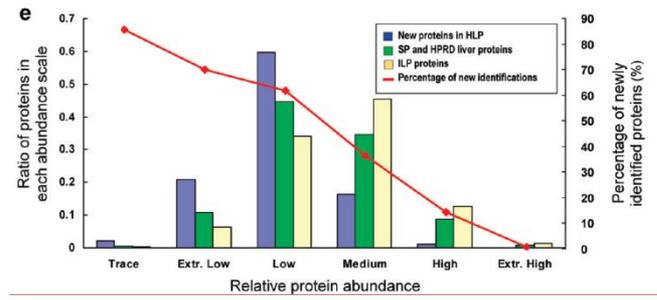
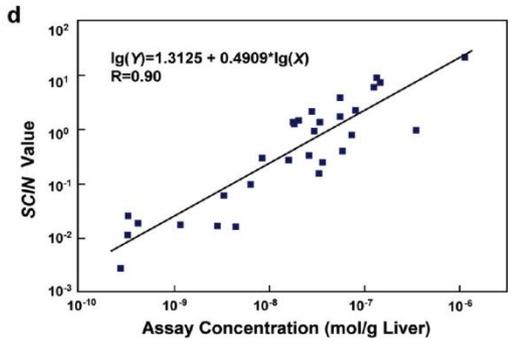
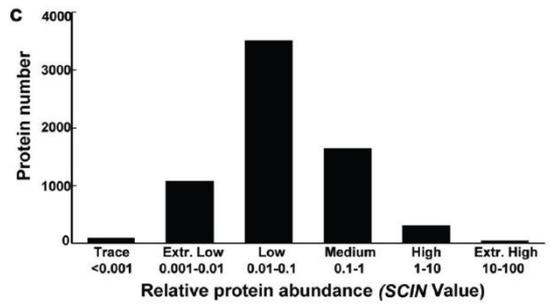
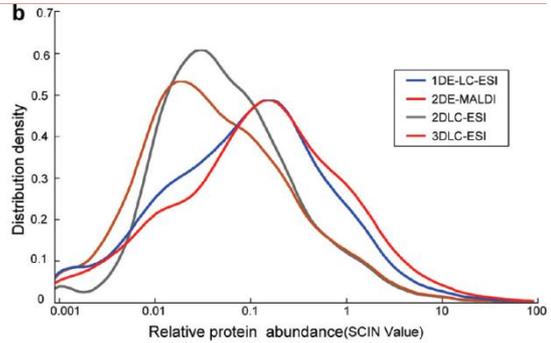
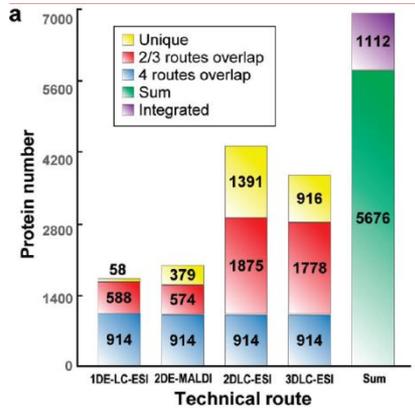
首届中国计算蛋白质组学研讨会

# “首届中国计算蛋白质组学研讨会”是中国蛋白质组学领域发展的里程碑



# J Proteome Res, 2009

## First Insight into the Human Liver Proteome from PROTEOMESKY-LIVERHu 1.0, a Publicly Available Database Chinese Human Liver Proteome Profiling Consortium



**12000 unique proteins so far**

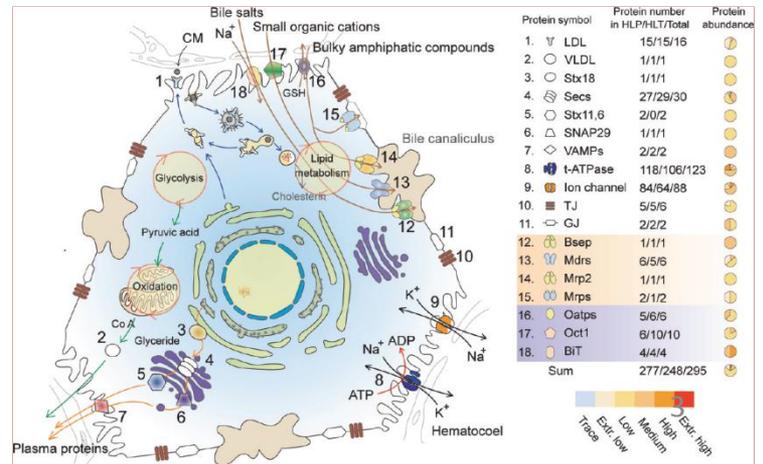
贺福初院士领衔

6788 unique proteins

军事医学科学院

复旦大学

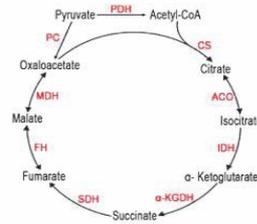
中科院上海生命科学院



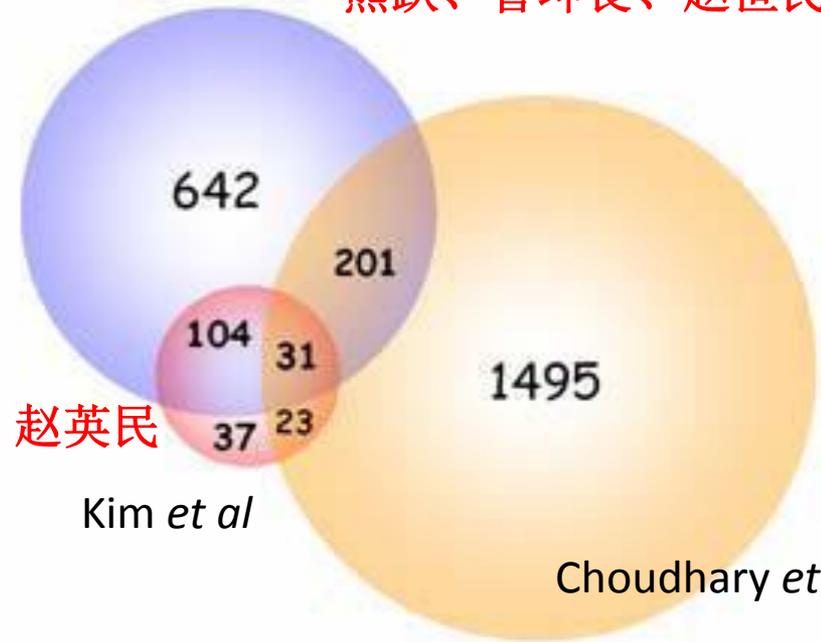
Regulation of Cellular Metabolism by Protein Lysine Acetylation

Shimin Zhao,1,2 Wei Xu,1,2\* Wenqing Jiang,1,2\* Wei Yu,1,2 Yan Lin,2 Tengfei Zhang,1,2 Jun Yao,3 Li Zhou,4 Yaxue Zeng,4 Hong Li,5 Yixue Li,6 Jiong Shi,6 Wenlin An,7 Susan M. Hancock,7 Fuchu He,3 Lunxiu Qin,5 Jason Chin,7 Pengyuan Yang,3 Xian Chen,3,4 Qunying Lei,1,2,8 Yue Xiong,1,2,4† Kun-Liang Guan1,2,8,9†

乙酰化保守, 广泛, 代谢特异



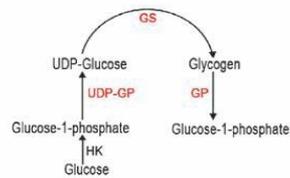
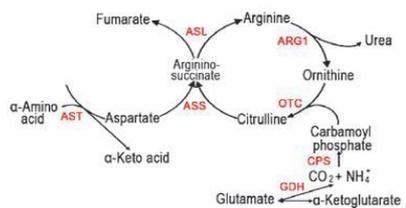
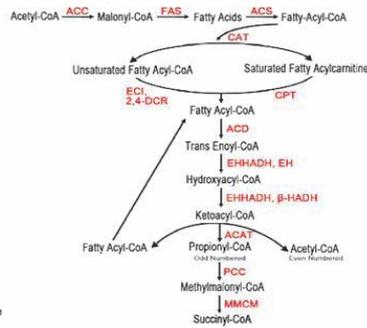
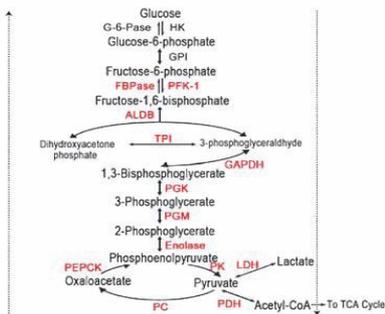
熊跃、管坤良、赵世民



赵英民

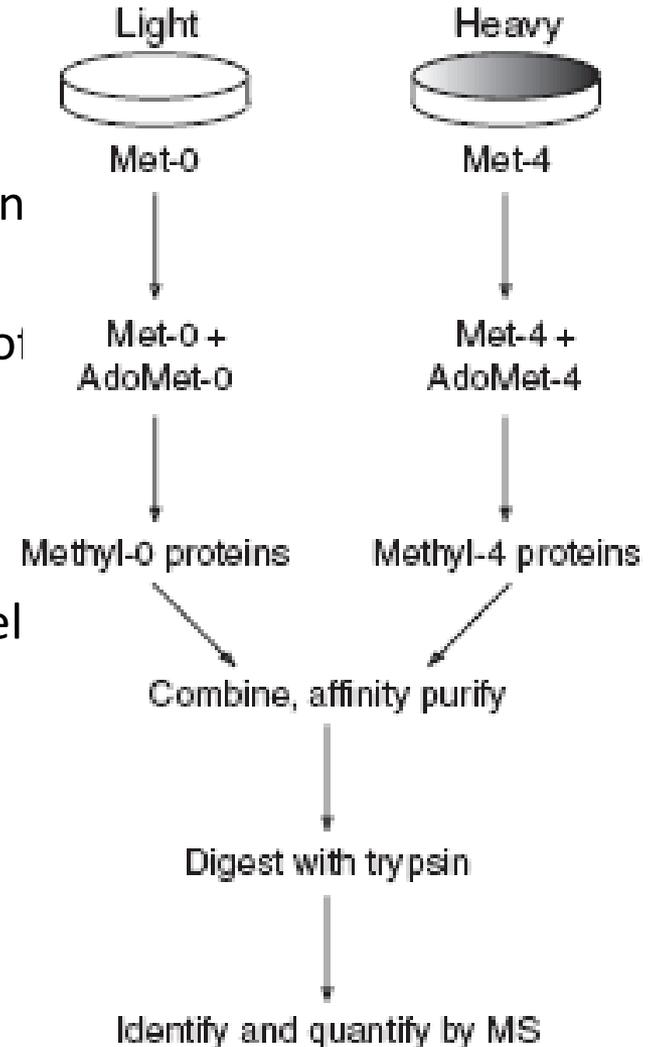
Kim et al

Choudhary et al.



# AACT/SILAC for Modification Quantitation

- Also possible to label modifications through addition of a labeled version of the donor.
- S-adenosyl methionine (AdoMet) is the sole donor of methyl groups for protein (and DNA, RNA) methylation.
- It is synthesized from methionine
- By adding  $^{13}\text{C}^2\text{H}_3$  methionine in culture one can label lysine and arginine methylations e.g. in histones.



发明人：陈先教授

**Chen X, Smith LM, Bradbury EM. Site-specific mass tagging with stable isotopes in proteins for accurate and efficient protein identification.**

***Anal Chem*, 2000, 72: 1134–1143**

# pFIND, 第一个具有中国知识产权的大型蛋白质组搜索软件

BIOINFORMATICS

Vol. 20 no. 12 2004, pages 1948–1954  
doi:10.1093/bioinformatics/bth186



## ***Exploiting the kernel trick to correlate fragment ions for peptide identification via tandem mass spectrometry***

Yan Fu<sup>1,2,\*</sup>, Qiang Yang<sup>3</sup>, Ruixiang Sun<sup>2</sup>, Dequan Li<sup>1</sup>, Rong Zeng<sup>4</sup>, Charles X. Ling<sup>5</sup> and Wen Gao<sup>1,2</sup>

<sup>1</sup>Institute of Computing Technology, Chinese Academy of Sciences, Beijing 100080, China, <sup>2</sup>Graduate School of Chinese Academy of Sciences, Beijing 100039, China, <sup>3</sup>Department of Computer Science, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, <sup>4</sup>Research Center for Proteome Analysis, Key Lab of Proteomics, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China and <sup>5</sup>Department of Computer Science, The University of Western Ontario, London, Ontario, Canada N6A 5B7

Received on September 4, 2003; revised on January 6, 2004; accepted on February 10, 2004  
Advance Access publication March 25 2004

## 近20年的质谱仪器研究历史

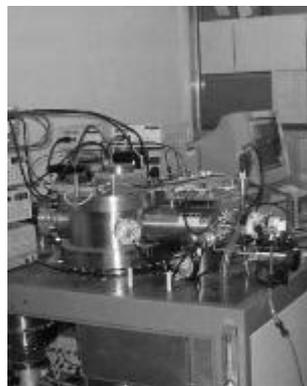
[biomass.fudan.edu.cn](http://biomass.fudan.edu.cn) 复旦大学化学系, IBS

主要技术人员——杨芾原、杭伟、周振、何坚、徐国宾

技术引进——A.F. Dodonov

厦门大学、复旦大学、上海大学、广州地化所

自主知识产权的仪器和软件?



## 其他有影响力的研究工作（MCP, JPR, Proteomics, Anal Chem, Angew Chem, Bioinform, 其他专业刊物）

分离富集：张玉奎，张丽华，张祥民，陆豪杰，邓春辉，邹汉发，叶明亮，曾嵘

糖修饰：钱小红，应万涛，杨芃原，陆豪杰

其他修饰：徐平，陈正军，

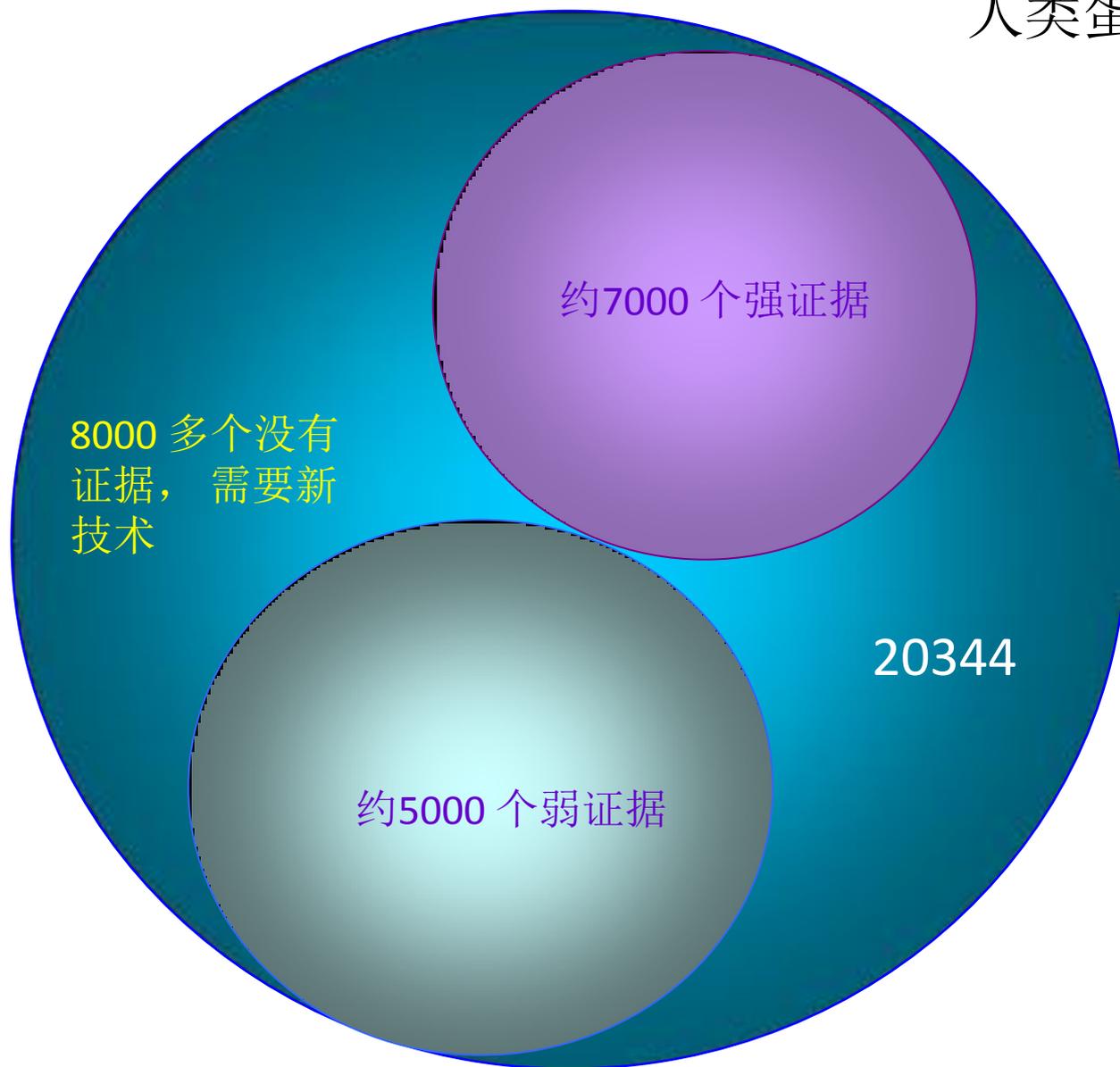
PPI：杨晓明，王建，陈先，

疾病蛋白质组：刘银坤，杨芃原，高友鹤，纪建国，钱小红，姜颖，刘思奇，施前，何庆瑜，徐宁志，

生理蛋白质组：姜颖，刘思奇，钱小红

蛋白质组生物信息学：李亦学，谢鹭，曹志伟，朱云平，贺思敏，孙瑞祥，张勇，盛泉虎，

# 人类蛋白质库的现状

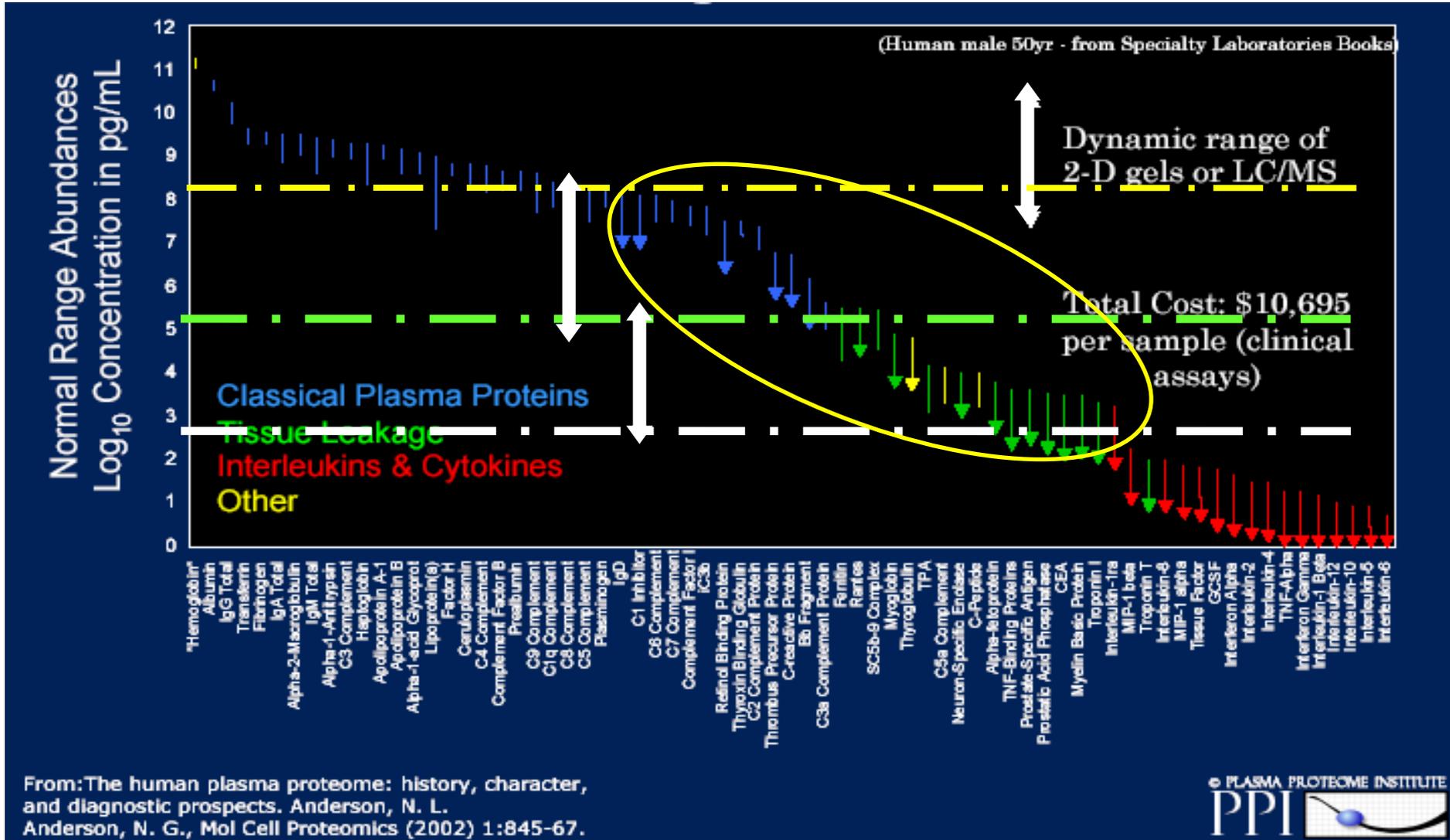


1. 没有证据和弱证据的蛋白在那些细胞通路中？有什么功能？

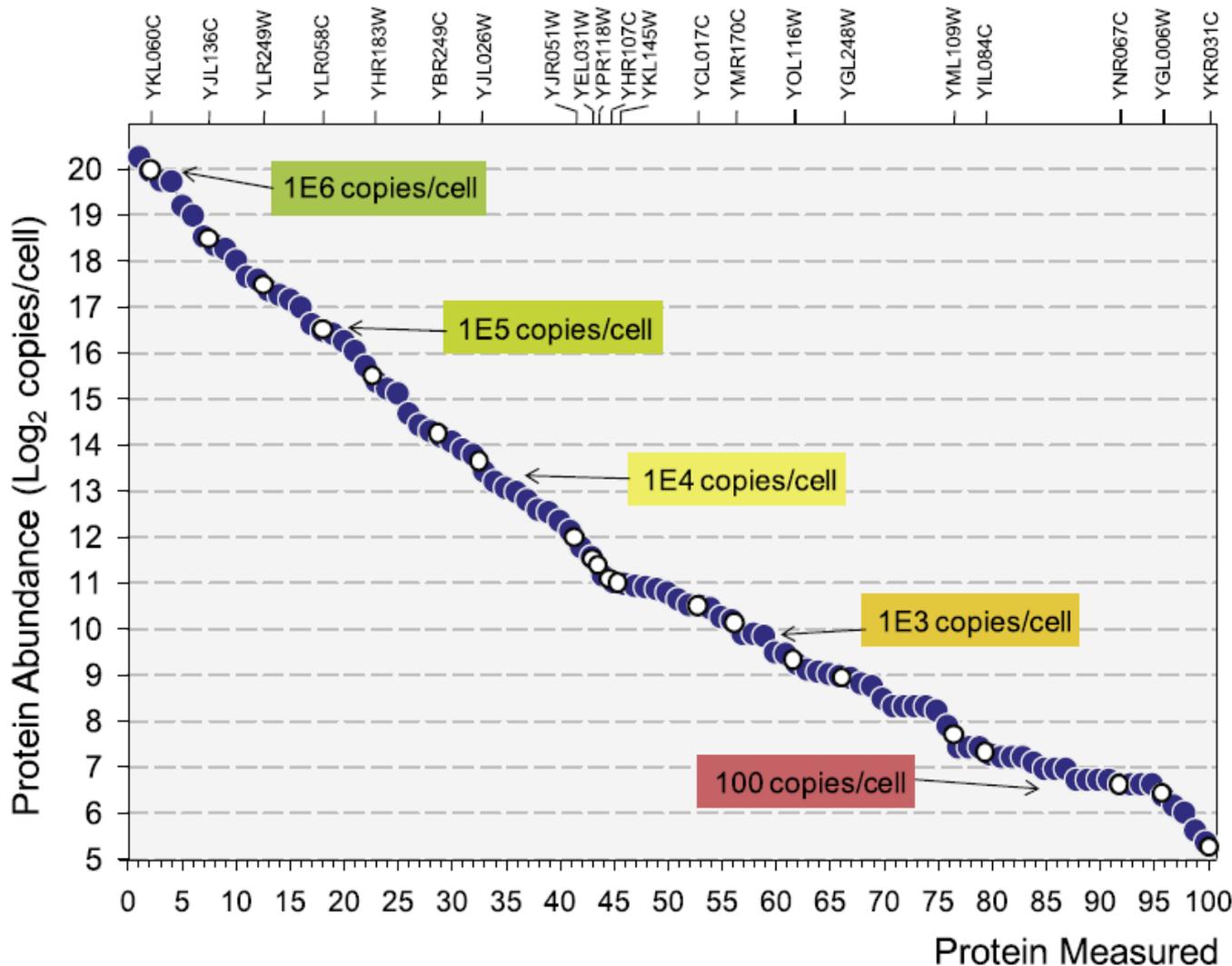
2. 疾病分子标志物和药靶很可能在8000个没有被发现的蛋白中？

3. 是不是有的蛋白从来不要也不会被人类基因表达？

# 蛋白质组分析技术的发展



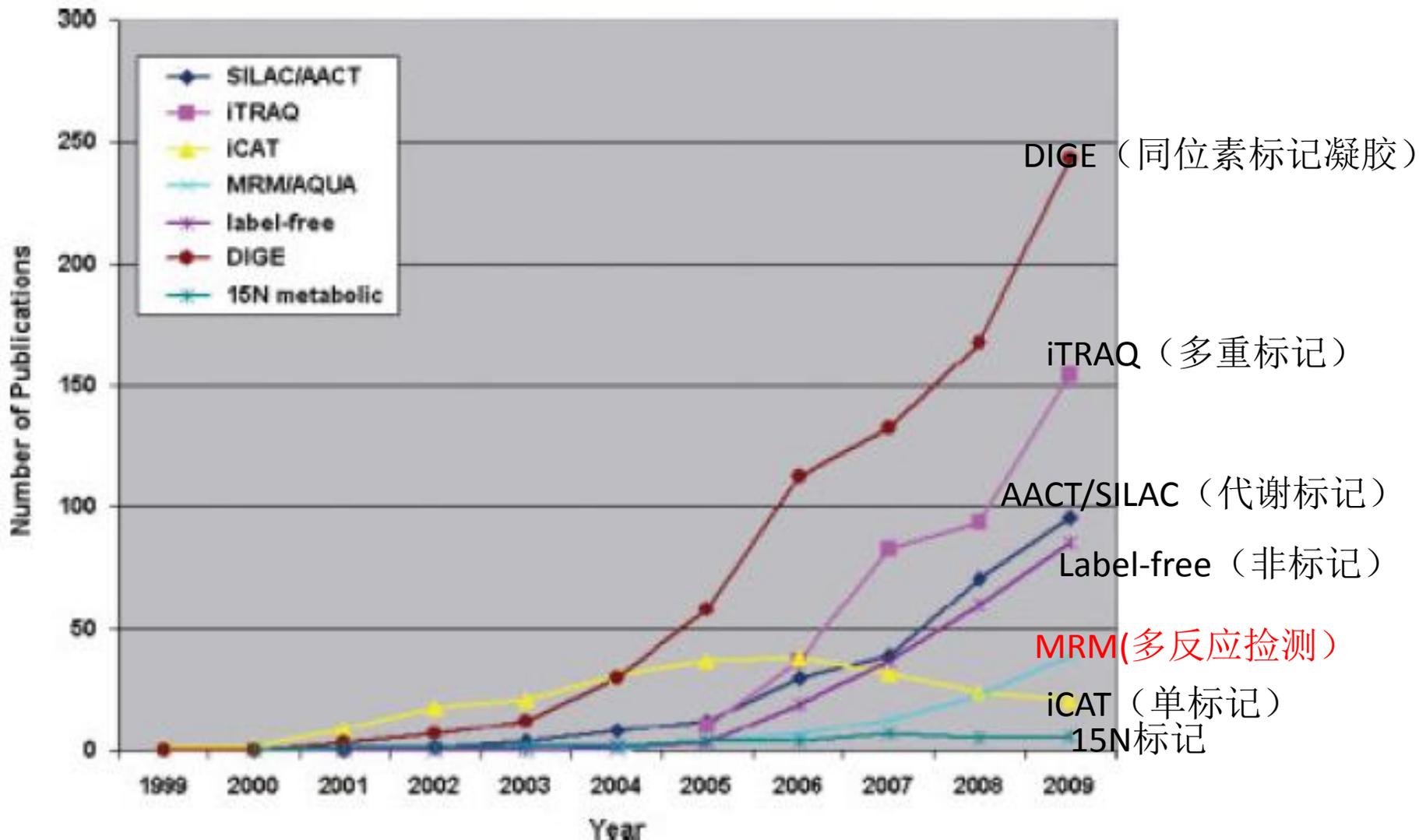
蛋白质的丰度



- |              |               |
|--------------|---------------|
| 1, YGL008C;  | 2, YKL060C;   |
| 3, YLR355C;  | 4, YLR249W;   |
| 5, YDR382W;  | 6, YJR104C;   |
| 7, YML028W;  | 8, YMR116C;   |
| 9, YCR012W;  | 10, YER091C;  |
| 11, YDR050C; | 12, YER165W;  |
| 13, YGR192C; | 14, YER177W;  |
| 15, YNL178W; | 16, YBR127C;  |
| 17, YHR183W; | 18, YKL182W;  |
| 19, YHR208W; | 20, YDL126C;  |
| 21, YLR058C; | 22, YML008C;  |
| 23, YIL078W; | 24, YAL012W;  |
| 25, YGR204W; | 26, YBR249C;  |
| 27, YJR105W; | 28, YNR016C;  |
| 29, YLR216C; | 30, YGR209C;  |
| 31, YJL136C; | 32, YDR368W;  |
| 33, YJL130C; | 34, YOR007C;  |
| 35, YMR099C; | 36, YKR048C;  |
| 37, YER006W; | 38, YML086C;  |
| 39, YKR001C; | 40, YER003C;  |
| 41, YFL014W; | 42, YDR129C;  |
| 43, YPL235W; | 44, YOL140W;  |
| 45, YMR170C; | 46, YDL021W;  |
| 47, YML100W; | 48, YKL150W;  |
| 49, YEL031W; | 50, YGL202W;  |
| 51, YDL017W; | 52, YGR080W;  |
| 53, YPL049C; | 54, YGL248W;  |
| 55, YEL011W; | 56, YHR107C;  |
| 57, YGL100W; | 58, YBR208C;  |
| 59, YPR118W; | 60, YJL172W;  |
| 61, YBR283C; | 62, YCR088W;  |
| 63, YGR256W; | 64, YJL026W;  |
| 65, YCL030C; | 66, YCL017C;  |
| 67, YOL116W; | 68, YNL161W;  |
| 69, YJR051W; | 70, YKL068W;  |
| 71, YHR138C; | 72, YGR232W;  |
| 73, YMR199W; | 74, YOR267C;  |
| 75, YJR134C; | 76, YKL141W;  |
| 77, YHR074W; | 78, YLR330W;  |
| 79, YDR436W; | 80, YKL129C;  |
| 81, YOR020C; | 82, YBR117C;  |
| 83, YBR125C; | 84, YKL073W;  |
| 85, YOL022C; | 86, YLL040C;  |
| 87, YNL014W; | 88, YML109W;  |
| 89, YIL092W; | 90, YIL084C;  |
| 91, YKL145W; | 92, YKL075C;  |
| 93, YIL002C; | 94, YHR015W;  |
| 95, YPL008W; | 96, YGL006W;  |
| 97, YLR035C; | 98, YNR067C;  |
| 99, YKR031C; | 100, YOR093C; |

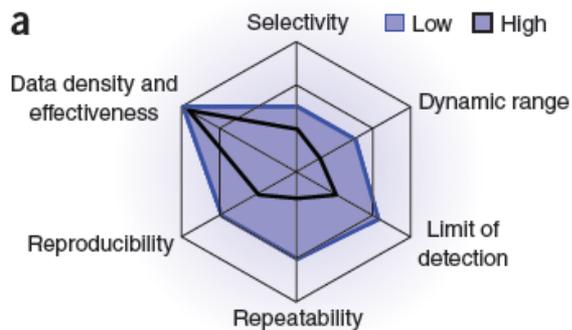
测得的该丰度下蛋白质的种类数

# 近10年不同定量方法每年发表的文章统计

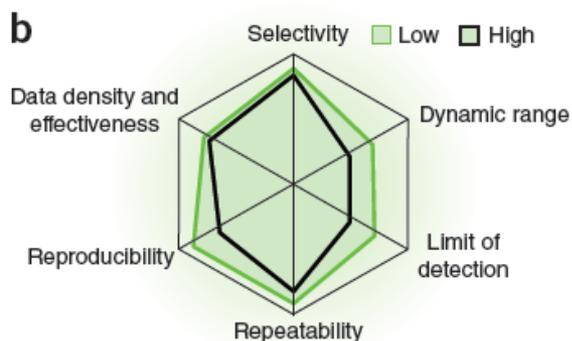


Trends in mass-spectrometry-based quantitation. Publications per year, based on a keyword search in SciFinder Scholar.

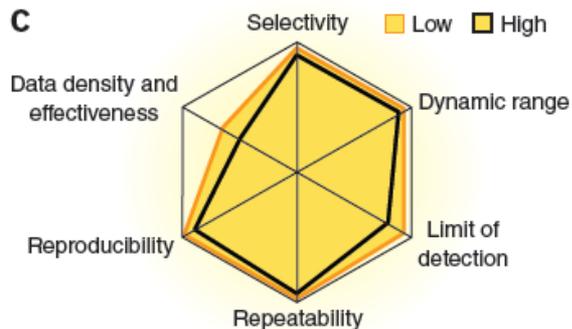
# 基于质谱的蛋白质定性定量策略



基于Shotgun酶解肽的分析策略：  
具有强的数据产出能力，重现性、动态检测范围、检测限不高

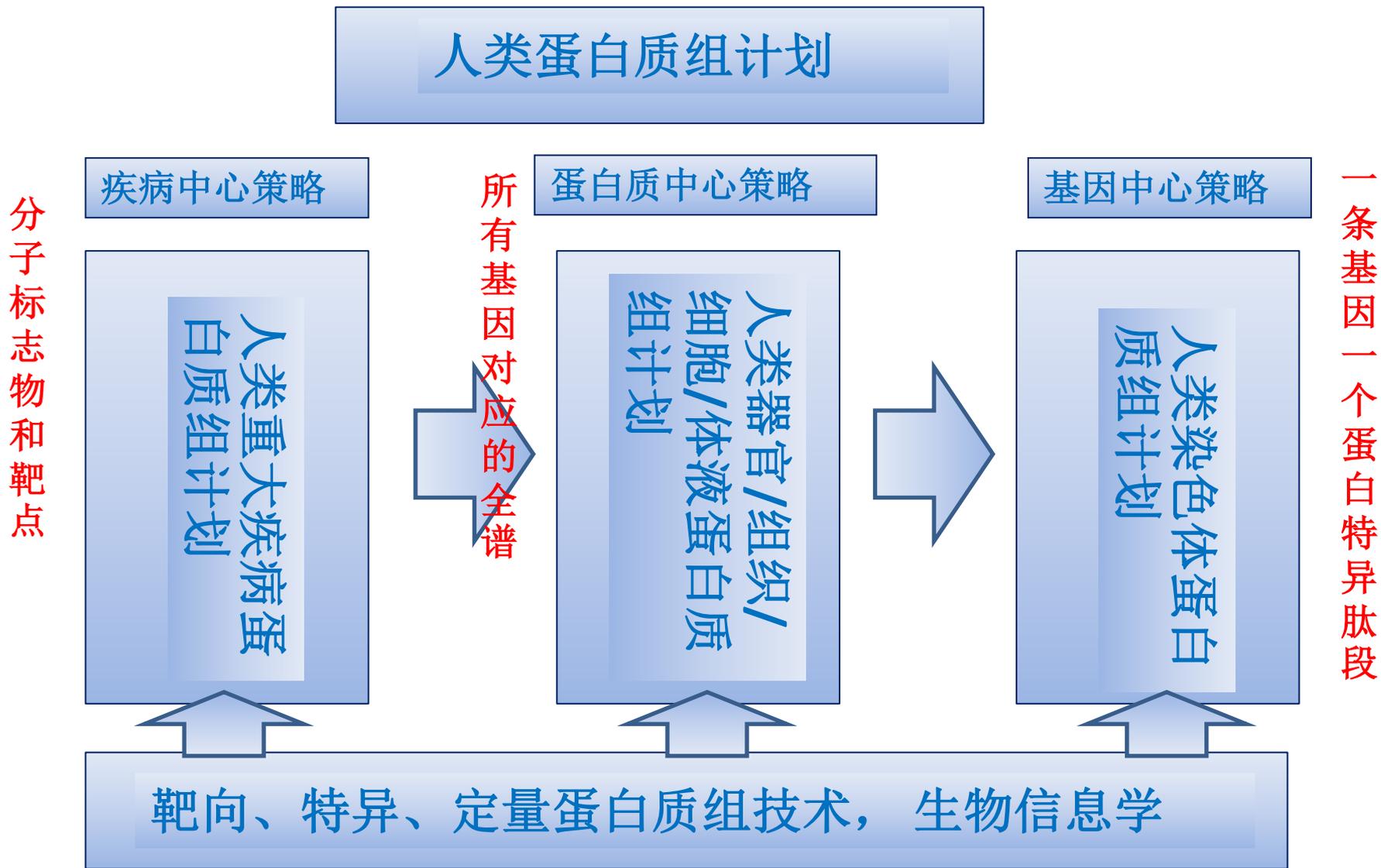


LC-MS/MS直接分析策略：  
各种优势不够突出



**LC-MS MRM**分析策略：  
选择性、动态范围、重复性好，定量具有明显优势！

2010年9月 在悉尼 正式 宣布启动人类蛋白质组计划， 定量技术是根基， 生物信息学面临挑战和机遇



# 中国计算蛋白质组学可以做的工作：

基因组、转录组、蛋白质组海量数据的整合、对接、解析和系统生物学分析？

我们到底能看到多少基因表达的蛋白？是否所有的编码蛋白的基因都会表达？如果不表达，什么原因？

所有表达蛋白的特异肽段是那些？质谱可见的特异肽段是那些？中国人疾病相关的蛋白的特异肽段是那些？

中国自主知识产权的程序和软件的开发和应用？中国蛋白质组研究基础设施中如何显示中国自主知识产权的仪器和软件（如pFIND）？

蛋白质后修饰研究和分析的软件，国际上才起步不久，中国人是否完全可以走在前沿？

生理和病理蛋白质组研究中明星分子和通路网络分析软件中（SAM, IPA, GSEA, Metacore)基本没有中国人发明的，如何改变这一局面？

最后我邀请大家一起，感谢贺思敏教授及其课题组成员的辛勤工作和努力，使本次会议获得了圆满成功