



博淼生物
BIOMIAO BIOLOGICAL
-SINCE2009-

Your own Laboratory
您的专属实验室

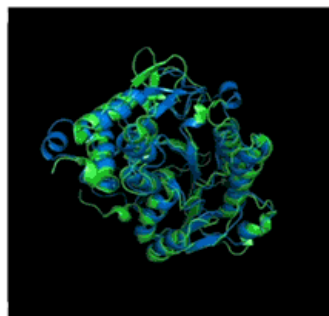
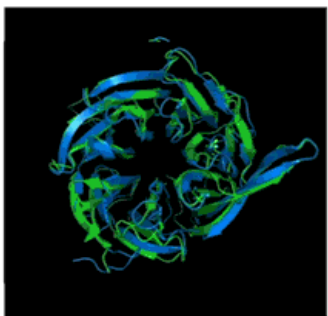
临床蛋白质组学与精准医疗整体解决方案

全国统一服务电话：400-6506-908

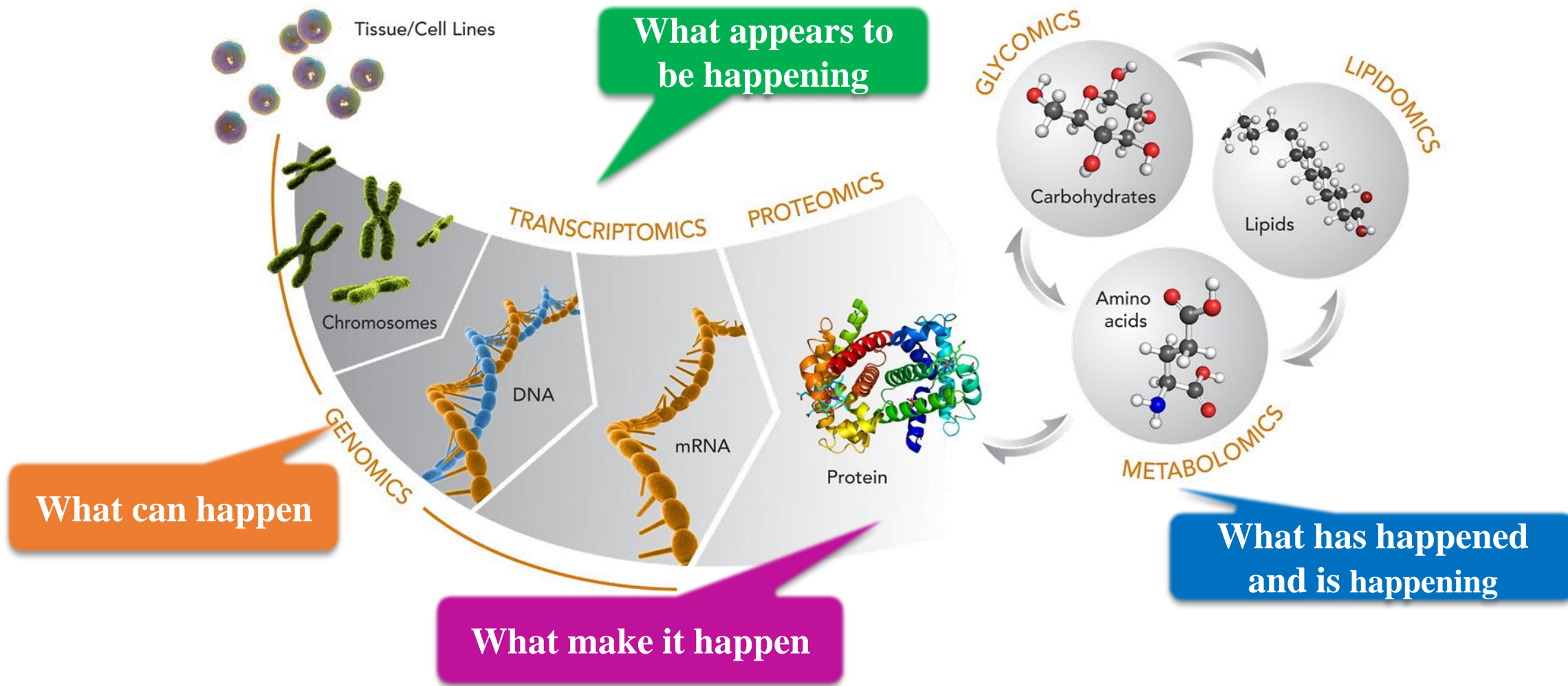
网址：www.biomiao.com

邮箱：marketing@biomiao.com

地址：北京市丰台区丰管路优橙创新中心



The central of molecular biology



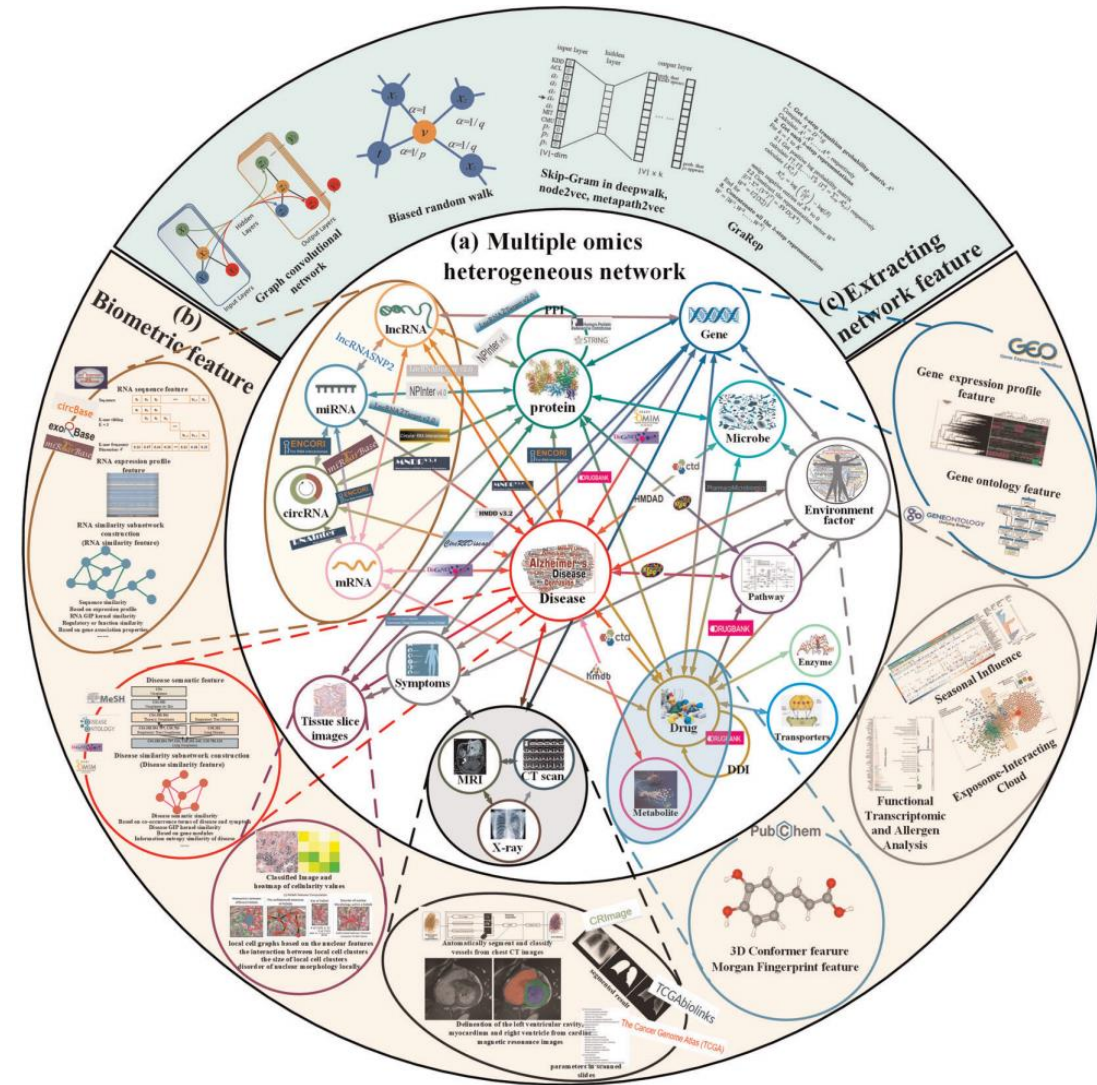
Future research direction: multi-omics combination

Fuse large-scale multi-omics data to comprehensively explore relationships between various biological entities.

Divided into three levels, the first is the collection and integration of multiple sets of data. By calculating the similarity between biological entities of the same type, sub-networks are constructed and associated with other sub-networks.

Then, according to the characteristics of the organism itself and the characteristics of the constructed network, the latent characteristics of biological entities are mined.

Finally, using these features, the relationship is predicted based on methods such as deep learning.

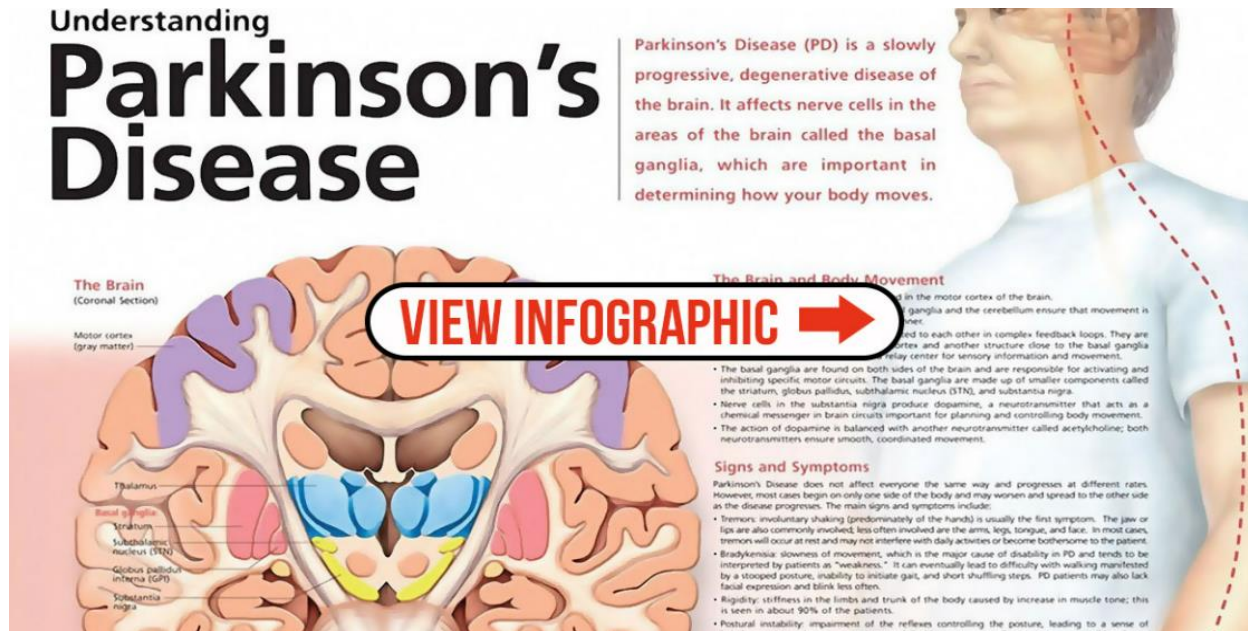


Proteomic and disease(neurodegenerative disease)

Protein is the executor of life functions, and almost no life activity can leave protein

Understanding Parkinson's Disease

Parkinson's Disease (PD) is a slowly progressive, degenerative disease of the brain. It affects nerve cells in the areas of the brain called the basal ganglia, which are important in determining how your body moves.



The Brain (Coronal Section)

Motor cortex (gray matter)

Thalamus

Basal ganglia

Striatum

Subthalamic nucleus (STN)

Globus pallidus interna (GPI)

Substantia nigra

The Brain and Body Movement

The basal ganglia are found on both sides of the brain and are responsible for activating and inhibiting specific motor circuits. The basal ganglia are made up of smaller components called the striatum, globus pallidus, subthalamic nucleus (STN), and substantia nigra.

Nerve cells in the substantia nigra produce dopamine, a neurotransmitter that acts as a chemical messenger in brain circuits important for planning and controlling body movements.

The action of dopamine is balanced with another neurotransmitter called acetylcholine; both neurotransmitters ensure smooth, coordinated movement.

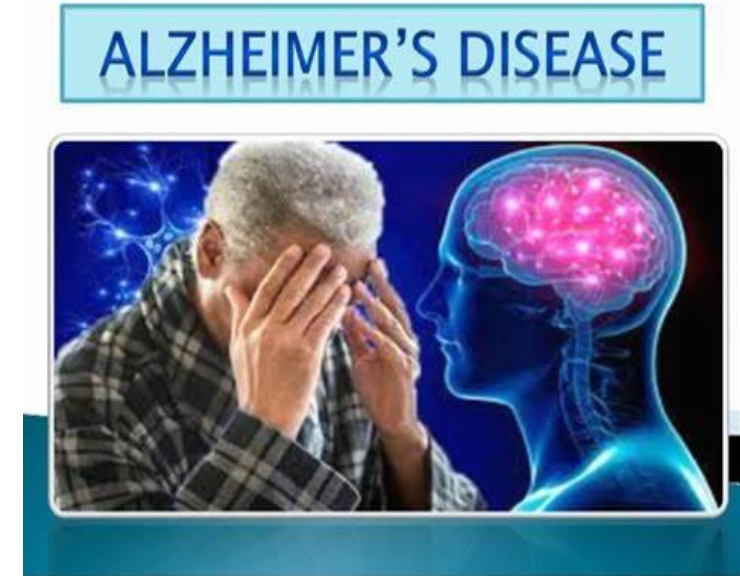
Signs and Symptoms

Parkinson's Disease does not affect everyone the same way and progresses at different rates. However, most cases begin on only one side of the body and may worsen and spread to the other side as the disease progresses. The main signs and symptoms include:

- Tremors: involuntary shaking (predominately of the hands) is usually the first symptom. The jaw or lips are also commonly involved; less often involved are the arms, legs, tongue, and face. In most cases, tremor will occur at rest and may not interfere with daily activities or become bothersome to the patient.
- Bradykinesia: slowness of movement, which is the major cause of disability in PD and tends to be interpreted by patients as "weakness." It can eventually lead to difficulty with walking manifested by a stooped posture, inability to initiate gait, and short shuffling steps. PD patients may also lack facial expression and blink less often.
- Rigidity: stiffness in the limbs and trunk of the body caused by increase in muscle tone; this is seen in about 90% of the patients.
- Postural instability: impairment of the reflexes controlling the posture, leading to a sense of

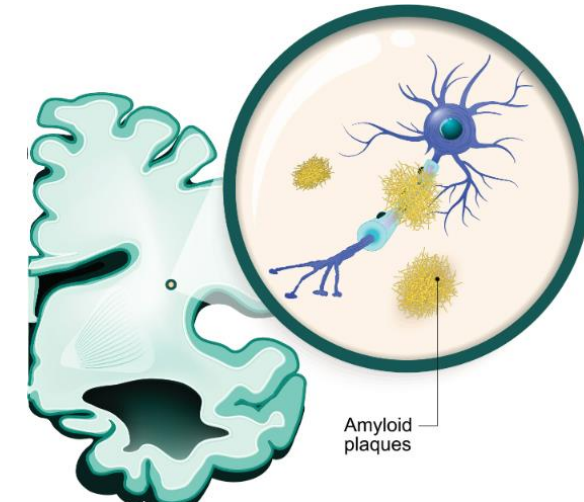
VIEW INFOGRAPHIC →

ALZHEIMER'S DISEASE



Alpha-synuclein (alpha-synuclein) is a soluble protein expressed presynaptic and perinuclear in the central nervous system, which is closely related to the pathogenesis and related dysfunction of Parkinson's disease.

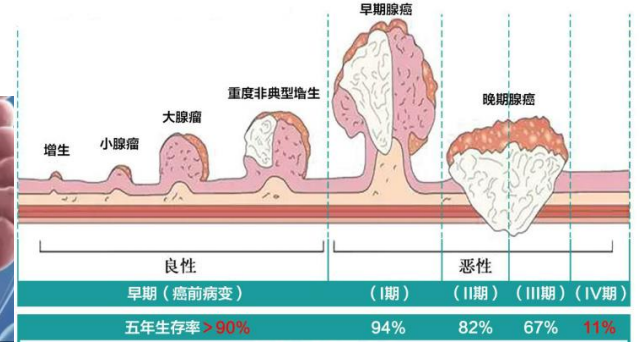
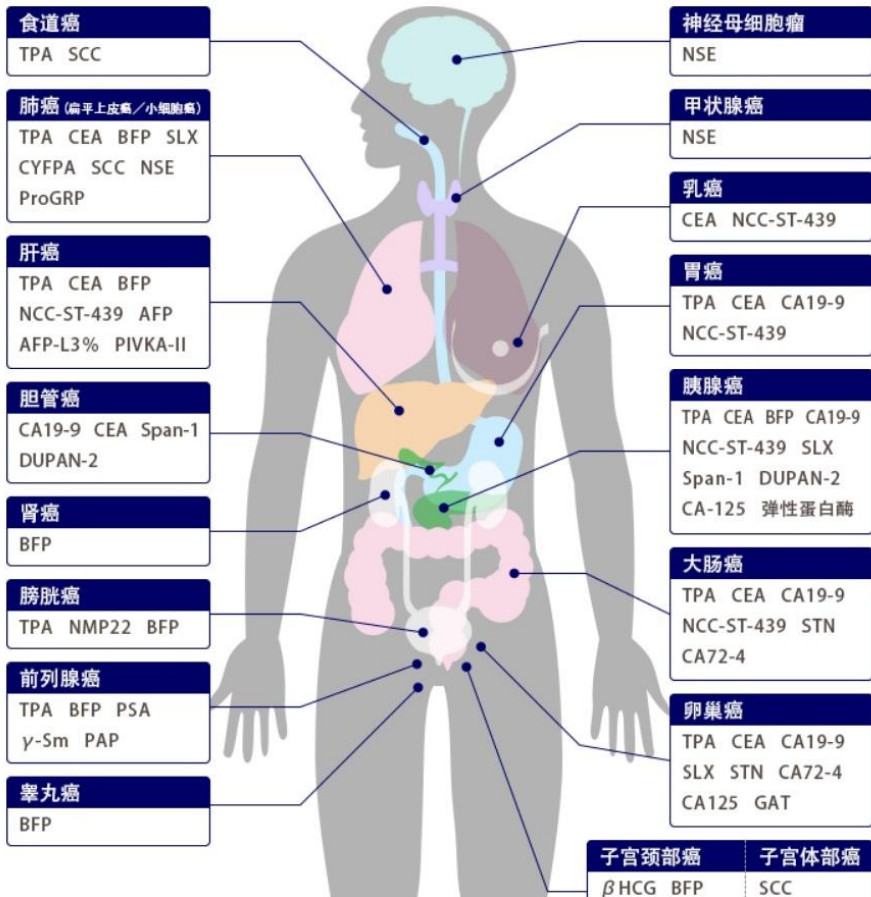
The etiology of AD is the deposition of β -amyloid ($A\beta$) and tau protein, which causes a large number of neurons to die, and cis-P-tau protein, which can drive neuronal degeneration. Antibodies targeting cis-P-tau improve neurodegeneration and memory loss in mouse models of vascular dementia and Alzheimer's disease. Can be used as a target for the treatment of vascular dementia or early Alzheimer's disease.



Proteomic and disease

Distinguishing disease by monitoring abnormal protein signatures

Tumor biomarkers: refers to the substances produced by malignant tumor cells or the host's stimulatory response to tumors, and can reflect the occurrence and development of tumors, and monitor the response of tumors to treatment.



nature medicine ARTICLES
<https://doi.org/10.1038/s41591-022-01850-y>
 Check for updates

OPEN
Noninvasive proteomic biomarkers for alcohol-related liver disease

Cell Resource

Extracellular Vesicle and Particle Biomarkers Define Multiple Human Cancers

LETTER
<https://doi.org/10.1038/s41586-019-1173-8>

Proteomics reveals NNMT as a master metabolic regulator of cancer-associated fibroblasts

Cell Reports Medicine Article

Proteome profiling of cerebrospinal fluid reveals biomarker candidates for Parkinson's disease

Proteomic and disease-biomarker

Distinguishing disease by monitoring abnormal protein signatures



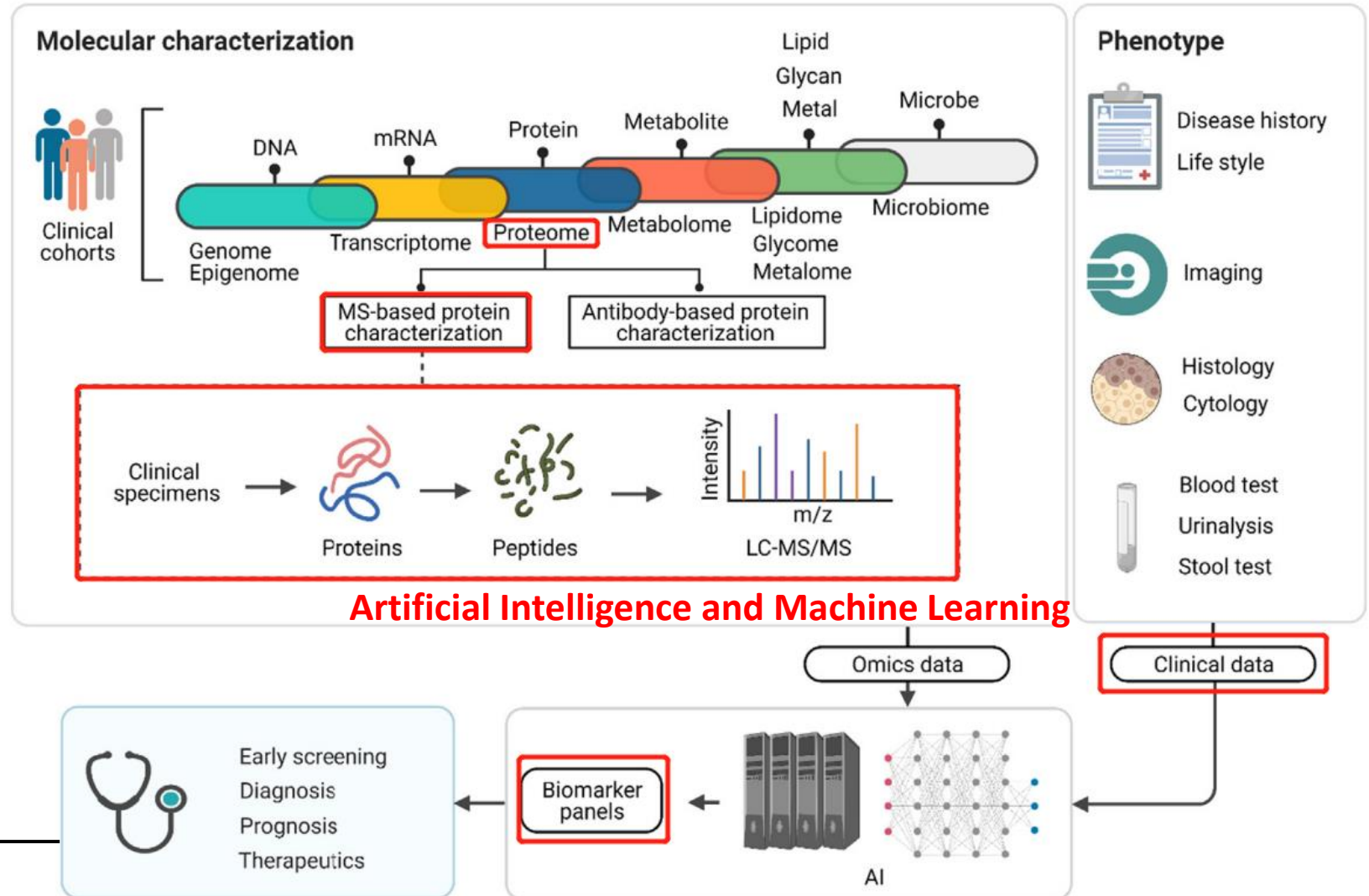
Potential diagnostic markers in healthy and diseased patients

Biomarkers at different stages of development in patients with disease

Different types of disease biomarkers

Relapse markers after disease treatment

disease treatment prognostic markers



Proteomic and disease

Distinguishing disease by monitoring abnormal protein signatures

GLOBAL CANCER BIOMARKER MARKET FORECAST 2019-2027



TOP COMPANIES

ABBOTT LABORATORIES

AFFYMETRIX, INC.

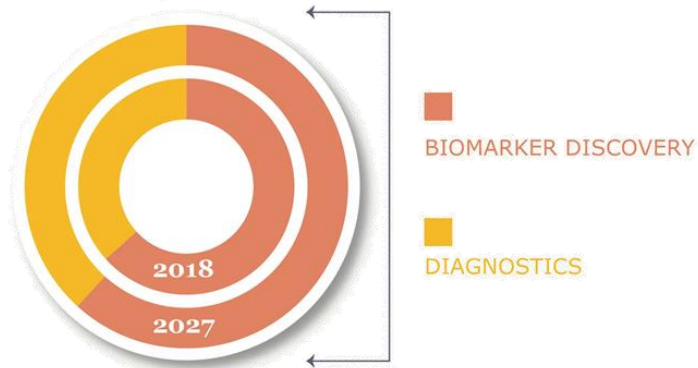
AGENDIA N.V.

AGILENT TECHNOLOGIES, INC.

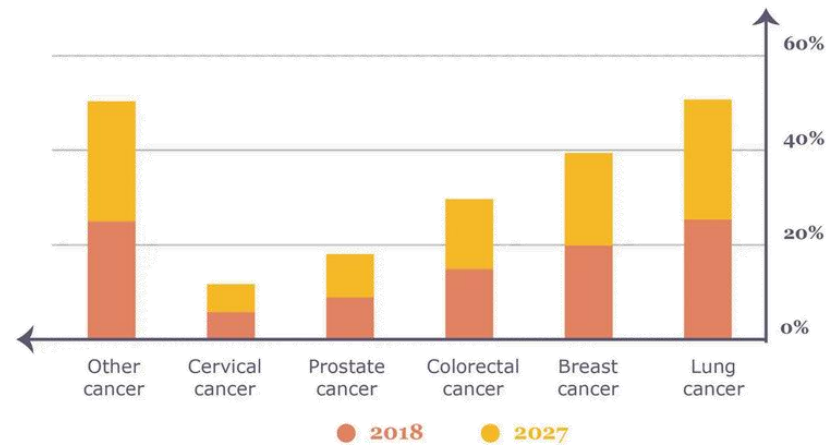


藻糖基化甲胎蛋白试剂盒

GLOBAL CANCER BIOMARKER MARKET, BY DISCOVERY AND DIAGNOSTICS 2019-2027



MARKET SHARE BY DISEASE



禽流感治疗药物Tamiflu

2021年国自然蛋白组获批项目标题	所属学部	项目类型	金额（万）	单位
基于代谢/蛋白质组学的西黄丸抗乳腺增生作用机制研究	医学科学部	地区科学基金项目	33.00	甘肃中医药大学
蛋白质组学下泌尿系草酸钙结石的分子机理研究	医学科学部	地区科学基金项目	34.00	兰州大学第二医院
中心体蛋白质组学及其与卵巢癌发生的分子关联研究	医学科学部	青年科学基金项目	30.00	北京大学
基于Label-free-PRM蛋白质组学技术的联合梅毒抗原标志物筛选策略	医学科学部	青年科学基金项目	30.00	厦门大学
基于TMT蛋白质组学的知母抗癫痫的皂苷类成分发现及作用机制研究	医学科学部	青年科学基金项目	30.00	黑龙江中医药大学
蛋白质乳酸化修饰产生和调控机制及其与沙门菌毒力的关系研究	医学科学部	青年科学基金项目	30.00	上海交通大学
基于LRT-R2*Mapping成像及蛋白质组学分析探讨铁死亡介导梗死后心肌出血性损伤及其不良预后的机制研究	医学科学部	面上项目	55.00	中国医科大学
蛋白质琥珀酰化修饰在恶性疟原虫青蒿素耐受机制中的作用研究	医学科学部	青年科学基金项目	30.00	江苏省血吸虫病防治研究所
氧化应激通过蛋白质降解体系调控结直肠癌转移的分子机制研究	医学科学部	重点项目	290.00	四川大学
血浆外泌体蛋白质与骨质疏松症疾病风险关联评价及其机制研究	医学科学部	面上项目	55.00	苏州大学
COG5基因突变导致神经细胞蛋白质糖基化改变的分子机制研究	医学科学部	面上项目	55.00	中南大学
影像组学评估脑白质异质性与病理改变及认知异常的相关性研究	医学科学部	青年科学基金项目	30.00	杭州医学院
GBP5通过影响蛋白质乳酸化修饰调控巨噬细胞抗结核免疫应答的机制研究	医学科学部	面上项目	55.00	首都医科大学
蛋白质翻译后巴豆酰化修饰在冠心病旁路移植术后房颤发生中的作用及机制的研究	医学科学部	面上项目	55.00	中国医学科学院
基于乳腺组织细胞外囊泡的生物学特性及蛋白组学的分析	医学科学部	青年科学基金项目	30.00	青岛大学
基于高灵敏蛋白质组学技术的结直肠癌原发性耐药机制研究	生命科学部	面上项目	58.00	暨南大学



Proteomic and disease-therapeutic target

Discover new potential drug targets; Undifferentiated identification of target proteins directly acting on drugs

By comparing normal and diseased variants, and changes in protein profiles before and after administration, proteomics technology can provide information on the molecular mechanisms of disease occurrence, drug effects, and adverse drug reactions. Specific biomarkers identified by proteomics can be used to investigate drug efficacy, resistance.

Review **TPP:热蛋白组学** OPEN ACCESS **molecular systems biology**

Thermal proteome profiling for interrogating protein interactions

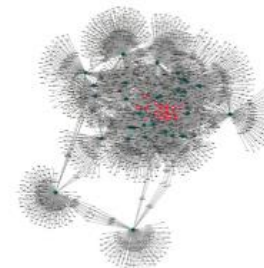
André Mateus^{1,†}, Nils Kurzawa^{1,2,†}, Isabelle Becher¹, Sindhuja Sridharan¹, Dominic Helm³, Frank Stein³, Athanasios Typas¹ & Mikhail M Savitski^{1,*}

Mol Syst Biol. 2020 Mar;16(3):e9232

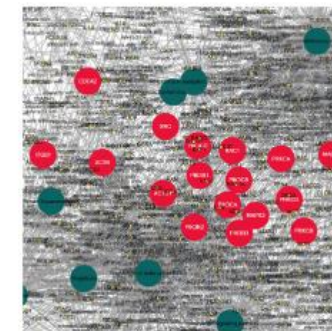


Multiple Processes May Involve in the IgG4-RD Pathogenesis: An Integrative Study via Proteomic and Transcriptomic Analysis

Network-Overview



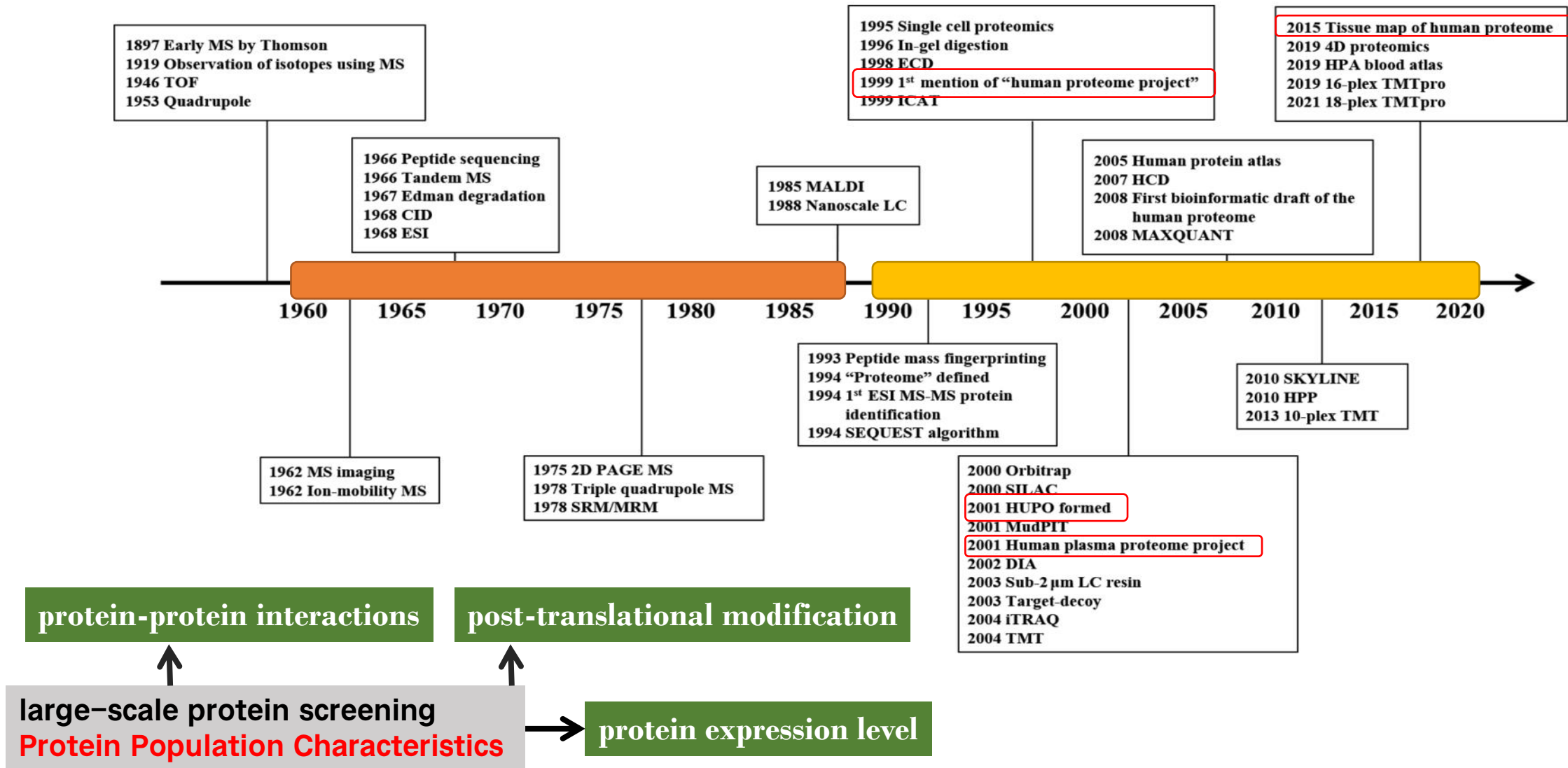
Network-Focus



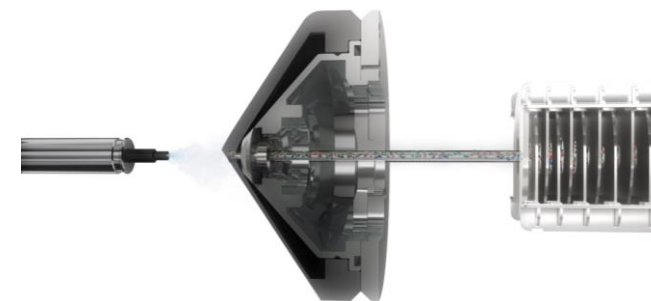
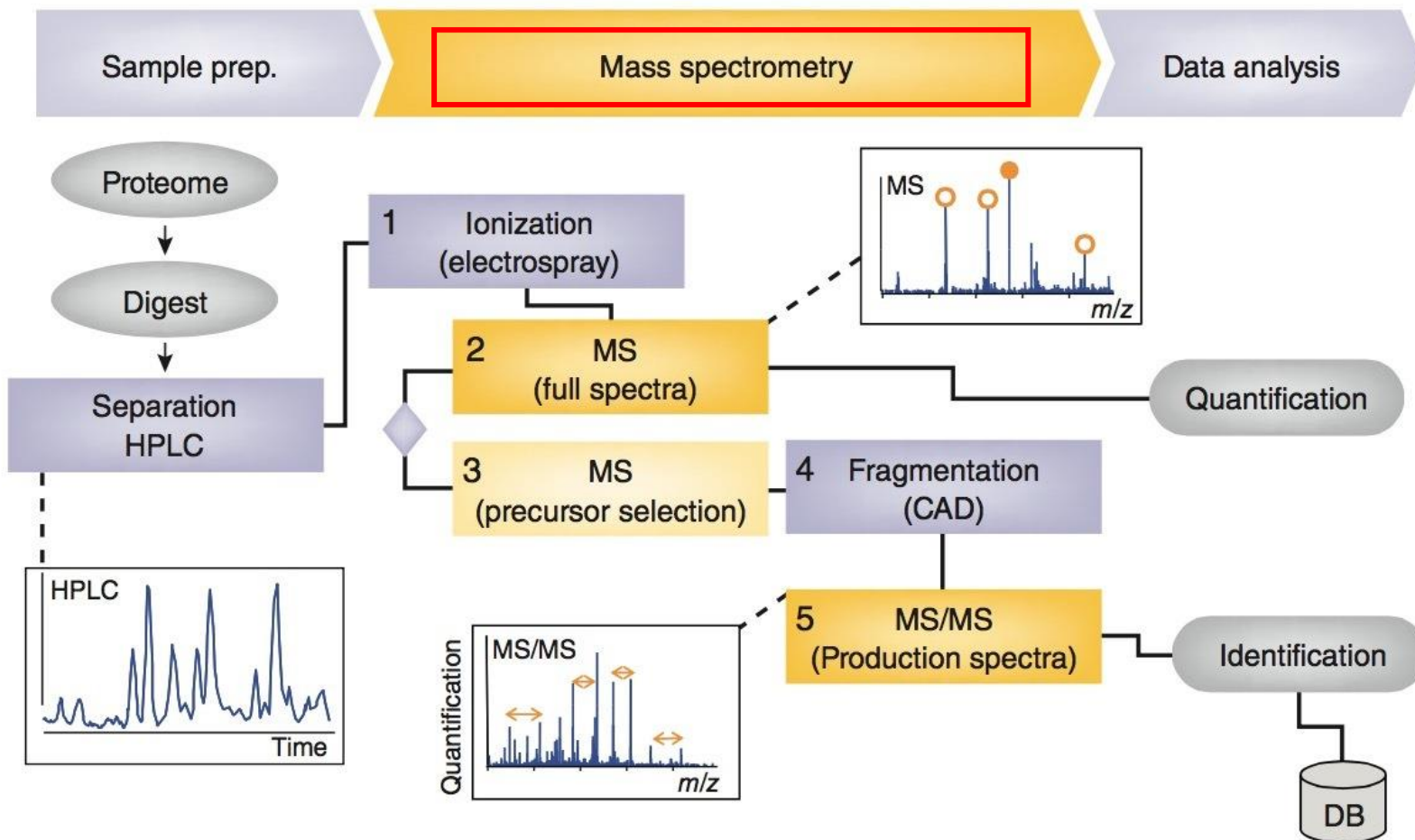
Top 15 Hub proteins

Gene Symbol	Degree
RAC1	14
ITGB1	12
MAPK1	12
MAPK3	12
ACTB	12
ACTG1	12
CDC42	12
PRKCB	12
PRKCA	11
PIK3CA	10
PIK3CB	10
PIK3CD	10
PIK3R1	10
PIK3R2	10
PIK3R3	10
PRKCG	10
SRC	10

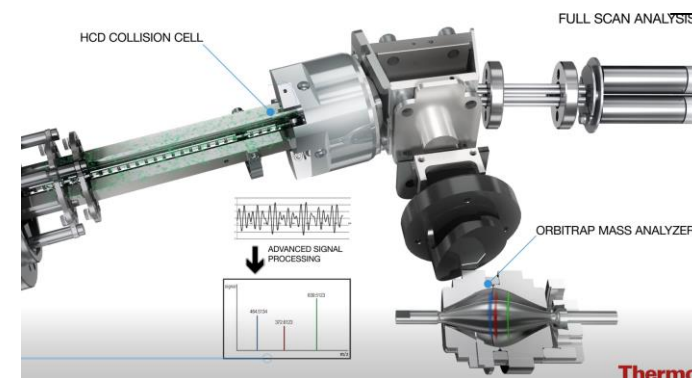
proteomics features and development history



Proteomics experimental workflow—shot gun/bottom up



Thermo SCIENTIFIC



Thermo



Mass Spectrometry Instrument Platform



Q Exactive™ HF-X

仪器名称	分辨率	质量范围	扫描速度
Q Exactive™	140000	50 ~ 6000 m/z	12HZ
Q Exactive HF-X	240000	50 ~ 6000 m/z	40HZ
Orbitrap Exploris™480	480000	40~6000/8000m/z	40HZ
Orbitrap Eclipse	240000	50~8000m/z	40HZ

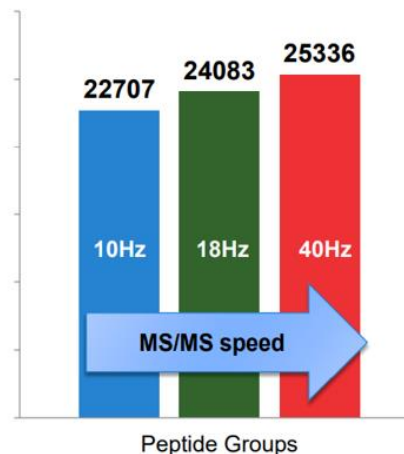
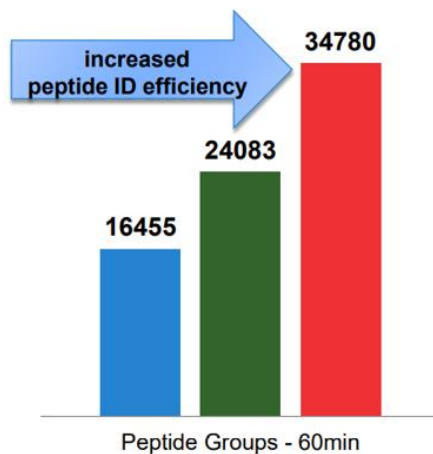


Orbitrap Exploris™
480 Mass Spectrometer

Deeper Dive into Proteome - More Productivity with Thermo Scientific Q Exactive HF-X MS

■ Q Exactive Plus MS
■ Q Exactive HF MS
■ Q Exactive HF-X MS

■ Q Exactive Plus MS 120 min
■ Q Exactive HF MS 60 min
■ Q Exactive HF-X MS 30 min



Maximizing peptide identifications

- Highest peptide coverage
- Deep proteome analysis
- Spectral library building
- **2x** productivity increase vs. Q Exactive HF
- **4x** productivity increase vs. Q Exactive Plus
- Sample: 1 ug Pierce HeLa digest



Orbitrap Eclipse™ Tribrid™
Mass Spectrometer

software

Latest version of commercial software: PD2.4, Spectronaut 16, Peaks, byonic

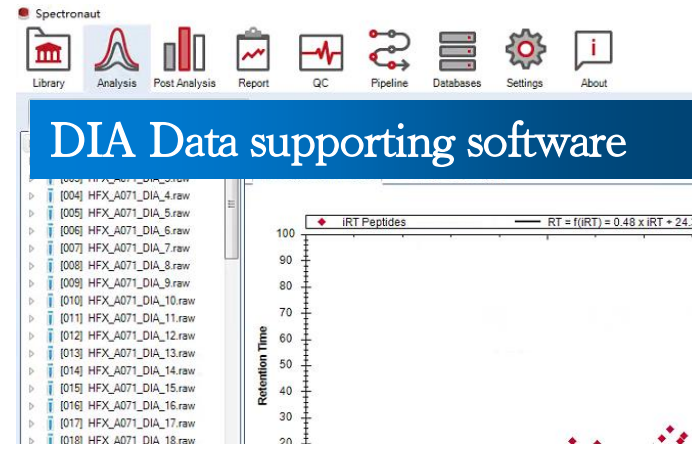
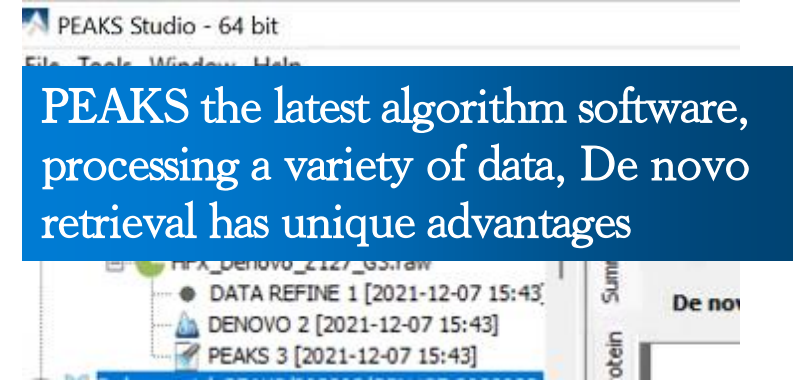


Thermo Official search software

New Study/Analysis

Open Study...
Open Result...

- CJKR048-20210310
- New Study
- New Study 2
- New Study 1
- W067-20210317
- W068-20210317

PEAKS Studio - 64 bit

File Tools Window Help

PEAKS the latest algorithm software, processing a variety of data, De novo retrieval has unique advantages

DATA REFINE 1 [2021-12-07 15:43]
DENOVO 2 [2021-12-07 15:43]
PEAKS 3 [2021-12-07 15:43]

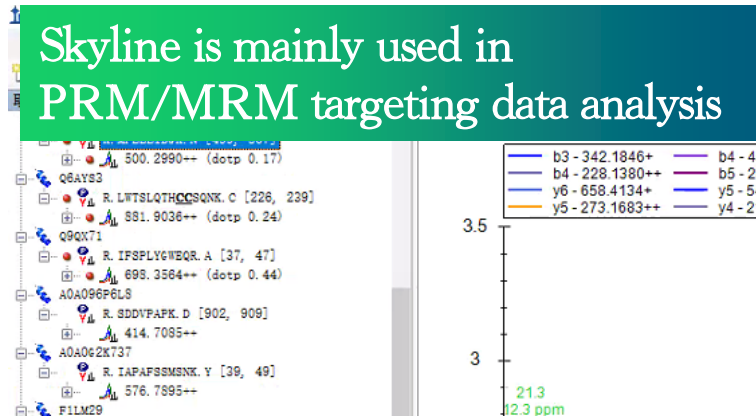
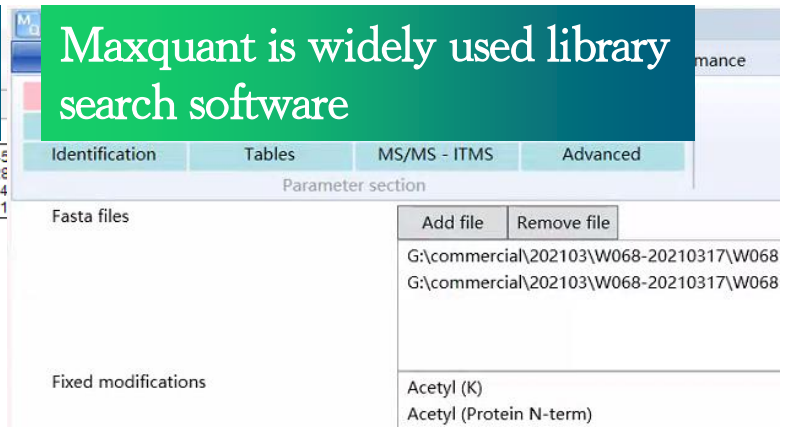


PMI-Byos - Protein Metrics Inc.

File Help

Simultaneous completion of peptide sequence search and glycoform search

Integrated Application Templated Workflow

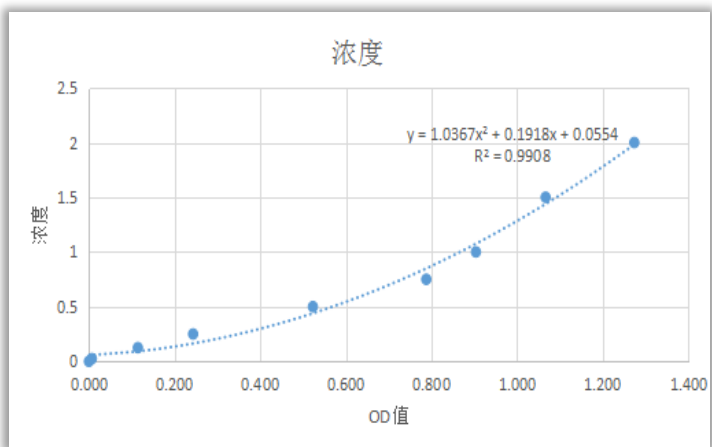
Maxquant is widely used library search software

Identification	Tables	MS/MS - ITMS	Advanced
Parameter section			
Fasta files	Add file Remove file		
	G:\commercial\202103\W068-20210317\W068		
	G:\commercial\202103\W068-20210317\W068		
Fixed modifications	Acetyl (K) Acetyl (Protein N-term)		

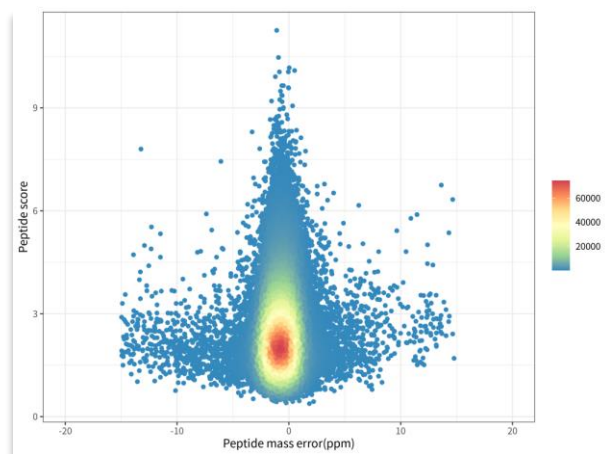


quality control process

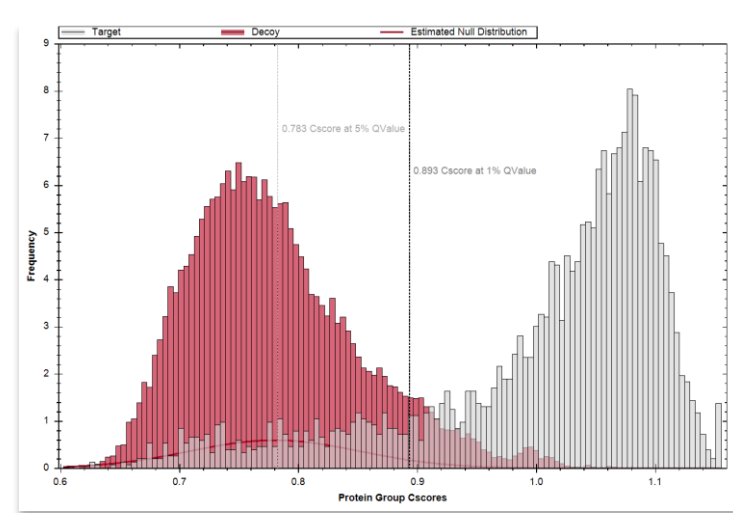
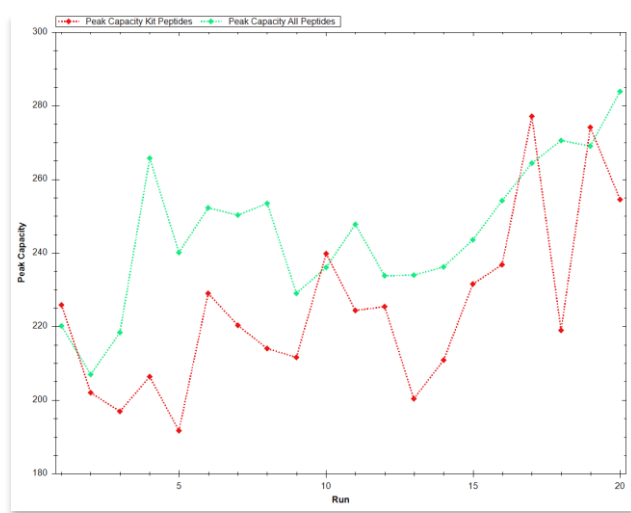
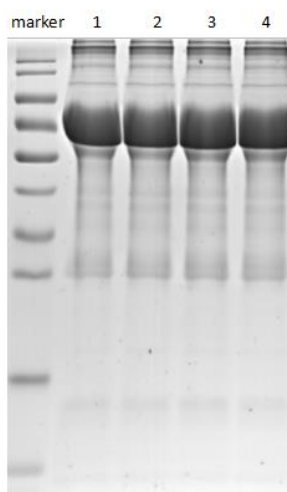
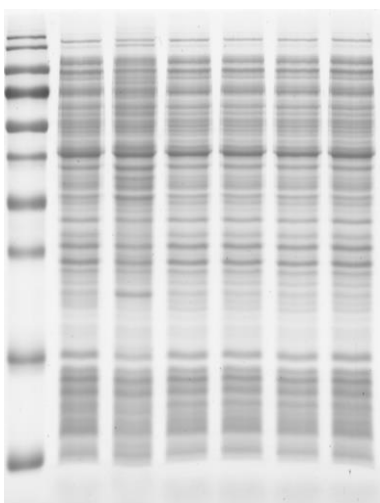
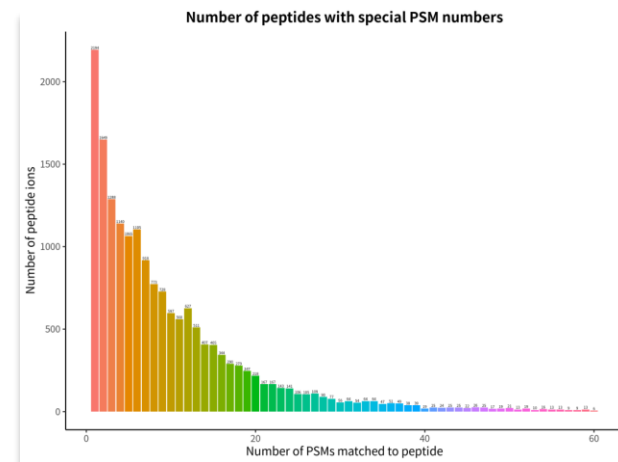
Sample quality control



Instrument quality control

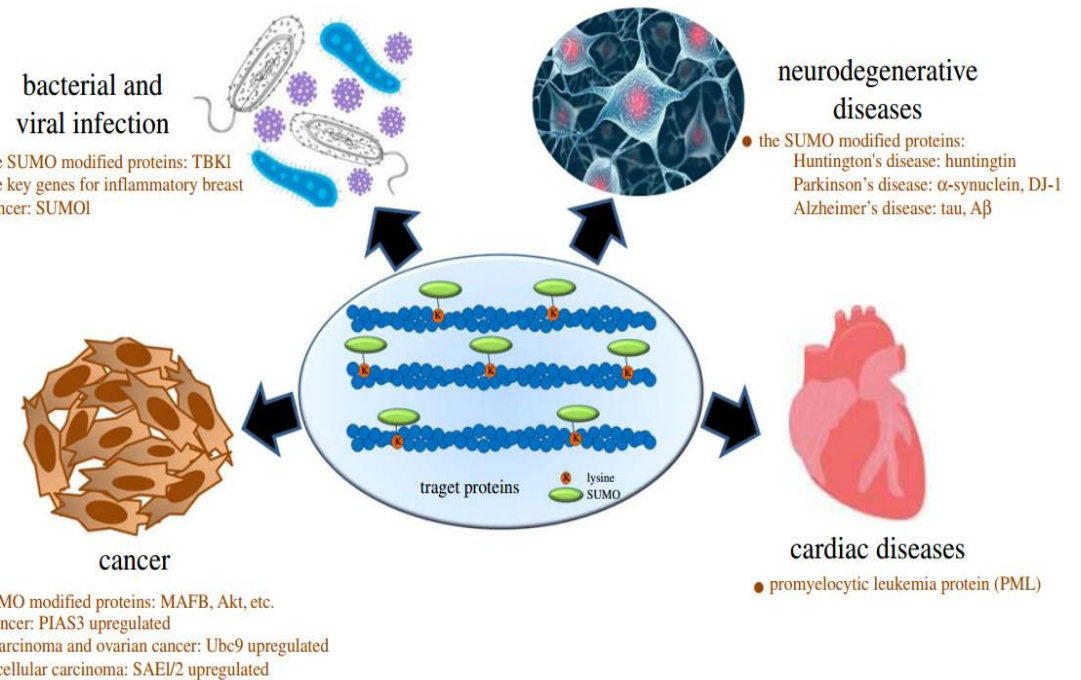
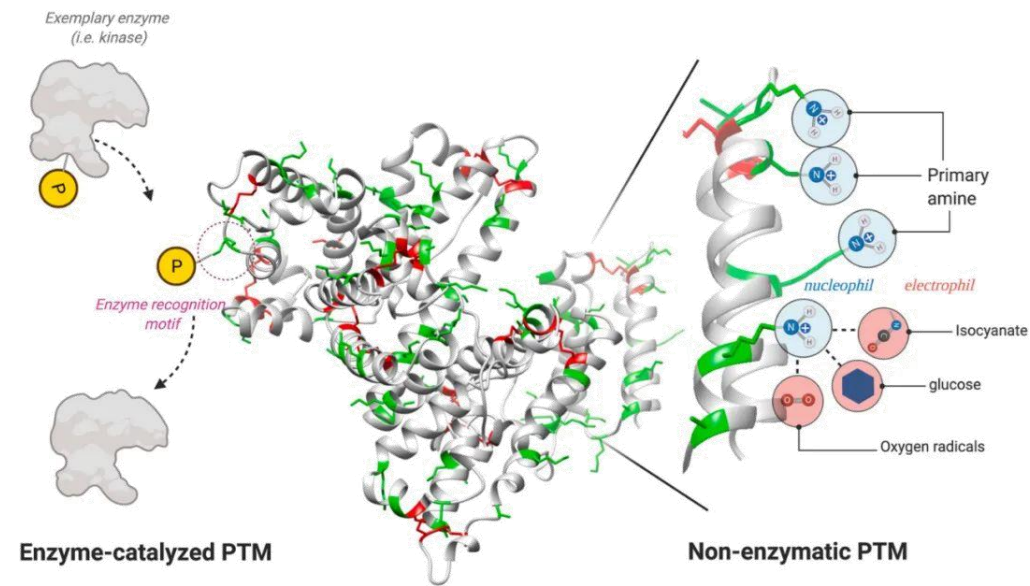


Data quality control



Protein translational modifications proteomics

Protein post-translational modification (PTM) can change the physical and chemical properties of proteins by adding modification groups to one or more amino acid residues, thereby affecting protein spatial conformation, activity, subcellular localization, protein folding and protein-protein interaction.



Mainly driven by enzymes, PTMs are important tools for regulating cellular and protein functions and maintaining cellular homeostasis

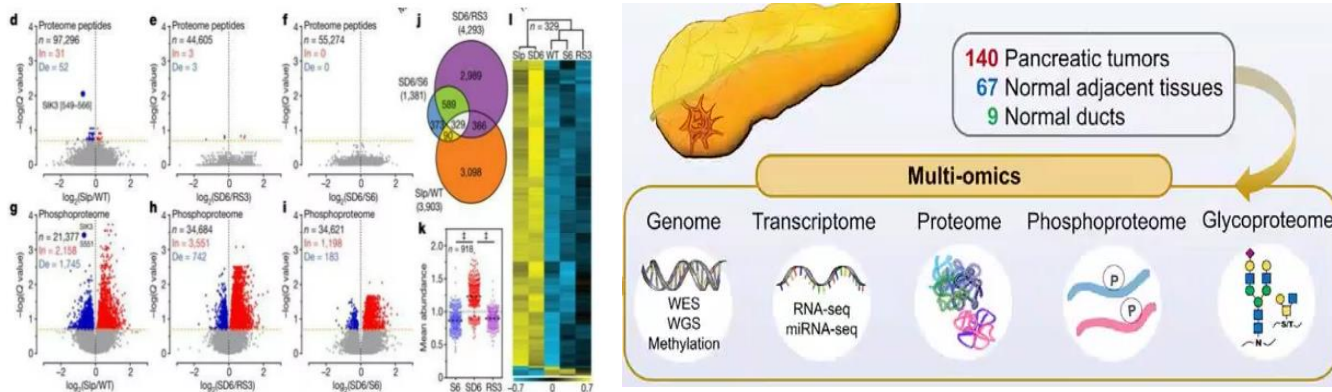
- PTM对蛋白功能影响是多样性的，表现在以下三个方面：
- (1) 同一蛋白质，即使只发生一种类型的修饰，也会赋予其多种功能；
 - (2) 同一个蛋白的同一种翻译后修饰，发生在不同的氨基酸上，其功能也不同；
 - (3) 同一蛋白还可能具有不同的修饰，其功能和参与的生物过程就更为复杂

The necessity of post-translational modification proteome research

生命活动和疾病发生等不仅与蛋白质表达丰度相关，与PTM相关

蛋白质组学领域的研究热点，与蛋白组学相比，更具有新颖性

PTM更有助于解释生命活动的分子调控机制，生物标志物和药物靶点的筛选



PTMD. PTMs that are associated with human diseases
Version 1.0

The CUCKOO Workgroup

THE CUCKOO WORKGROUP
HUST

HOME BROWSE ADVANCE ENRICHMENT DOCUMENTATION LINK CONTACT DOWNLOAD

PRODUCTS OF CUCKOO

- + PTMs Predictor
- + Tools
- + Databases

Introduction

Post translational modification (PTM) is an important biochemical process, which occurs after the mRNA is translated into the protein sequence in ribosomes. PTM process the protein by adding different biochemical group (such as phosphorylation (Moorhead *et al.*, 2009), methylation (Chen *et al.*, 2006)), by adding different small protein molecule (such as ubiquitination (Gao *et al.*, 2013), sumoylation (Ren *et al.*, 2009)), and by splicing protein sequence at specific sites (such as caspase cascade (Eamshaw *et al.*, 1999)). PTM is involved in nearly all aspect of biological processes by regulation of protein function. Abnormal PTM status has been reported to be associated with a variety of diseases, including cancers and neurologic diseases (Cohen *et al.*, 2001, Aletta *et al.*, 2008, Sakamoto *et al.*, 2002, McIlwain *et al.*, 2013).

nature methods ARTICLES
https://doi.org/10.1038/s41592-022-01523-1

Cyclic immonium ion of lactyllysine reveals widespread lactylation in the human proteome

Signal Transduction and Targeted Therapy www.nature.com/sigtrans

LETTER OPEN
Phosphoproteomics reveals therapeutic targets of esophageal squamous cell carcinoma

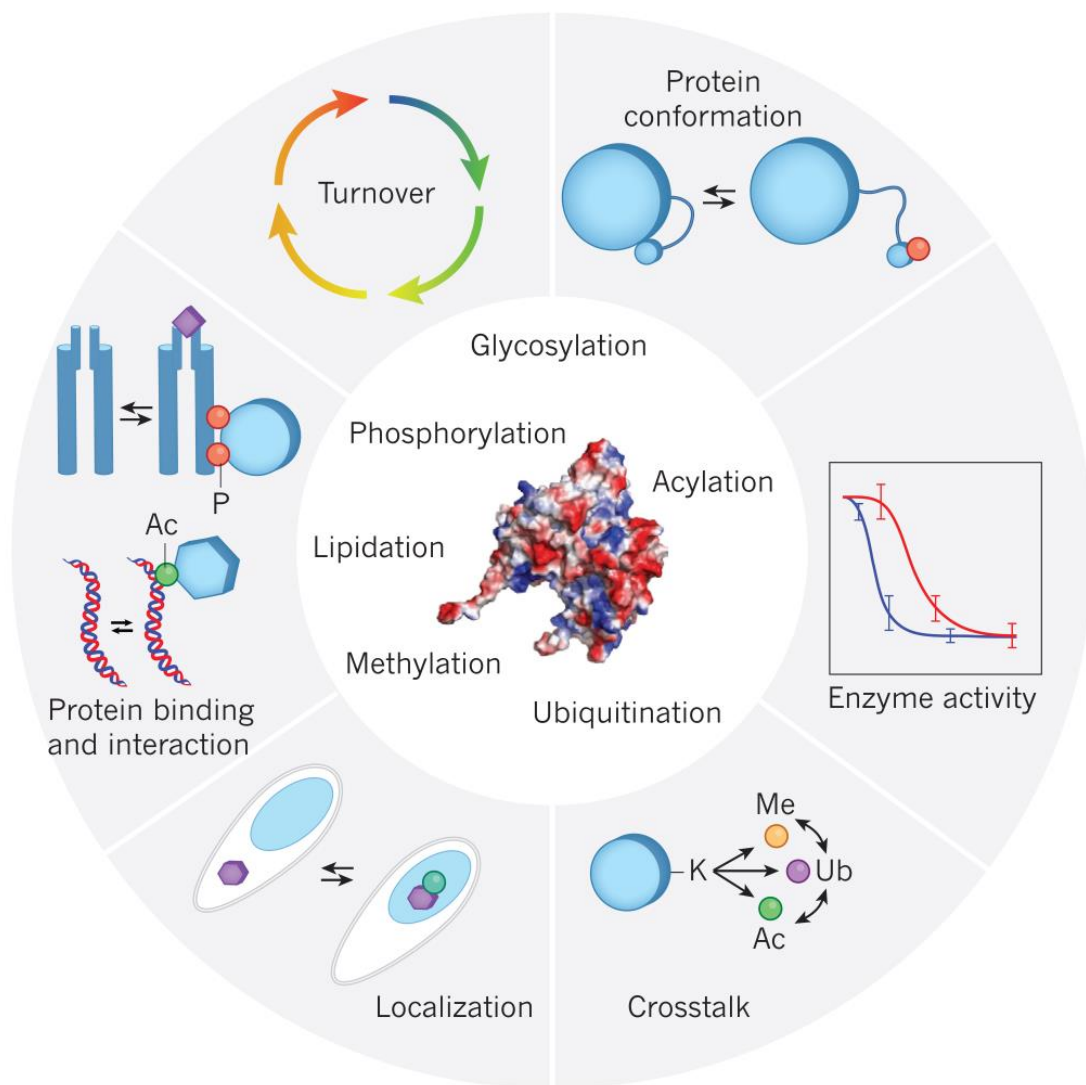
Cancer Cell

Article
Increased glucose metabolism in TAMs fuels O-GlcNAcylation of lysosomal Cathepsin B to promote cancer metastasis and chemoresistance

Cell Reports

Article
Macrophage K63-Linked Ubiquitination of YAP Promotes Its Nuclear Localization and Exacerbates Atherosclerosis

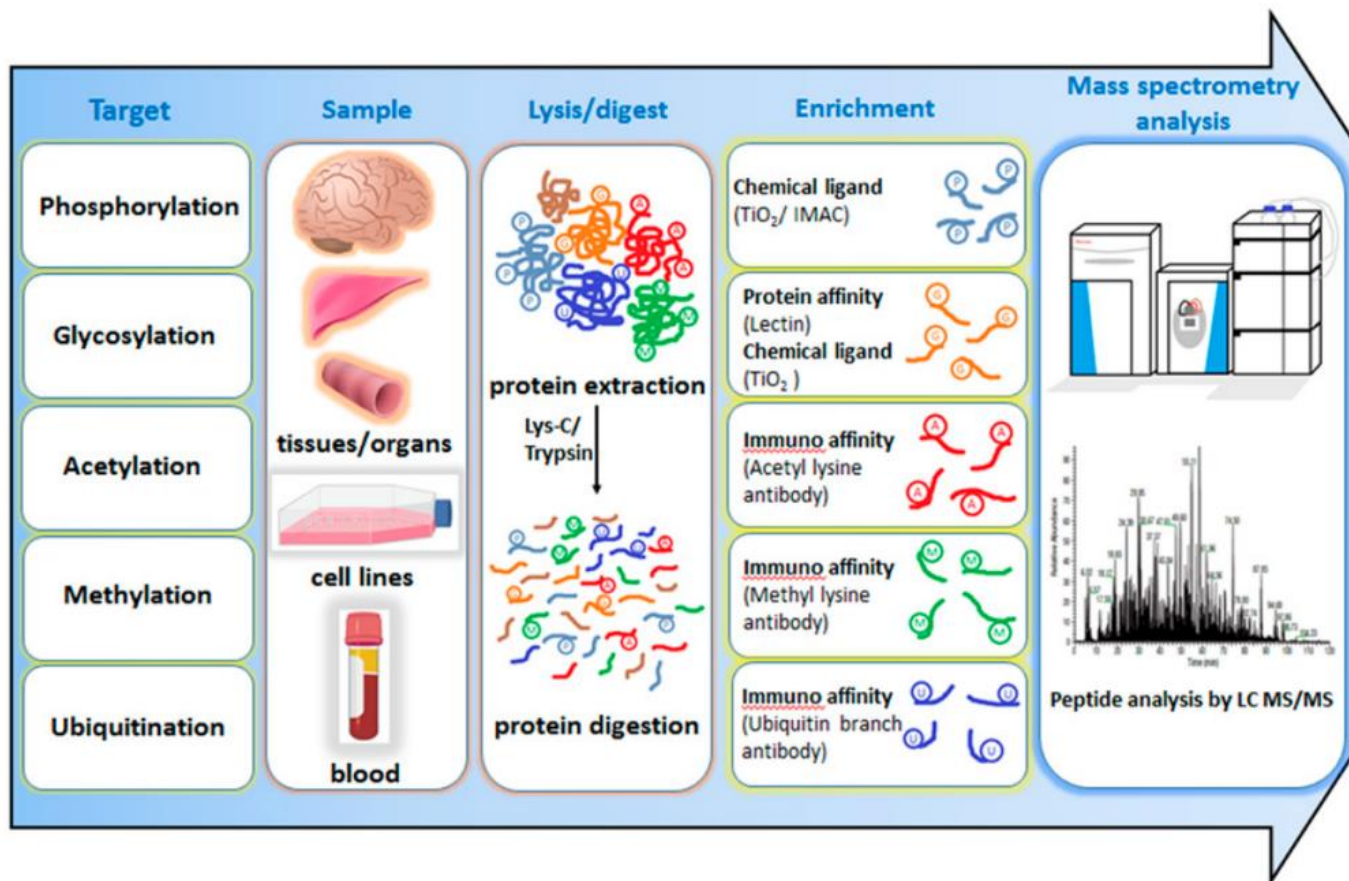
Protein translational modifications proteomics



修饰类型	单甲基化	调控生物过程
methylation	单甲基化	
dimethylation	赖氨酸双甲基化	染色质结构以及转录调控；稳定蛋白质，调控蛋白转录以及结合活性、DNA复制和损伤
trimethylation	赖氨酸三甲基化	
aDMA	精氨酸不对称二甲基化	
sDMA	精氨酸对称二甲基化	
malonylation	丙二酰化	
succinylation	琥珀酰化	基因表达调控、细胞凋亡、细胞代谢
glutarylation	戊二酰化	
Acetylation	乙酰化	
N-Acetylation	N端乙酰化	
HexHAcylation	O-乙酰葡萄糖胺修饰	代谢、生长、形态发生、凋亡、转录等
phosphopropargyl	磷酸化	信号转导、细胞周期、生长发育以及癌症机理
GG-Ub	泛素化/SUMO化	细胞周期调控、增殖与分化、凋亡以及蛋白质周转代谢

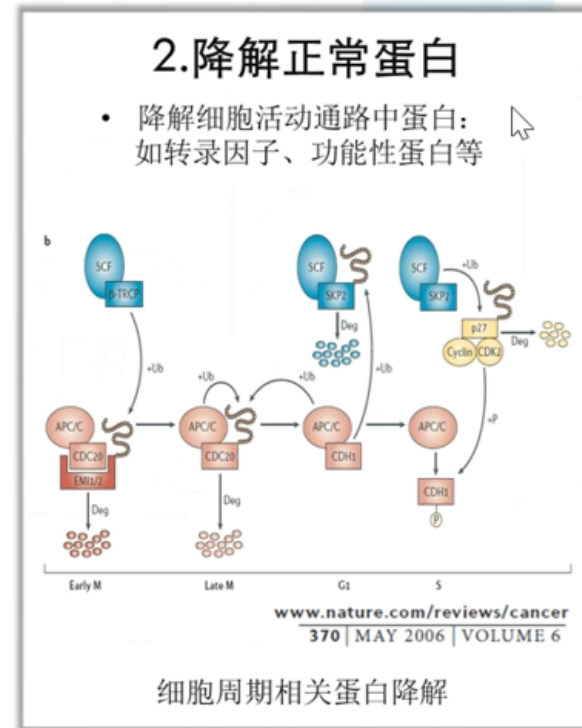
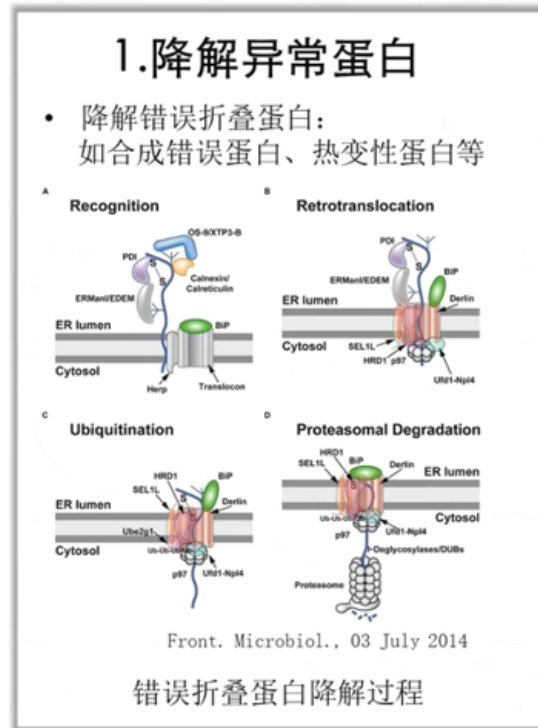
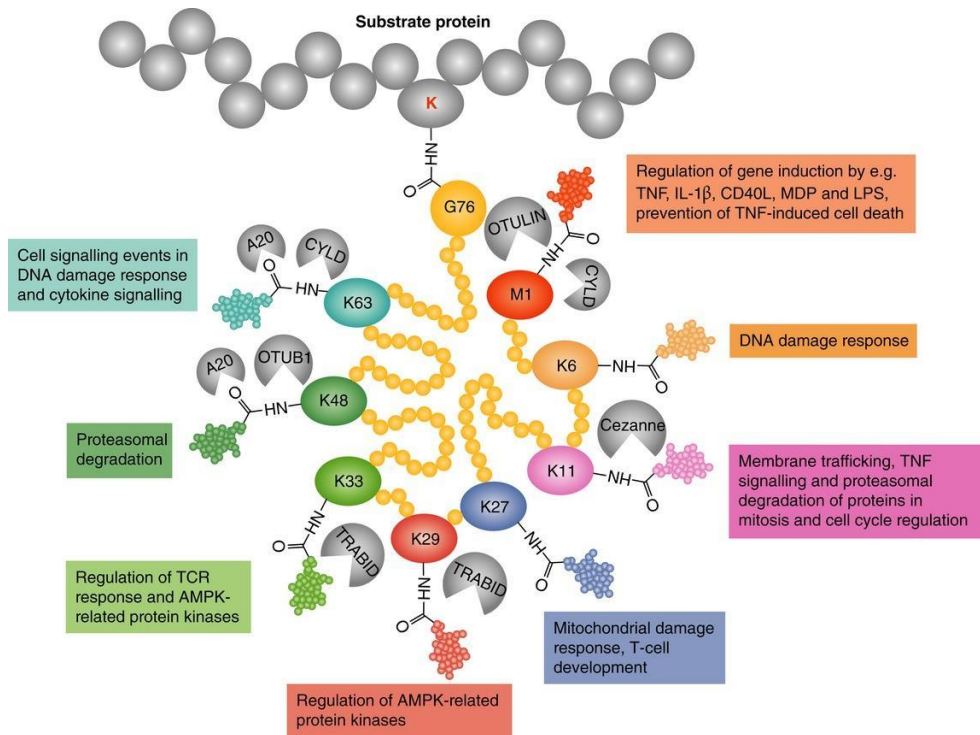
Protein translational modifications proteomics

质谱鉴定翻译后修饰的原理主要是利用蛋白修饰后的质量偏移来实现



热点	2021年医学部 中标数	热点	2021年医学部中标数
免疫调节	852	缺氧、低氧	211
血管生成、重构	531	泛素化	186
线粒体	485	乙酰化	135
外泌体	430	细胞焦亡	118
miRNA	413	代谢重编程	118
干细胞	371	单细胞	105
lncRNA	371	内质网	76
细胞自噬	358	炎性小体	76
肠道菌群	312	类器官	46
circRNA	287	超级增强子	25
m6A m5C m7G	270	相分离	21
铁死亡	257	乳酸化修饰	21
转录调控	232	迁移体	4

Protein translational modifications proteomics—ubiquitination



The Nobel Prize in Chemistry 2004

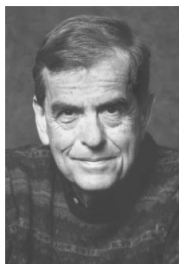


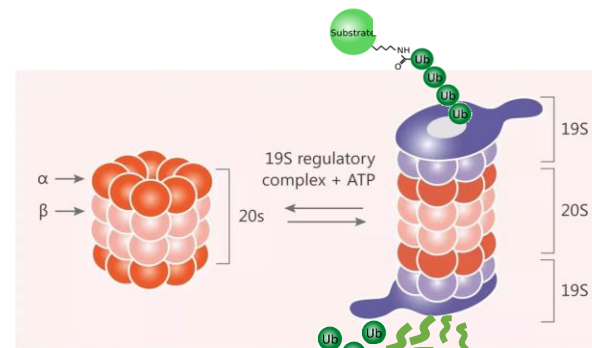
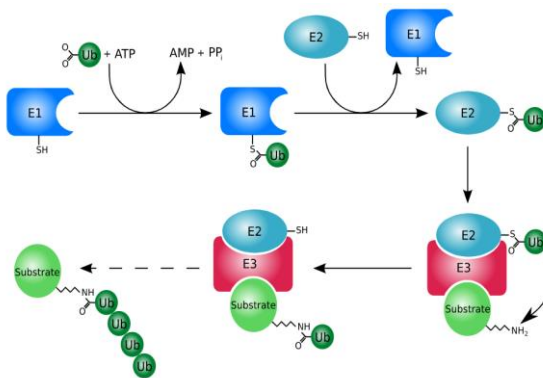
Photo: D. Porges
Aaron Ciechanover



Photo: D. Porges
Avram Hershko



Photo from the Nobel Foundation archive.
Irwin Rose



蛋白质组学常规分析内容

一数据质控

鉴定蛋白和肽段评估和统计分析：PSM数、覆盖率、分子量、漏切位点，肽段长度等

二、全局鉴定结果统计分析（数据总览、样本分布、重合性分析）

三、归一化数据分析（全局聚类热图、相关性分析、主成分分析）

四、差异蛋白筛选（差异蛋白火山图、热图、小提琴图、ROC曲线分析）

五、功能富集分析

1、COG功能注释

2、GO分析（GO注释三联图、差异蛋白柱状图、富集分析柱形图、气泡图、和弦图、有向无环图）

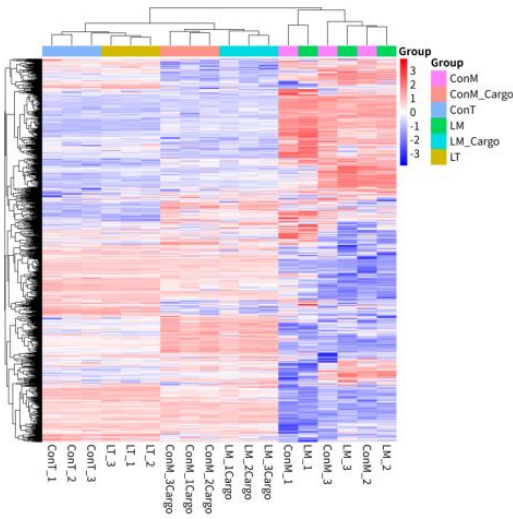
3、GOslim分析（GOslim注释三联图、差异蛋白柱状图、富集分析柱形图、气泡图、和弦图）

4、KEGG分析（差异蛋白柱状图、富集分析柱形、气泡图、和弦图、通路图）

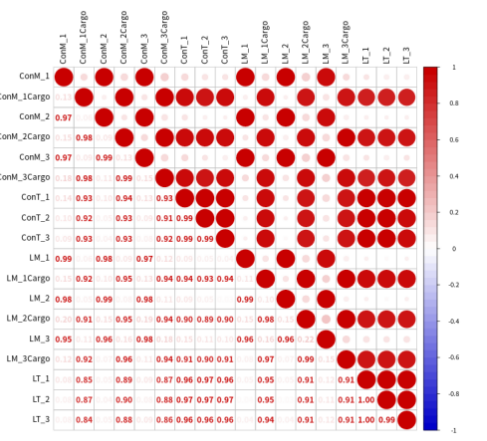
5、Reactome分析（差异蛋白柱状图、富集分析柱形、气泡图、和弦图、有向无环图）

6、Pfam富集分析（差异蛋白柱状图、富集分析柱形、气泡图、和弦图）

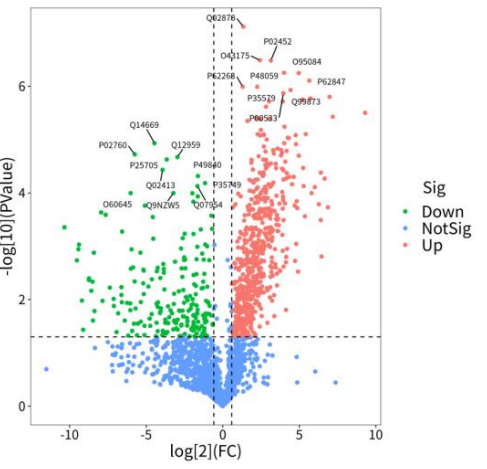
7、蛋白相互作用分析PPI（相互作用网络分析、Hub节点分析）



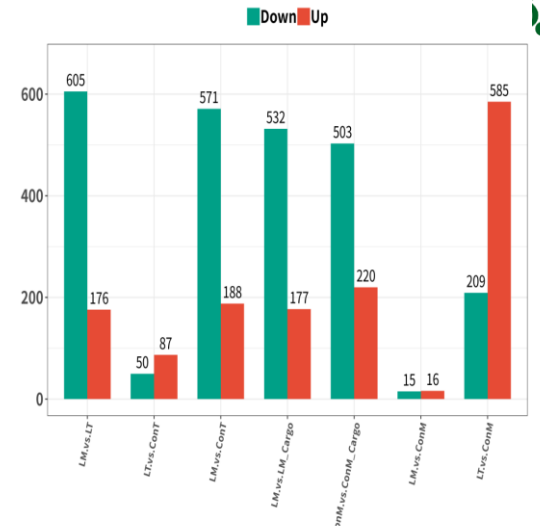
全局分析聚类热图



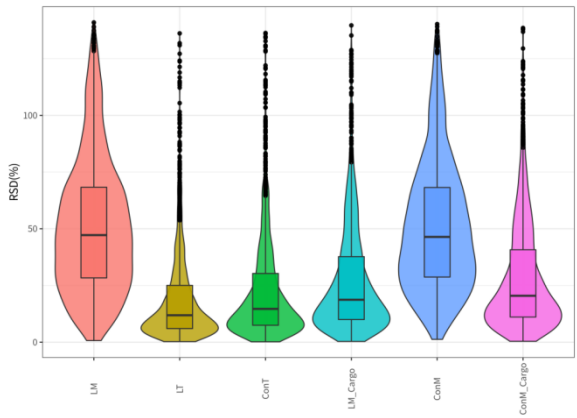
样本相关性图



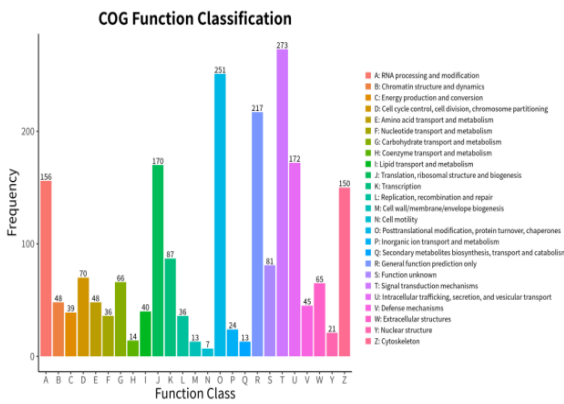
差异蛋白火山图



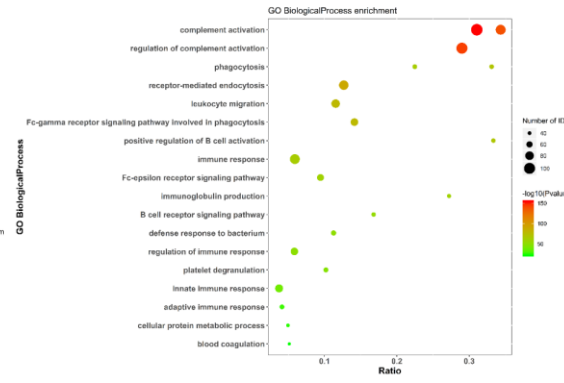
差异蛋白柱状图



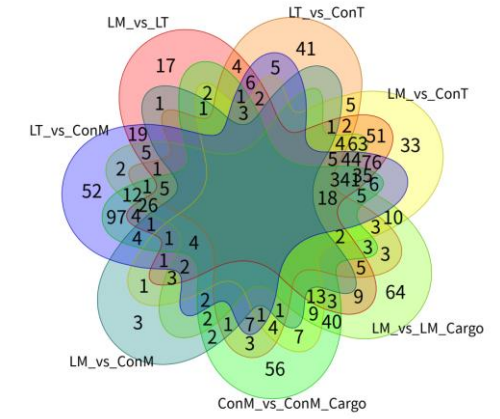
小提琴图



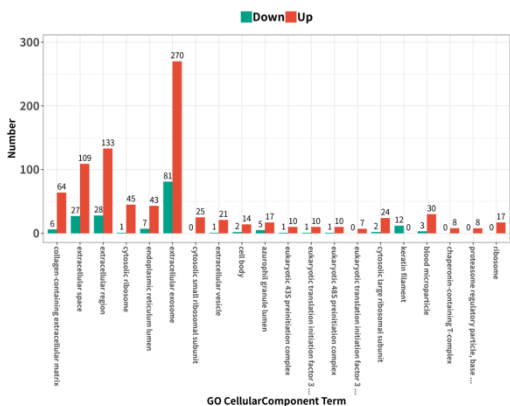
COG 功能分类统计图



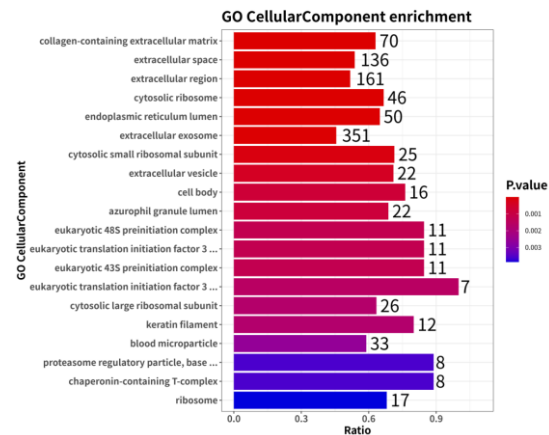
富集度气泡图



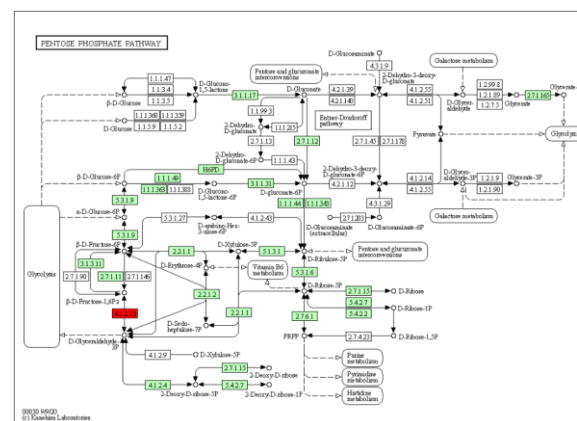
花瓣图



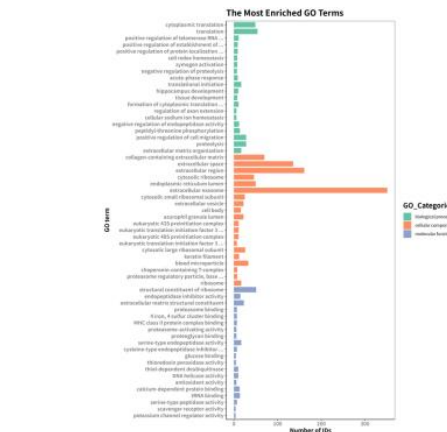
GO差异蛋白柱状图



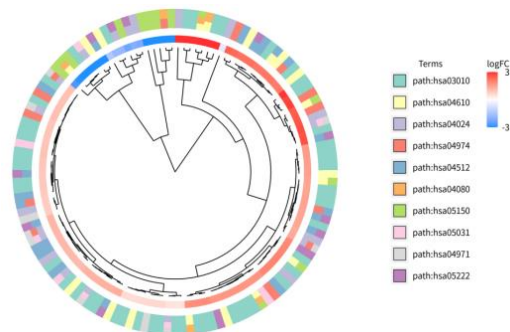
GO富集柱状图



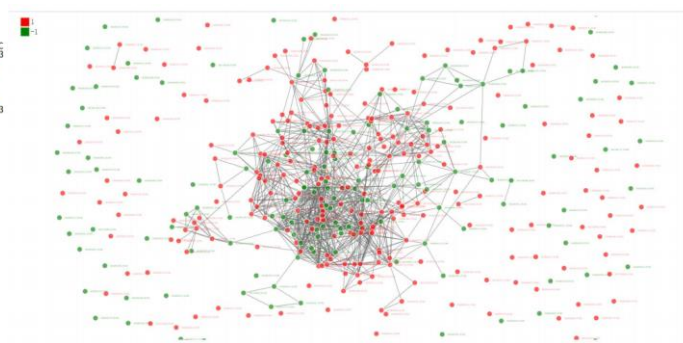
KEGG 信号通路图



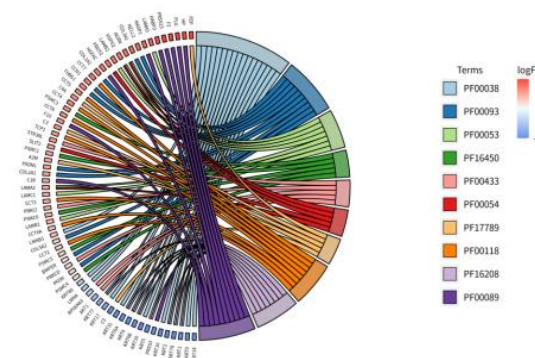
GO富集三联柱状图



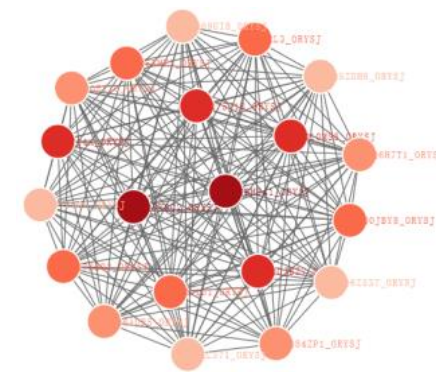
富集结果聚类图



相互作用网络示意图

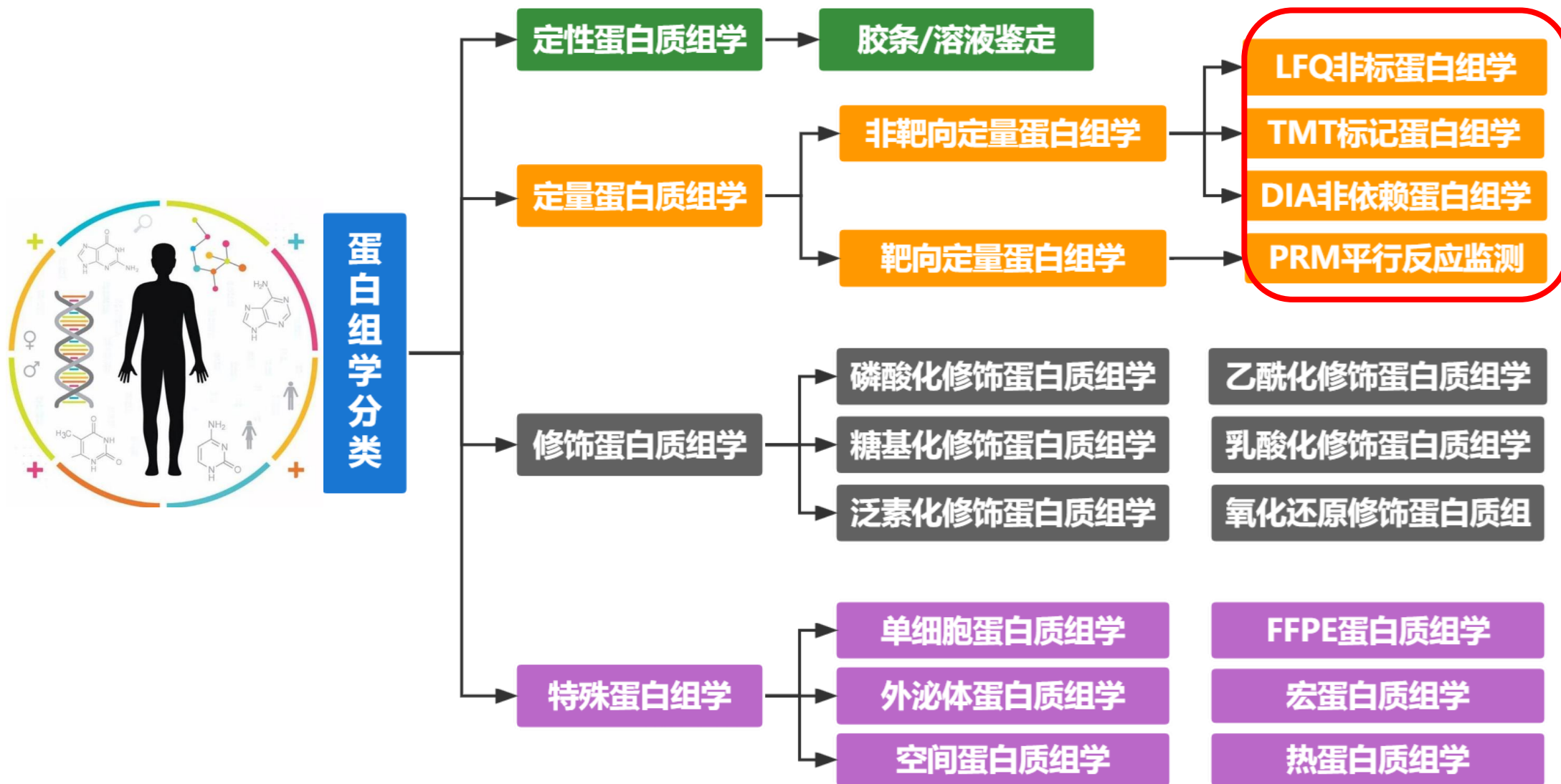


Pfam富集结果和弦图

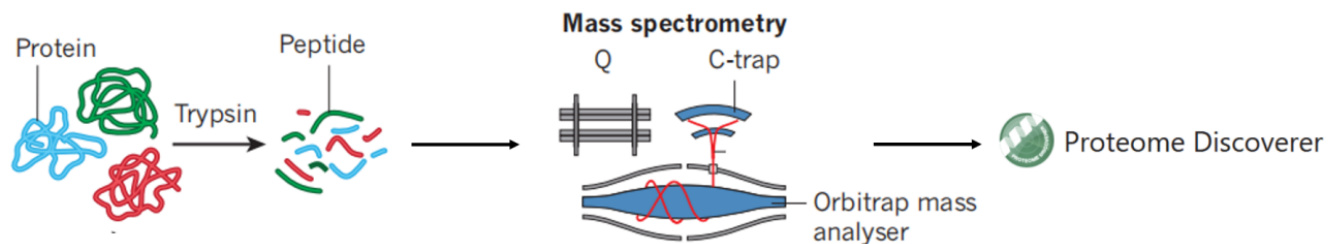
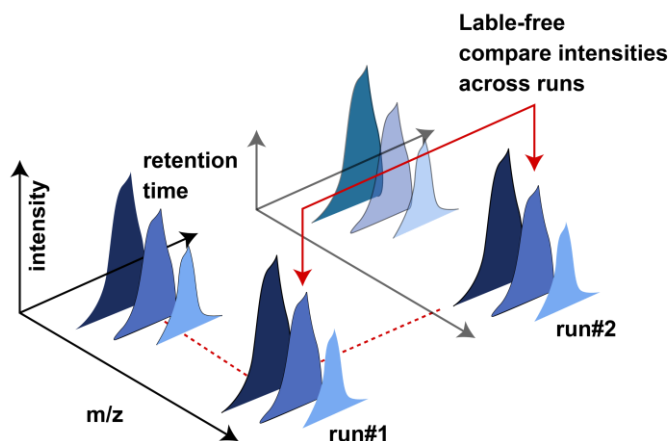


相互作用Hub网络图

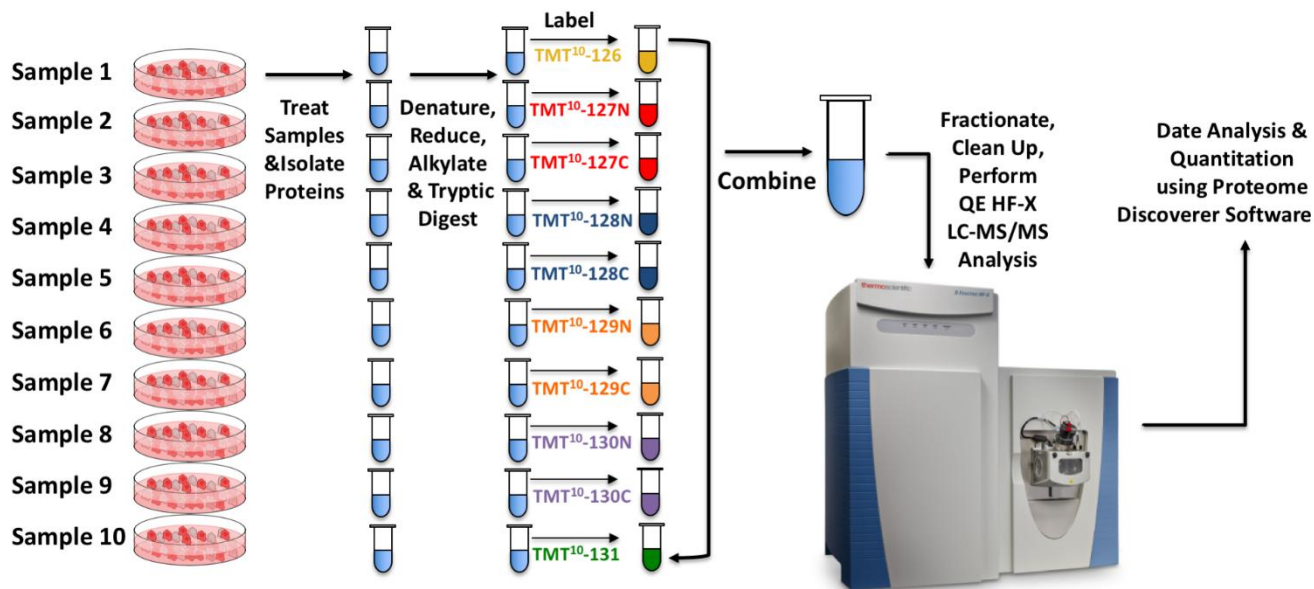
proteomic classification



proteomic techniques(LFQ/TMT/DIA)



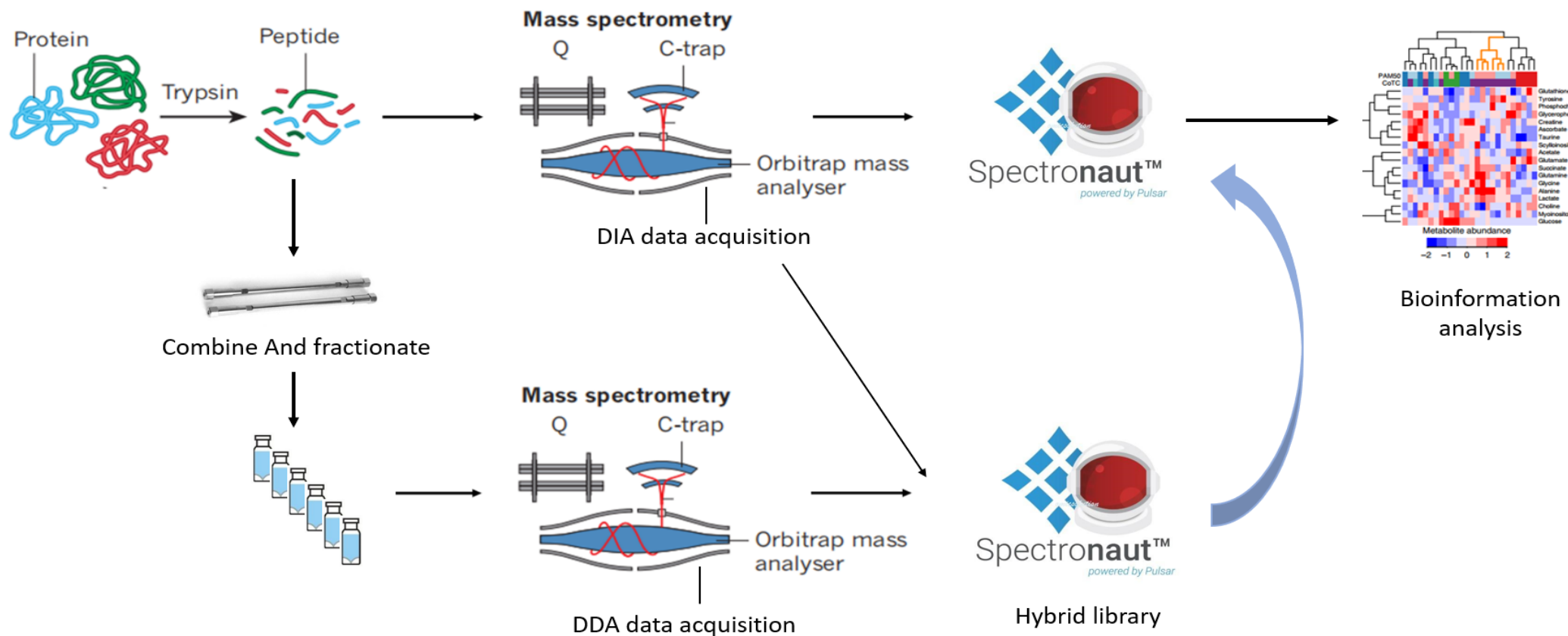
LFQ (label-free quantification), **非标记定量技术**, 无需对肽段进行特殊处理, 直接使用液相质谱联用仪对干净的多肽样本进行数据采集, 通过**比较不同样品中相应肽段的信号强度**, 从而对肽段对应的蛋白质进行相对定量。



TMT-标记定量技术。**(2-16) 稳定同位素标签**, 特异性标记多肽的氨基基团进行串联质谱分析, 在一级质谱图中, TMT™试剂标记的不同样本的同一肽段表现为相同的质荷比。在二级质谱中, 可剪切臂能够优先断裂以便释放报告离子。报告离子的峰强度能够反应出所标记的多肽的样品丰度, 再经过软件处理得到蛋白质的定量信息。

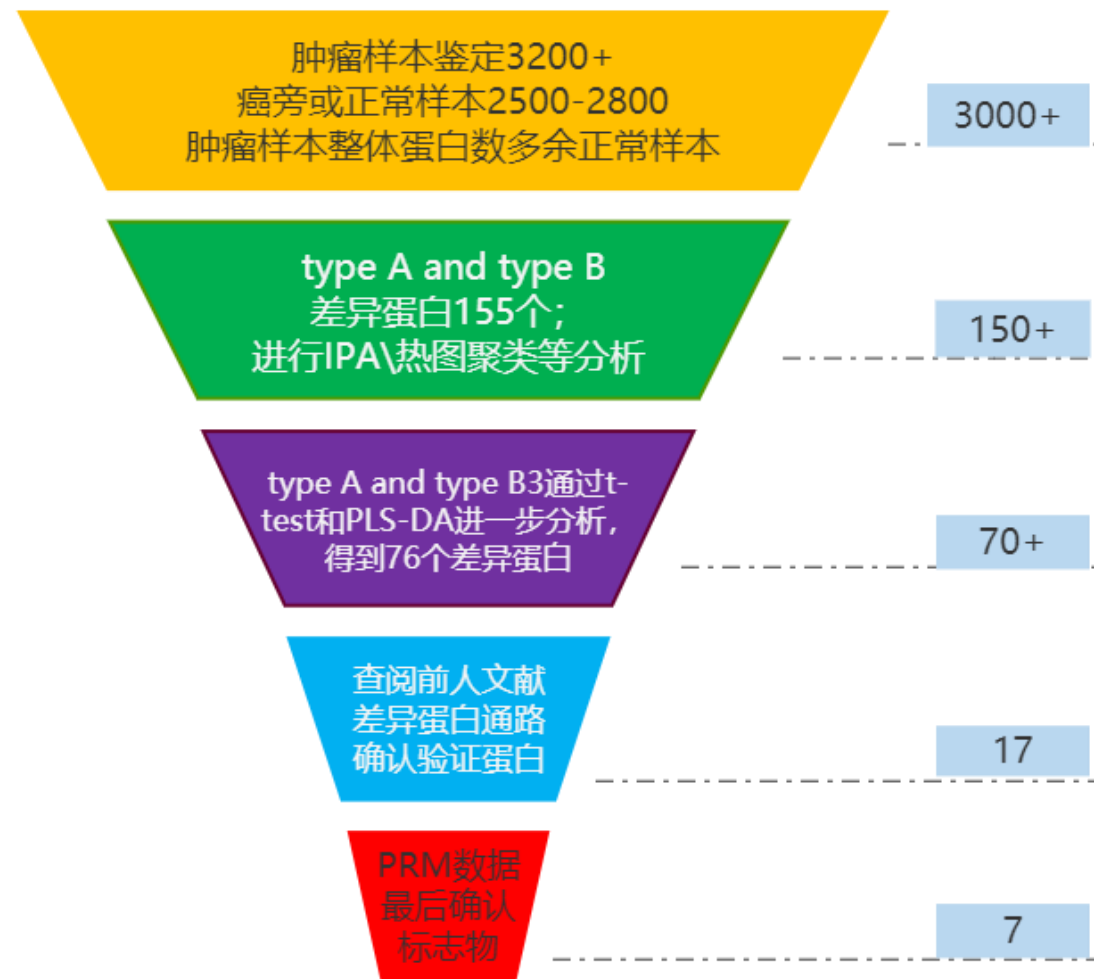
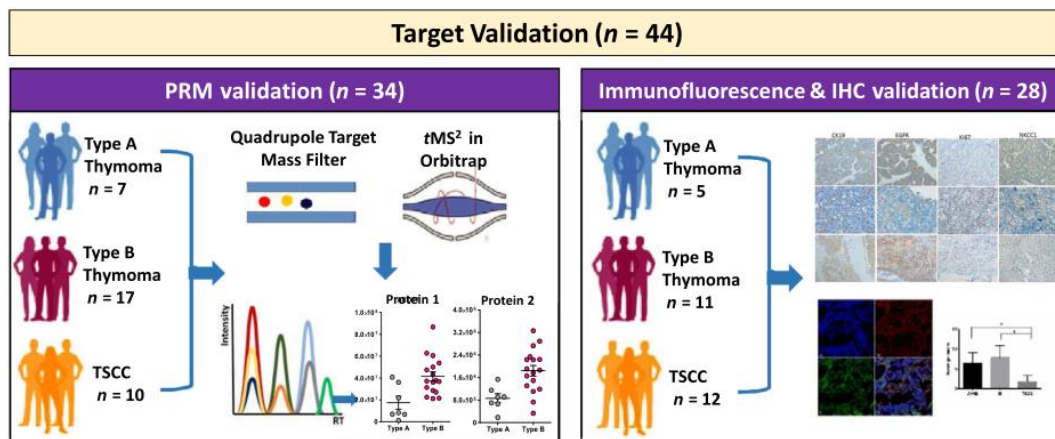
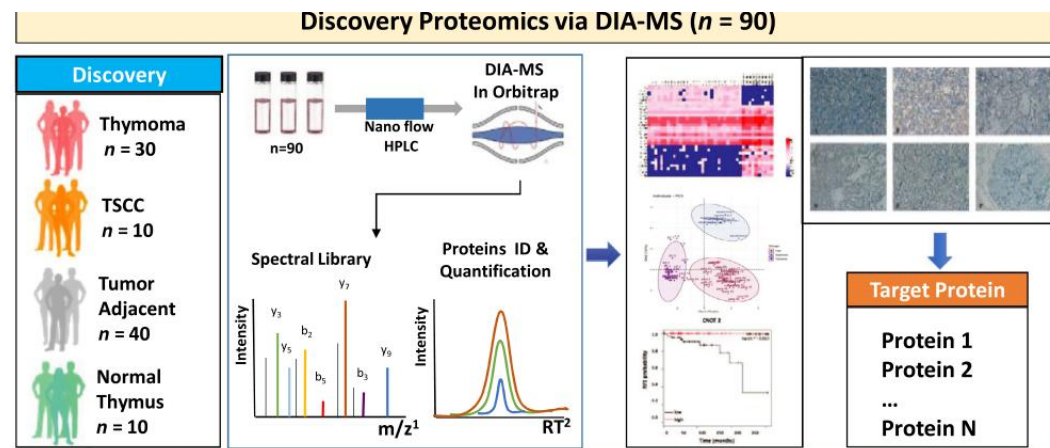
proteomic techniques(LFQ/TMT/DIA)

数据非依赖性采集 (Data Independent Acquisition, DIA)：是指样品在进入二级质谱时，按照设定的质荷比m/z范围，对该范围内所有的母离子进行碎片化，而不是依赖信号强度进行母离子的挑选。与传统的**数据依赖性采集 (Data Dependent Acquisition, DDA)**模式相比，DIA方法具有重复性好，蛋白质覆盖率高，定量准确性高等特点。



解密基于组织的蛋白质组特征揭示了胸腺上皮肿瘤的新亚型和预后标记

Deciphering tissue-based proteome signatures revealed novel subtyping and prognostic markers for thymic epithelial tumors

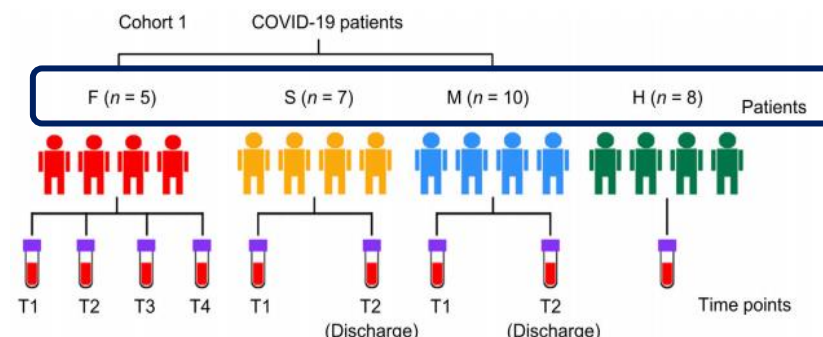


Immunity IF: 22+ 发表期刊: Immunity, 2020

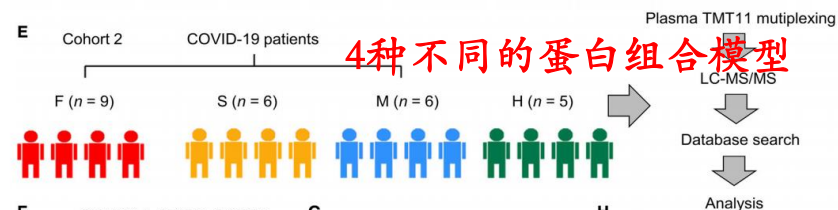
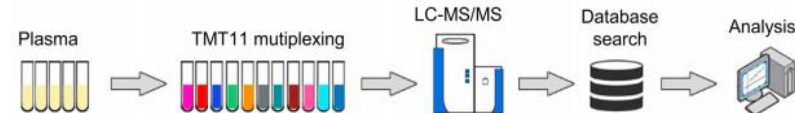
Plasma Proteomics Identify Biomarkers and Pathogenesis of COVID-19

Highlights

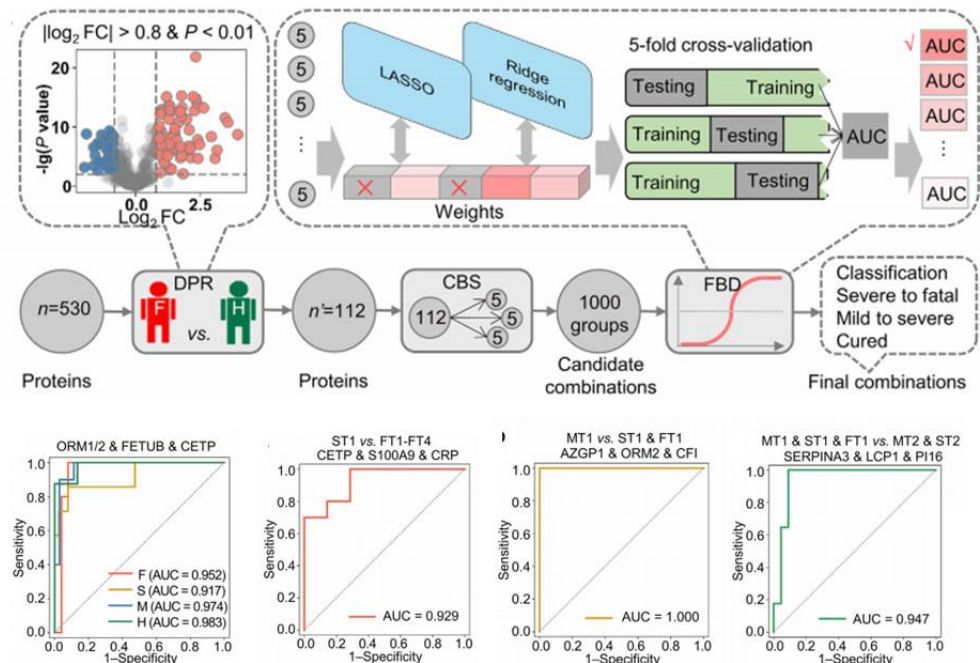
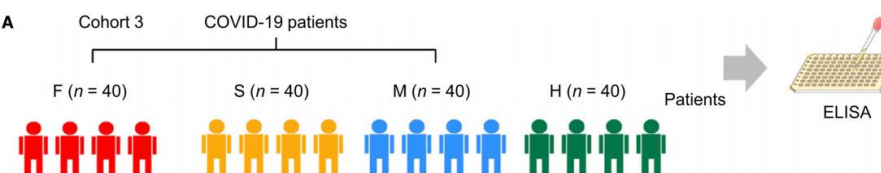
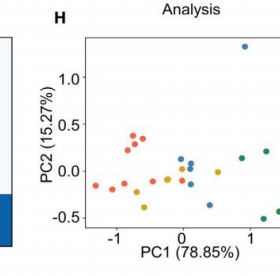
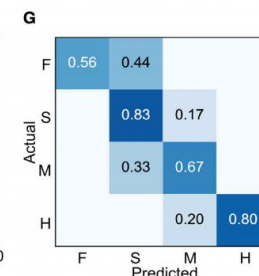
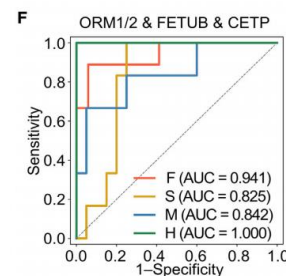
- ◆ 新冠肺炎患者不同症状和时间点的血浆蛋白质组学
- ◆ 宿主血浆蛋白的变化与新冠肺炎的发展有关
- ◆ 机器学习的模型区分不同严重程度的患者
- ◆ 生物标志物组合预测新冠肺炎临床结果



62例血浆样本 → 872个蛋白定量



4种不同的蛋白组合模型



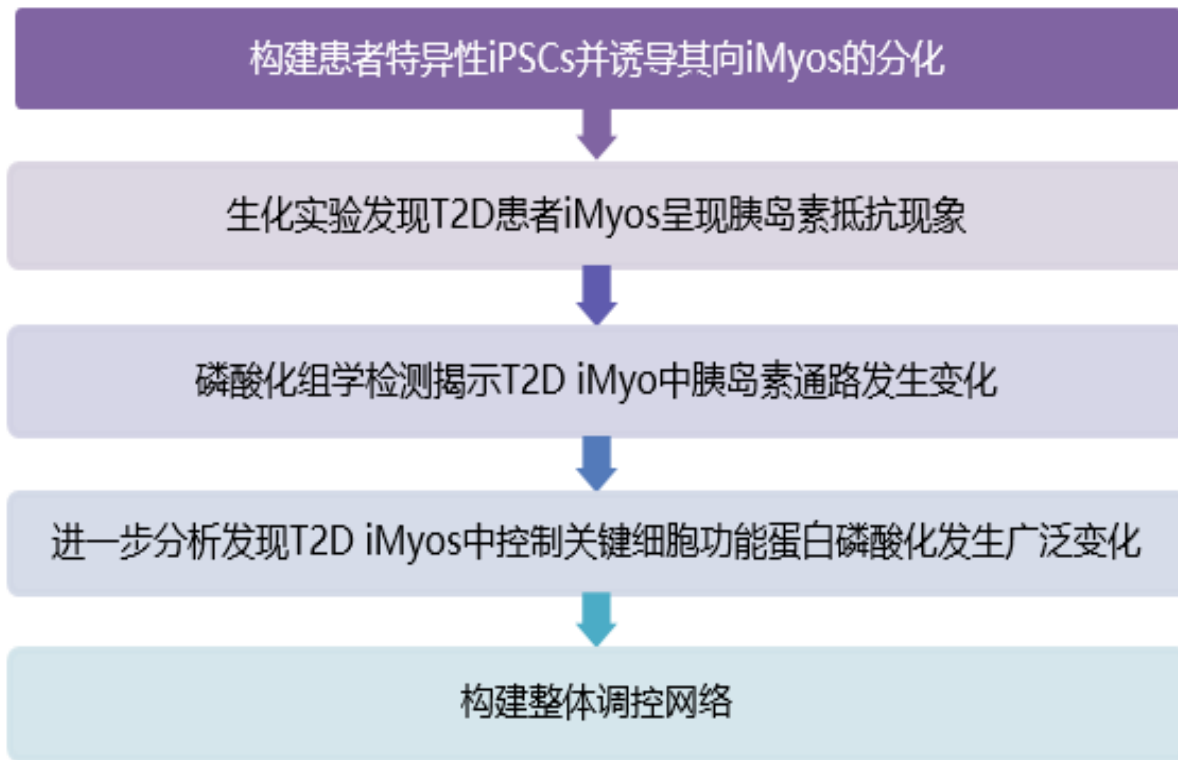
Cell Metabolism

Article

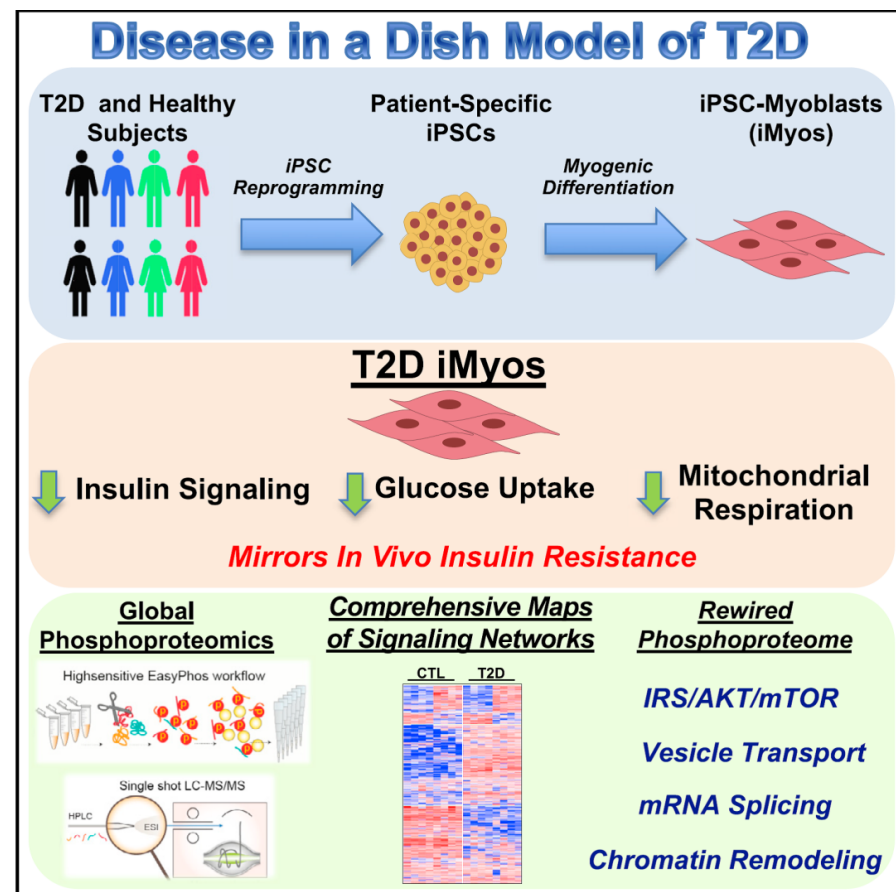
解析2型糖尿病致病背后机制

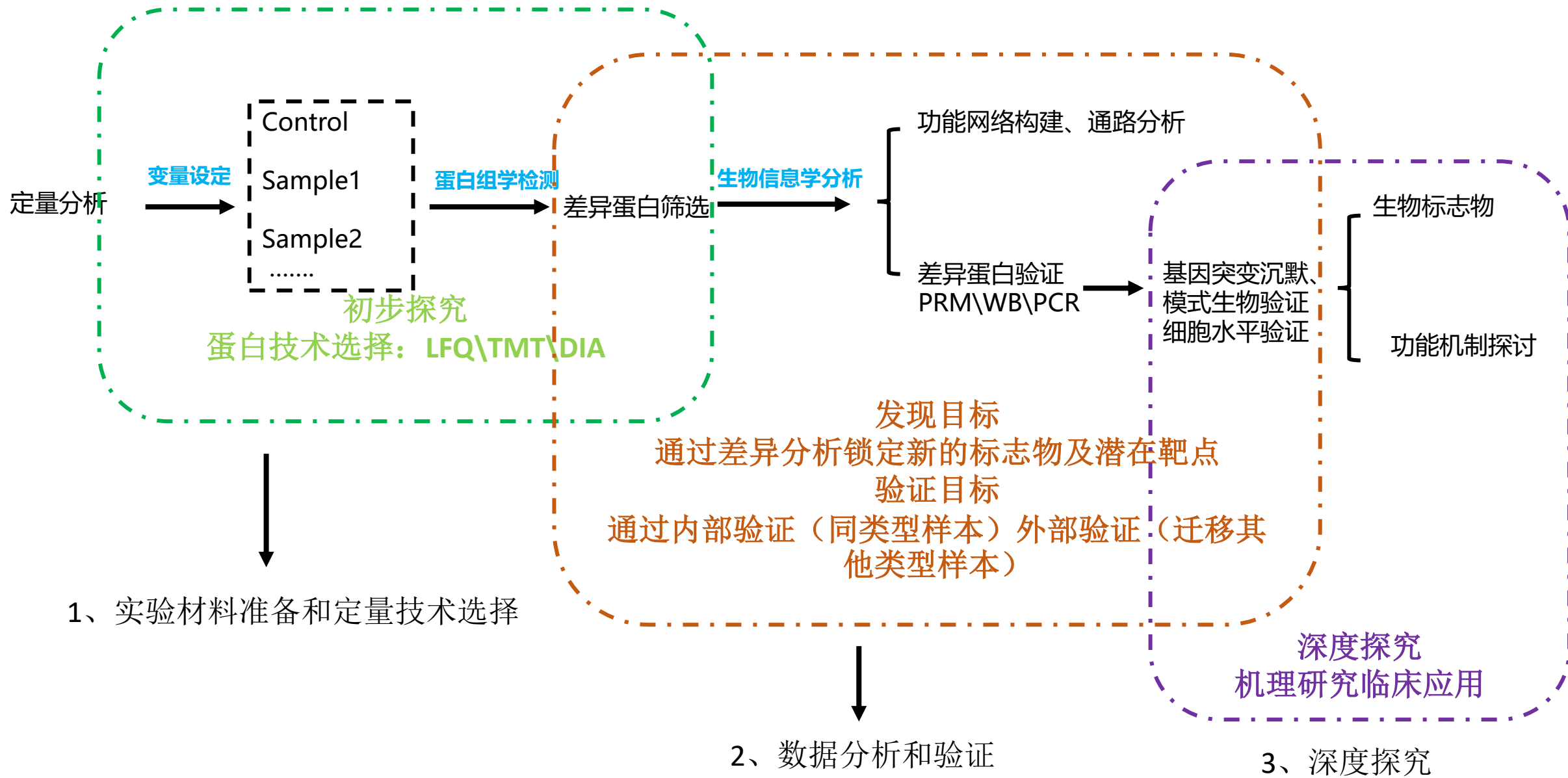
A Cell-Autonomous Signature of Dysregulated Protein Phosphorylation Underlies Muscle Insulin Resistance in Type 2 Diabetes

骨骼肌胰岛素抵抗在T2D的发生发展中具有重要作用，但其具体机制仍存在争议



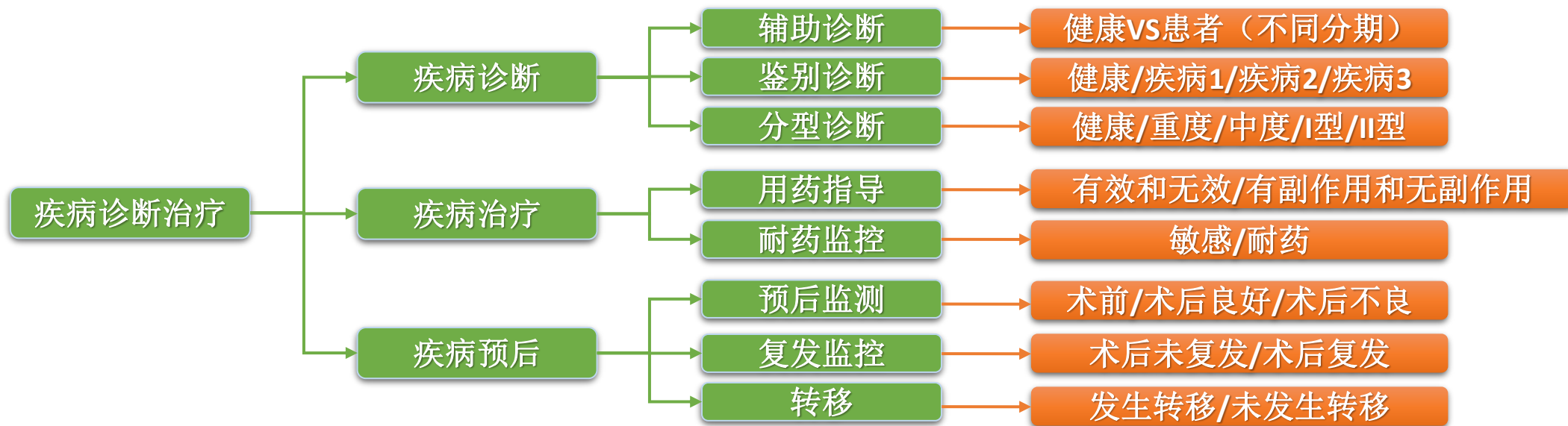
研究材料：健康对照（CTL，8人，4男4女）
 T2D患者（8人，4男4女）
 iPS细胞分化成的成肌细胞（iMyos）
 技术方法：磷酸化蛋白组学







组学类型	样本来源	样本数量	样本类型
蛋白组学	模式动物	3--10样本/组	体液类（血液、尿液、汗液、唾液、泪液等.....） 组织类（常规器官组织-心脏、肝脏、胃组织.....等） FFPE样本
	临床病人	>10样本/组	



感谢各位的聆听

Your own Laboratory

——您的专属实验室

