



## **Proposed Projects:** Identification of potential biomarkers for

- 1) pancreatic ductal adenocarcinoma
- 2) respiratory viral and bacterial infections

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# Identification of Biomarkers

mRNA, microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs)

1) Experimental Validation

2) High-throughput data analysis

- Identification of Differentially expressed genes (DEGs)
- Finding linear or non-linear relationships among genes expression
- Machine Learning



**Weighted Gene Co-Expression  
Network Analysis**

# Philosophy of Weighted Gene Co-Expression Network Analysis

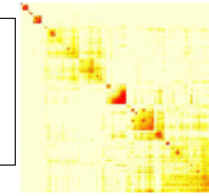
- Understand the “system” instead of reporting a list of individual parts
- Describe the functioning of the engine instead of enumerating individual nuts and bolts
- Focus on modules (clusters) as opposed to individual genes

# Weighted Gene Co-Expression Network Analysis

## Construct a gene co-expression network

**Rationale:** make use of interaction patterns among genes

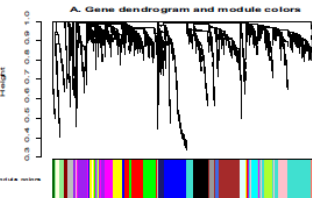
**Tools:** correlation as a measure of co-expression



## Identify modules

**Rationale:** module (pathway) based analysis

**Tools:** hierarchical clustering, Dynamic Tree Cut

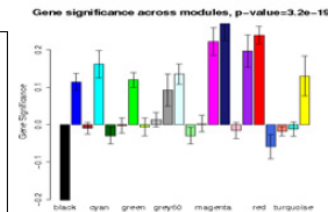


## Relate modules to external information

Array Information: clinical data, SNPs, proteomics

Gene Information: ontology, functional enrichment

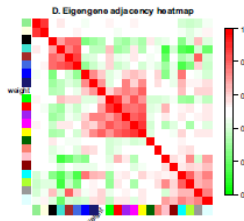
**Rationale:** find biologically interesting modules



## Study module relationships

**Rationale:** biological data reduction, systems-level view

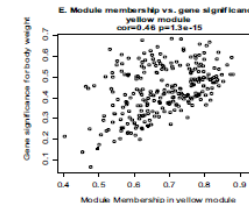
**Tools:** Eigengene Networks



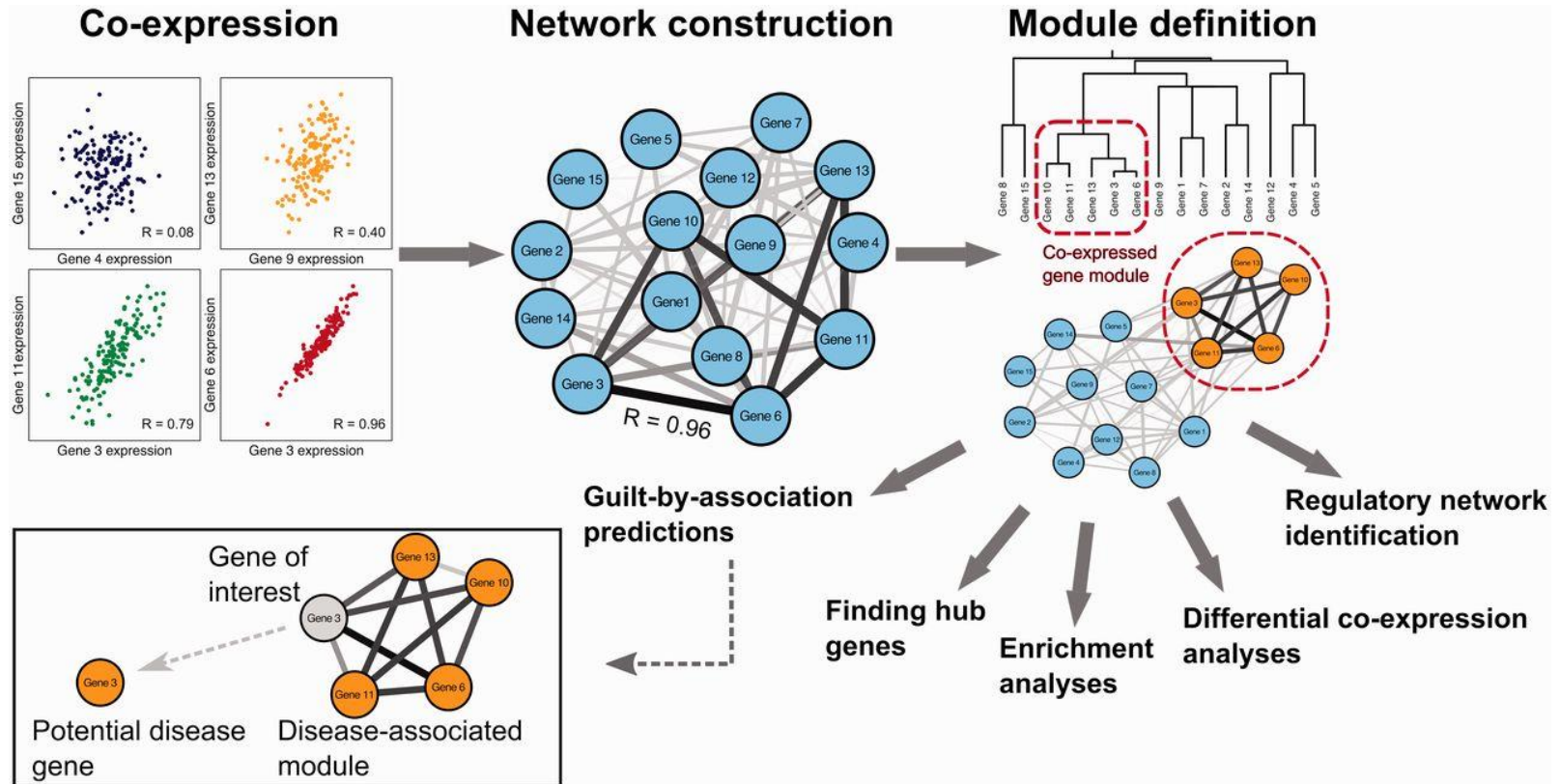
## Find the key drivers in interesting modules

**Rationale:** experimental validation, biomarkers

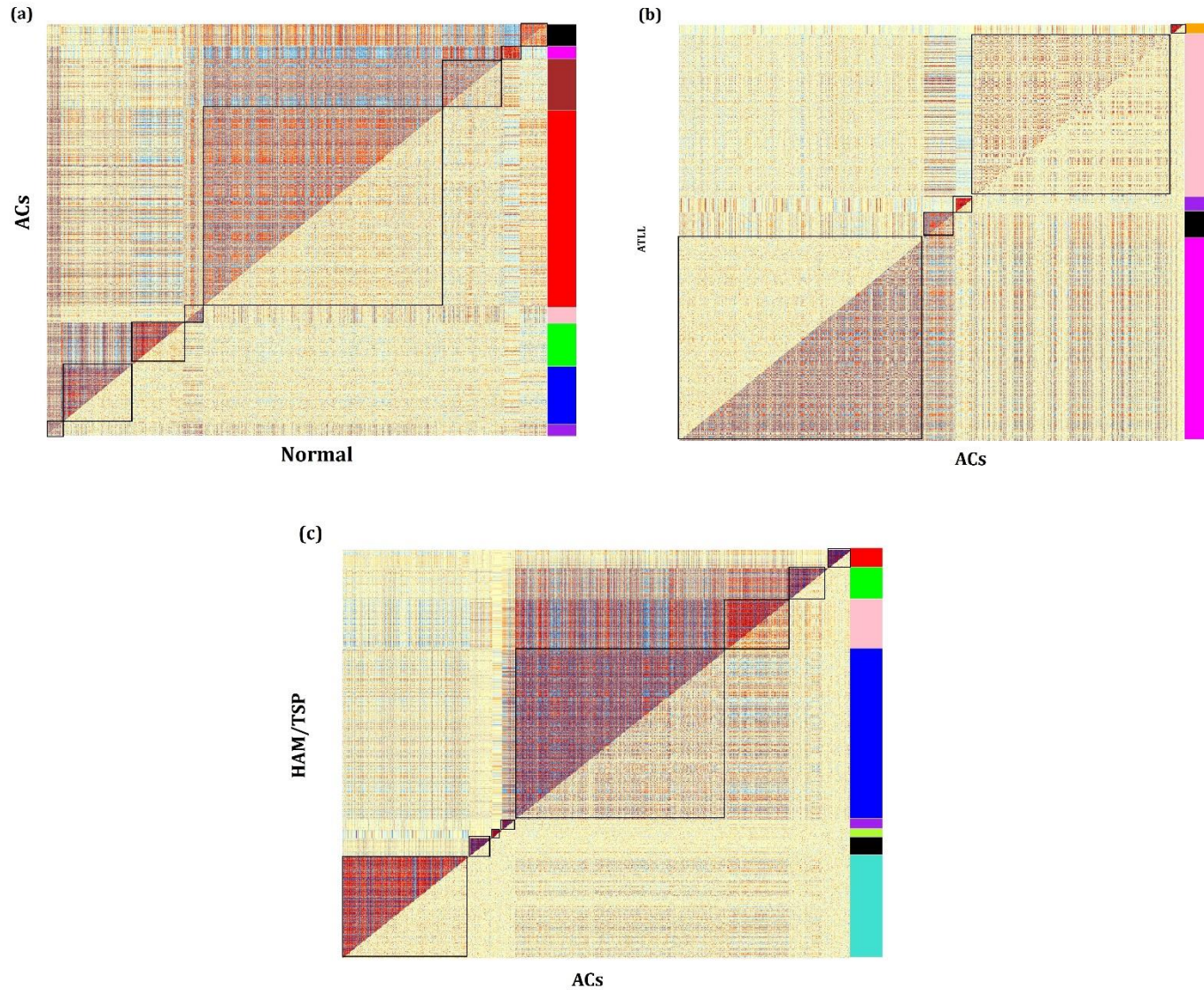
**Tools:** intramodular connectivity, causality testing



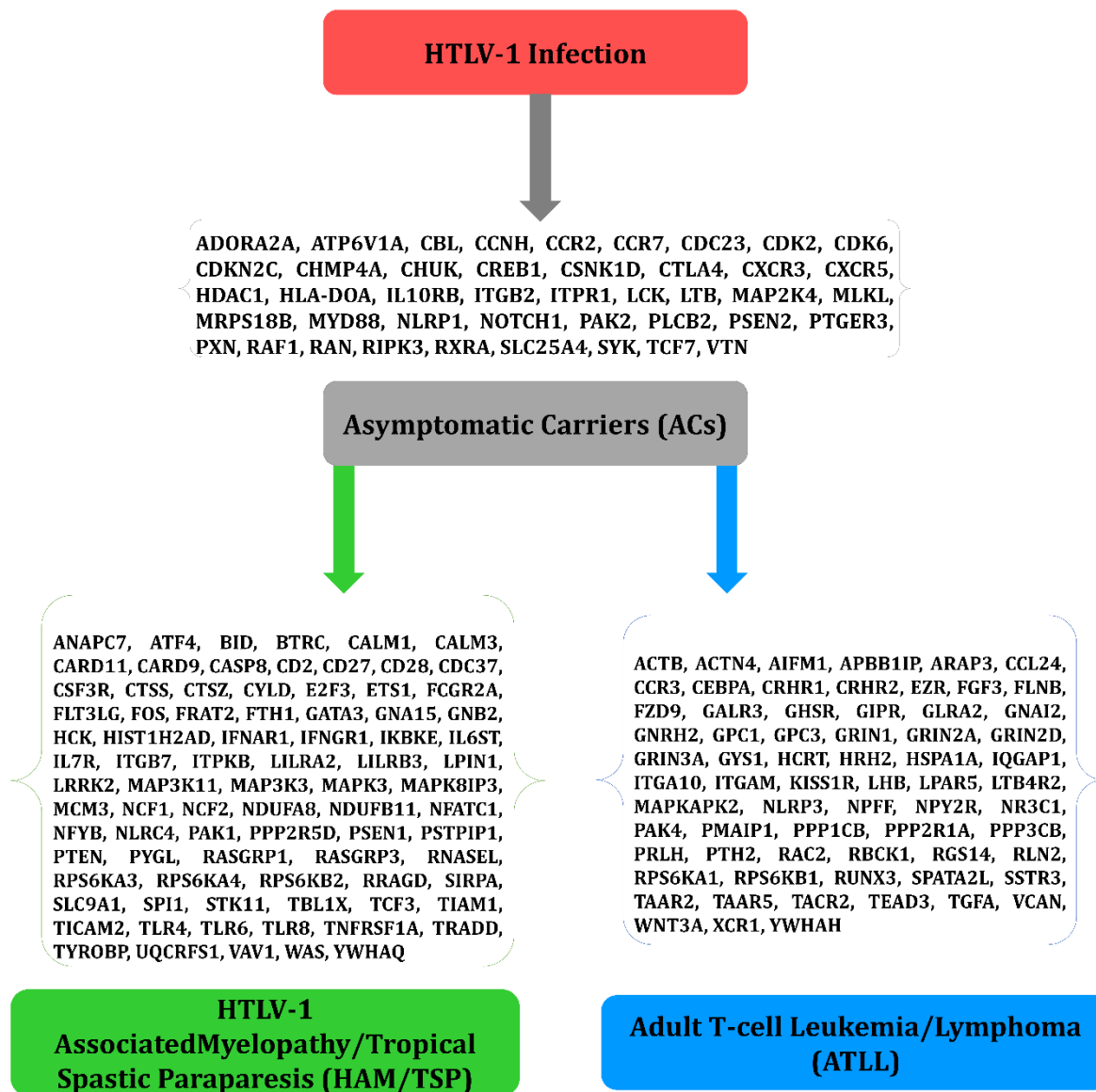
# Weighted Gene Co-Expression Network Analysis



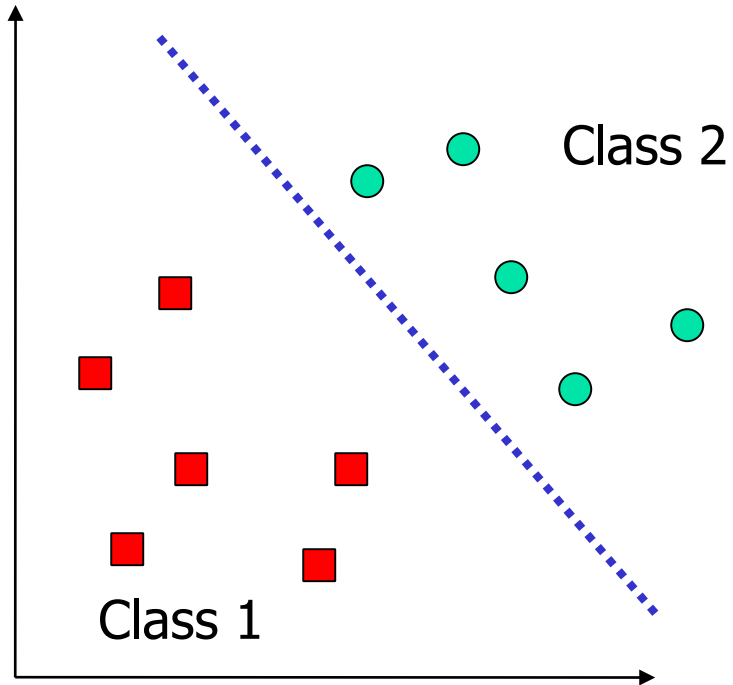
# Differentially co-expressed modules (DiffCoEx)



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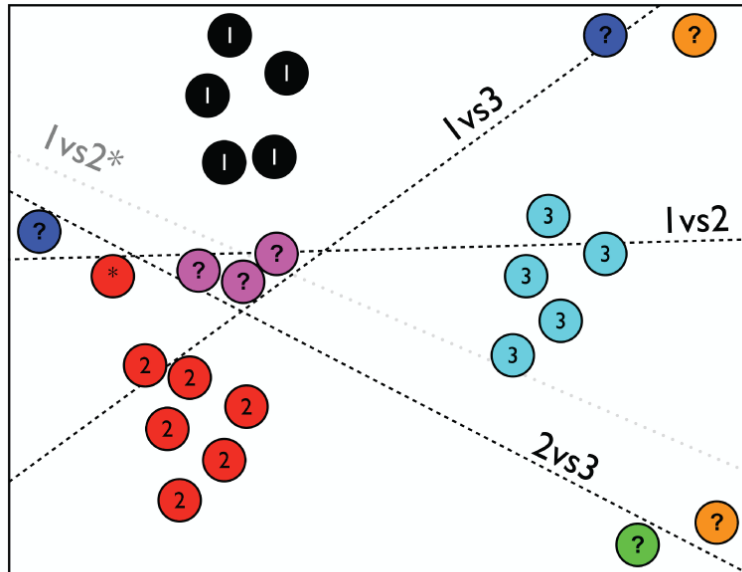


# Machine Learning: Classification

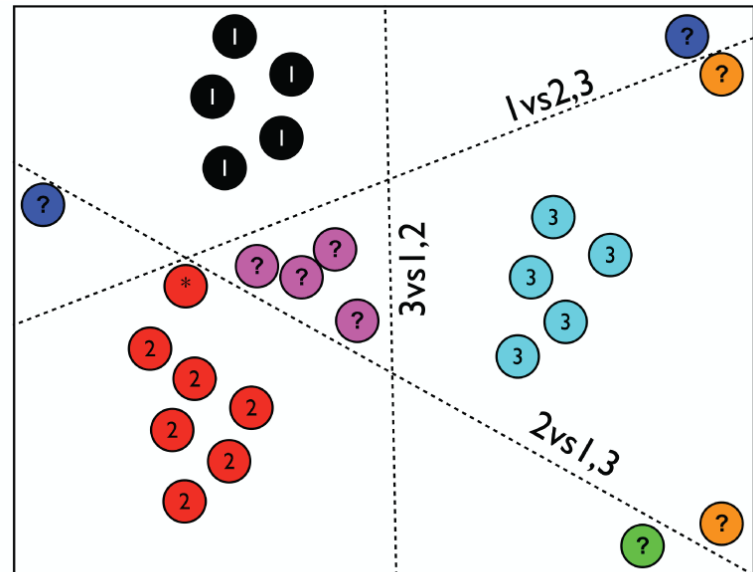




# Support Vector Machine (SVM): one-vs-one and one-vs-rest

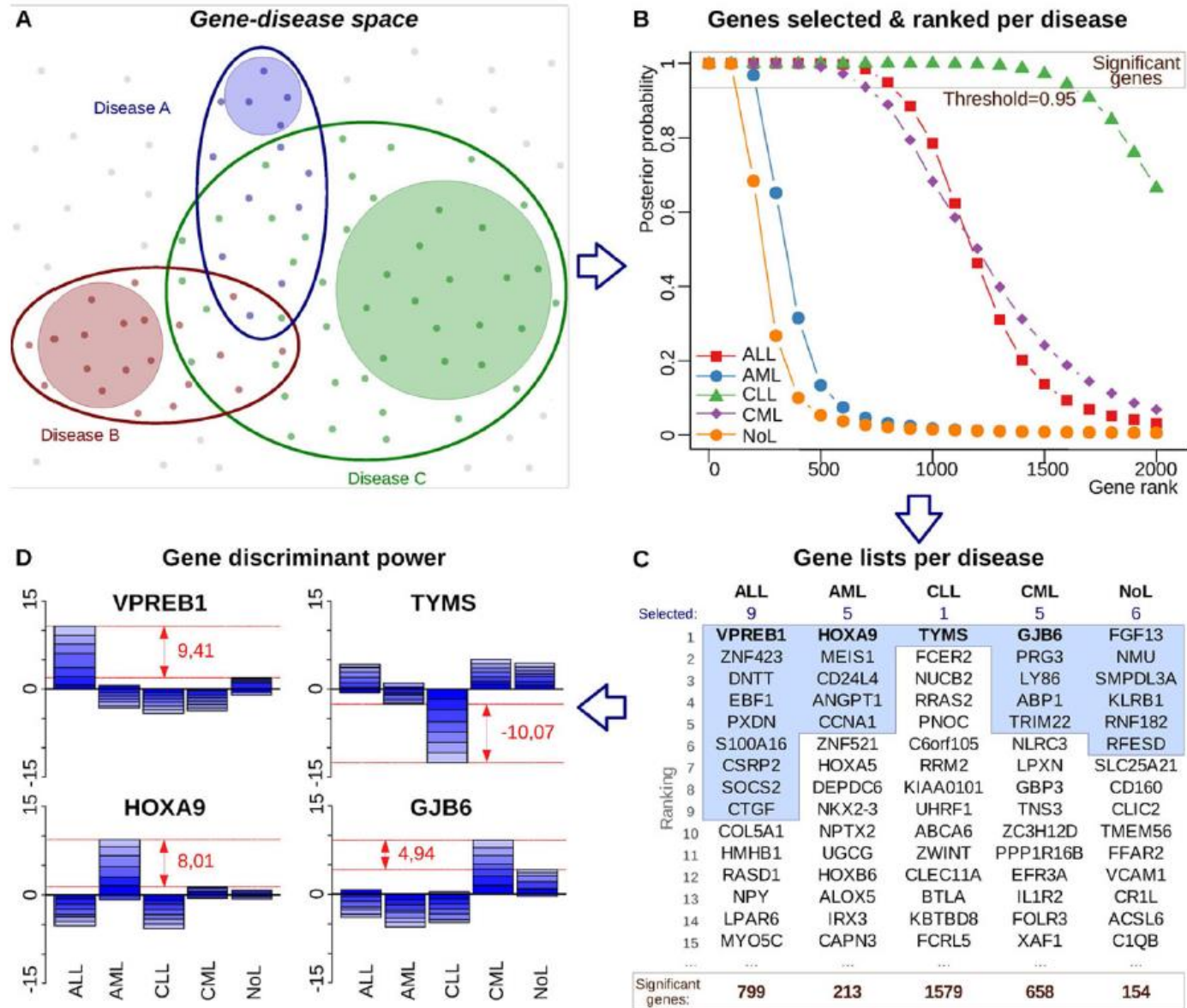


(a) 1-vs-1



(b) 1-vs-All

# Application of SVM in classification of diseases

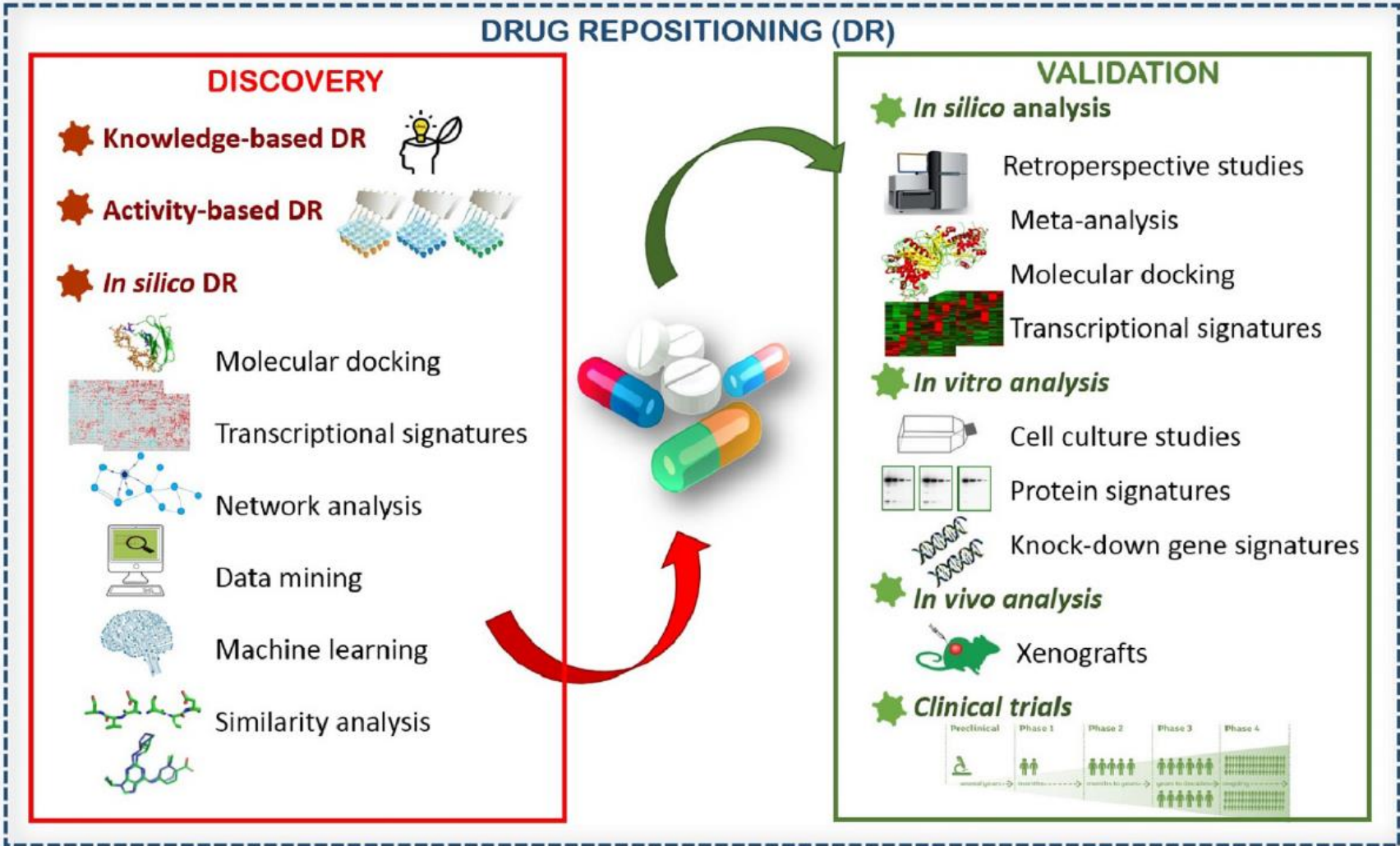


# Drug repurposing

Repurposing of a drug includes use of drugs approved by regulatory agencies such as the FDA, the European Medicines Agency (EMA), the Medicines and Healthcare Products Regulatory Agency (MHRA), among others, for a new indication.

Owing to immense promise of a shortened development cycle, many pharmaceutical companies are currently adopting drug repurposing to redevelop some of their FDA-approved and previously unsuccessful pipeline molecules as novel therapies for diverse disease conditions.

# Drug repurposing



# **Proposed Projects**

(Pancreatic ductal adenocarcinoma )



# Identifying potential prognostic biomarkers for pancreatic ductal adenocarcinoma

# Risk factors and biomarkers for early diagnosis of pancreatic ductal adenocarcinoma

## Conventional

- Carbohydrate antigen 19-9 (CA 19-9) is a Lewis antigen of the mucin 1 protein class (Limitations: CA 19-9 is elevated in patients with nonmalignant diseases, including liver cirrhosis, chronic pancreatitis (CP), cholangitis, and other cancers of the gastrointestinal system. Moreover, CA 19-9 is not expressed in Lewis blood-type-negative patients (approximately 5–10% of the population).
- CA-125, CA-242,  $\alpha$ -fetoprotein, and CEA), cytokines/chemokines (IL-2, IL-10, IL-13, and tumor necrosis factor- $\alpha$ )

# Problem

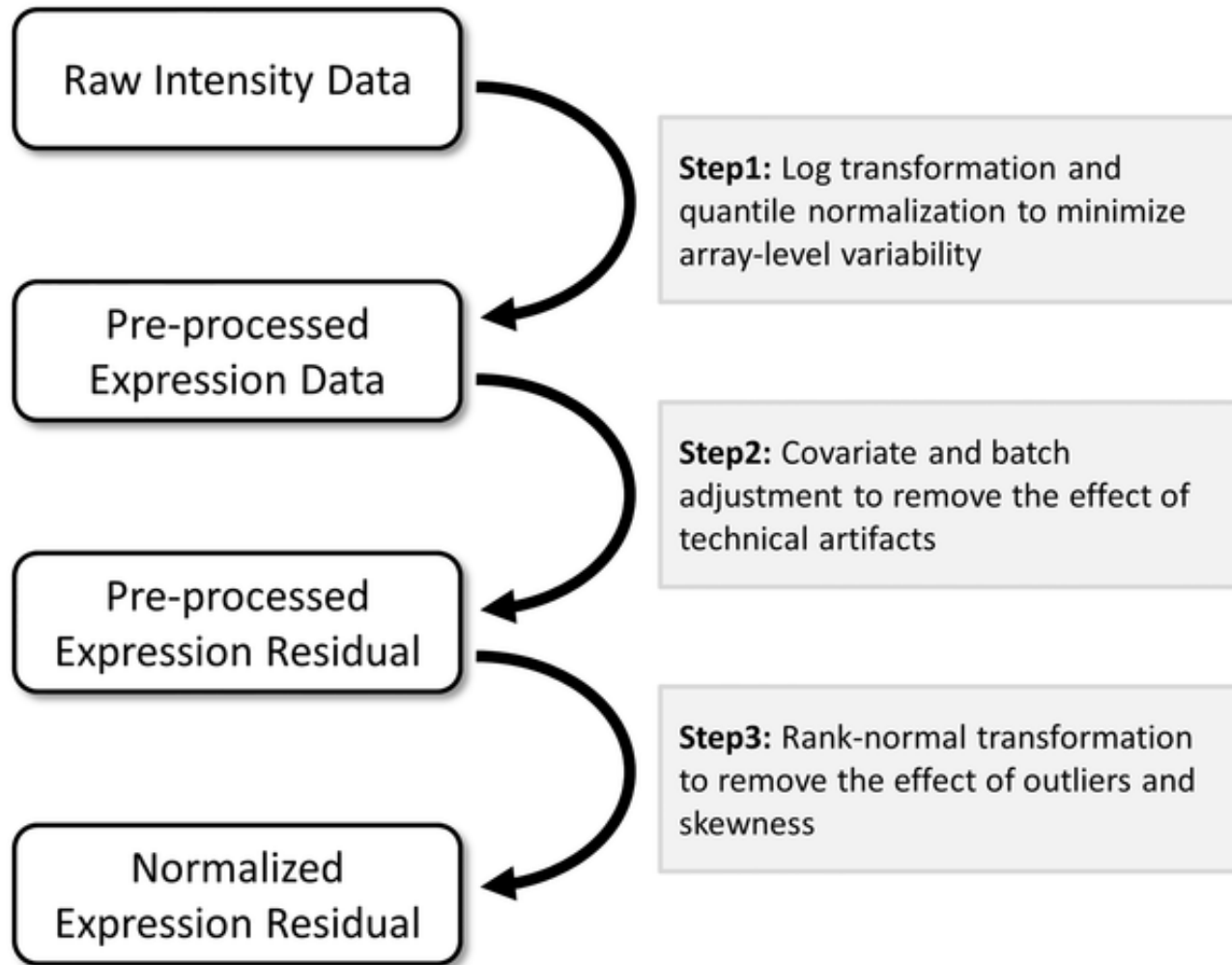
There is no promising and specific biomarkers for early diagnosis of pancreatic ductal adenocarcinoma



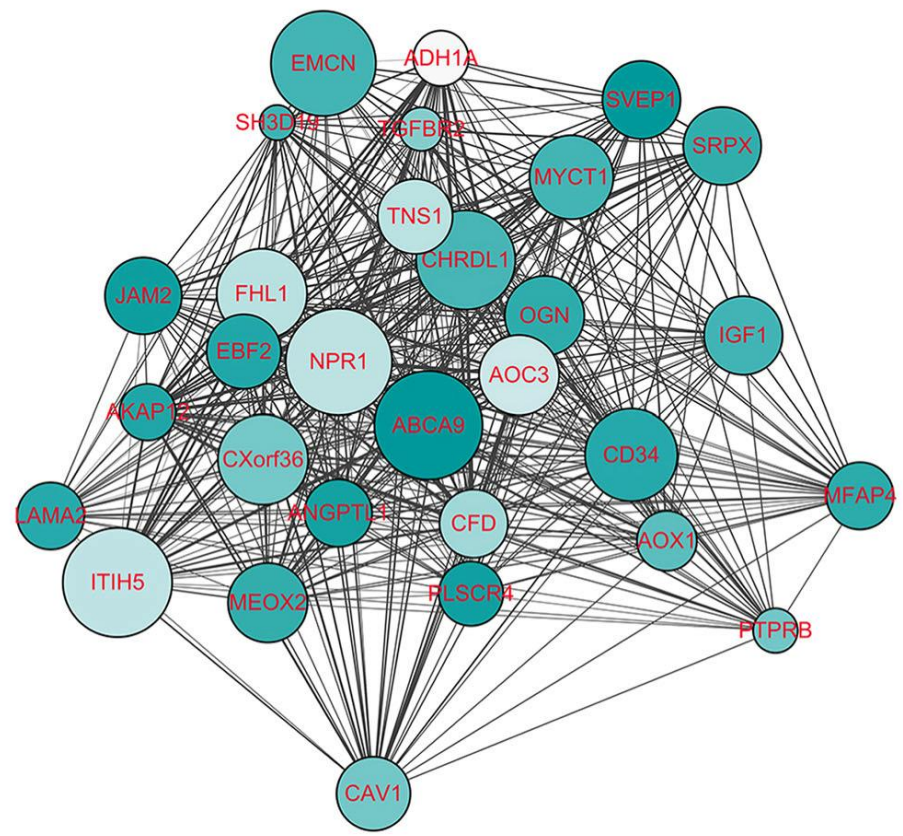
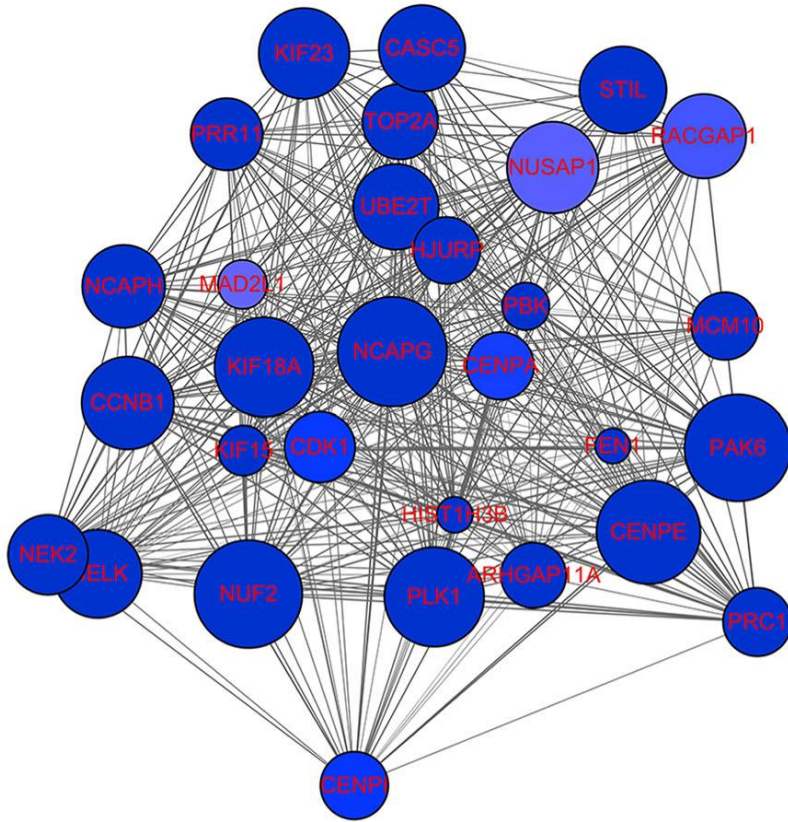
# Project

- 1) Exploring mRNA/non-coding datasets: Pancreatic ductal adenocarcinoma (different stages), cholangiocarcinoma, liver cirrhosis, chronic pancreatitis (CP), cholangitis, and colon cancer  
[Websites: [Gene expression omnibus](#) and [TCGA](#)]
- 2) Finding discriminant mRNA/non-coding panels for each disease using co-expression, differential coexpression and machine learning methods
- 3) Proposing promising biomarkers for pancreatic ductal adenocarcinoma

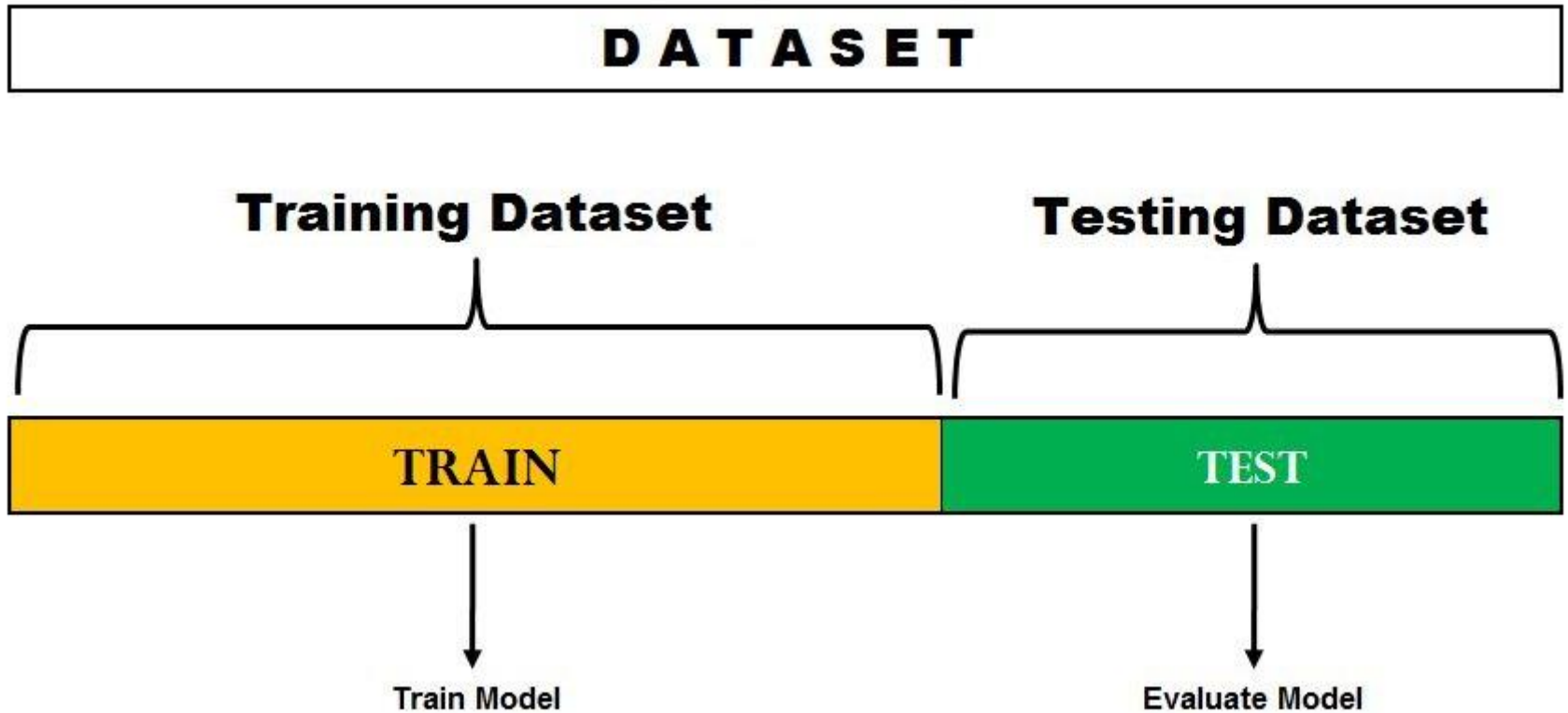
## Data pre-processing and normalization



# Finding specific and common panels by DiffCoEx and SVM



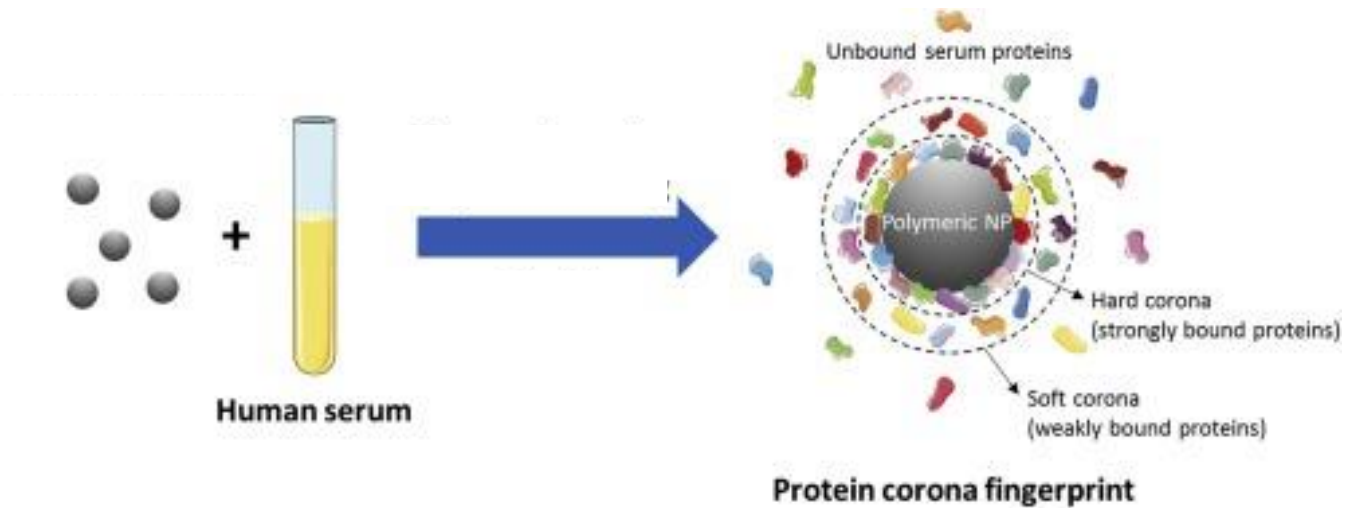
# Validation of results by external datasets



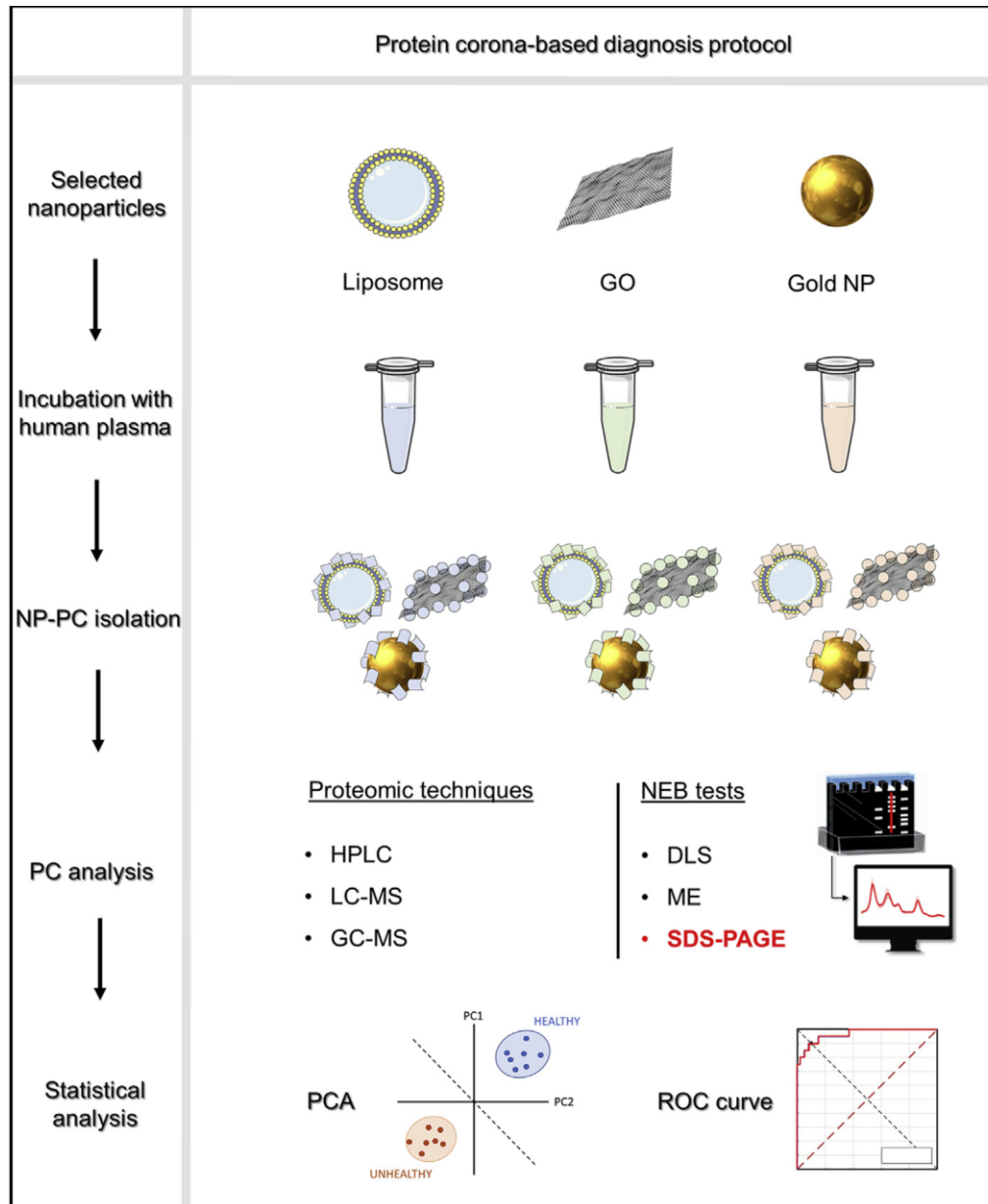


# Protein corona-enabled blood test for early detection of pancreatic ductal adenocarcinoma

# Protein corona



# Protein corona

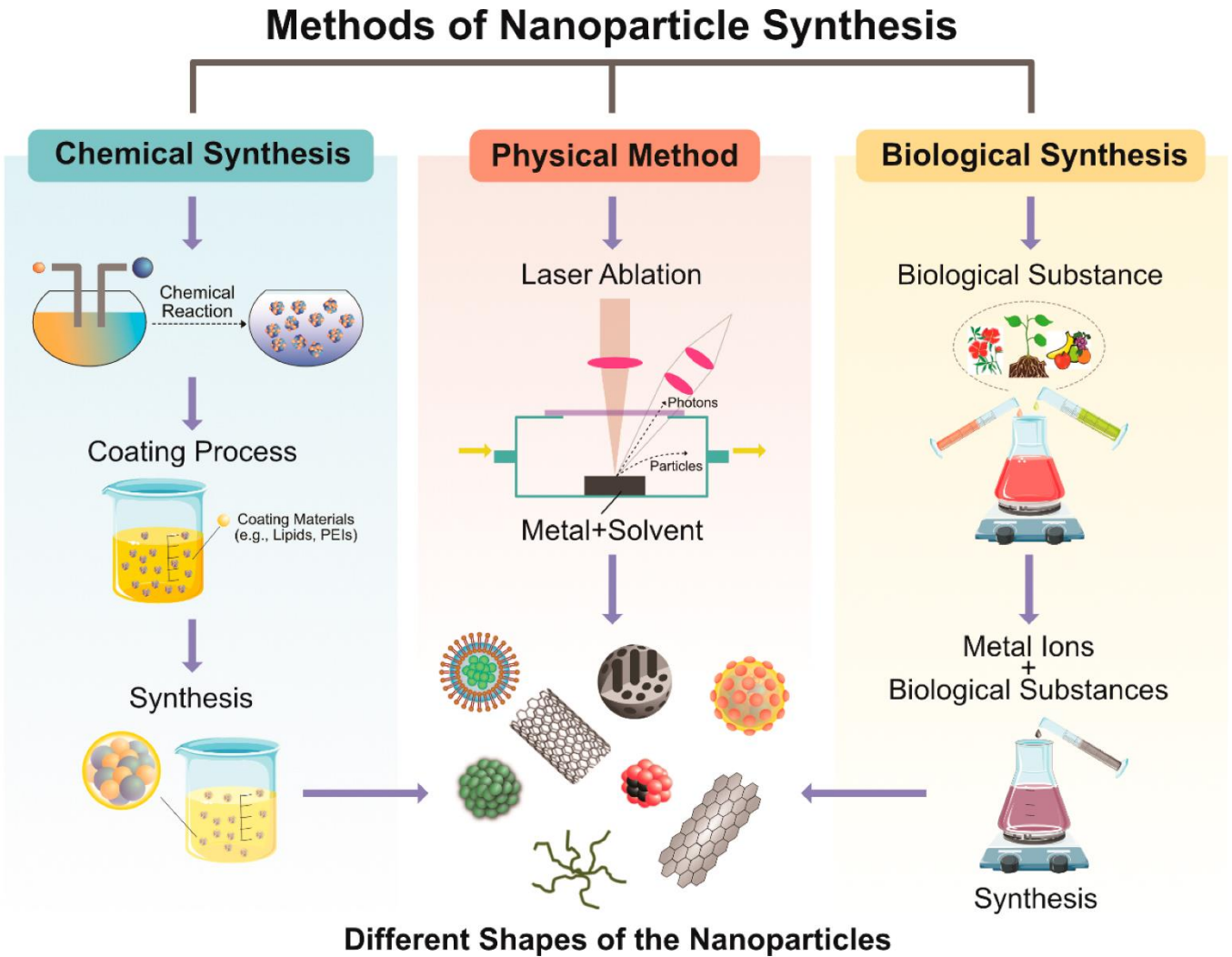


1) Collecting patient samples: Pancreatic ductal adenocarcinoma (different stages), cholangiocarcinoma, liver cirrhosis, chronic pancreatitis (CP), cholangitis, and colon cancer

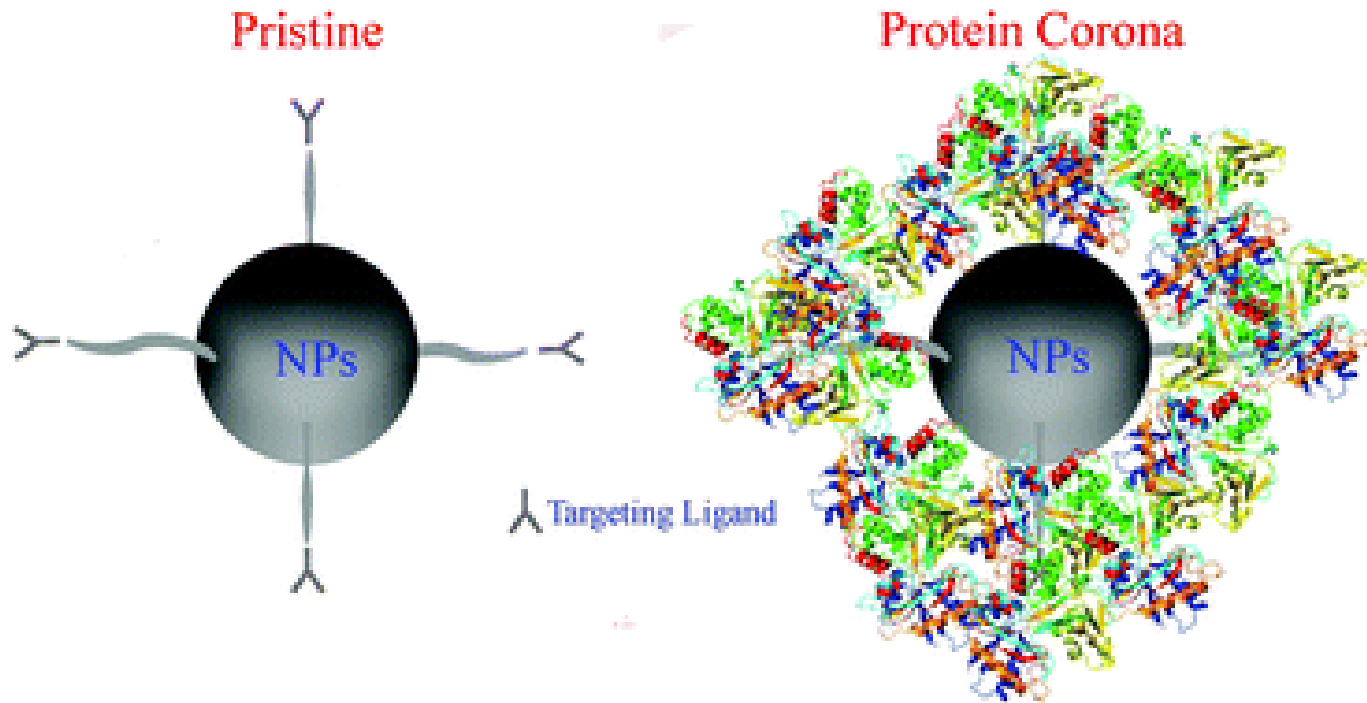




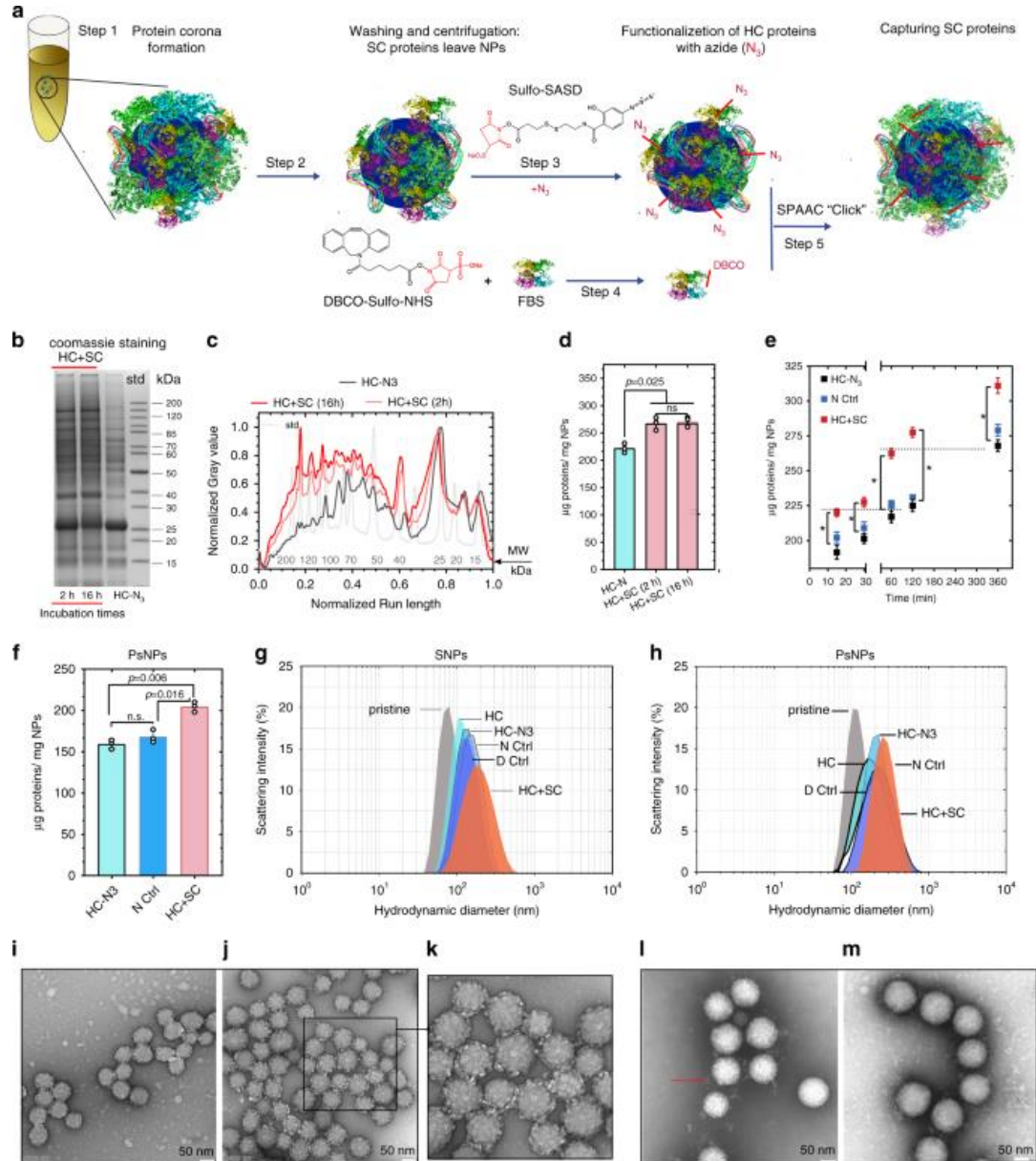
# 2) Synthesis of various nanoparticles (AuNPs capped by polymers, Carbon-based nanoparticles, liposomes nanoparticles)



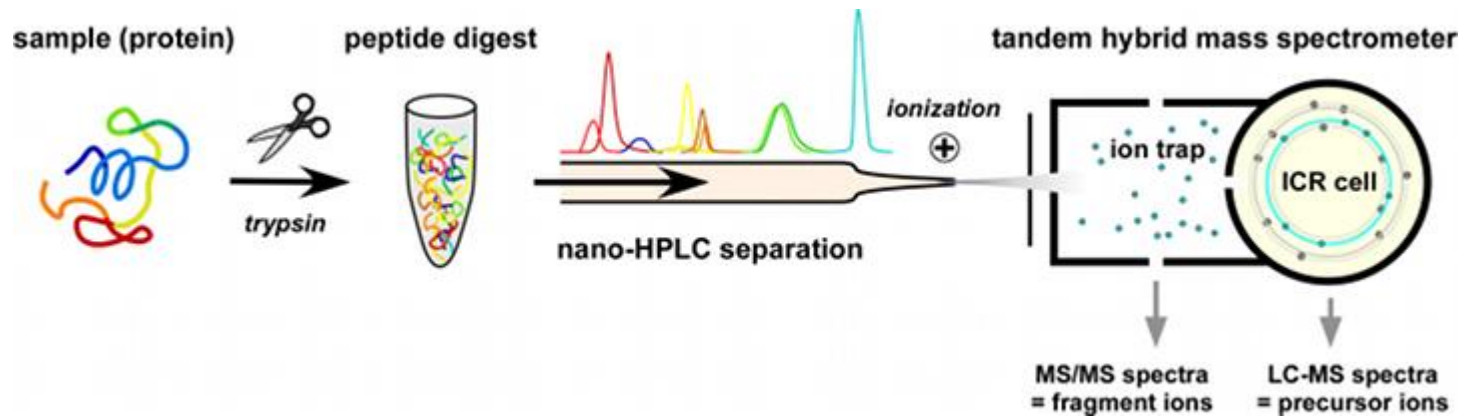
### 3) Constitution of protein corona on the nanoparticle's surface



# 4) Characterization of protein coronas by TEM, DLS, and 1-dimensional (1D) SDS-PAGE

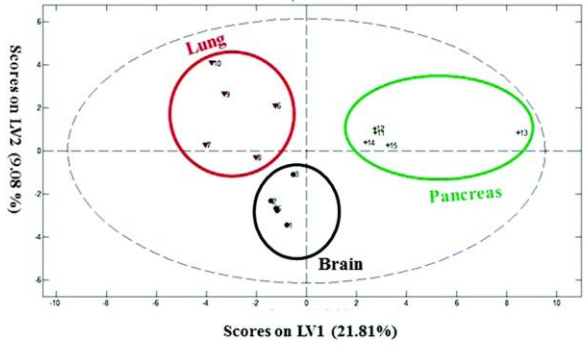


## 5) Determining proteins by nanoLC/MS/MS

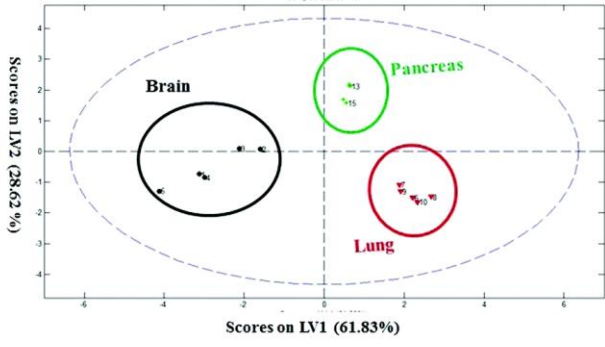


6) Construction of proper model to discriminate between control and various diseases and finding promising protein biomarkers

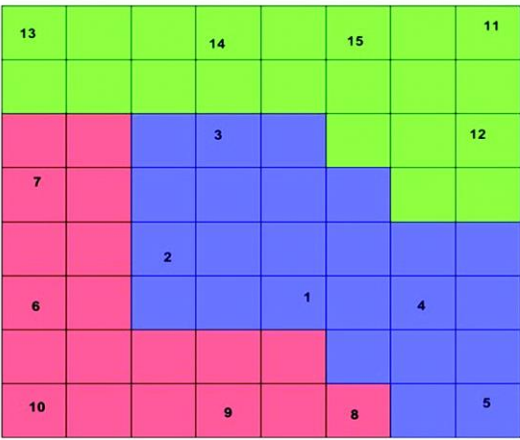
**A**



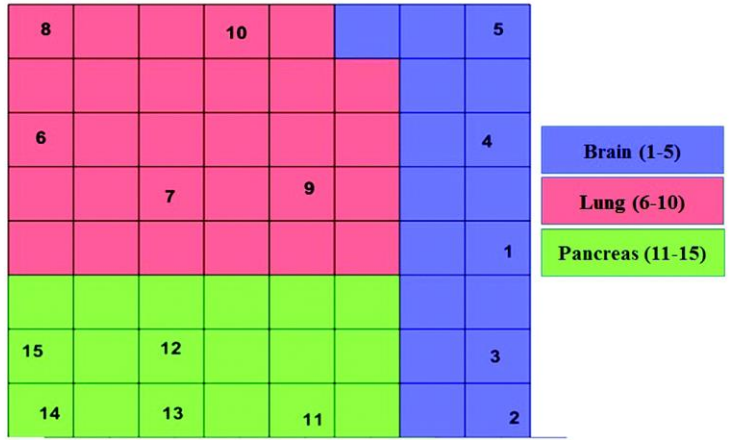
**B**



**C**



**D**





# Classification of respiratory viral and bacterial infections: insight into similarities and differences

Respiratory tract infections caused 3.2 million deaths worldwide and 164 million disability-adjusted life years lost.

Improved diagnostics for acute infections could decrease morbidity and mortality by increasing early antibiotics for patients with bacterial infections and reducing unnecessary antibiotics for patients without bacterial infections. The mortality rate of bacterial sepsis increases by 8% for each hour by which antibiotics are delayed.

Indiscriminate prescription of antibiotics to patients without bacterial infections increases rates of morbidity and antimicrobial resistance. The rate of inappropriate antibiotic prescriptions in the hospital setting is estimated at 30 to 50% and would be decreased by improved diagnostics.



Fridkin, S., et al. (2014). Vital signs: improving antibiotic use among hospitalized patients. *MMWR. Morbidity and mortality weekly report*, 63(9), 194.

Grijalva, C. G., et al. (2009). Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *Jama*, 302(7), 758-766.

# Problem

There is currently no gold standard point-of-care diagnostic that can broadly determine the presence and type of infection. Thus, the White House has established the *National Action Plan for Combating Antibiotic-Resistant Bacteria*, which called for “point-of-need diagnostic tests to distinguish rapidly between bacterial and viral infections”.



# Proposed Project

# 1) Collecting datasets related to respiratory viral and bacteria infection from Gene Expression Omnibus (GEO) and ArrayExpress)

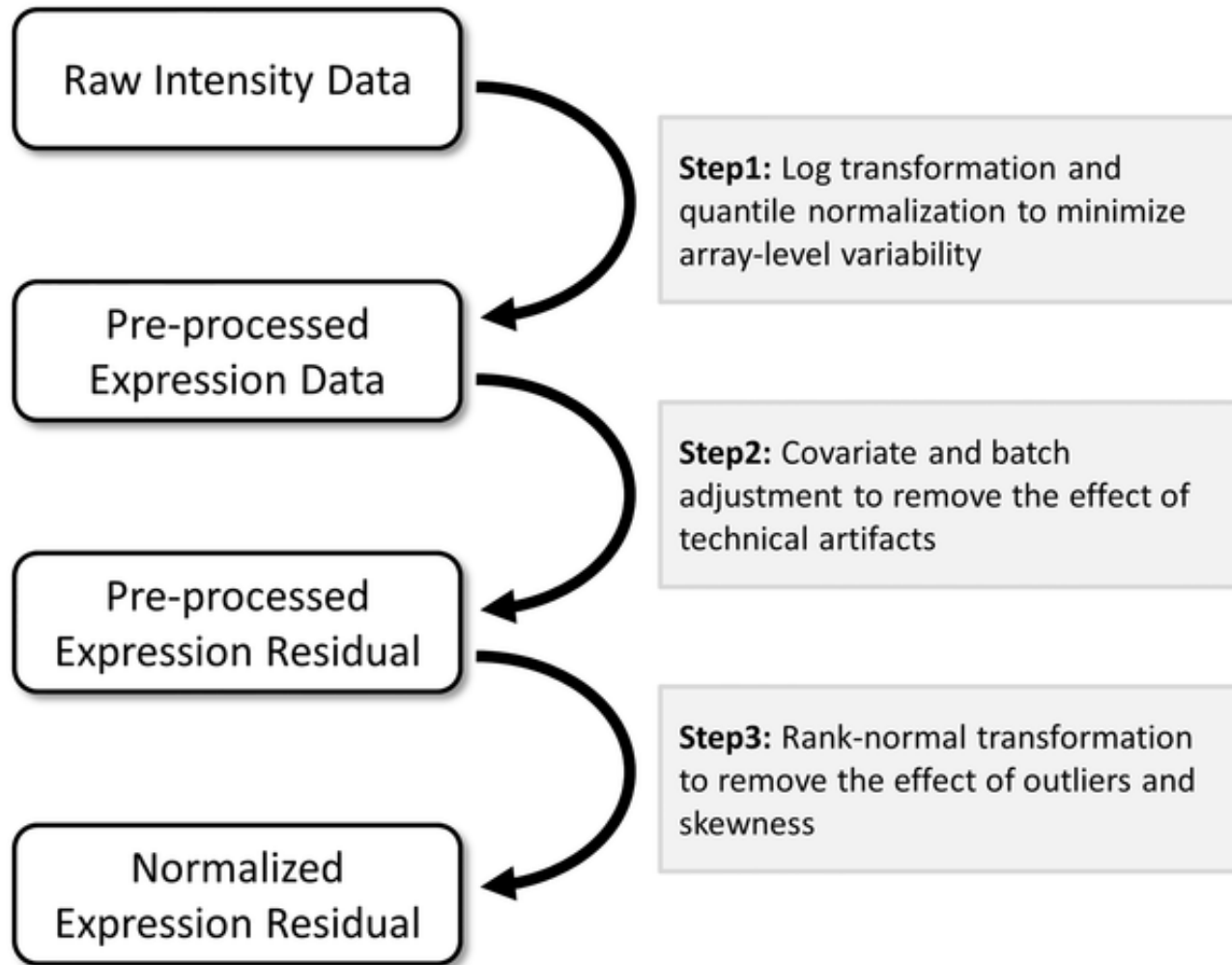
## Human respiratory viruses

- Respiratory Syncytial Virus (RSV)
- Rhinovirus (RV)
- Adenovirus (ADV)
- influenza virus (types B and A)
- Bocavirus (BoV)
- Enterovirus (EV)
- Parainfluenza virus (PIV)
- Metapneumovirus (MPV)
- Middle East respiratory syndrome (MERS)
- Severe Acute Respiratory Syndrome  
Coronavirus 2 (SARS-CoV-2)
- Severe Acute Respiratory Syndrome  
Coronavirus (SARS-CoV)

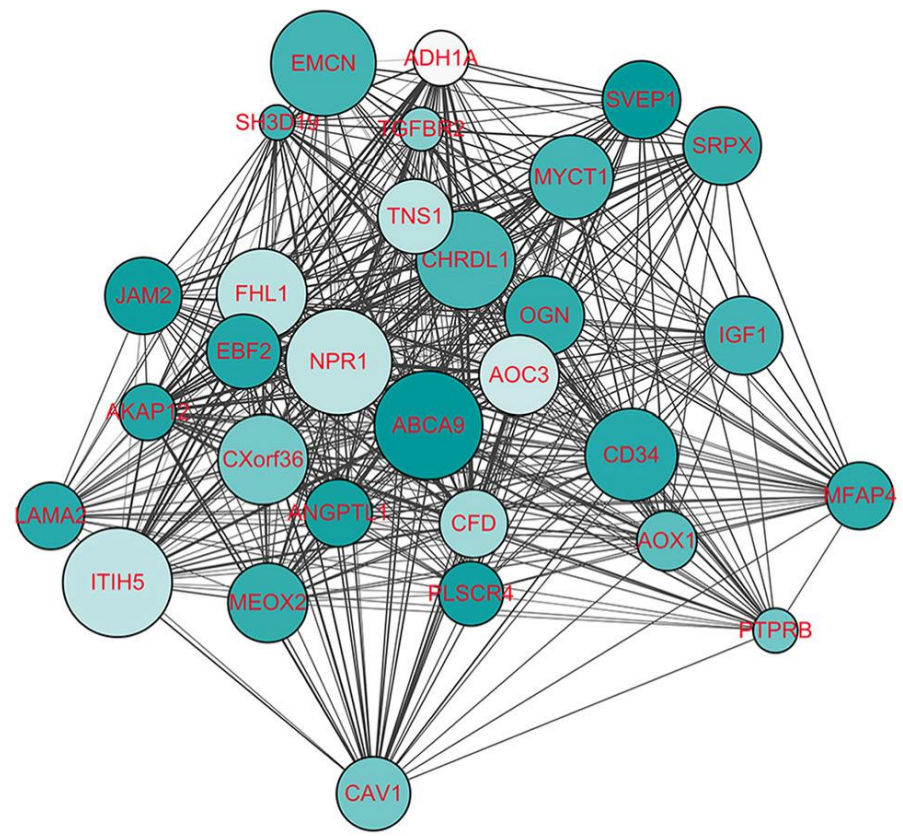
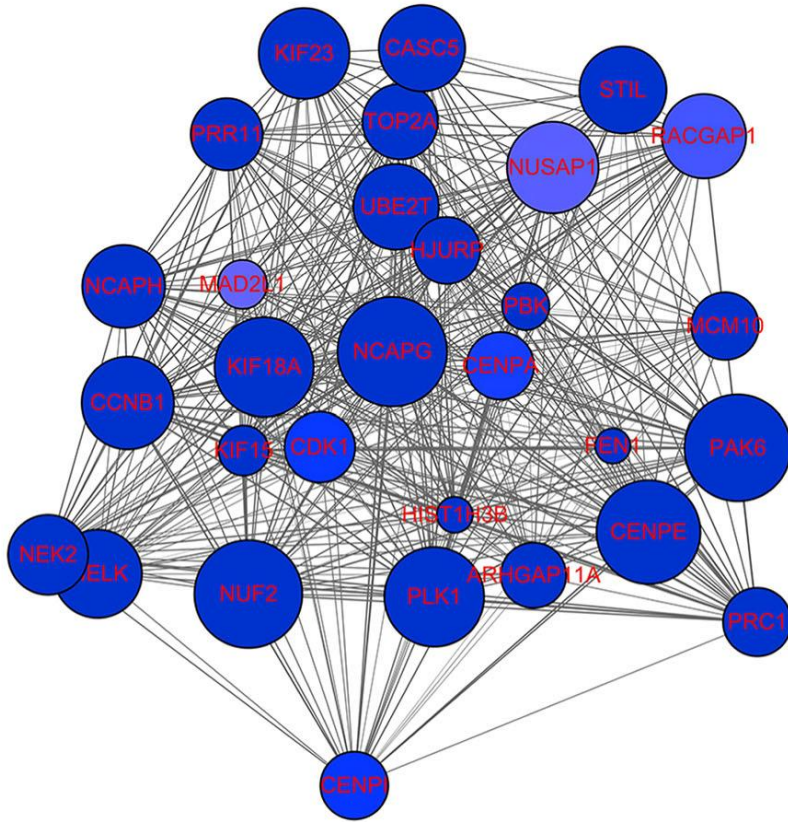
## Human respiratory bacteria

- Streptococcus pneumoniae (pneumococcus)
- streptococcal pharyngitis
- Haemophilus influenza
- Moraxella catarrhalis
- Staphylococcus aureus
- Mycoplasma pneumonia
- Chlamydophila pneumonia
- Chlamydophila psittaci
- Chlamydia trachomatis
- Klebsiella pneumonia
- Staphylococcus aureus
- Pseudomonas aeruginosa
- Mycobacterium tuberculosis
- Bordetella pertussis
- Legionella pneumophila

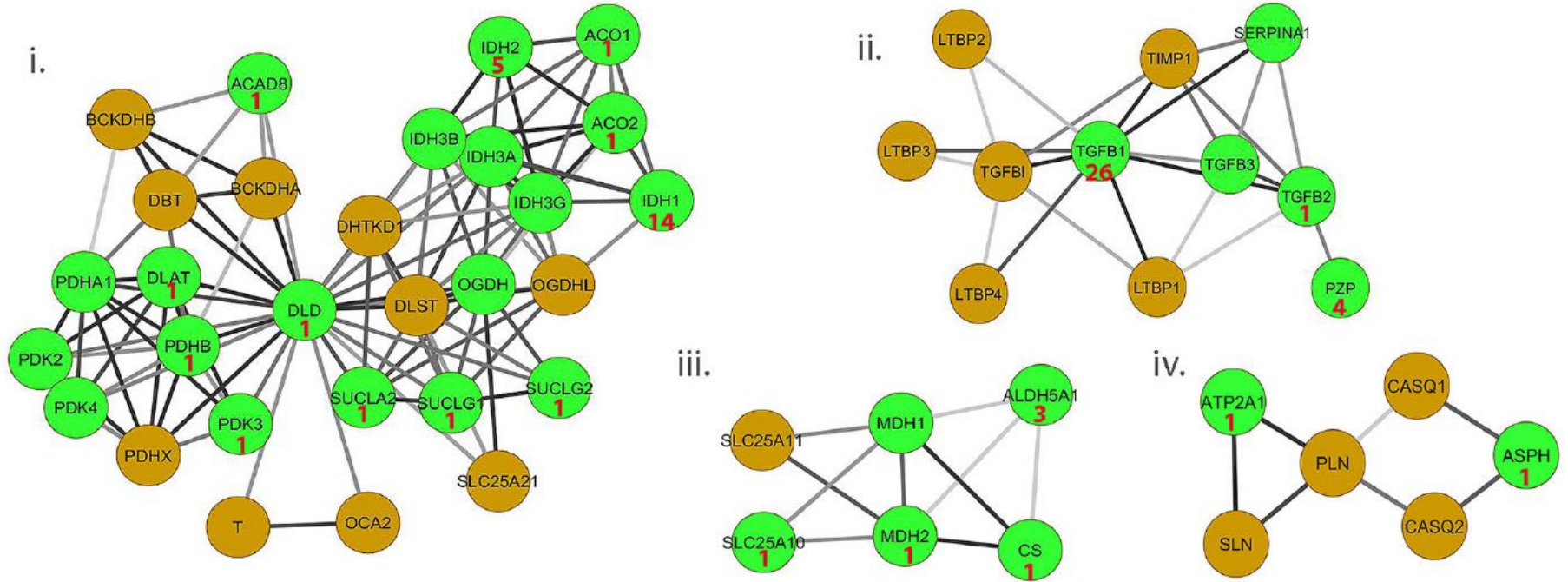
## 2) Data pre-processing and normalization



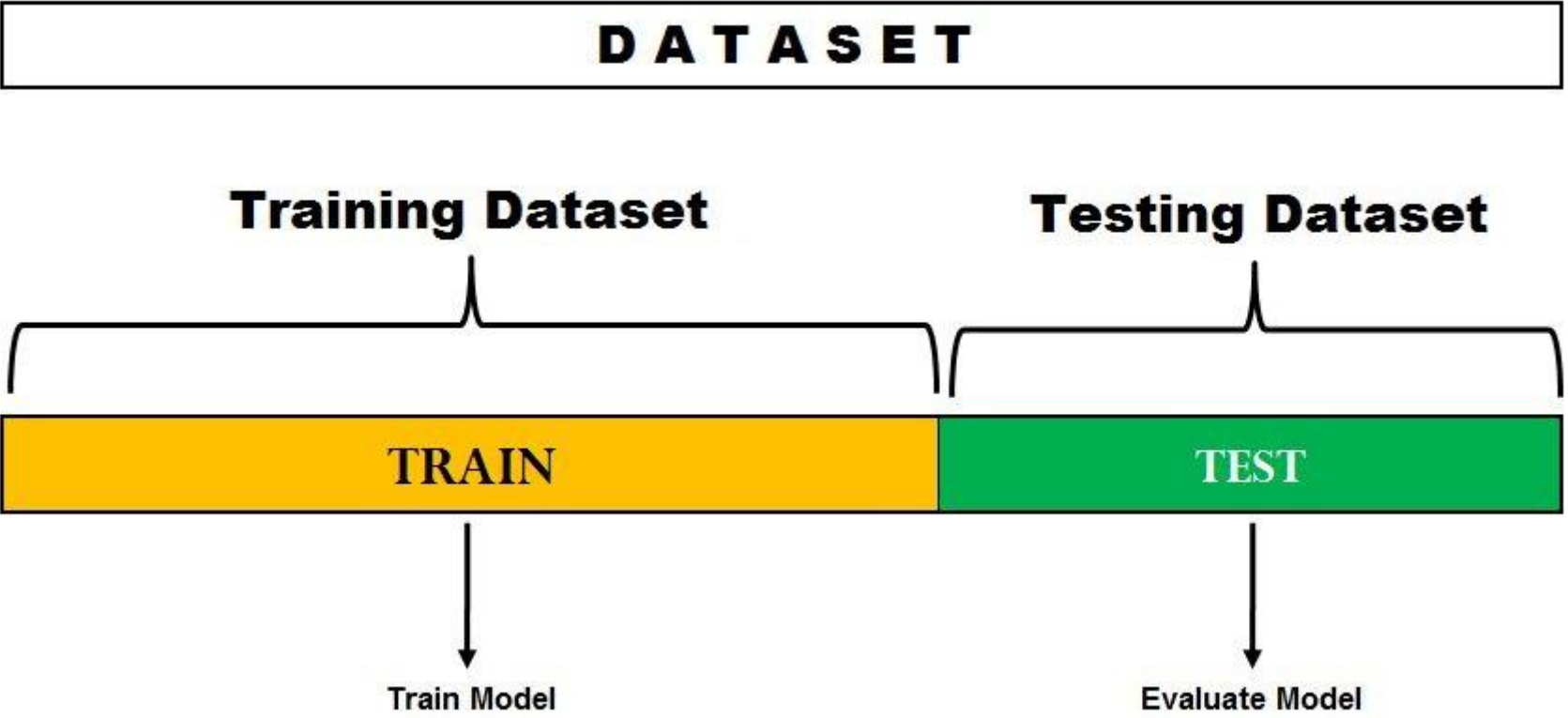
### 3) Classification of viral and bacteria infection by DiffCoex and SVM: Finding specific and common genes



# 4) Classification of viral and bacteria infection, individually based on specific gene patterns

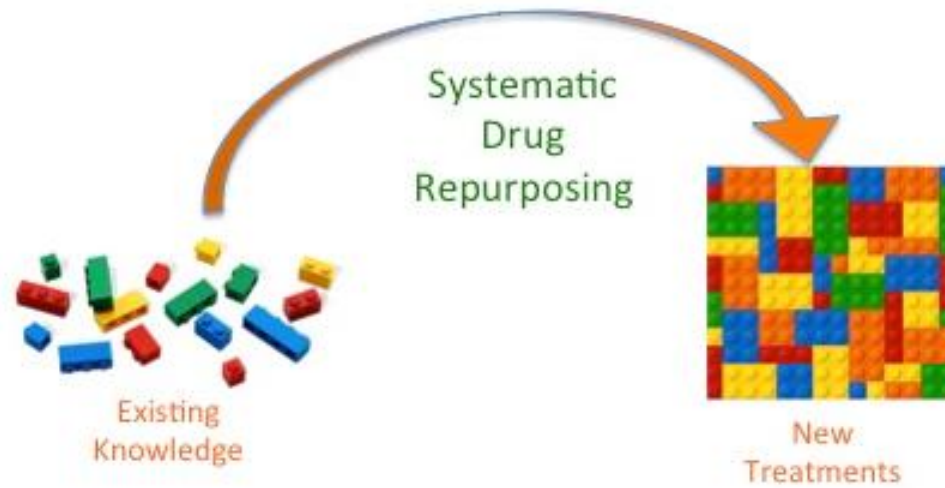


# 5) Validation of results by external datasets





## 7) Drug repurposing





**Thank you for your attention**