CLINICAL METAPROTEOMICS WORKFLOW TO STUDY HOST-MICROBIOME DYNAMICS

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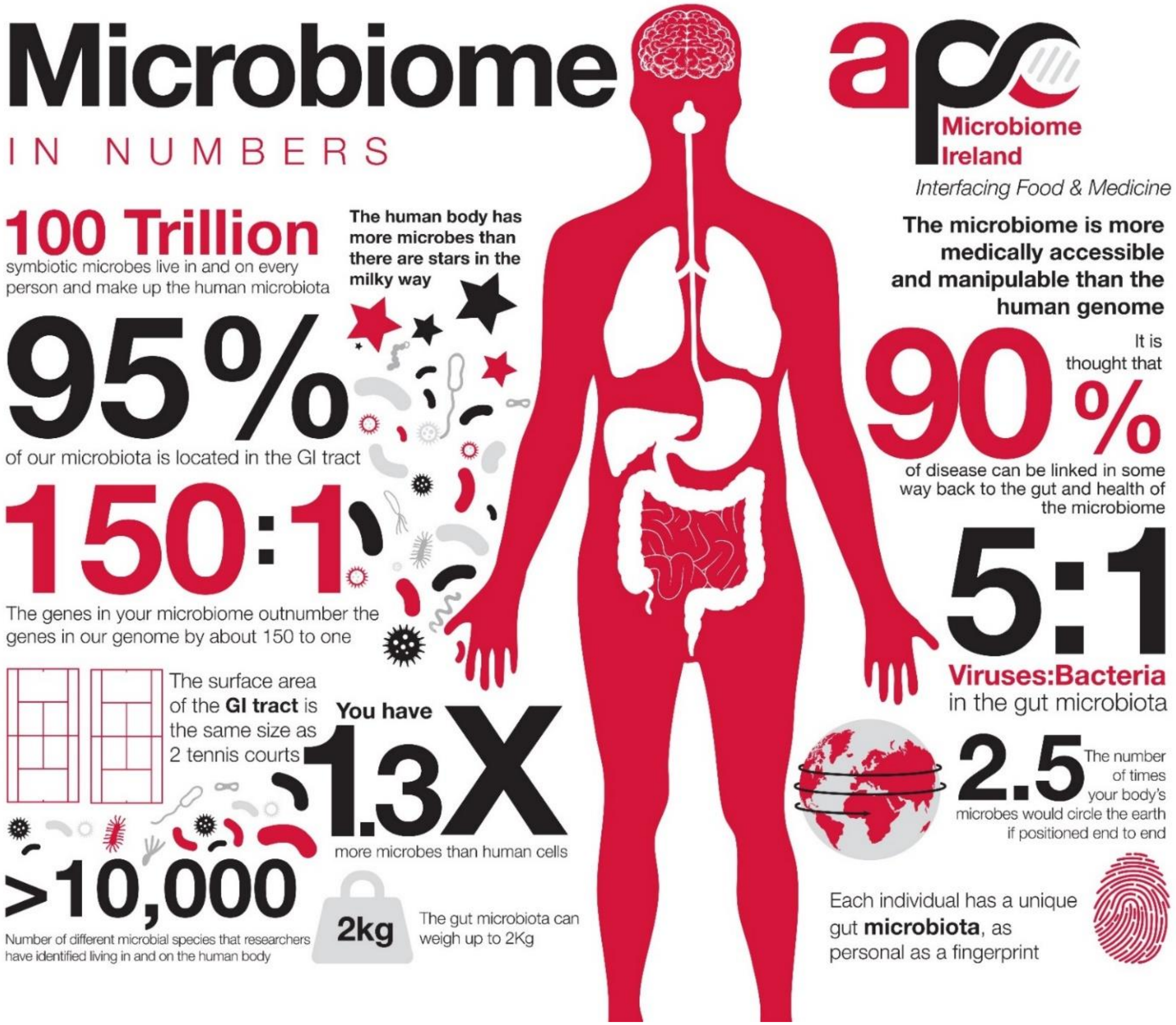
CLINICAL METAPROTEOMICS WORKFLOW TO STUDY HOST-MICROBIOME DYNAMICS

- ***MICROBIOME RESEARCH***
- ***METAPROTEOMICS RESEARCH***
- ***CLINICAL METAPROTEOMICS WORKFLOW***
- ***CLINICAL METAPROTEOMICS:COVID-19 PANDEMIC***
- ***CLINICAL METAPROTEOMICS:CYSTIC FIBROSIS***
- ***CLINICAL METAPROTEOMICS: OVARIAN CANCER***

MICROBIOME RESEARCH



Microbiome
IN NUMBERS

apc Microbiome Ireland
Interfacing Food & Medicine

100 Trillion symbiotic microbes live in and on every person and make up the human microbiota

The human body has more microbes than there are stars in the milky way

95% of our microbiota is located in the GI tract

150:1 The genes in your microbiome outnumber the genes in our genome by about 150 to one

The surface area of the **GI tract** is the same size as 2 tennis courts

You have 1.3X more microbes than human cells

>10,000 Number of different microbial species that researchers have identified living in and on the human body

2kg The gut microbiota can weigh up to 2Kg

The microbiome is more medically accessible and manipulable than the human genome

It is thought that **90%** of disease can be linked in some way back to the gut and health of the microbiome

5:1 **Viruses:Bacteria** in the gut microbiota

2.5 The number of times your body's microbes would circle the earth if positioned end to end

Each individual has a unique gut **microbiota**, as personal as a fingerprint

https://worldmicrobiomeday.com/resources/

MICROBIOME

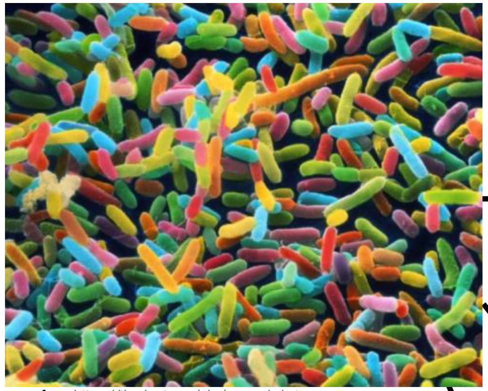


Image from https://thedoctorweighsin.com/what-everyone-should-know-about-the-infant-microbiome/

Potential to unravel the **mechanistic details of microbial interactions with host / environment** by analyzing the **functional dynamics of the microbiome.**

METAGENOMICS

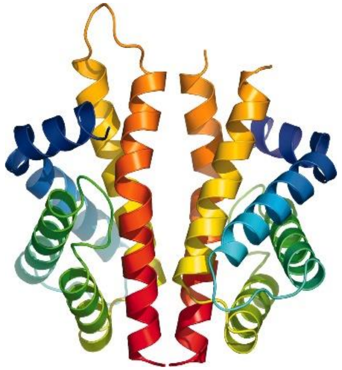
TAXONOMY

function

METATRANSCRIPTOMICS

TAXONOMY

function

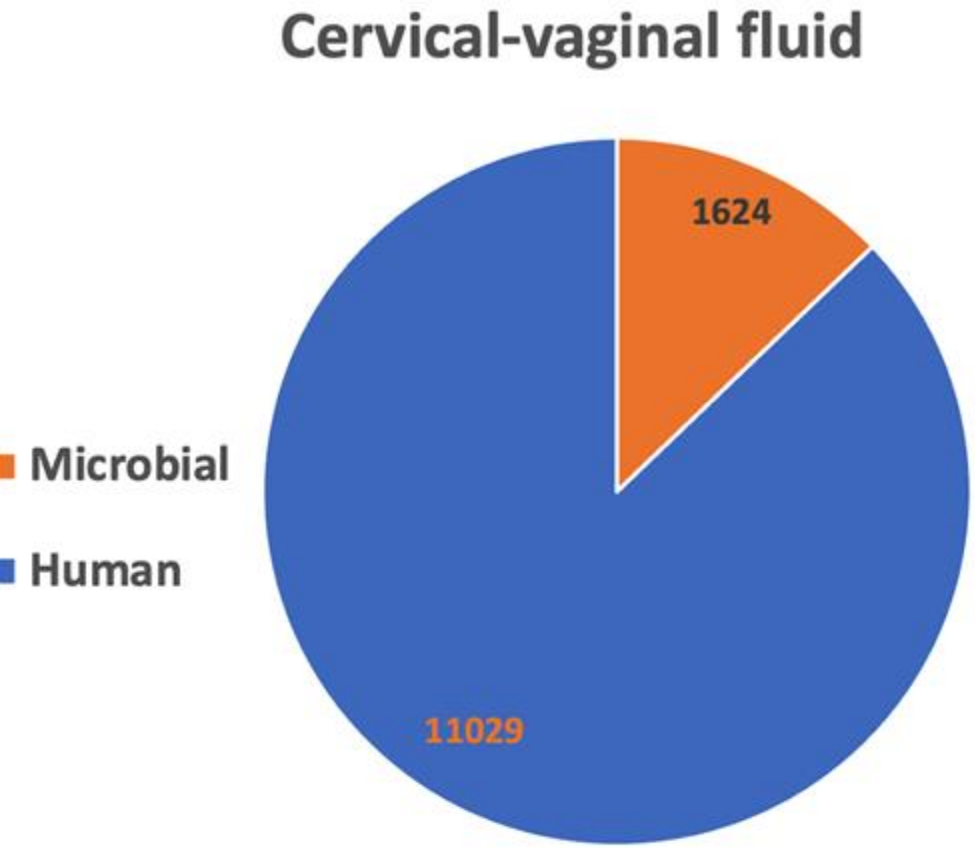


METAPROTEOMICS

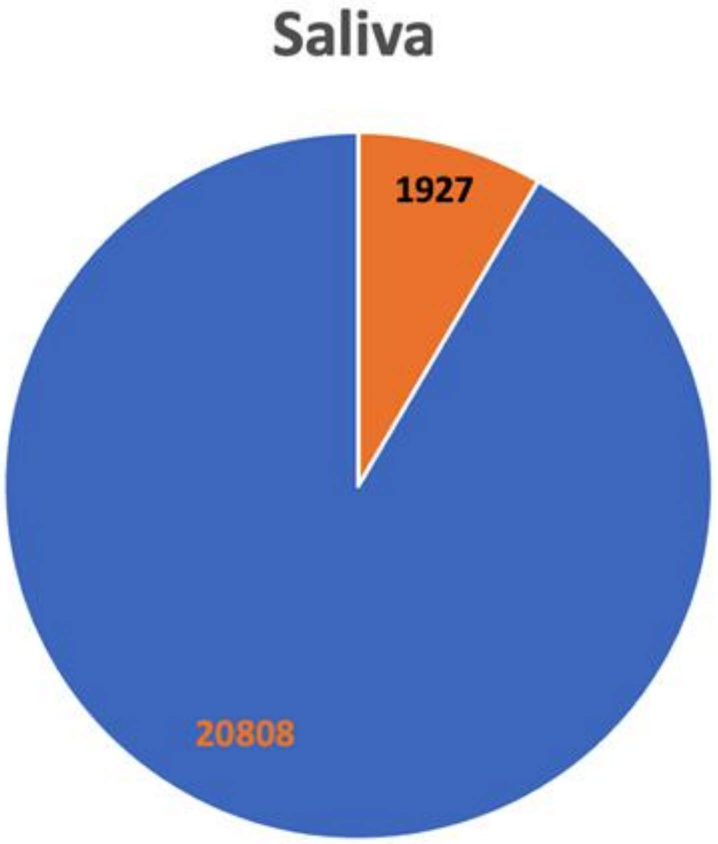
TAXONOMY

FUNCTION

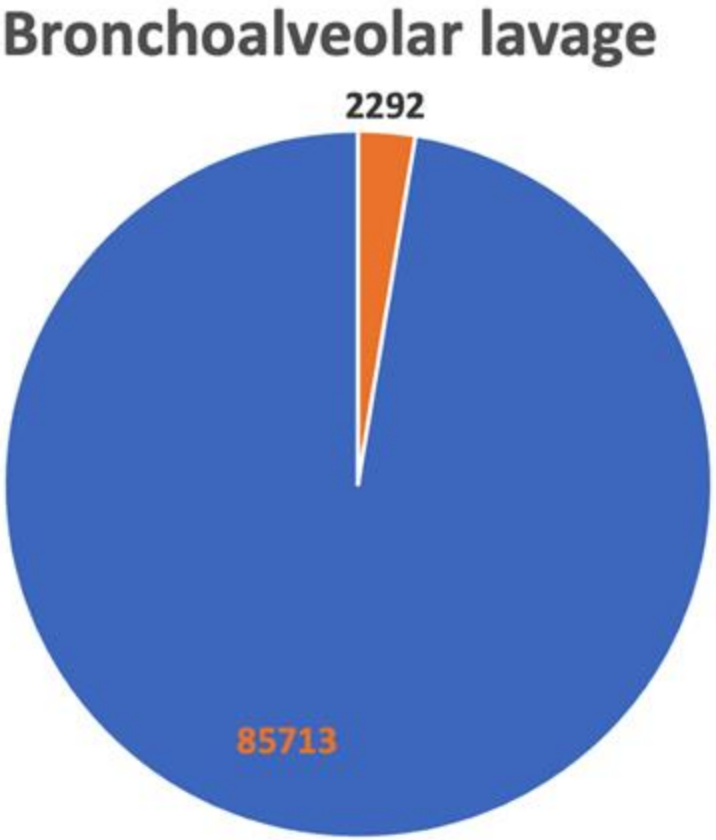
CLINICAL METAPROTEOMIC STUDIES DETECT LIMITED NUMBER OF MICROBIAL PEPTIDES



Afiuni-Zadeh *et al* (2018) Sci Rep . 8(1):10868.
doi: 10.1038/s41598-018-29092-4.

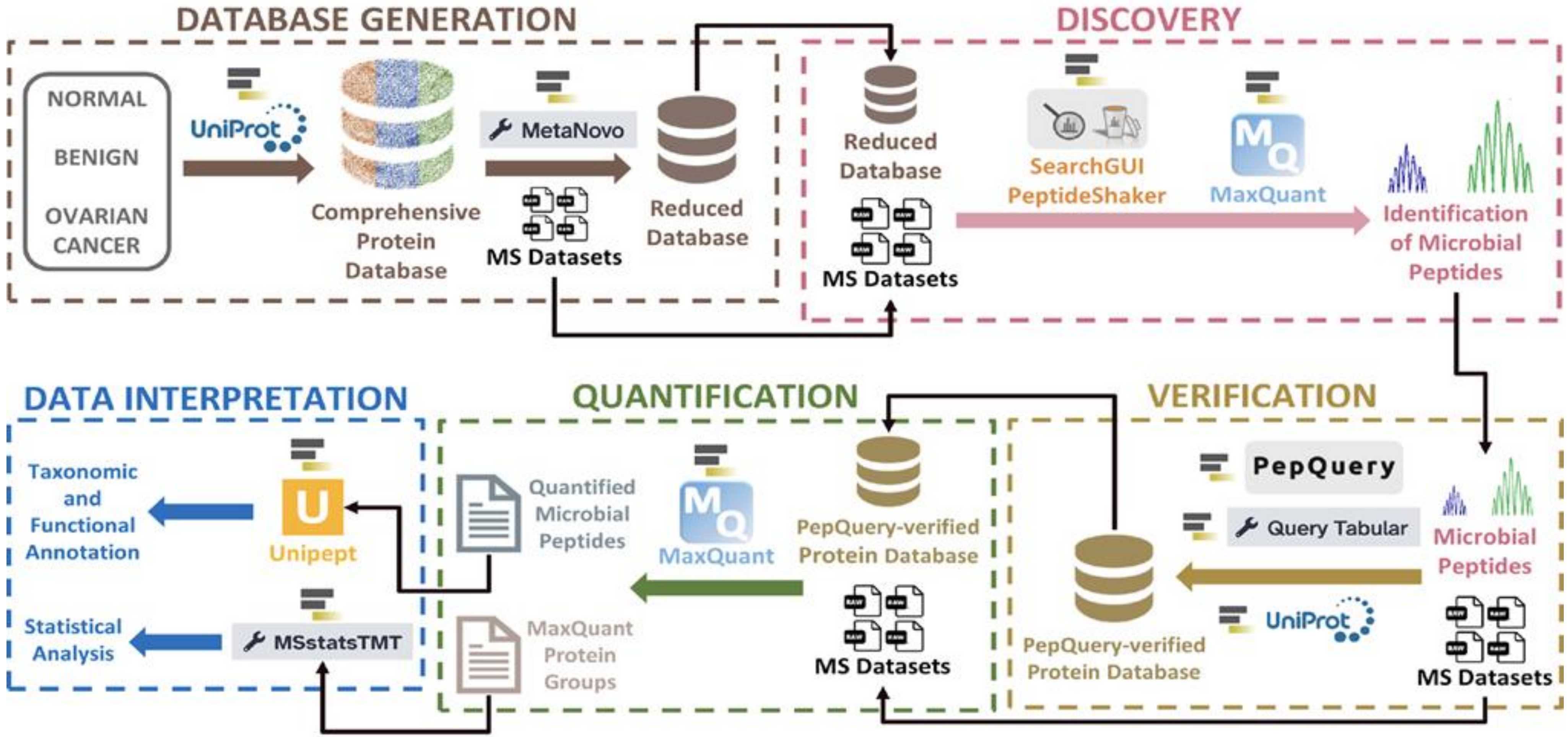


Jagtap *et al* (2012) Proteomics 12(7): 992–1001.
doi: 10.1002/pmic.201100503



Kruk *et al* (2024) mSystems
doi: 10.1128/msystems.00929-23

OVERVIEW OF CLINICAL METAPROTEOMICS WORKFLOW



We have developed a MS-based Galaxy-driven <u>bioinformatics workflow</u> for processing of microbial and host proteins, generating <u>verified microbial peptide candidates</u> suitable for <u>targeted analysis</u> within individual patient samples.

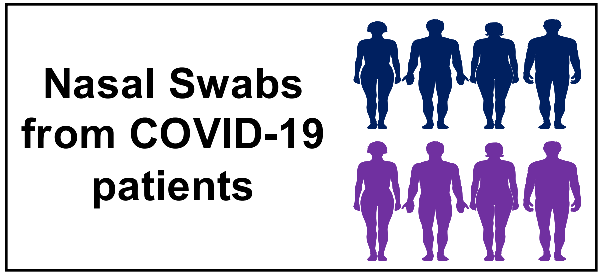
Do K *et al* (2024). mSphere <u>https://doi.org/10.1128/msphere.00793-23</u>

CLINICAL METAPROTEOMICS: COVID-19 PANDEMIC

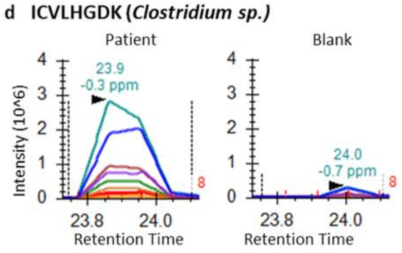
Bihani S *et al* (2023) Metaproteomic Analysis of Nasopharyngeal Swab Samples to Identify Microbial Peptides in COVID-19 Patients. J Proteome Res 22(8):2608-2619. doi: 10.1021/acs.jproteome.3c00040.

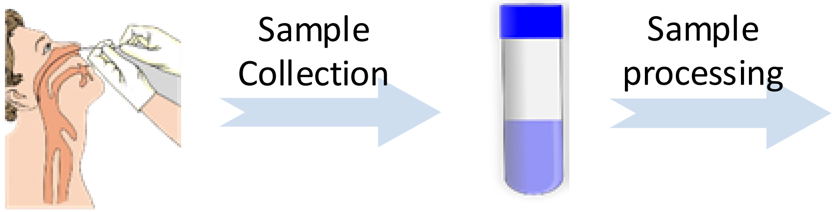
Surbhi Bihani

IIT BOMBAY



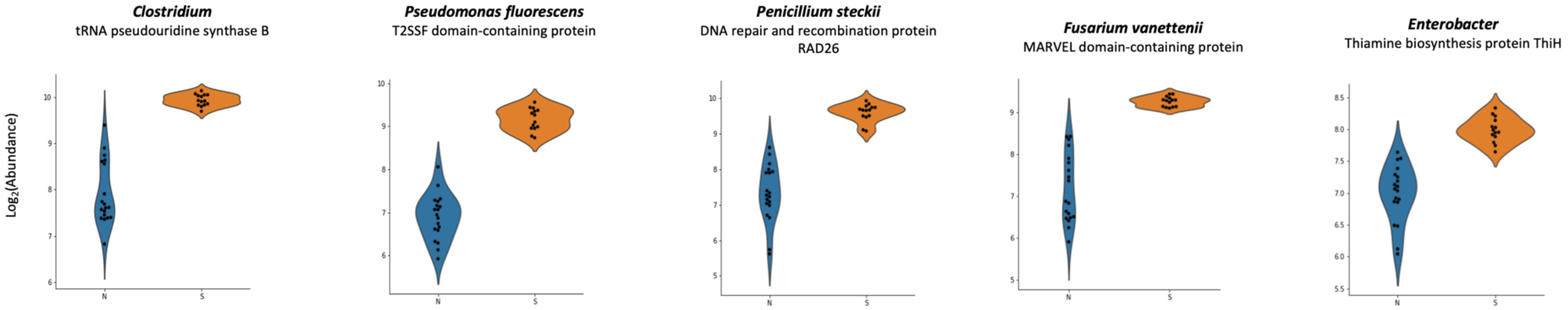
Nasal Swabs from COVID-19 patients

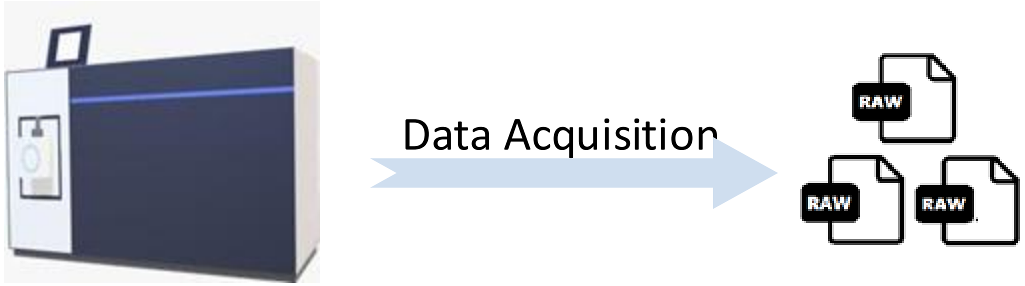




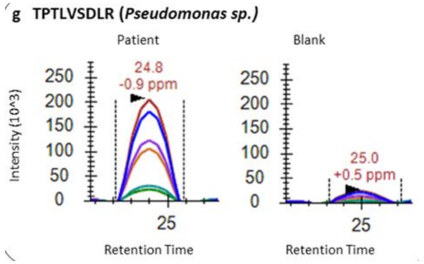
Sample Collection

Sample processing

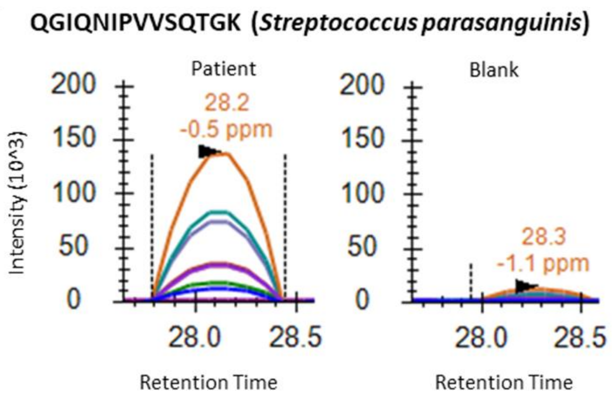




Data Acquisition



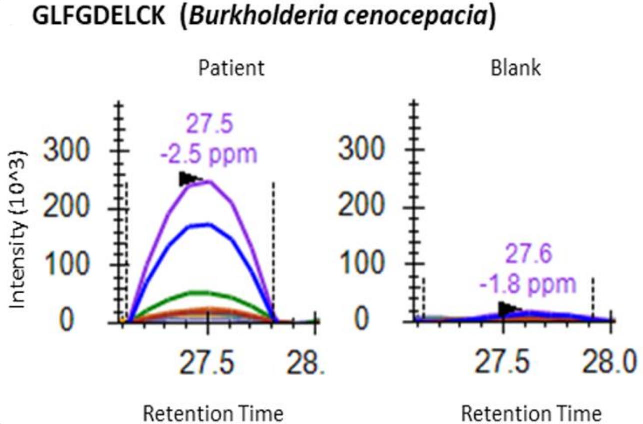
TARGETED ANALYSIS OF POTENTIAL PATHOGENS IN COVID PATIENTS



Streptococcus parasanguinis

Dominant isolate of dental plaque

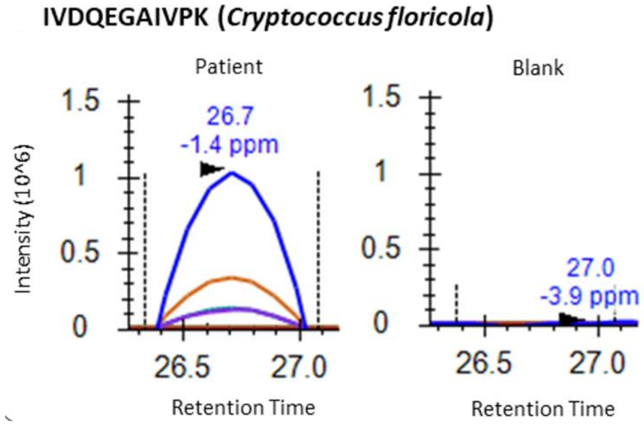
Opportunistic pathogen associated with subacute endocarditis



Burkholderia cenocepacia

Opportunistic pathogen

Cause systemic infections in immunocompromised individuals including cystic fibrosis patients.



Cryptococcus floricola

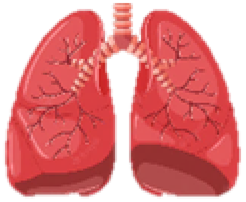
Infect immunocompromised hosts

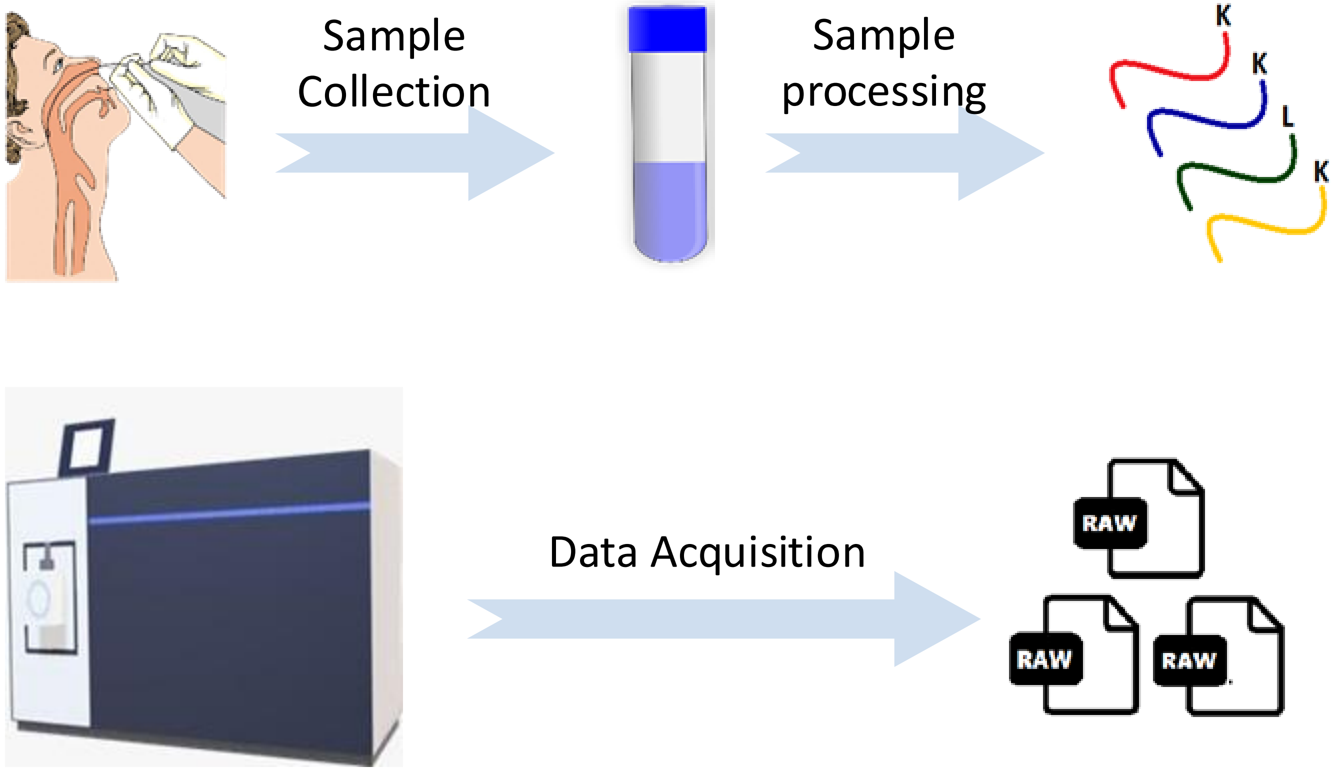
Infection initiates in the lungs.

CYSTIC FIBROSIS DATASETS

Kruk M *et al* (2024) An integrated metaproteomics workflow for studying host-microbe dynamics in bronchoalveolar lavage samples applied to cystic fibrosis disease. mSystems (https://doi.org/10.1128/msystems.00929-23).

BALF from
Cystic Fibrosis
or
Disease Control
Samples





Sample Collection

Sample processing

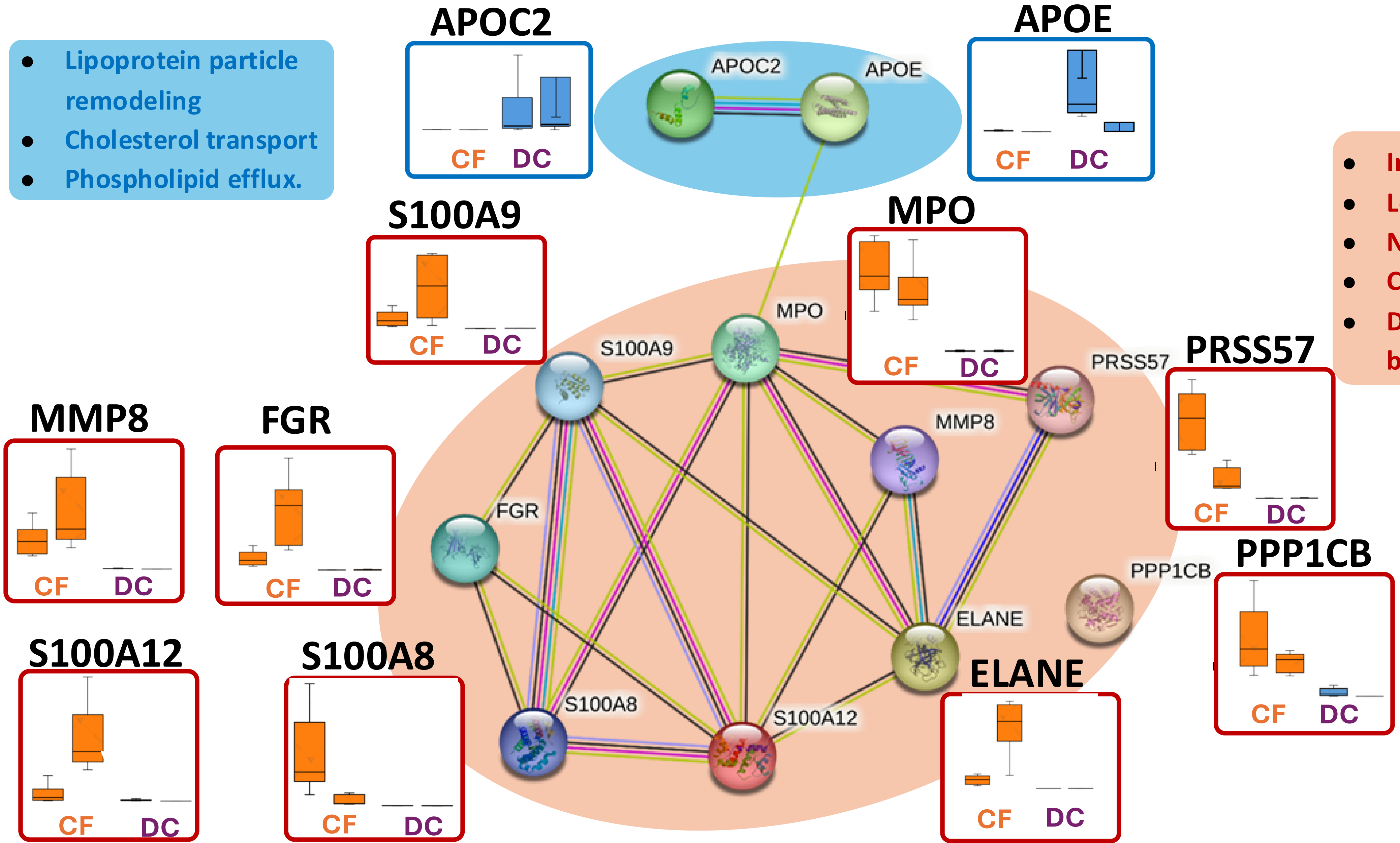
Data Acquisition

Monica E. Kruk

TARGETED ASSAY FOR HOST-MICROBIAL PROTEIN DYNAMICS IN CLINICAL CF SAMPLES

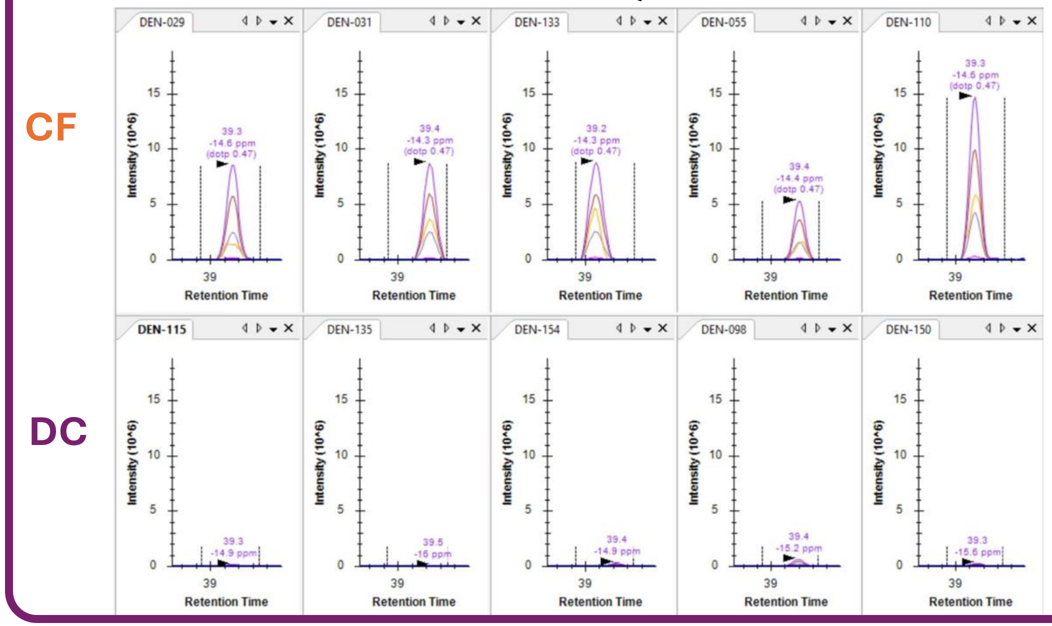
- Lipoprotein particle remodeling
- Cholesterol transport
- Phospholipid efflux.

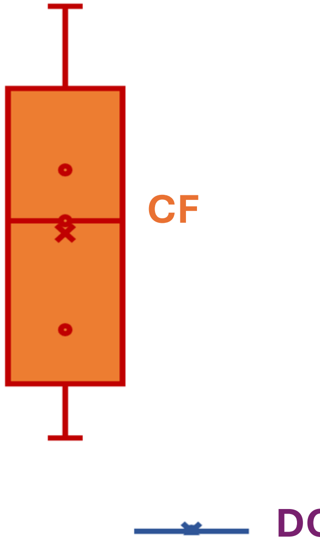
- Inflammatory response
- Leukocyte migration
- Neutrophil degranulation
- Cytokine production
- Defense response to bacteria

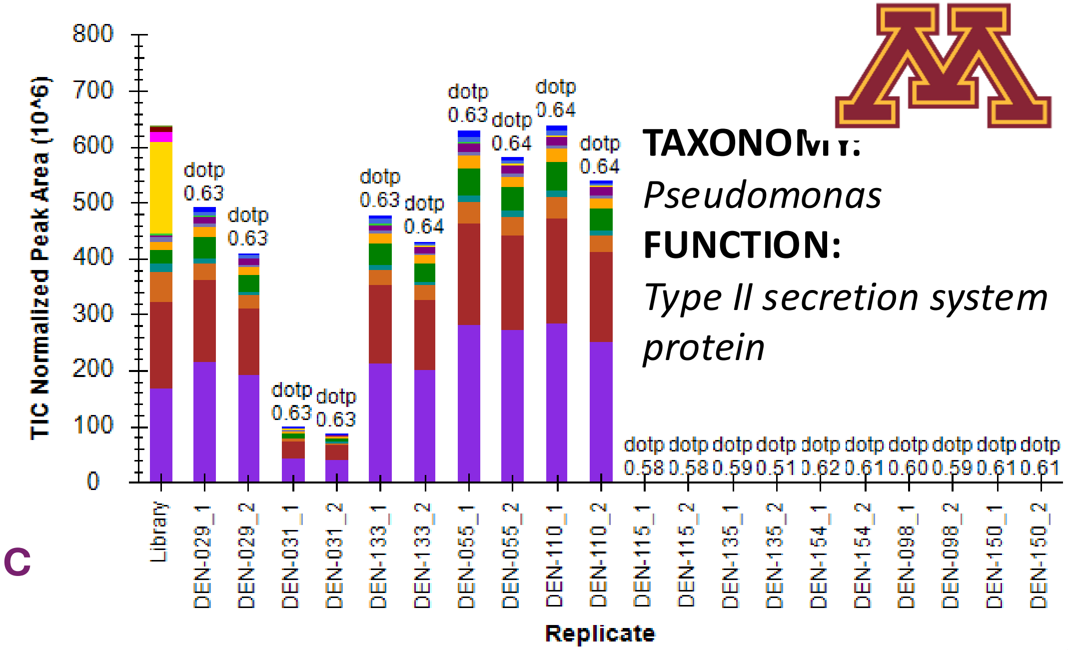


MICROBIAL PEPTIDES FROM CYSTIC FIBROSIS PATIENTS

DWLDSLLQR

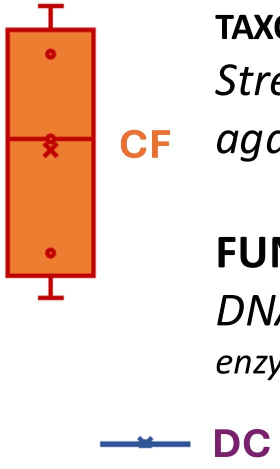






TAXONOMY:
Pseudomonas
FUNCTION:
Type II secretion system protein

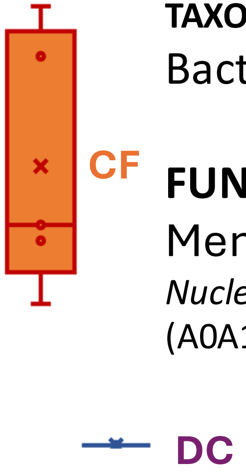
MKIGNLGGAYR



TAXONOMY:
Streptococcus agalactiae

FUNCTION:
DNA recombination enzyme

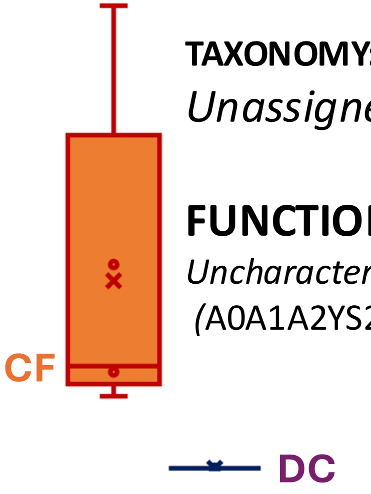
VLGARGHR



TAXONOMY:
Bacteria *(UniPept)*

FUNCTION:
Membrane kinase activity
Nucleoside triphosphate hydrolase
(A0A119BW38)

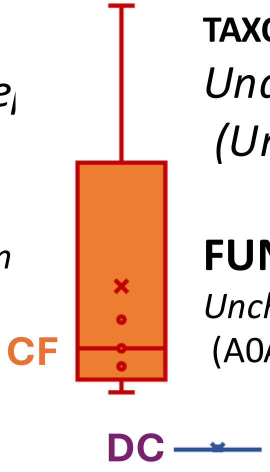
AALGAYDLR



TAXONOMY:
Unassigned (UniPe

FUNCTION:
Uncharacterized protein
(A0A1A2YS21)

ATVEELHLEGI



TAXONOMY:
Unassigned (UniPept)

FUNCTION:
Uncharacterized
(A0A1H9MU03)

The workflow modules, training data and documentation are available via the Galaxy Training Network.
https://training.galaxyproject.org/training-material/learning-pathways/clinical-metaproteomics.html

Galaxy Training Network

https://galaxyproject.org/events/gcc2021/training/

https://training.galaxyproject.org/training-material/topics/proteomics/

CLINICAL METAPROTEOMICS

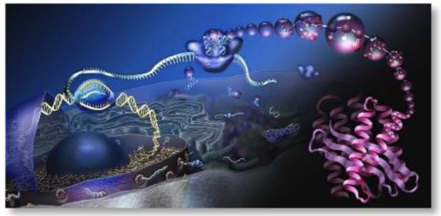
- We have developed a MS-based Galaxy-driven bioinformatics workflow for processing of microbial and host proteins, generating verified microbial peptide candidates suitable for targeted analysis within individual patient samples.

- We have utilized this workflow to detect and validate microbial peptides during a) co-infection during the COVID-19 pandemic (Bihani *et al* 2023, JPR); b) CF disease progression studies by comparing it with disease control (Kruk *et al* 2024, mSystems (In Press)) and c) Ovarian cancer studies (Mehta *et al*, work in progress).

- We hope that the workflow availability through Galaxy Training Network will help users detect differentially expressed host and microbial proteins in disease state.

PROTEOGENOMICS SHARED RESOURCE

Masonic Cancer Center
University of Minnesota

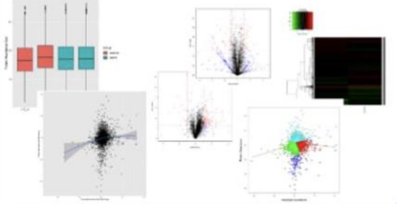


PROTEOGENOMICS

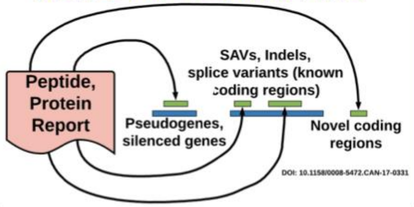
INTEGRATE RNA-SEQ AND MS-BASED PROTEOMICS DATA TO IDENTIFY EXPRESSED VARIANTS AND MECHANISMS OF FUNCTIONAL REGULATION

- ***IDENTIFY FUNCTIONAL DRIVERS AND BIOMARKERS***
- ***PATHWAY ANALYSIS OF CANCER DEVELOPMENT, PROGRESSION AND INTERVENTION***
- ***PEPTIDE NEOANTIGEN IDENTIFICATION***

RNA – PROTEIN RESPONSE



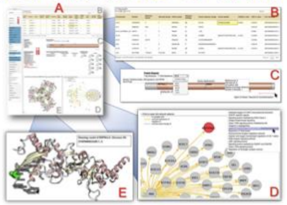
NOVEL PEPTIDE MAPPING



DOI: 10.1158/0008-5472.CAN-17-0331

RESULTS VISUALIZATION

IMPACT ANALYSIS OF VARIANTS



POWERED BY:

HIGH RESOLUTION MS

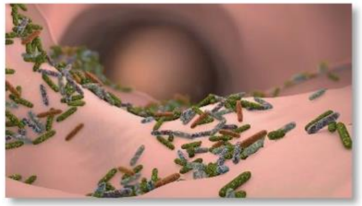
\+

NEXT-GEN SEQUENCING

\+

GalaxyP
galaxyp.org

CUSTOMIZED BIOINFORMATICS

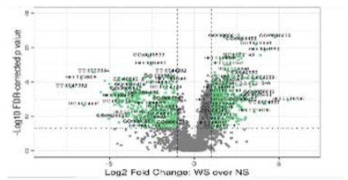


METAPROTEOMICS

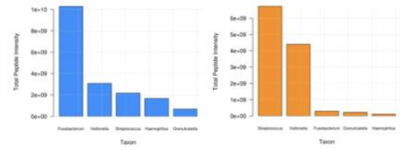
INTEGRATE METAGENOMICS AND PROTEOMICS DATA TO STUDY DYNAMIC HOST-MICROBIOME INTERACTIONS

- ***IDENTIFY FUNCTIONAL MARKERS EXPRESSED BY MICROBES AND HOST***
- ***FUNCTIONAL VERSUS TAXONOMY RESPONSE UNDER DIFFERENT CONDITIONS***
- ***FUNCTIONAL-TAXONOMIC INTERACTIONS***

DIFFERENTIAL EXPRESSION

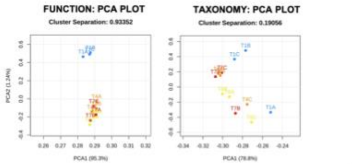


TAXONOMIC ABUNDANCE



FUNCTION-TAXONOMY INTERACTION

STATISTICAL ANALYSIS



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Informatics Technology for Cancer Research

MOCA
MINNESOTA OVARIAN CANCER ALLIANCE

MASONIC CANCER CENTER
UNIVERSITY OF MINNESOTA

http://galaxyp.org/contact/

galaxyp.org