Metaproteomics as a tool to reveal microbial contributions to cancer

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Microbiome research

https://worldmicrobiomeday.com/resources/

https://www.nature.com/articles/d41586-020-00193-3
Abundant evidence exists that links altered microbiota to oncogenesis.
Microbiome potential to unravel the mechanistic details of microbial interactions with host/environment by analyzing the functional dynamics of the microbiome.
Metaproteomics analytical challenges

**Single-organism proteomics**

- **Search Database**
  - Size: Small to medium size (10 K to 100K sequences)
  - Complexity: Single + contaminants

**Metaproteomics**

- **Search Database**
  - Large (1 million and above)
  - Multi-organism database with homologous proteins

Disparate tools and multiple processing steps.

- **Search algorithms** being developed to address large and complex database searches
- **Protein grouping** at multi-organism level
- **Identification statistics** affected by large databases
- **Taxonomy** based on unique peptide identifications
- **Functional analysis** based on proteins identified
Gastric and Head-and-neck (HNSCC) samples from CPTAC used in this pilot study
Metaproteomics Workflow

- Raw MS/MS data
  - Metanovo
  - Unipept
    - Major taxonomic matches
    - Uniprot.org
  - combined FASTA files
- MaxQuant
  - Matched Microbial Peptides
- PepQuery
  - Validated Microbial Peptides
Gastric Cancer LC-MS data reveals taxonomic information about the microbiome
PepQuery-validated microbial peptides from gastric cancer demonstrate varied taxonomy and functionality.

**Microbial Genera of Validated Peptides**

- Bacteroides
- Butyricicoccus
- Clostridium
- Desulfovibrio
- Enterococcus
- Eubacterium
- Faecalibacterium
- Finegoldia
- Faecalibacterium

**GO Biological Processes in validated microbial peptides of Gastric Cancer data**

- DNA
- Metabolic process
- Biosynthetic process
- Regulation
- Protein binding
- Transcription
- Translation
- Cell signaling
- Carbohydrate metabolism
- Nucleotide metabolism
- Amino acid metabolism
- Metal ion binding
HNSCC LC-MS data reveals taxonomic information about the microbiome
PepQuery-validated microbial peptides from HNSCC data demonstrate varied taxonomy and functionality.
Future Directions

• Assess the degree of agreement between metagenomic and metaproteomic analyses of cancer data sets for taxonomic identification of the microbiome
• Employ enrichment strategies to remove human peptides from the LC-MS data
• Optimize quantitative metaproteomic analyses of cancer patient data
• Apply metaproteomic analyses to other cancer data sets in CPTAC
Accessing Functional Microbiome Galaxy Workflows

Proteogenomics Core at the Masonic Cancer Center

Tools and Workflows also available at:
https://proteomics.usegalaxy.eu/

Galaxy Training Network:
https://training.galaxyproject.org/training-material/topics/proteomics

Galaxy Europe: https://proteomics.usegalaxy.eu/

Contact: http://galaxyp.org/contact/