Towards an integrated microbiome-host protein biomarker panel for early detection of ovarian cancer in routinely collected clinical samples

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**Proteogenomics Core**

**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

**Meta-omics:** Integrate meta-genomics, transcriptomics and proteomics (and metabolomics) 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

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**Results Visualization**

**Impact analysis of variants**

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**Pathway/functional analysis**

**Taxonomic Abundance**

**Function-Taxonomy Interaction**

**Statistical classification**

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Pratik Jagtap
Significance and Rationale

- Ovarian cancer lacks reliable early detection methods.
- Dysbiosis in the female reproductive tract disrupts homeostasis between bacterial communities and host cells, linked to ovarian cancer.
- Microbiome-derived molecular markers, such as expressed proteins (the metaproteome), integrated with proteins expressed by the human host, may hold a key for early detection.
- Residual fluid from liquid Pap tests, routinely collected in the clinic, are a rich source of microbiome-expressed and human host proteins (our past collaborative work).

We hypothesize that quantitative metaproteomic and proteomic analysis of MS-based data collected from Pap test fluid from non-cancer and high grade serous ovarian cancer (HGSOC) individuals will reveal bacterial-host protein signatures with promise for early detection of ovarian cancer in commonly collected samples.
Bacterial proteins are detectable (along with host proteins) in Pap fluid samples using MS-based metaproteomics.
Re-analysis of a quantitative proteomics dataset in clinical Pap fluid samples: a metaproteomics perspective

20 non-cancer controls

20 HGSOC patients

Quantitative proteomics data

MetaNovo

GalaxyP

PepQuery

Human proteome database

Reduced metaproteome database

Quantified proteins and peptides
Preliminary results: Partial analysis of the full dataset

Relative amounts of bacterial and host proteins

Taxonomic distributions
Metaproteomics reveals unique taxonomic-functional relationships

Lactobacillus

Glycolytic metabolic enzyme network (fold-change cancer/non-cancer)

(from string-db.org)
Integrating bacterial-host protein signatures: diagnostic potential in Pap fluid samples

Glioma pathogenesis-related protein 1 performs dual functions in tumor cells

Junjie Wang, Zeyu Li, Fenfen Yin, Rui Zhang, Ying Zhang, Zhengxin Wang & Xiumei Sheng

Cancer Gene Therapy 29, 253–263 (2022) | Cite this article
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GLIPR cancer/non-cancer

Bacterial “Metabolic protein panel”
**Aim 1**

Shoot DNA sequencing

**Aim 2**

Quantitative proteomics dataset

**Aim 3**

Microbiome-host diagnostic peptide panel

**Next steps**

Figure 4. Overview of integrated Aims.
Thank You!

Questions welcome!