A novel imaging mass spectrometry method for visualizing chemical communication in metastasis

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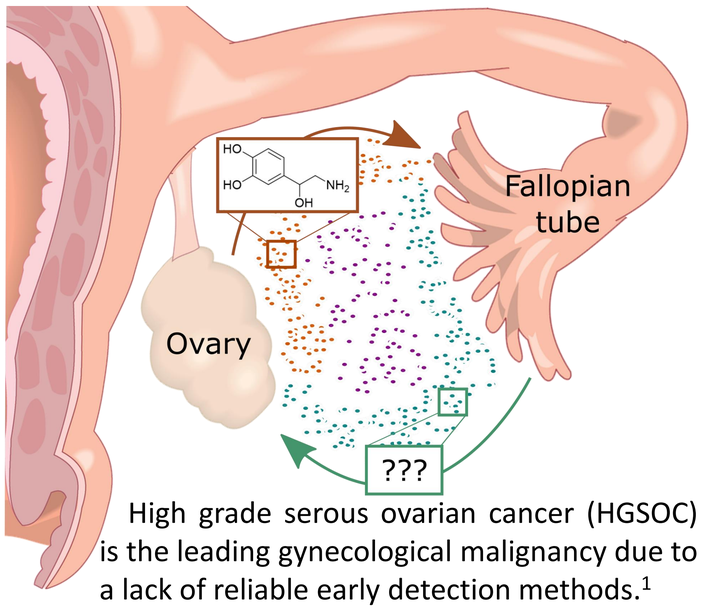
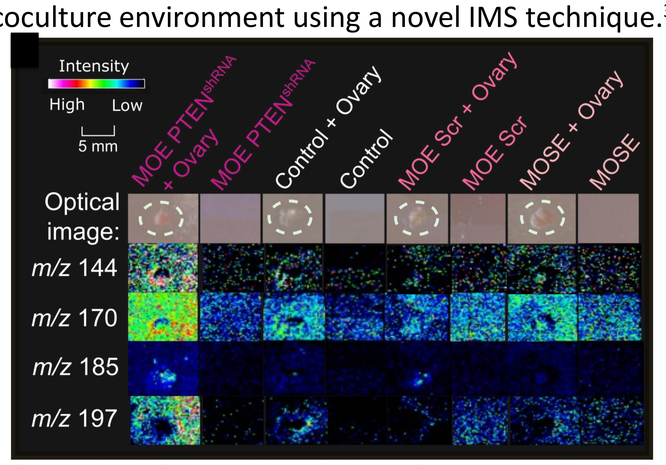
Introduction



High grade serous ovarian cancer (HGSOC) is the leading gynecological malignancy due to a lack of reliable early detection methods.[1]

HGSOC begins in the fallopian tube epithelium (FTE) and migrates to the ovary during ovulation.[2] Norepinephrine (NE) has been detected in the coculture environment using a novel IMS technique.[3]



This method is capable of detecting molecules using any cell type and a wide range of tissue types.

Aims

Aim I: Detect signals being produced from the fallopian tube cells relevant to primary metastasis. Ascertain the order of communication between the organ structures.

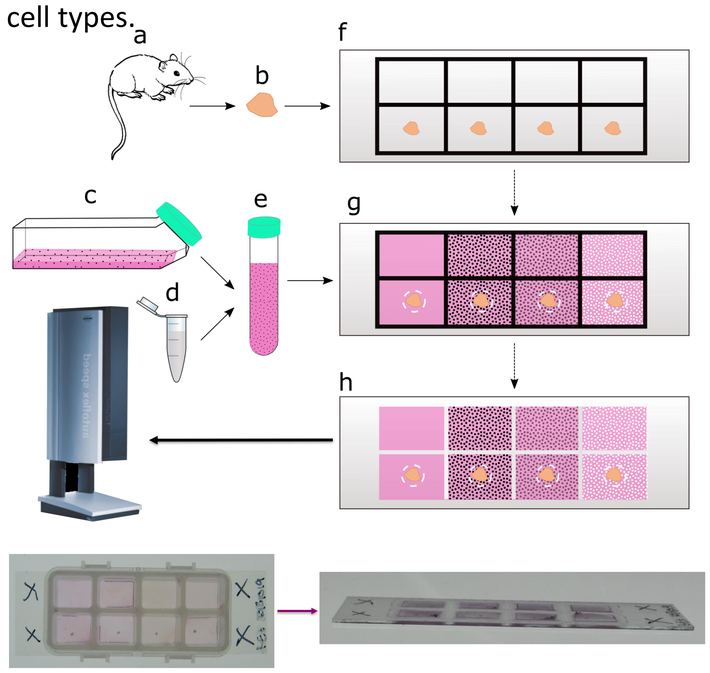
Aim II: Unveil chemical cues that indicate or drive secondary metastasis to the omentum.

Hypothesis

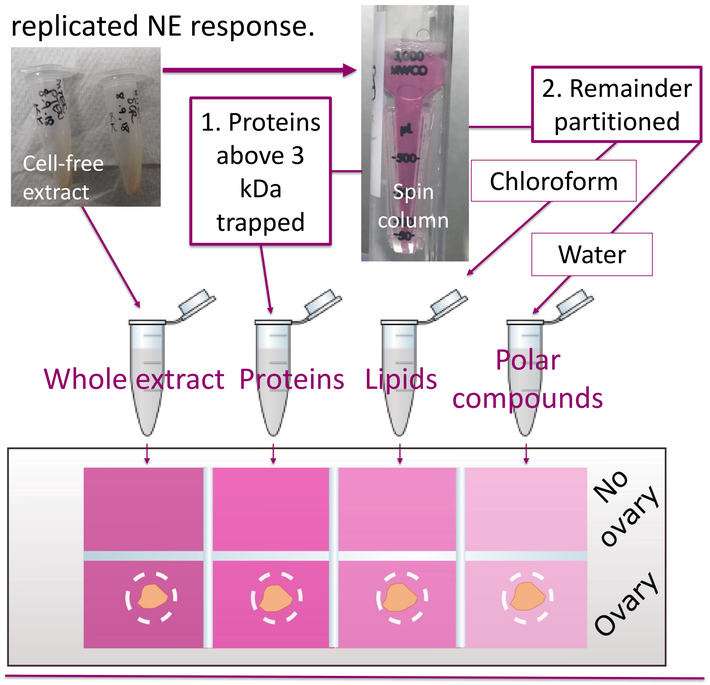
Small molecules may drive the communication that results in primary and secondary metastases of HGSOC, and can be detected using this novel IMS technique.

A Novel IMS Method

Sample preparation[3]: Murine ovaries are collected from mice and cocultured with a cell culture of tumorigenic FTE cells embedded in agarose. The platform is IMS-compatible and is amenable to many cell types.

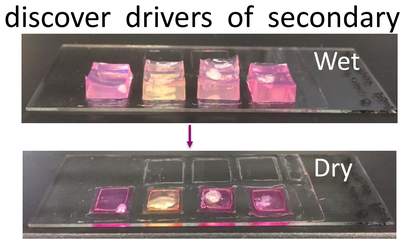


Aim I: Cell-free conditioned media from tumorigenic FTE cells is fractionated and evaluated via IMS for replicated NE response.



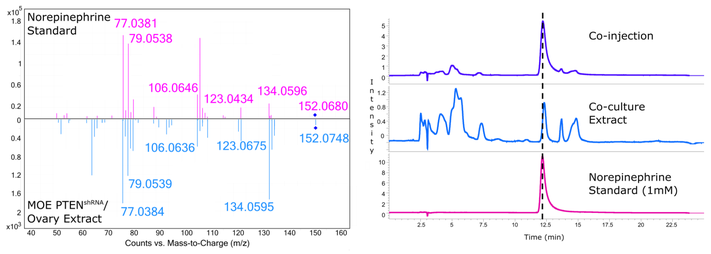
Aim II: Optimize conditions to embed omental tissue into agarose plug to discover drivers of secondary metastasis.

The omentum is the site of secondary metastasis of HGSOC from the ovary.

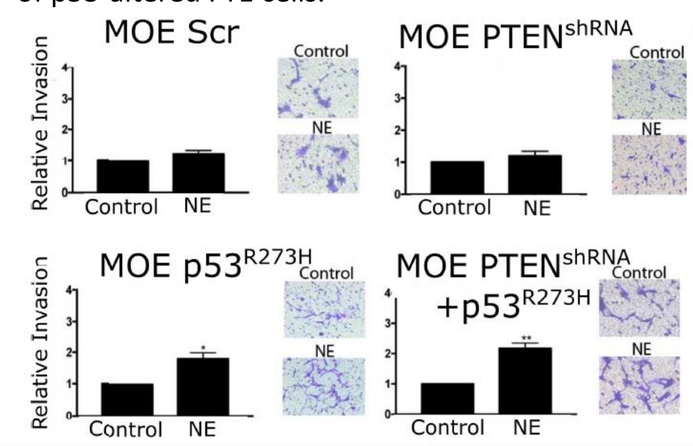


Results

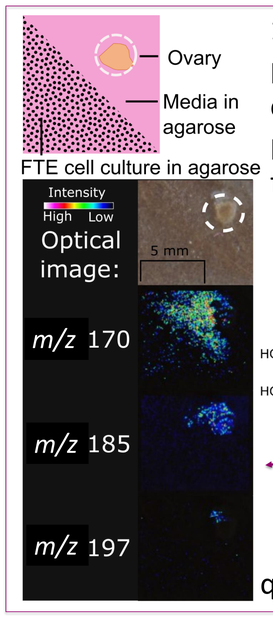
Orthogonal methods of dereplication have validated that the ovarian tissue releases norepinephrine.



NE has previously been implicated in HGSOC, and further evidence suggests it influences the invasion of p53-altered FTE cells.[3]



Future Directions



1. Identify remaining molecules produced by ovary in coculture conditions.[3] Known biosynthesis pathways provide starting point for dereplication.

2. Develop LC-MS methods to quantify metabolites in extracts.

References & Acknowledgements

[1]Siegel et al, *CA Cancer J Clin.* **2018**, 68, 7–30
[2]Labidi-Galy, S. et al, *Nat. Commun.* **2017**, *8, 1,* 1093
[3]Zink et al, ACS Cent Sci. **2018**, 4, 10, 1360-1370

Funding provided by the Chicago Biomedical Consortium with support from the Searle Funds at The Chicago Community Trust (C-076); the National Institute of Child Health and Human Development (NICHD) and the National Institutes of Health Office of Research on Women's Health (ORWH); UIC Startup Funds; T32 and the Ovarian Cancer Research Fund Alliance and UG3 ES029073.