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A Multi-Omic Liquid Biopsy Test:
High Sensitivity for Ovarian Cancer, High Specificity under Stress-Testing, and Expansion into Broader Gynecologic Cancer Detection

Check out our newest publication in *Diagnostics!*

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Check out our publication in *Cancer Research Communications!*

Early Detection of Cancer Conference
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Background and Rationale

Ovarian cancer (OC) remains highly lethal primarily due to late-stage diagnosis[1]. Existing diagnostic tools lack sensitivity and specificity to detect early-stage disease[2].

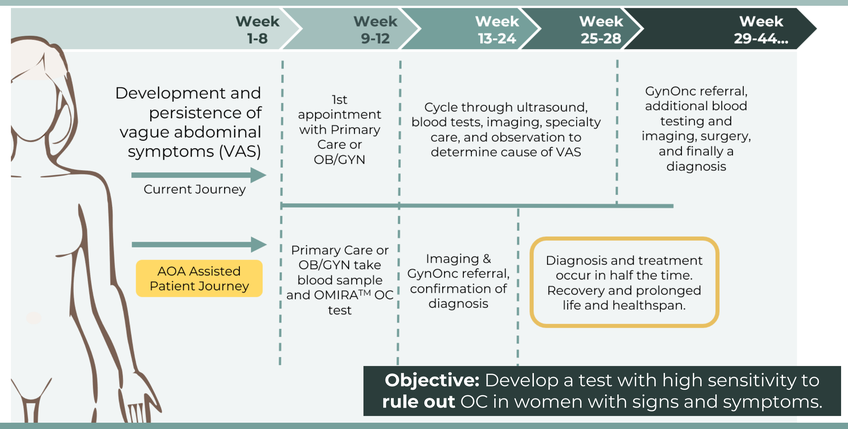
30%

5-year survival rates for stage I are >90%, but OC is often detected **at late stages (III/IV)** when **survival is <30%**[1].

~85% of patients present with symptoms[3], but they are often vague and misattributed, leading to a 9-month diagnostic delay[4].

There is a clear **unmet need for improved diagnostic tools** to accurately triage symptomatic women and enable earlier detection.

Patient Journey to OC Diagnosis



Objective: Develop a test with high sensitivity to **rule out** OC in women with signs and symptoms.

Why Real-World Performance Matters

Diagnostic tools built in controlled cohorts often lose sensitivity and specificity in real-world, clinically diverse populations, especially patients with masses or nonspecific symptoms, where clinical decisions matter most. Existing biomarkers are especially prone to poor specificity in benign conditions.

✓ **Strong performance in early-stage OC**

Our assay shows 90.8% sensitivity / 83.5% specificity in early-stage OC vs. symptomatic controls

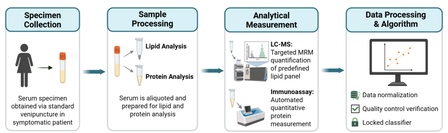
✓ **Holds up in challenge groups**

>80% specificity maintained across conditions impacting proteins and lipid profiles

✓ **Extends to other gynecologic cancers**

100% sensitivity for cervical cancer and 95.7% sensitivity for endometrial cancer at 90% specificity

Study Design + Methods



Serum samples were analyzed across the following groups for model training:
- Ovarian cancer (OC) cases
- Benign adnexal masses
- Symptomatic controls with confirmed absence of malignancy

Three biomarker-impacting groups were included to stress-test specificity in challenging conditions:
- Conditions affecting protein biomarkers
- Conditions affecting lipid profiles
- Conditions affecting both protein + lipids

Other gynecological cancers were included to investigate the potential of novel lipids as biomarkers beyond OC:
- Endometrial cancer
- Cervical cancer

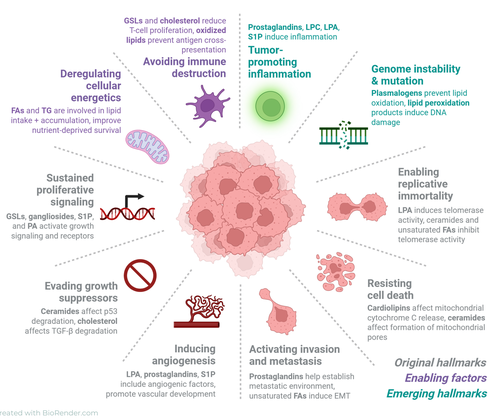
Specimens were prospectively collected and supplemented by commercial vendors. Lipids were measured by mass spectrometry (LC-HRMS for discovery lipidomics, LC-QqQ for targeted analysis); proteins by immunoassay. A logistic regression model, with coefficients and threshold locked on the OC/control cohort (≥90% prespecified sensitivity) was applied without retraining to each challenge group.

Model Training Categories	N
Ovarian cancer	105
Early-stage (I/II) OC	*65*
Late-stage (III/IV) OC	*40*
Benign adnexal masses	37
Symptomatic controls	115

Specificity Challenge Groups	Condition	N
Protein interference	Endometriosis	24
Lipid interference	Obesity with T2D	25
	Pregnancy	17
Combined Impact	Hypothyroidism	13
	Liver Disease	63
	PCOS	24

Other Gynecologic Cancers	N (early/late stage)
Cervical Cancer	18 / 2
Endometrial Cancer	23 / 0

Lipids are fundamental to cancer biology



- Tumors undergo metabolic reprogramming
- Reprogramming supports proliferation, invasion, and more
- Lipids…
  - are involved in multiple cancer hallmarks[5]
  - Reflect tumor metabolism and signaling
  - Capture biology not represented by protein biomarkers alone

Why MS? Proven + Scalable

Mass spectrometry is already widely deployed in clinical labs[6]:

Endocrinology	Newborn Screening	Vitamins	Clinical Toxicology
• **Comprehensive hormone panels** (congenital adrenal hyperplasia) • **Cortisol** (Cushing's syndrome) • **Sex steroid panels** (hypogonadism, PCOS)	• **Newborn screening panels** (>30–60 inborn metabolic errors) • **Acylcarnitine profiling** (fatty acid oxidation disorders) • **Amino acid analysis** (phenylketonuria)	• **Vitamin D** (deficiency diagnosis) • **Vitamin B6** (nutritional, metabolic assessment) • **Vitamin A + E** (malabsorption, deficiency disorders)	• **Opioid + drug panels** (pain management) • **Therapeutic drug monitoring** (anti-epileptics) • **Toxicology** (overdose evaluation)

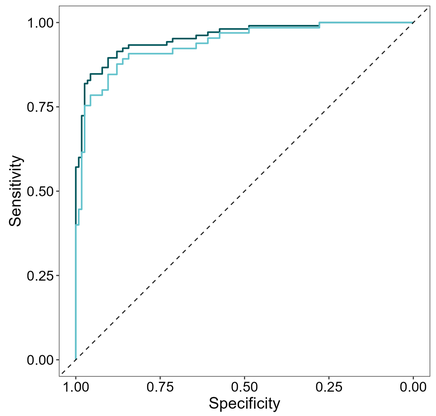
Compatible with standard clinical workflows and automation, providing robust and reproducible measurements.

90.8% sensitivity for early-stage OC while maintaining specificity

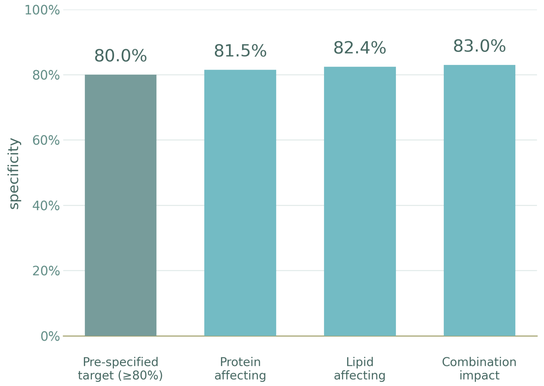
High performance in both all-stage OC and early-stage OC using a targeted panel of <10 lipid + protein features

Early-Stage OC vs. Symptomatic
Sensitivity: 90.8%
Specificity: 83.5%
AUC: 0.94 (0.90–0.97)

OC vs. Symptomatic
Sensitivity: 93.3%
Specificity: 83.5%
AUC: 0.96 (0.93–0.98)



- Conditions were grouped by biomarker mechanism:
  - **Protein interference:** documented in endometriosis [8]
  - **Lipid interference:** documented in obesity + type 2 diabetes [14,15] and pregnancy [16]
  - **Combined-impact (protein + lipid interference)**: hypothyroidism [13], liver disease [11,12], and PCOS [9,10]
  - Mechanism-first structure stress-tests the model against each interference pathway independently
- Coefficients and threshold locked on the model training, applied without retraining
- All three challenge groups clearly maintain >80% specificity at fixed 90% sensitivity threshold

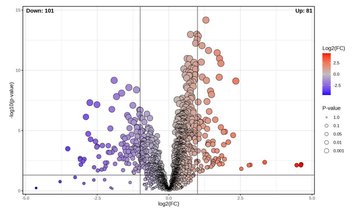


Potential of lipids for detection of other gyn. cancers

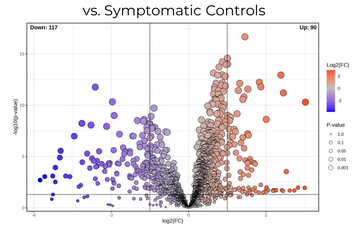
Cervical and endometrial show **unique lipid profiles in discovery data**, even in a cohort enriched for early-stage disease, which can be leveraged to build biomarker panels for additional cancer indications

Discovery Lipidomics

Cervical Cancer
vs. Symptomatic Controls



Endometrial Cancer
vs. Symptomatic Controls



Preliminary data shows that a **targeted panel of lipid biomarkers** shows high sensitivity and specificity in other early-stage gynecological cancers; future analyses will leverage multi-omics to optimize performance in additional cohorts

Targeted Lipid Panel

Cancer Type	N	Sens @ 80% Spec	Sens @ 90% Spec
Early-stage Cervical	18	100%	100%
Early-stage Endometrial	23	95.7%	95.7%

References
1. Siegel RL, et al. CA Cancer J Clin. 2025;75(1):10-45. 2. Menon U, et al. Lancet Oncol. 2021;22(3):e115-e130. 3. Goff BA, et al. Gynecol Oncol. 2000;77(3):436-442. 4. Olawaiye AB, et al. Cancer. 2021;127(20):3771-3780. 5. Hanahan D, Weinberg RA. Cell. 2011;144(5):646-674. 6. Rifai N, et al. Nat Biotechnol. 2006;24(8):971-983.