

From discovery to validation:
**Serum Marker Panels for
Early Detection of Ovarian Cancer**

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Candidate markers were discovered by existing technologies

- Tissue (and matched blood) samples obtained at time of primary surgery
- Multiple rounds of **cDNA microarray** interrogation
 - malignant ovarian tumors: 85
 - benign ovarian tumors: 19
 - ovarian tissue from healthy women: 66
- RT-PCR to confirm and quantify **over-expression**

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Schummer et al, *Gene*, 1999.

A sandwich ELISA was developed for **Mesothelin** to facilitate its evaluation in serum samples

- ROC curve analysis was used to evaluate the value added of **Mesothelin (sMSLNs)** to a composite marker including CA125
 - 53 cases
 - 220 controls
- Performance of the markers was evaluated
 - CA125 alone
 - sMSLNs alone
 - Composite marker of CA125 + sMSLNs

Scholler et al, *PNAS*, 1999; McIntosh et al, *Gyn Oncol*, 2004.

Logistic regression was used to define a **composite marker (CM)** including CA125 and sMSLNs

A CM is a linear combination of the markers in the panel

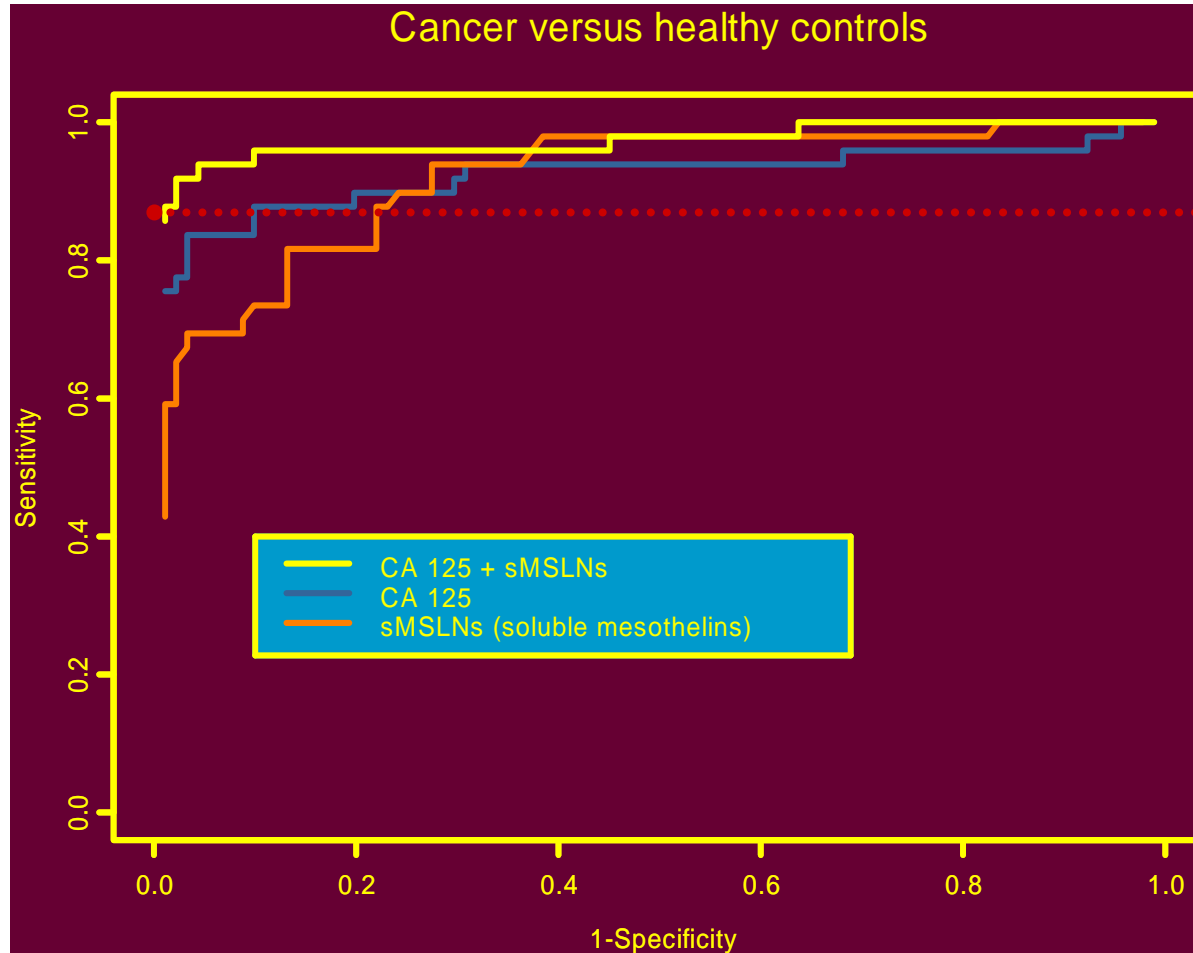
- Marker levels were converted to logs and standardized
- Logistic regression was used to estimate the weights for each marker, controlling for menopausal status
- $CM = 1.388 \times CA\ 125 + 0.998 \times sMSLNs$

The composite marker can be analyzed just as if it were a single marker

- In ROC curves
- In longitudinal algorithms for use in screening

• McIntosh & Pepe, *Biometrics*, 2002

Addition of sMSLNs to CA125 improves detection of ovarian cancer



Development of bead-based assays to evaluate lead time in validation studies

- Use multiple, commercially available antibodies pairs on bead-based platform and assess
 - Assay feasibility (affinity)
 - Accuracy in assessing known CA125 concentrations
- Measure CA125 using a bead-based assay with most promising antibody pairs in ovarian cases (n=66) and controls (n=138).
- Evaluate
 - Reproducibility
 - Validity
 - Screening performance

Diagnostic performance for 2 CA125 bead-based assays, an HE4 bead-based assay, and the standard RIA CA125 assay (64 cases vs 125 controls)

