

GD2 and GD3 gangliosides as diagnostic biomarkers for all stages and subtypes of ovarian cancer.

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Background: Ovarian cancer (OC) is the deadliest gynecological cancer, often diagnosed at advanced stages. A fast and accurate diagnostic method for early-stage OC is needed. The tumor marker gangliosides, GD2 and GD3, exhibit properties that make them ideal potential diagnostic biomarkers but they have never before been quantified in OC. We investigated the diagnostic utility GD2 and GD3 for diagnosis of all subtypes and stages of OC.

Methods: This retrospective study evaluated GD2 and GD3 expression in biobanked tissue and serum samples from patients with invasive epithelial OC, healthy donors, non-malignant gynecological conditions, and other cancers. GD2 and GD3 levels were evaluated in tissue samples by immunohistochemistry (n = 299), and in two cohorts of serum samples by quantitative ELISA. A Discovery Cohort (n = 379) showed feasibility of GD2 and GD3 quantitative ELISA for diagnosing OC, and a subsequent Model Cohort (n = 200) was used to train and cross-validate a diagnostic model.

Results: GD2 and GD3 were expressed in tissues of all OC subtypes and FIGO stages but not in surrounding healthy tissue or other controls. In serum, GD2 and GD3 were elevated in patients with OC. A novel diagnostic model that included serum levels of GD2 and GD3 was superior to the standard of care (CA125, $p < 0.001$) at detecting OC, as well as, in early-stage (1/11) OC samples.

Conclusions: GD2 and GD3 are high value candidates for building a novel diagnostic panel. A diagnostic model combining GD2 and GD3 quantification in serum had diagnostic power for all subtypes and all stages of OC, including early-stage. Further research exploring the utility GD2 and GD3 for diagnosis of OC is warranted. Future work will aim to validate these biomarkers in independent prospective studies.

Overall Predictive Model (N = 200)

	Predictive Model AUC	95%CI		p-value vs CA125	Sx Cross Validation AUC	95%CI
CA125	0.876	0.823	0.942		0.877	0.777-0.971
HE4	0.903	0.858	0.947	0.208	0.904	0.884-0.924
GD2	0.957	0.928	0.985	0.010	0.952	0.922-0.982
GD3	0.965	0.944	0.987	0.001	0.963	0.943-0.983
Novel Panel	0.988	0.977	0.998	< 0.001	0.976	0.956-0.996

Early-Stage Predictive Model (N = 173)

	Predictive Model AUC	95%CI		p-value vs CA125	3x Cross Validation AUC	95%CI
CA125	0.801	0.675	0.939		0.773	0.613-0.933
HE4	0.888	0.813	0.964	0.059	0.898	0.838-0.958
GD2	0.952	0.889	1.000	0.010	0.952	0.922-0.982
GD3	0.967	0.936	0.997	0.014	0.973	0.963-0.983
Novel Panel	0.988	0.971	1.000	0.002	0.979	0.969-0.989