Biomarker Datasheet

Human Folate Receptor Alpha OmniVUE™ Biomarker

Product Overview

Folate Receptor alpha (FRα) is a high-affinity cell surface protein involved in the transport of folate into cells. It is highly expressed in various epithelial cancers, including ovarian, lung, breast, and renal cancers, while being minimally expressed in most normal tissues. Folate Receptor's restricted expression in normal cells and its overexpression in cancerous tissues make it an attractive target for cancer therapies, especially Antibody-Drug Conjugates (ADCs). By linking cytotoxic drugs to antibodies that specifically target Folate Receptor, ADCs exploit this overexpression for precise delivery of anticancer agents, limiting toxicity to healthy tissues. Folate Receptor also plays roles in mediating immune responses and in cellular growth and differentiation.

Overview

Target	Other names	Isotype	Primary cell type	Subcellular location	Relevant indications
Folate Receptor Alpha	FBP, FOLR1, FR-α, Folate binding protein	Rabbit IgG	Epithelial cancer cells, placental cells	Plasma Membrane	Ovarian and Kidney cancer

*Clone available upon request

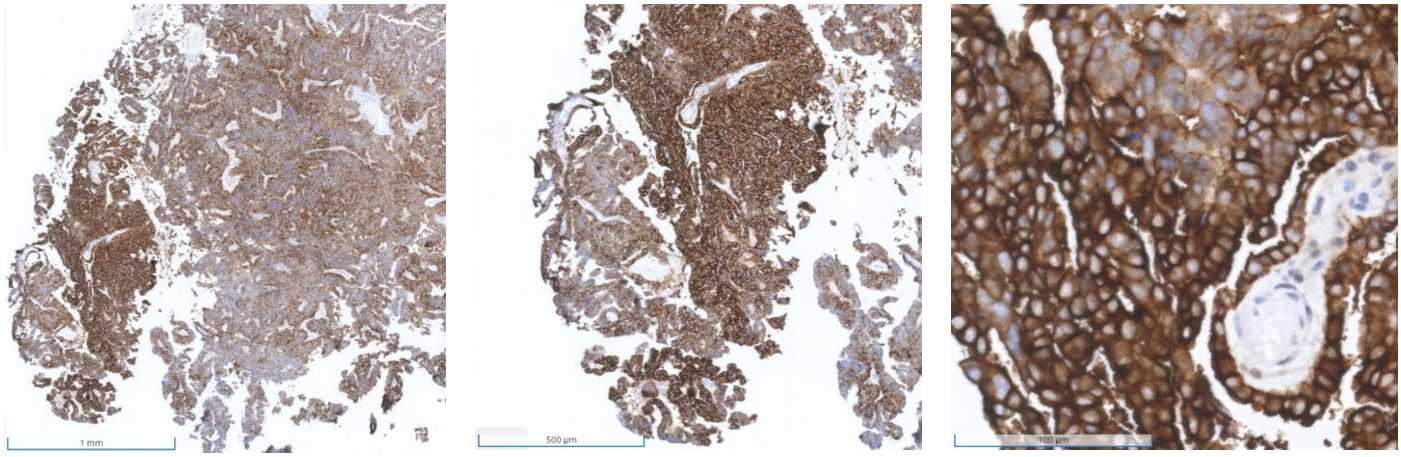
Quality Control

Each lot of Antibody-barcode conjugate reagent is tested on the appropriate positive control tissue and reviewed by Ultivue's pathologists and image analysis experts to ensure expected staining pattern and positive signal intensity, through qualitative as well as quantitative analysis. Lot-to-lot consistency is evaluated and strictly maintained through quantitative comparison of a new lot of reagent with the predicate (previous lot) with an accepted variability of ±20% for positive signal intensity, which is at par with the current standards practiced in pathology.

Predicate Comparison

Serial sections of ovarian cancer tissue were stained with traditional chromogenic DAB using unconjugated antibodies and with the InSituPlex® (ISP) monoplex assay to demonstrate concordance between staining modalities.

Folate Receptor Alpha DAB staining in Ovarian Cancer



Folate Receptor Alpha ISP staining in Ovarian Cancer

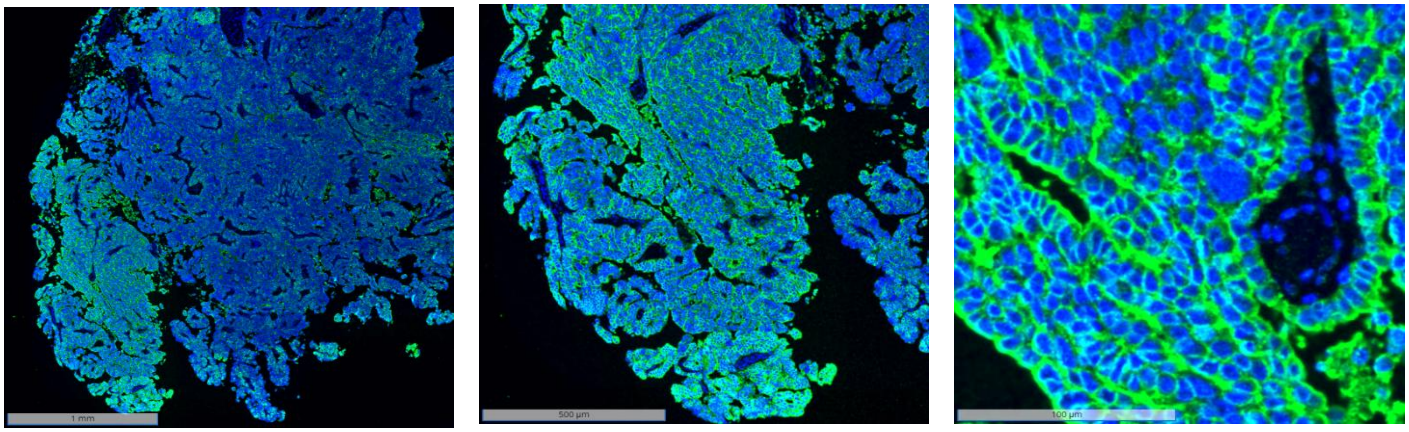


Figure 1: Comparison of unconjugated DAB and InSituPlex® monoplex assay in Ovarian Cancer tissue. Chromogenic DAB (top panel), fluorescent ISP staining (bottom panel).

Assay Performance testing

Precision of the InSituPlex® monoplex assay was evaluated by assessing intra-run precision and repeatability across serial sections of Ovarian Cancer tissue on the BOND RX autostainer by Leica Biosystems. For assessment of intra-run precision (Figure 2), 7 serial sections were stained within the same Bond RX run, imaged and analyzed in order to calculate the coefficient of variation (CV) for intra-run densities (number of positive cells/mm^2) and intra-run mean positive cell intensities. Inter-day precision (Figure 3) was assessed by staining 3 serial sections across 3 different days on multiple Bond RX staining runs. Stained slides were imaged and analyzed to calculate the CV for the same two key metrics: cell densities and mean positive cell intensities. Staining performance was found to be qualitatively and quantitatively concordant across all slides within a single run (intra-run precision testing) as demonstrated by CVs of both positive cell density and signal intensity. CVs for positive cell density and mean positive cell intensity were within the acceptance value of 30% for the Ovarian Cancer tissue (5.2% and 8.2%, respectively) (Figure 2). Similarly, staining performance demonstrated high concordance between slides stained across multiple runs. CVs for positive cell density and mean positive cell intensity remained within 30% for Ovarian Cancer tissue (21.1% and 10.0%, respectively) across the three independent runs (Figure 3).

We demonstrated excellent assay performance for the tumor tissue for which CVs were below the highest accepted value of 30% CV for tumor indications. To note, for tumor indications, the acceptance range is increased to 30% (from the accepted value of 20% CV[6]) to accommodate possible tumor heterogeneity.

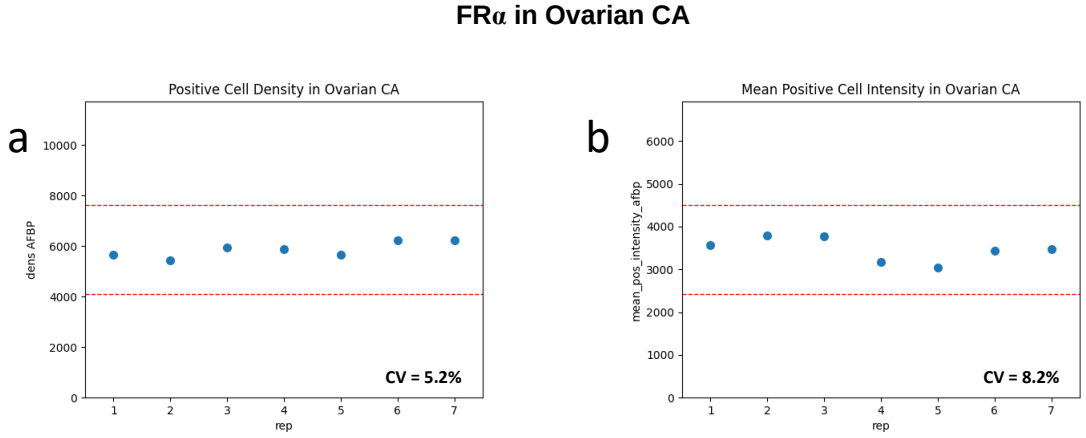


Figure 2: Intra-run precision of the InSituPlex® monoplex assay a. Number of positive cells/mm^2 per slide on Ovarian Cancer tissue. **b.** Mean positive signal intensity per slide on Ovarian Cancer tissue. For Ovarian Cancer tissue, thresholds (red dotted lines) mark +30% and -30% of the mean of all samples.

FRα in Ovarian CA

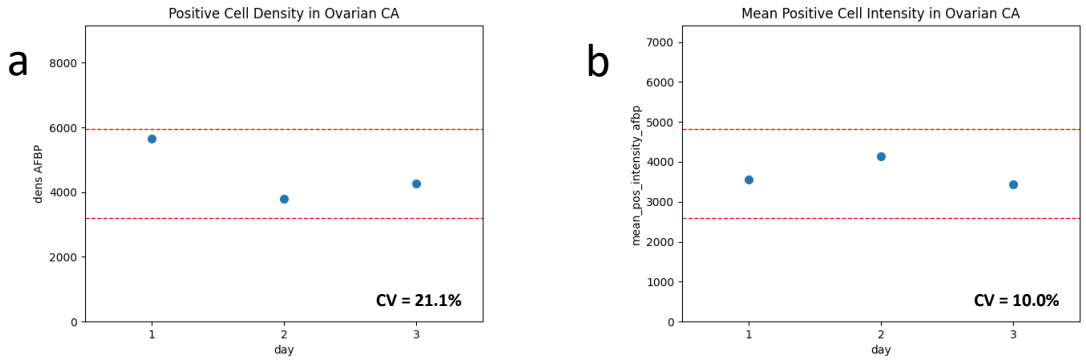


Figure 3: Inter-run precision of the InSituPlex® monoplex assay a. Number of positive cells/mm^2 per slide on Ovarian Cancer tissue. **b.** Mean positive signal intensity per slide on Ovarian Cancer tissue. For Ovarian Cancer tissue, thresholds (red dotted lines) mark +30% and -30% of the mean of all samples.

References

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3. Shen, Y., & Low, P. S. (2010). "Folate receptor-targeted cancer chemotherapeutics: Mechanism and therapeutic potential." *Advanced Drug Delivery Reviews, 62(10)*, 1299-1306.
4. Ab, O., Whiteman, K. R., Bartle, L. M., et al. (2013). "IMGN853, a Folate Receptor-Alpha (FRα)-Targeting Antibody–Drug Conjugate, Exhibits Potent Targeted Antitumor Activity Against FRα-Expressing Tumors." *Molecular Cancer Therapeutics, 12(10)*, 2126-2136.
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