Biomarker Datasheet

Human Tissue Factor OmniVUE™ Biomarker

Product Overview

Tissue Factor (TF) is a transmembrane protein that plays a critical role in the initiation of blood coagulation. It is expressed in various cells, including epithelial cells, macrophages, and tumor cells, where it acts as a receptor for Factor VII/VIIa, triggering the clotting cascade. Beyond its role in hemostasis, TF is involved in various pathophysiological processes such as cancer progression, metastasis, and inflammation. Due to its role in promoting tumor angiogenesis and metastasis, TF is a promising target in cancer therapies, including Antibody-Drug Conjugates (ADCs), which exploit TF's overexpression in tumors for targeted delivery of cytotoxic drugs.

Overview

Target	Other names	Isotype	Primary cell type	Subcellular location	Positive control(s) and relevant indications
Tissue Factor	TF, Coagulation factor III, CD142	Rabbit IgG	Epithelial cells, macrophages, tumor cells	Plasma Membrane	Tonsil, Placenta, kidney and most tumor tissues

*Clone available upon request

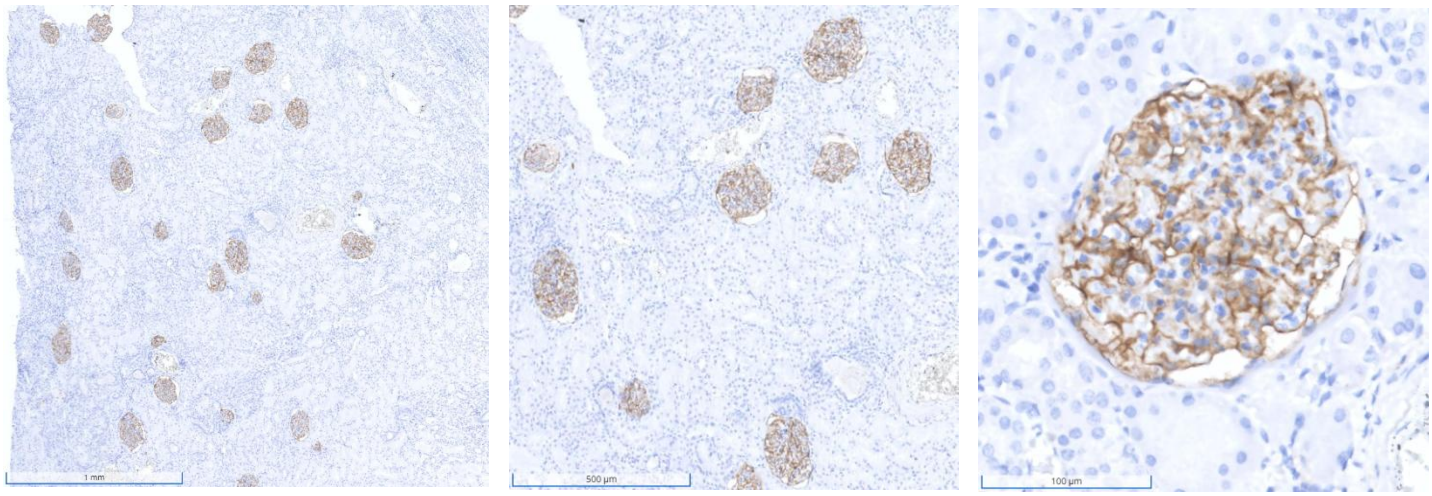
Quality Control

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 kidney positive control tissue and a relevant tumor tissue (non-small cell lung cancer NSCLC) were stained with traditional chromogenic DAB using unconjugated antibodies and with the InSituPlex® (ISP) monoplex assay to demonstrate concordance between staining modalities.

Tissue Factor DAB staining in Kidney



Tissue Factor ISP staining in Kidney

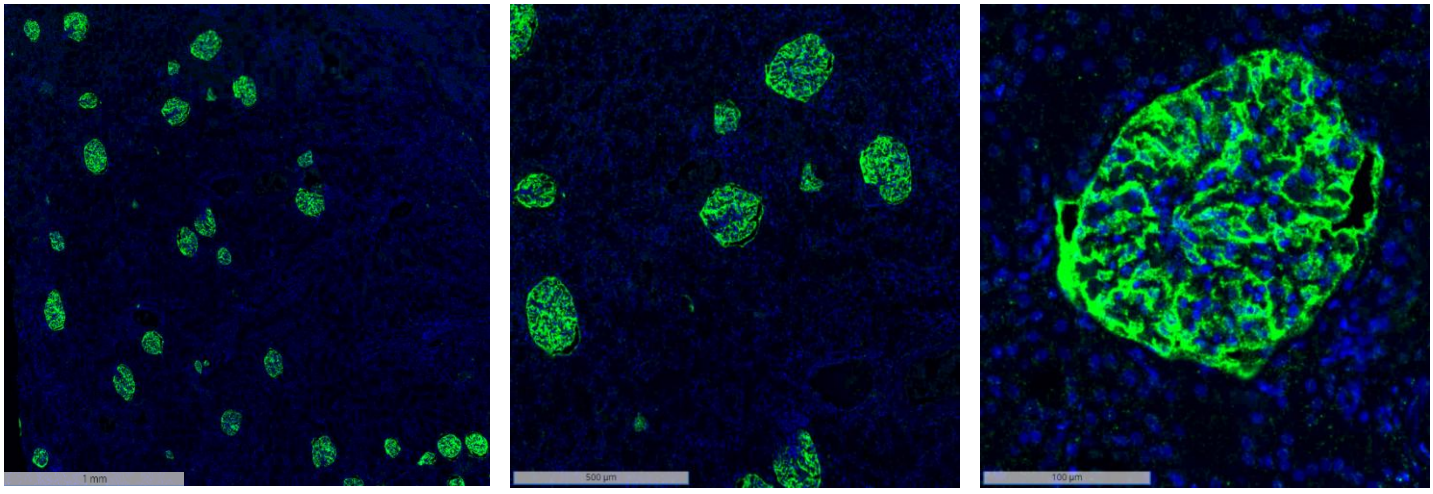
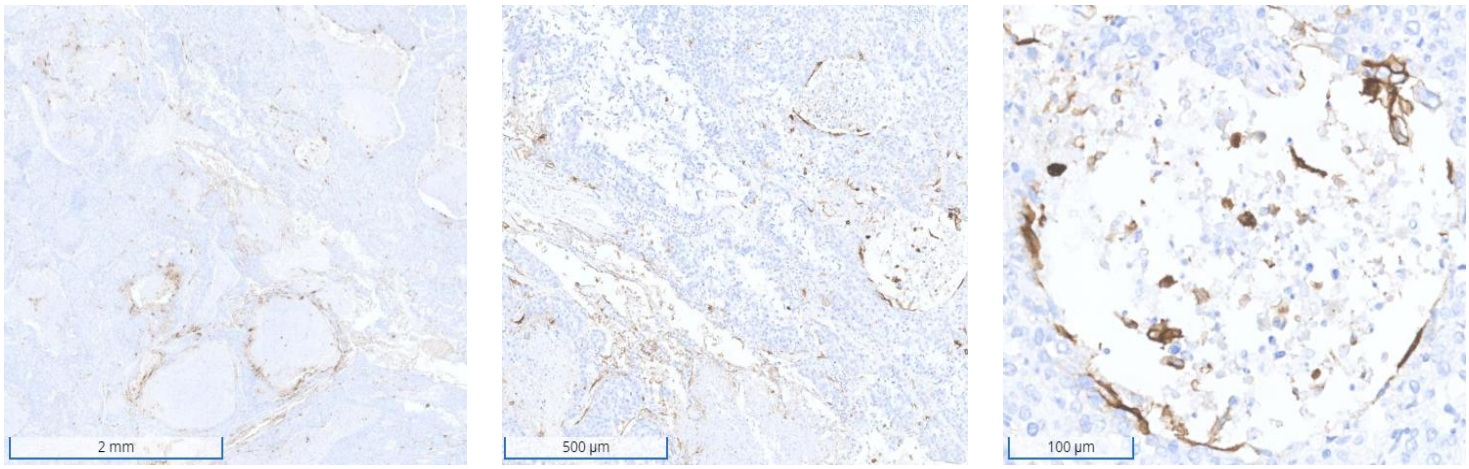


Figure 1: Comparison of unconjugated DAB and InSituPlex® monoplex assay in Kidney tissue. Chromogenic DAB (top panel), fluorescent ISP staining (bottom panel).

Tissue Factor DAB staining in NSCLC



Tissue Factor ISP staining in NSCLC

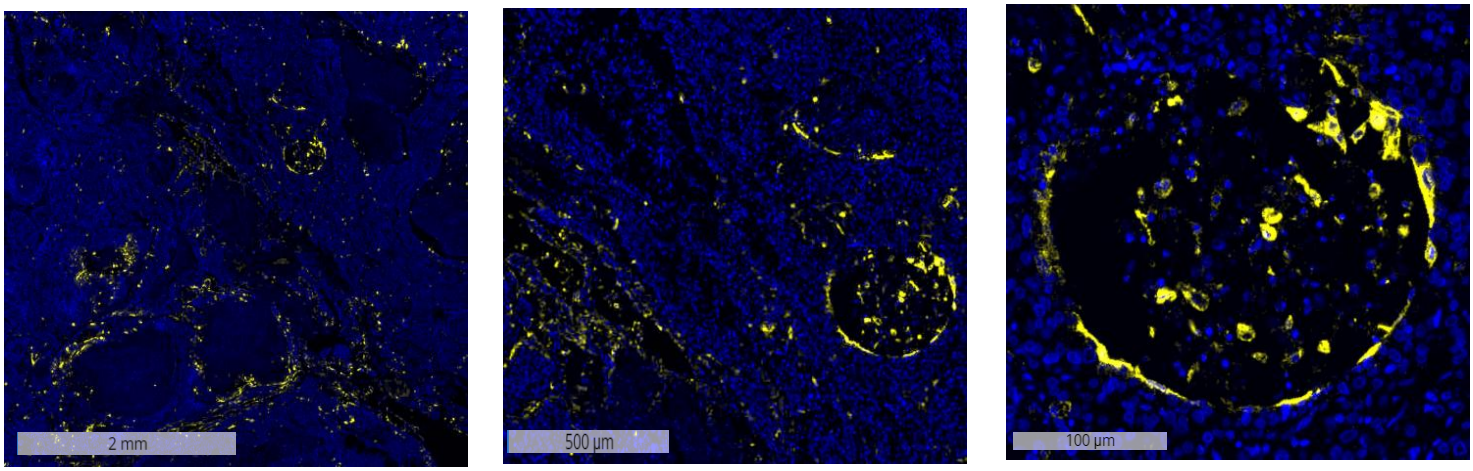


Figure 2: Comparison of unconjugated DAB and InSituPlex® monoplex assay in NSCLC tissue. Chromogenic DAB (top panel), fluorescent ISP staining (bottom panel).

Assay Performance testing

Precision of the InSituPlex® monoplex assay was evaluated by assessing intra-run precision and repeatability across serial sections of kidney and Non-small cell lung cancer (NSCLC) tissue on the BOND RX autostainer by Leica Biosystems. For assessment of intra-run precision (Figure 3), 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 4) 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 20% for the positive control kidney (13.0% and 6.8%, respectively) and the acceptance value of 30% for the NSCLC tissue (9.2% and 10.6%, respectively) (Figure 3). Similarly, staining performance demonstrated high concordance between slides stained across multiple runs. CVs for positive cell density and mean positive cell intensity remained within 20% for kidney tissue (11.1% and 3.3%, respectively) and within 30% for NSCLC tissue (19.4% and 21.5%, respectively) across the three independent runs (Figure 4).

We demonstrated excellent assay performance for both the positive control tissue and tumor tissue for which CVs were below the highest accepted value of 20% CV[5] for normal tissue and 30% CV for tumor indications. To note, for tumor indications, the acceptance range is increased to 30% to accommodate possible tumor heterogeneity.

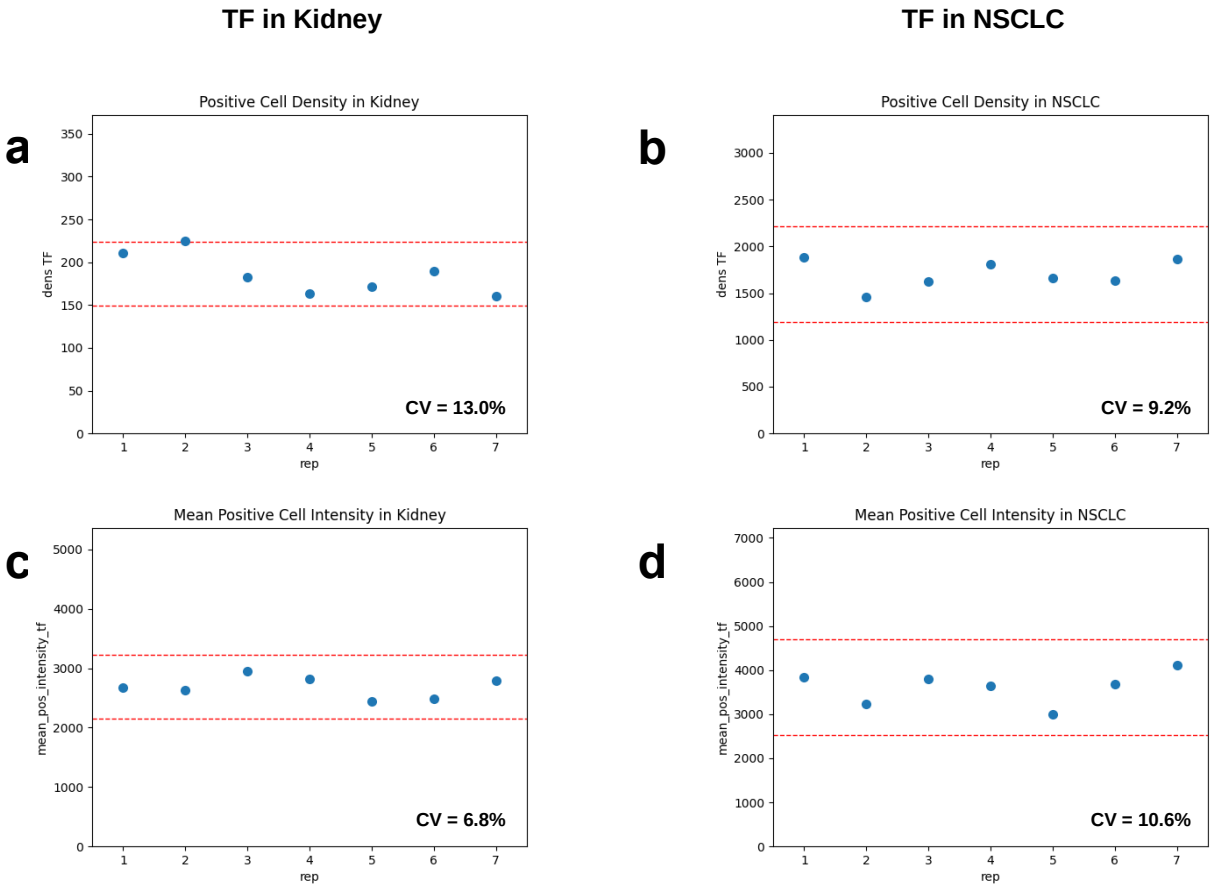


Figure 3: Intra-run precision of the InSituPlex® monoplex assay a. Number of positive cells/mm^2 per slide on kidney tissue. **b.** Number of positive cells/mm^2 per slide on NSCLC tissue. **c.** Mean positive signal intensity per slide on kidney tissue. **d.** Mean positive signal intensity per slide on NSCLC tissue. For kidney tissue, thresholds (red dotted lines) mark +20% and -20% of the mean of all samples. For NSCLC tissue, thresholds (red dotted lines) mark +30% and -30% of the mean of all samples.

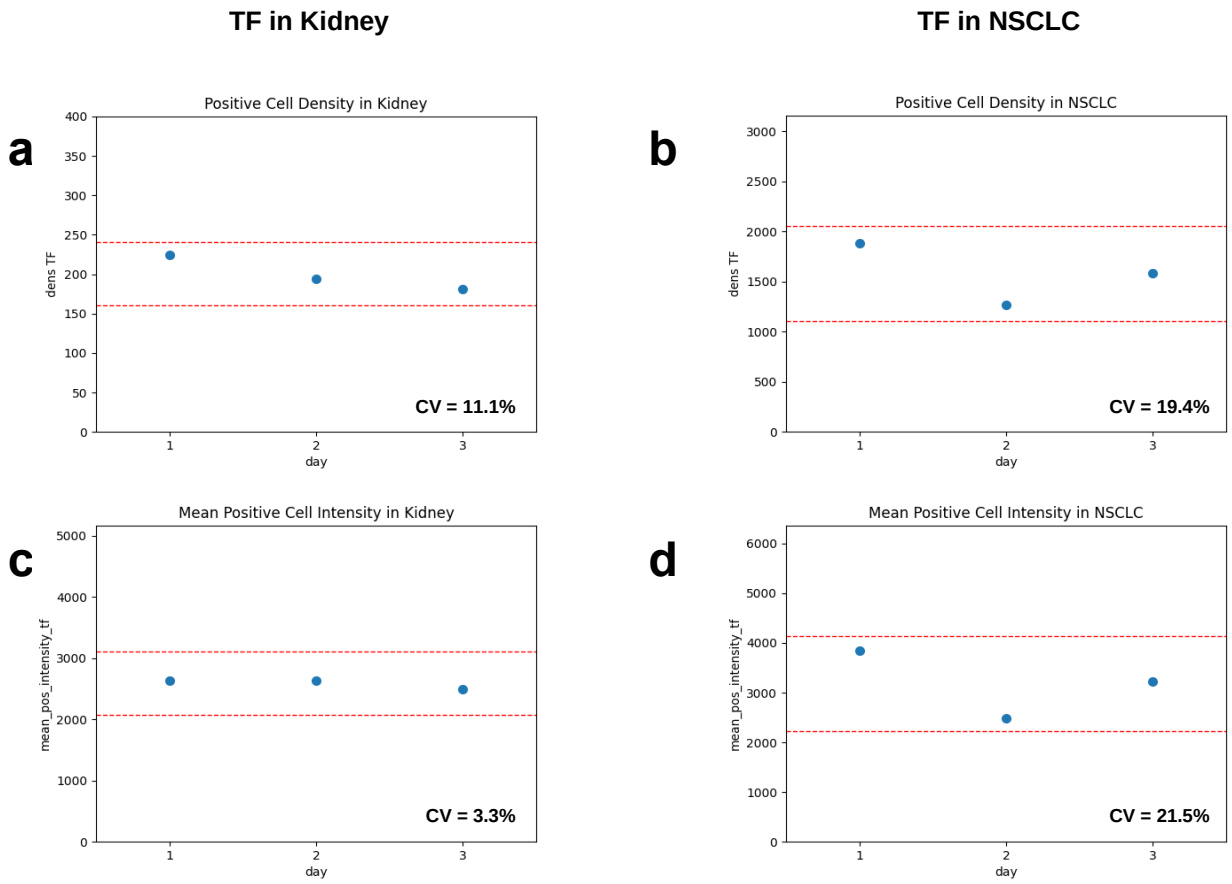


Figure 4: Inter-run precision of the InSituPlex® monoplex assay a. Number of positive cells/mm^2 per slide on kidney tissue. **b.** Number of positive cells/mm^2 per slide on NSCLC tissue. **c.** Mean positive signal intensity per slide on kidney tissue. **d.** Mean positive signal intensity per slide on NSCLC tissue. For kidney tissue, thresholds (red dotted lines) mark +20% and -20% of the mean of all samples. For NSCLC tissue, thresholds (red dotted lines) mark +30% and -30% of the mean of all samples.

References

1. Bogdanov, V. Y., & Versteeg, H. H. (2015). "Tissue Factor: A Major Mediator of Hemostasis and Thrombosis." *Thrombosis Research, 135(Suppl 1)*, S5-S9.
2. van den Berg, Y. W., Osanto, S., Reitsma, P. H., & Versteeg, H. H. (2012). "The Relationship Between Tissue Factor and Cancer Progression: Insights into Tumor Biology and Coagulation." *Thrombosis Research, 129(Suppl 1)*, S80-S85.
3. Hu, Z., & Rao, A. V. (2020). "Tissue Factor as a Target in Cancer: Innovations in the Development of Antibody-Drug Conjugates." *Cancer Research, 80(8)*, 1628-1635..
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