

Application Note

High Quality Tissue Essential in Developing Predictive Biomarker Assays

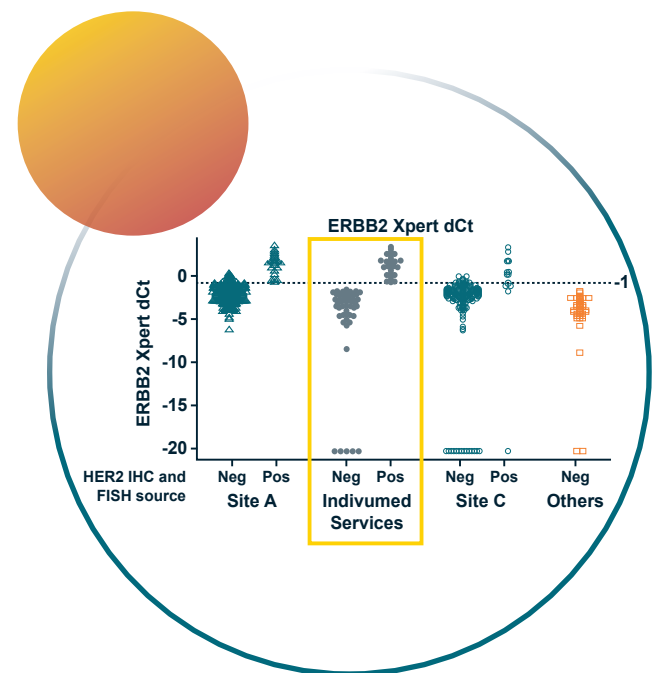
Overview

Results from any analytical assay are only as reliable as the quality of the analytes that are being evaluated. The tissue sample quality is of the utmost important factor for accurately assessing genes and proteins as closely presented/expressed clinically in the patient's tumor. Here, breast cancer patient samples sourced from Indivumed Services as well as other biobanks were assessed for HER2 (ERBB2) gene amplification and protein overexpression using three different analytical methods. Indivumed Services's high quality tissues (low ischemic time and high standard tissue processing procedure) showed the highest concordance rate of HER2 status as determined by the new GeneXpert Breast Cancer Biomarker Assay (Xpert BC) and the two standard method of analyzes immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH).

Study Summary

- Xpert BC is a semi-quantitative real-time PCR test that utilizes cutoff values that were empirically derived from comparison analysis studies of PCR and corresponding FISH and IHC data for the ERBB2 gene and protein (Figure 1).
- In order to validate the new Xpert BC assay, breast cancer tissues from Indivumed Services's biobank (117 samples) as well as other biobanks (384 total samples from different sources) were analyzed for (ERBB2) overexpression and gene amplification by the two standard companion diagnostic assays IHC (Herceptest) and FISH (PathVysion) respectively. The results obtained from the companion diagnostic assays were compared to those obtained from the Xpert BC assay.
- The accuracy of the established Xpert BC assay was assessed by deriving positive (PPA) and negative (NPA) measured agreements as well as overall percent agreement (OPA) when compared to the standard assays (IHC and FISH).
- Samples from Indivumed Services showed the highest concordance rate (100%) in all measured agreement including the OPA for high concordance in comparison to other tissue sources (Figure 2 A and 2 B).

Figure 1: Cutoff value (delta cycle threshold (dCt)) as determined by Xpert BC and compared to IHC and FISH Results



The delta cycle threshold (dCt) value is the normalized expression level of the mRNA compared to an endogenous control

Figure 2: Comparison Study (IHC, FISH and Xpert BC). a) Individumed Services Samples b) Other Sites Sourced Samples

Figure 2 A

ERBB2		IHC/FISH		Total
		POS	NEG	
Xpert	POS	35	0	35
	NEG	0	82	82
	Total	35	82	117

OPA: 100 % (95% CI: 96.9-100)

PPA: 100 % (95% CI: 90.0-100)

NPA: 100 % (95% CI: 95.6-100)

Figure 2 B

ERBB2		IHC/FISH		Total
		POS	NEG	
Xpert	POS	31	29	60
	NEG	5	317	322
	Total	36	346	382

OPA: 93 % (95%CI:87.8-93.8)

PPA: 86 % (95%CI:70.5-95.3)

NPA: 92 % (95%CI:88.2-94.3)

Indivumed Services' Advantage

- The high concordance results observed for Indivumed Services' samples is due to the high quality of the tissues.
- Tissue quality is affected by various factors including pre-analytical conditions such as ischemic time, sample processing/handling post-resection as well as the surgical procedure.
- Indivumed Services has established a distinctive infrastructure within the clinical networks in which its clinical teams are imbedded in the surgical OR. This unique arrangement allows the implementation of stringent tissue collection and processing protocols. Tissues are immediately fixed or frozen right after resection ensuring short ischemia time (on average 10 minutes)
- In depth clinical data (over 250 points) per patient is also annotated for every collection
- Quantity of the biological specimens and the data is guaranteed by a stringent validation process that is certified according to ISO 9001:2008

Implications

- In cancer biomarker assay development, tissue quality used for validating the assay is paramount in ensuring proper determination of cutoff values
- Whether an assay will be used as a part of diagnostic, prognostic or predictive tool, a proper stratification of patients starts with accurately determined cutoff values acquired from highly validated assays with high quality tissues

About Indivumed Services

Indivumed Services, a Crown Bioscience Company, is a global contract research organization (CRO) that offers an industry-leading oncology biobank and a range of service platforms to advance oncology and immuno-oncology drug discovery and development.

Holding a unique biobank of clinical specimens, unrivalled in quality and associated clinical history, which currently totals almost one million patient samples, the company partners with extensive clinical network of more than 60 entities in the United States, Europe, and Asia providing direct and controlled access to relevant surgical biospecimens and blood samples.

Further known for their enhanced immunohistochemistry and spatial transcriptomics, Indivumed Services' platforms complement a range of established Crown Bioscience capabilities supporting biomarker discovery.

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