Prosigna® Breast Cancer Prognostic Gene Signature Assay

The UNC Hospitals Molecular Genetics Laboratory offers the Prosigna® Breast Cancer Prognostic Gene Signature Assay to generate a risk score predicting distance recurrence of breast cancer.

Background: The Prosigna® Breast Cancer Prognostic Gene Signature Assay is an FDA 510(k)-cleared in vitro diagnostic assay performed on the NanoString nCounter® Dx Analysis System. This multigene RNA expression assay assesses prognosis in postmenopausal women with hormone receptor positive invasive breast carcinoma. The Prosigna® assay is based on the PAM50 signature developed at UNC by Dr. Charles Perou and colleagues. The assay measures 50 mRNAs (PAM50), along with 8 housekeeping RNAs for signal normalization, 6 spiked transcripts, and 8 negative controls. The Prosigna Score relies on a proprietary algorithm, resulting in a numerical value on a 0 to 100 scale that reflects low, intermediate or high probability of distant recurrence within 10 years.

Clinical Indications: Postmenopausal female hormone receptor positive (ER and/or PR expressing) breast cancer patient with one of the following tumor histologies: invasive ductal carcinoma, invasive lobular carcinoma, invasive carcinoma with ductal and lobular features ("mixed type carcinoma"), or not otherwise specified, who had surgery in conjunction with locoregional treatment for lymph node-negative stage I or II breast cancer, or for l stage II lymph node-positive breast cancer (1–3 positive nodes; micrometastases are considered node negative).

Laboratory testing: Six unstained 10 micron thick paraffin sections from a formalin-fixed paraffin-embedded (FFPE) breast carcinoma tissue specimen are required along with an H&E-stained slide on which the surgical pathologist has marked areas of invasive carcinoma. In those areas, malignant cell proportion must be ≥ 10% and the total circled area must be ≥ 4 mm2. A copy of the surgical pathology report is requested. Specify if the tumor is <= 2cm or >2cm, and if nodal status is negative or 1 to 3 nodes positive. After macrodissection of >100 mm2 of tumor, RNA is isolated and transcripts are quantified and score calculated on a NanoString nCounter Dx Analysis System. Results are interpreted by a pathologist and a "risk of recurrence" (ROR) score and risk category are reported.

References:

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2. Gnant M, et al. Predicting distant recurrence in receptor-positive breast cancer patients with limited clinicopathological risk: using the PAM50 Risk of Recurrence score in 1478 postmenopausal patients of the ABCSG-8 trial treated with adjuvant endocrine therapy alone. Ann Oncol. 2014, PMID:24347518
3. Filipits M, Nielsen TO, Gnant M et al. The PAM50 Risk-of-Recurrence Score Predicts Risk for Late Distant Recurrence after Endocrine Therapy in Postmenopausal Women with Endocrine-Responsive Early Breast Cancer. Clin Cancer Res. 2014, PMID: 24520097
4. Wallden B et al. Development and verification of the PAM50-based **Prosigna** breast cancer gene signature assay. BMC Med Genomics. 2015;8:54. PMID: 26297356

Questions? Consult a pathologist in the Molecular Genetics Lab at 984-974-1825 or email Dr. Weck at kweck@unc.edu

Website, http://www.uncmedicalcenter.org/uncmc/professional-education-services/mclendon-clinical-laboratories/directory/molecular-pathology-and-genetics