
We report the development of a gene expression (GE) based test to detect endometrial cancer (EC). Validation of the test in a multicenter validation study conducted in over 10 different hospitals in Spain is ongoing.

**Discovery:** Seventy tissue samples (60 EC + 10 normal) were collected from women with abnormal uterine bleeding (AUB) that were submitted to biopsy or tumor resection. Microarray based GE analysis was performed at Oryzon to yield a candidate gene set.

**Initial validation:** An independent cohort of normal (n = 20) and tumor tissue (n = 20) samples as well normal (n = 48) and tumor (n = 33) uterine aspirate samples was obtained for validation. GE analysis was performed using TaqMan LDAs containing an EC-specific signature in a 64-gene assay format.

**Translation:** Expression profiles from 9 tumor tissue and aspirates from the same patients were compared in Taqman LDAs and showed high correlation. This opened the possibility to perform the GE analysis on a sample type which can be obtained by a procedure that is considerably less invasive than hysteroscopy.

**ROC scores of the individual markers as secretory / proliferative and/or tumor/ no tumor markers were assessed. The best markers and endogenous controls were selected and 5 test score algorithms (4, 5, 6, 12, 20 genes) developed.**

The 5 scoring algorithms classified the 81 aspirates from subjects in the validation cohort as positive or negative for EC with high specificities and sensitivities (near 100%). Inclusion of markers that distinguish between secretory and proliferative phase is essential to correctly diagnose pre or perimenopausal women. One sample recorded as negative on histologic basis was classified as a tumor sample according to our algorithms. The histological revision of the EC-negative sample led to a reclassification of the sample, which may indicate that the GE assay could reduce diagnostic errors.

**Multi-center validation:** a cohort of 350-500 patients with AUB (20% is expected of being affected by EC) is being enrolled in a multicentric double blind study to evaluate 5 test algorithms. The LDA assay is being evolved to a small profile to produce a cost-effective assay.

**Conclusion:** The uterine aspirate based GE test shows high diagnostic potential. Inclusion of EC subtype specific and prognostic marker is expected to further increase the utility of the proposed diagnostic method.

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