EpiSwitch™ MIQE-Compliant PCR

A sensitive and reliable detection methodology enabling epigenomic precision medicine

Introduction: Getting the basics right

Oxford BioDynamics' (OBD) *EpiSwitch*™ biomarker discovery platform combined with their newly enhanced detection technology gives the company valuable quantitative insights into chromosome conformations (DNA protein complexes) that regulate normal and disease biology in individual patients. The company has developed an International Organization for Standardization (ISO) compliant clinical grade testing platform for quantitative real-time Polymerase Chain Reaction (qPCR) experiments and is actively working with their pharmaceutical and biotechnology industry partners to enable their precision medicine initiatives.

Approved genomic tests and the Food & Drug Administration (FDA)

PCR-based techniques are considered by the FDA as one of the 'gold-standard' technologies used for the validation of experimental results, and numerous PCR-based diagnostic assays have been approved in the last decade. In fact, approximately 40% of nucleic acid-based tests and companion diagnostics approved by the FDA through 2017 utilized PCR-based detection methodologies[1].

The speed, sensitivity, and quality of measuring chromosome conformations by *EpiSwitch* qPCR combined with the fact that in almost all circumstances, the development of new qPCR assays meet or exceed FDA standards for PCR assay validation, make *EpiSwitch* qPCR an industry leading biomarker measurement modality.

What is unique about the patented technology? OBD's *EpiSwitch* technology relies on a proprietary processing of chromatin templates into a robotically generated library, unique for each patient in which the protein/DNA complexes have been captured.

The qPCR experiments are rigorously controlled and exceed the guidelines for the Minimum Information for Publication of Quantitative Real-Time PCR experiments (MIQUE) published by Bustin et al., in 2009[2]: The company has also patented a unique range of sequenced internal standards and negative controls that validate near perfect diagnostic specificity.

Analytical sensitivity of qPCR

The analytical sensitivity of the *EpiSwitch* assays refers to the minimum number of copies in a sample that can be measured accurately, for OBD this is between 1-10 copies. For example, the FOXC1 chromosome conformation copy number varies in the blood of patients with non-malignant and advanced stage breast cancer. A typical calibration curve with tissue matched negative controls samples is shown in the figure on the following page. The amplification curves for the standards can be seen in pink (from a million copies, before cycle 20 on the x-axis to 1 copy), and the patient samples amplification curves are seen in blue. OBD's patented probe technology specifically detects the chromosome conformation and no products were detected in the non-template controls or concentration matched negative controls. The 3C assay shown below significantly discriminated advanced stage breast cancer from non-malignant samples using the FOXC1 chromosome conformation.

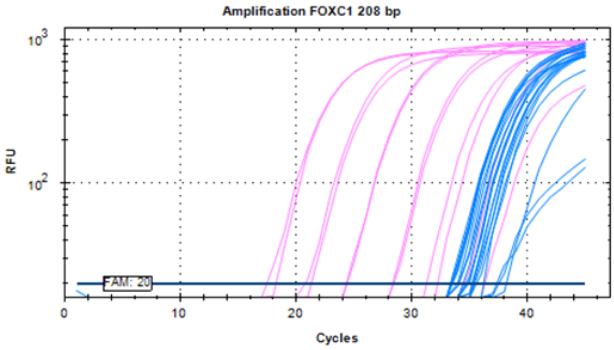

Figure 1: The amplification curves for standards (pink) and patient samples (blue), for the FOXC1 chromosome conformation qPCR assay.

Conclusion

The MIQE-compliant qPCR *EpiSwitch* assay technology is highly robust and reproducible and has been used in many collaborations with OBD's life science industry partners across a wide range of human disease indications. New insights into how the organization of the human genome contributes to pathological conditions coupled with quantitative insight into chromosome conformations is generating interesting answers to long standing questions in human health and disease. A host of recent academic publications and strategic developments related to patent protection for this proprietary technology have put the *EpiSwitch* biomarker discovery platform utilizing MIQE-compliant qPCR technology at the forefront of the rapidly expanding field of precision medicine.

References

1. https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm330711.htm
2. Bustin SA, Benes V, Garson JA, Hellemans J, Huggett J, Kubista M, Mueller R, Nolan T, Pfaffl MW, Shipley GL, Vandesompele J, Wittwer CT (2009). The MIQE guidelines: minimum information for publication of quantitative real-time PCR experiments. Clinical Chemistry. Apr;55(4):611-22.

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