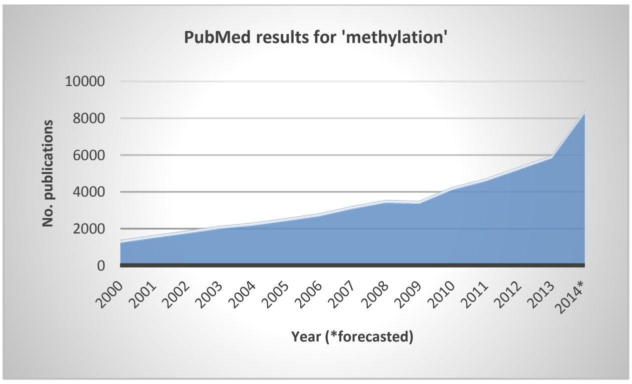
Methylation Specific-Quantitative Melt Analysis

Quantitative DNA methylation method

The opportunity

Interest in epigenetics, and in particular DNA methylation, is growing exponentially as more and more diseases are linked to changes in the "epigenome". Changes in methylation have been linked to diseases such as cancer, lupus, and a range of birth defects.



In the clinic, DNA methylation is being used to determine residual disease in prostate cancer patients and inform drug responsiveness in glioma patients.

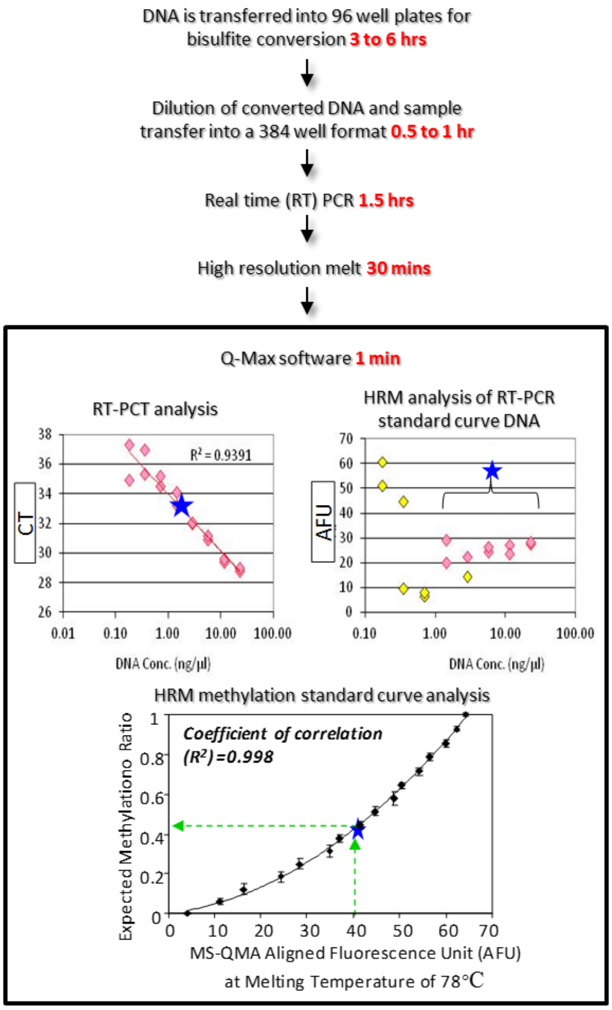
Researchers at MCRI have developed an assay and analysis method that has a quantitative limit of 2% and a qualitative limit of 1% for methylation at a target site within a DNA sample and enables high throughput screening in a 'closed tube' format.

The technology

The novel method referred to as "MS-QMA", combines the qualitative strengths of high resolution melt technology and the high-throughput, quantitative real-time PCR standard curve to provide accurate quantification of DNA methylation in a single assay.

MS-QMA has been shown to correlate with the more cumbersome reference methods of Southern blot and MALDI-TOF MS, and even to perform better with low quality DNA, e.g. DNA extracted from newborn blood spots. Analysis of MS-QMA raw data is by a custom designed computer algorithm, which simultaneously performs all analysis steps. The algorithm is available in the form of a user-friendly desktop application called **Q'Max**.

The performance of the method was assessed in Fragile X Syndrome (FXS), a neurodevelopmental disorder that is complex and heterogeneous in both clinical phenotype and epigenotype.



The present method was able to differentiate FXS affected individuals from controls, with sensitivity, specificity, positive and negative predictive values between 92 and 100%. The method was also shown to be sufficiently sensitive to provide prognostic information, as methylation ratios were significantly correlated with various measures of intellectual impairment (e.g. verbal IQ impairment P=0.002).

Applications

MS-QMA has the potential to be a powerful research tool for investigators examining the relationship between DNA methylation and disease.

MS-QMA has an immediate application in FXS diagnostics, including potential applications in newborn screening, prenatal testing and use in prognosis.

The method also has the potential to form the basis of diagnostic/prognostic tests for other conditions associated with aberrant DNA methylation, as well as companion diagnostics.

Opportunity for partnership

The Murdoch Childrens Research Institute is seeking a partner to develop the technology as a research tool, together with the **Q'Max** desktop application.

We are also seeking a partner to co-invest in the development of the technology for clinical applications.

Intellectual Property

The Murdoch Childrens Research Institute holds patents relating to the MS-QMA method (PCT/AU2014/000044).

The patent family describes the method broadly, as well as the use of the method to diagnose FXS, Prader-Willi syndrome/Angelman Syndrome and sex chromosome aneuploidies, as well as prognosis in FXS.

Intellectual property, in the form of copyright, also exists in the Q'Max desktop application.

Key publications

Godler DE et. al. Early Detection of Fragile X Syndrome: Applications of a Novel Approach for Improved Quantitative Methylation Analysis in Venous Blood and Newborn Blood Spots. Clinical Chemistry (2014) v. 60, p.963-973.

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