Detection of microsatellite instability (MSI) with the Idylla™ MSI Test in colorectal cancer samples

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Background

Detection of microsatellite instability (MSI) is recommended for all colorectal cancer (CRC) patients. Current clinical reference methods to detect MSI stain for mismatch repair proteins or analyze frequently mutated DNA repeat regions. The Idylla™ MSI Test is being developed using a unique set of novel biomarkers (Zhao et al. 2014; eLife) capable of faster detection with greater specificity and selectivity compared to current methods.

Methods

To assess the suitability of the novel marker set to detect MSI status in CRC, we profiled 8 or more markers in 870 CRC samples. Several clinical sites and different ethnic groups (Afro American, Caucasian, East-Asian, Hispanic and Indian) were included to assess robustness of marker selection. Repeat length was determined on FFPE DNA by PCR followed by melting curve analysis. Two-hundred and one samples were additionally screened with a reference methodology for MSI detection (Promega MSI analysis system).

Results

Hundred fifty-three samples (17.6%) were classified as MSI-H and 693 samples (79.7%) as MSS with the novel set of biomarkers, while 24 samples (2.8%) could not be classified. Concordance analysis was performed on 201 samples. The overall percent agreement with results available for both methods (173/201) was 93.6%. 11/173 (6.4%) were scored MSI-H for Idylla™ and MSS for the reference method; conversely no MSI-H cases for the reference method and MSS for Idylla™ were detected. 24/201 (11.9%) samples failed with the reference method, even after repeat testing, while only 8/201 (4.0%) samples failed with the Idylla™ methodology.

Conclusion

This study on a diverse set of CRC samples successfully demonstrated the validity of the novel MSI biomarkers to discriminate between MSI-H and MSS status. The Idylla™ MSI Test is currently under development on the most performant markers. Compatibility with the fully integrated Idylla™ platform will allow providing accurate, reliable results and actionable results generated within 150 minutes from just one tumor FFPE slice (no reference sample required).

Figure 1 Marker selection and development of the Idylla™ MSI Test

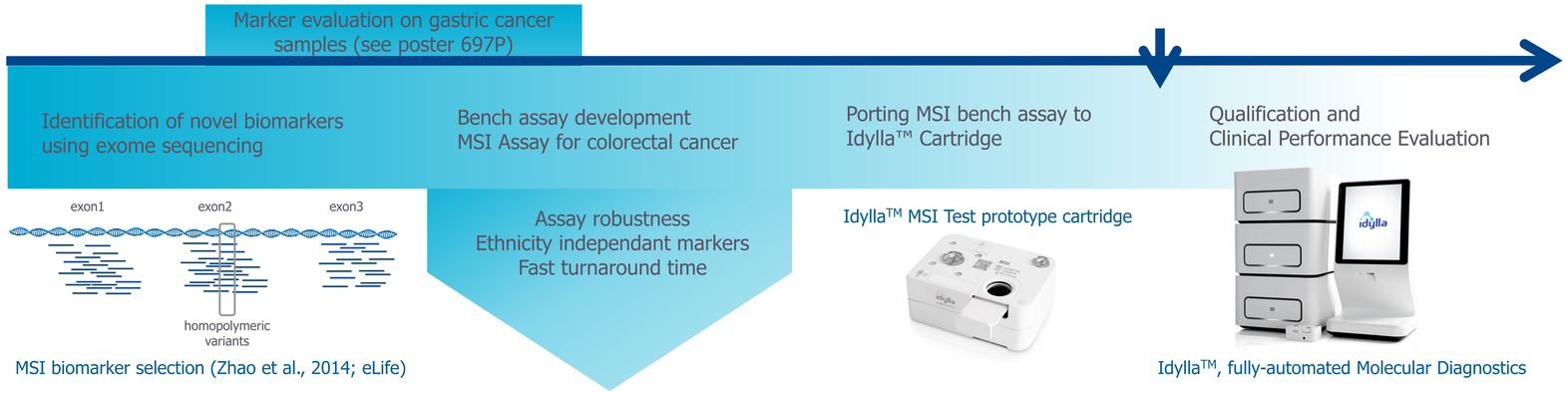


Figure 2 Screening of 870 colorectal cancer samples with novel biomarkers during Idylla™ MSI Test optimization

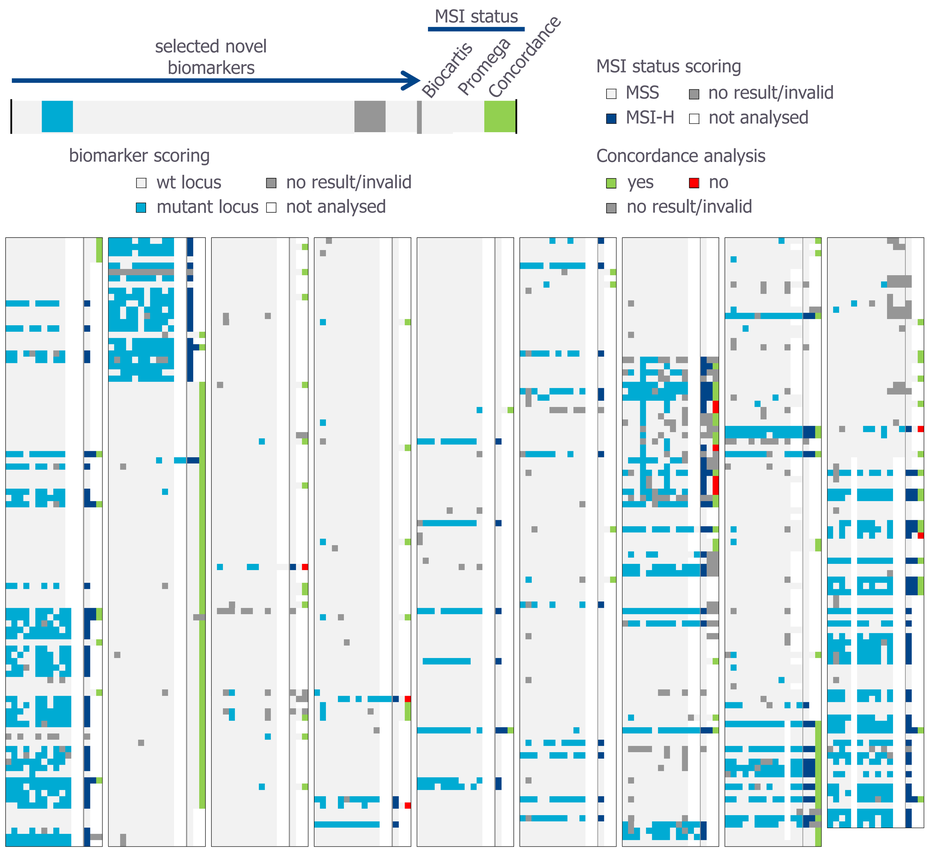
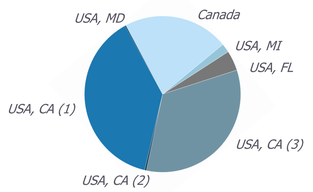


Figure 3 CRC sample characteristics

(n=870)	Biocartis MSI Test (at least 8 markers)			
	MSS	MSI-H	Failed	Total
Total	693	153	24	870

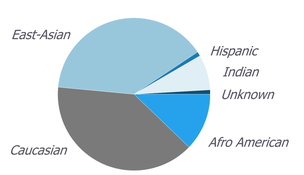
Distribution

Sample source



Samples acquired from several CROs (country of head office indicated), sourcing globally to ensure sample variability

Ethnicity



Several ethnicities were included to check marker length consistency and assay robustness

Figure 4 Concordance analysis Biocartis MSI vs Promega MSI biomarkers

(n=201)		Biocartis (at least 8 markers)			
		MSS	MSI-H	Failed	Total
Promega MSI analysis (5 markers)	MSS	123	11	4	138
	MSI-H	---	39	---	39
	Failed	9	11	4	24
	Total	132	61	8	201

93.6 % overall concordance on 173 samples

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