Detection of microsatellite instability (MSI) with a novel panel of biomarkers in gastric cancer samples

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Background
Detection of microsatellite instability (MSI) is recommended to identify colorectal cancer (CRC) patients with Lynch syndrome, but MSI is present in several other tumor types such as ovarian and gastric cancer. 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 for 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 gastric cancer, we performed a small-scale evaluation study: 10 novel MSI biomarkers with proven efficacy in CRC were tested in 150 gastric cancer samples. Repeat length was determined on FFPE DNA by PCR followed by melting curve analysis. Eighty-five samples were screened with a reference methodology for MSI detection (Promega MSI analysis system).

Results
Fifteen out of 150 samples (10%) were classified as MSI-H with the novel set of biomarkers. At least 5/10 (50%) of the markers scored mutant in each of these 15 samples. All of the 10 markers scored wild type in 131/150 samples. All samples with at least one mutant marker (n=19) and 66 randomly selected samples with no mutant markers were screened with the Promega MSI analysis system. 9/85 samples failed with the reference method, even after repeat testing, while the Idylla™ methodology did not generate any failures (0/150). For 76 samples with results available for both methods, the overall percent agreement was 100% (76/76).

Conclusion
This study on a limited number of samples successfully demonstrated the validity of the novel MSI biomarkers to discriminate between MSI-H and MSS samples in gastric cancer samples. The Idylla™ MSI Test will be compatible with the Idylla™ platform designed to provide rapid and reliable results, with actionable results generated within 150 minutes. Interestingly, recent scientific evidence is coupling MSI tumor status to eligibility for immunotherapy. As such our fast and personalized diagnostic solution could potentially be coupled to one of the most promising therapies harnessing the immune system to fight cancer.

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

Figure 2 Screening results of 150 gastric cancer samples

Figure 3 Number of positive Biocartis MSI biomarkers observed in gastric cancer samples with MSI-H status

Figure 4 Concordance analysis Biocartis MSI biomarkers vs Promega MSI markers

(n=85)