Innovative, rapid and easy to use diagnostic multiplex platforms that enable individualized care

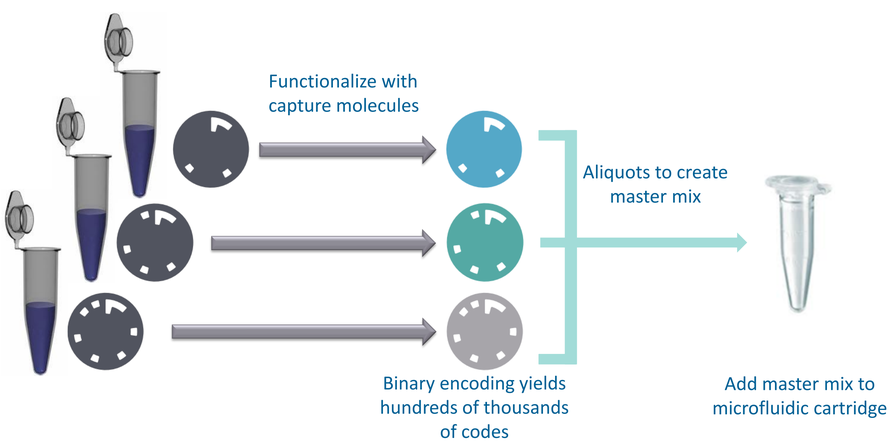
Ina Vandenbroucke, Benoit Devogelaere, Patrick van den Boogaard, Koen Van Acker, Bart Claes, Erwin Sablon and Geert Maertens
Biocartis, Generaal De Wittelaan 11B3, 2800 Mechelen, Belgium

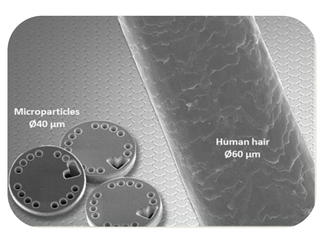
Introduction

Cancer therapy is in evolution from non-specific cytotoxic drugs that damage both tumor and normal cells to more specific agents and immunotherapy approaches. Targeted agents are directed at unique molecular features of cancer cells, and immunotherapeutics modulate the tumor immune response; both approaches aim to produce greater effectiveness with less toxicity. The development and use of such agents in biomarker-defined populations enable more individualized approaches that require easy-to-use, rapid diagnostics platforms that can operate at the point-of-need.
Biocartis has developed two platforms that are expected to meet such requirements.

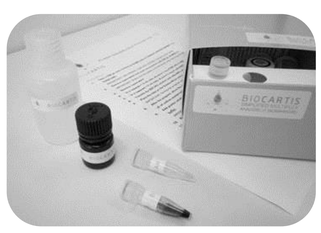
The High Multiplex platform

The Biocartis' high multiplex platform leverages advanced semi-conductor technologies and micro-fluidics to provide fast, flexible and multiplexed detection and quantification of nucleic acids and proteins. The platform accelerates biomarker research and yields robust and highly reproducible data over a wide range of analyte concentrations. Biocartis' proprietary digitally encoded microparticles allow for the simultaneous detection of up to 2,000 different analytes without deterioration in performance.





Silicon-based, digitally encoded microparticles - 40 µm in diameter


Conditioned microparticles ready for attachment of capture molecules


Novel microfluidic cartridge designed for accelerated and real-time assay protocols


Instrument, performing all steps of assays, including thermal control, fluidic activation, and fluorescence readout

The Molecular Diagnostics platform

The Molecular Diagnostics (MDx) platform is a sample-in, result-out system that enables the detection of up to 30 reportable nucleic acid (DNA, RNA, meDNA, miRNA) biomarkers in a single disposable cartridge with minimal user intervention. A wide range of solid and liquid sample types, including formalin-fixed, paraffin-embedded (FFPE) tissue can be used. A single FFPE shaving is directly placed in the cartridge. The complete process for sample preparation, PCR and reporting is less than 90 min, with <2 minutes hands-on time. A prototype *BRAF* V600 Mutation assay has shown superior analytical sensitivity (detection of <1% of mutant in wt background), ease of use, turnaround time, and detects a broader range of mutations (V600E, E2, D, K, R, and M) compared to existing diagnostic tests (Roche COBAS *BRAF*), as shown in a series of >65 FFPE samples (extract of this study in Table 1). Concordance with deep sequencing was 100% (MiSeq, Illumina).

					Anticipitated sensitivity	5%	~1%	1%
ID	Tumor type	Year	Pigmentation	% tumor (at purchase)	Benchmark BRAF qPCR assay (macrodisected)	Biocartis MDx BRAF (1 shaving)	Deep sequencing (1 shaving)
A1	Melanoma	1993	Low	30	WT	V600E	V600E (4.6%)
A3	Melanoma	1994	Low	5	Not tested*	WT	WT
A5	Melanoma	2001	Low	83	MUT	V600E	V600E (27%)
A6	Melanoma	2002	Low	90	WT	WT	WT
A7	Melanoma	2003	High**	85	WT	WT	WT
A8	Melanoma	2008	Low	90	WT	WT	WT
A9	Melanoma	2005	High**	65	WT	V600K/R	V600R (5.7%)
A16	Melanoma	2011	Low	80	WT	WT	WT
A20	Melanoma	2011	Low	92	MUT	V600E	V600E (37%)
A21	Melanoma	2011	High**	90	MUT	V600E	V600E (40%)
A22	Melanoma	2011	Low	20	WT	WT	WT
A23	Melanoma	2011	Low	100	MUT	V600K/R	V600K (40%)
O1	Melanoma	2002	High**	97	WT	WT	WT
O2	Melanoma	2002	High**	85	MUT	V600K/R	V600K (36%)
O3	Melanoma	2002	Low	99	WT	WT	WT

Table 1 Comparison of performance of the prototype BRAF V600 assay on the Biocartis MDx platform to the Cobas BRAF assay and MiSeq deep sequencing (*Not tested because no tumor. ** May contain high melanin),


Sample in

<2 min hands-on time


35 to 90 min processing time

Rapid result out

(Currently) up to 30 real time (q)PCR measurements

Sample liquefaction/ Swab rinsing

Cell lysis

DNA/RNA extraction (optional)

NA amplification and detection

Data analysis and reporting

The 1st International Congress on Controversies in Personalized Oncology (CONPO)
7-10 March, Barcelona, Spain