Bringing Personalized Medicine to the Clinic

A High Multiplex Open Platform Approach to Fusion Gene Test Development

Next Generation DX Summit

August 2011

PrimeraDx

Bringing Personalized Medicine to the Clinic

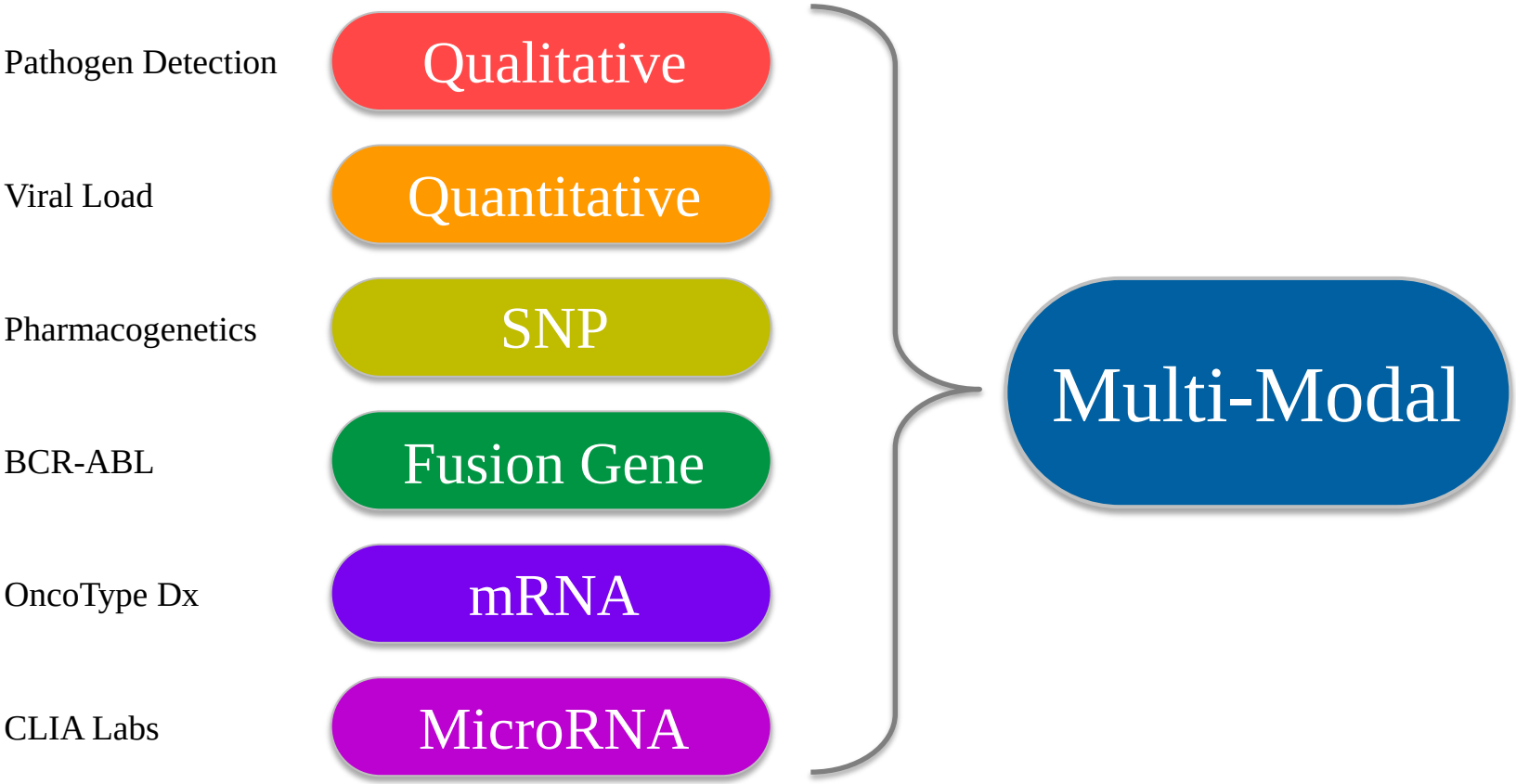
Providing a molecular platform for the robust detection and quantification of multiple target types in a single well.

Enabling clinical labs to easily develop cost-effective, high impact molecular diagnostic tests.

Bringing next generation products to patient care.

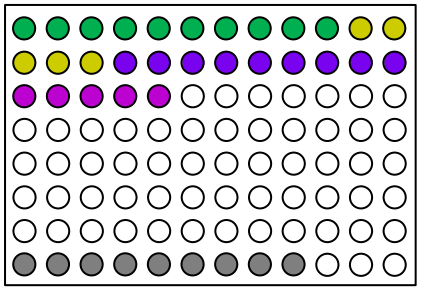
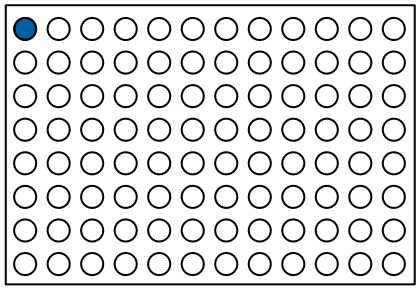
The Progression Towards Multi-Modal Testing

Clinical Market Now Needs "All-in-one Well" for Patient Care



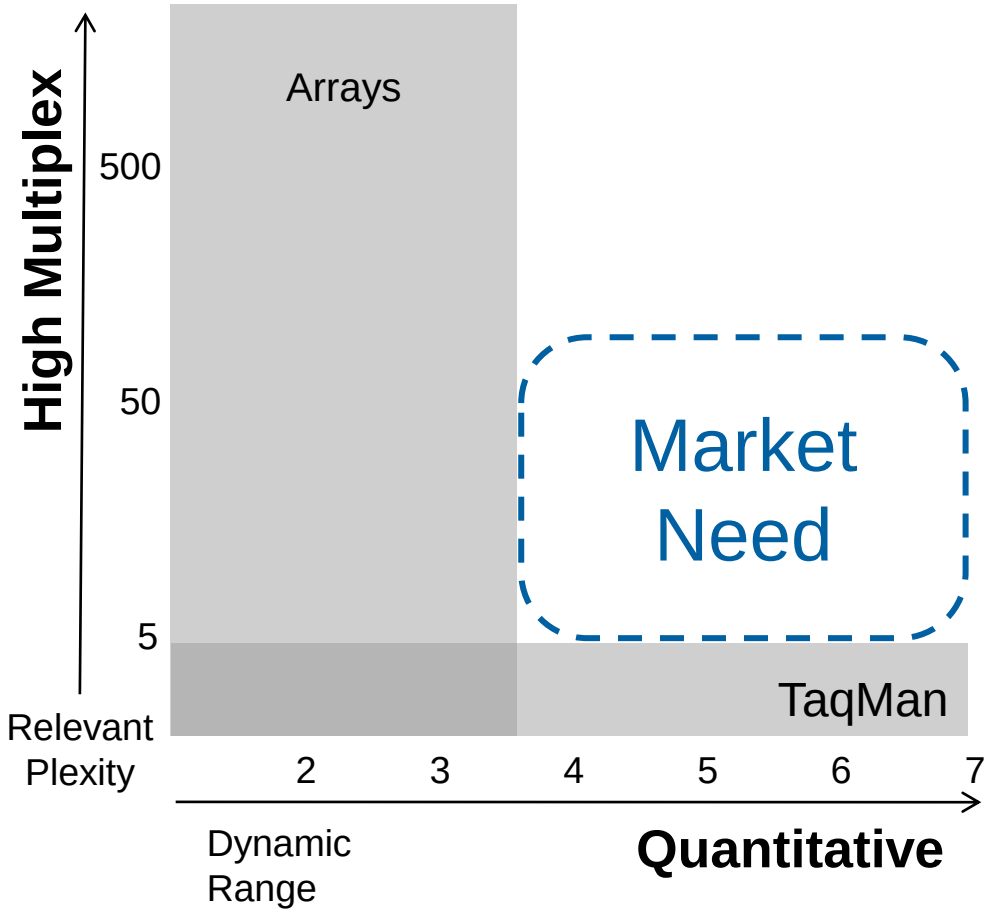
ICE*Plex*: High Quality / Low Cost / Simple Workflow

Technology that Redefines the Market

		Real-Time Instrument	PrimeraDx
Oncology Multi-Modal Panel: Fusion gene variants + Oncogene Gain-of-function SNPs + Gene Expression Signature + MicroRNAs	29 Targets + 9 Controls		
	96 Patient Samples	**6 days**	**1 morning**

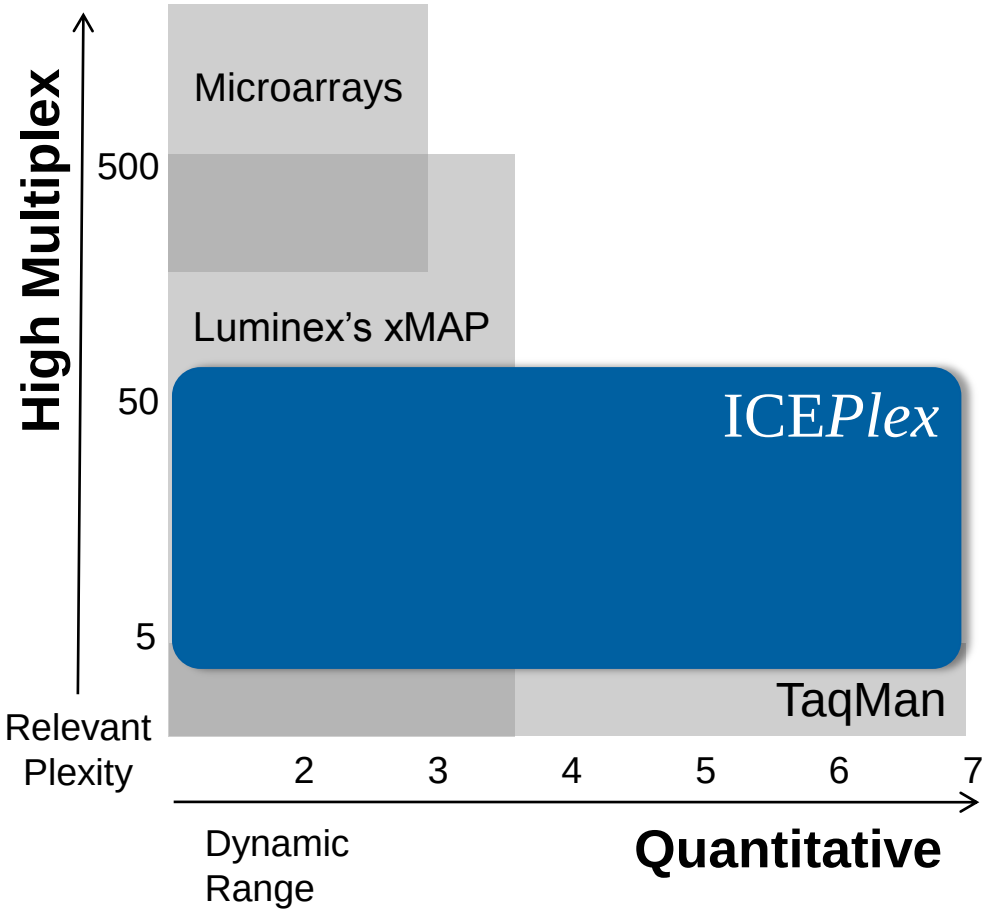
Current Technologies Lag Clinical Practice Requirements

Clinical Need: High Multiplex AND Dynamic Range



Only ICE*Plex* Can Solve this Market Need

Clinical Need: High Multiplex AND Dynamic Range



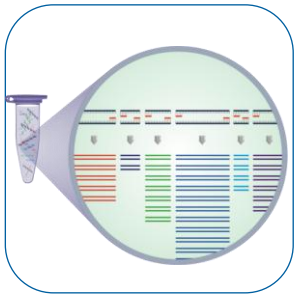
ICE*Plex* Technology: Providing Answers That Matter

The Marriage of PCR and Capillary Electrophoresis

Real-time detection of PCR products separates targets by size.

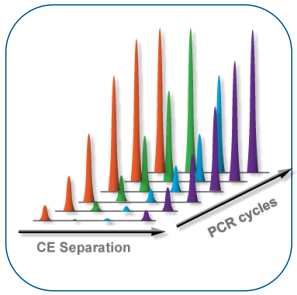
Sampling as the reaction progresses allows quantitation.

Multiplex quantitative results provide clinically actionable data.



PCR

+



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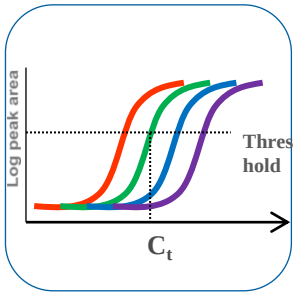

Quantification

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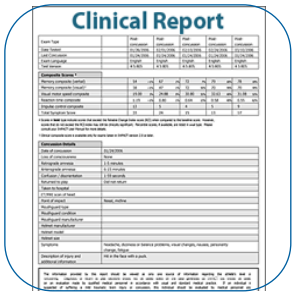


Clinically Actionable Results

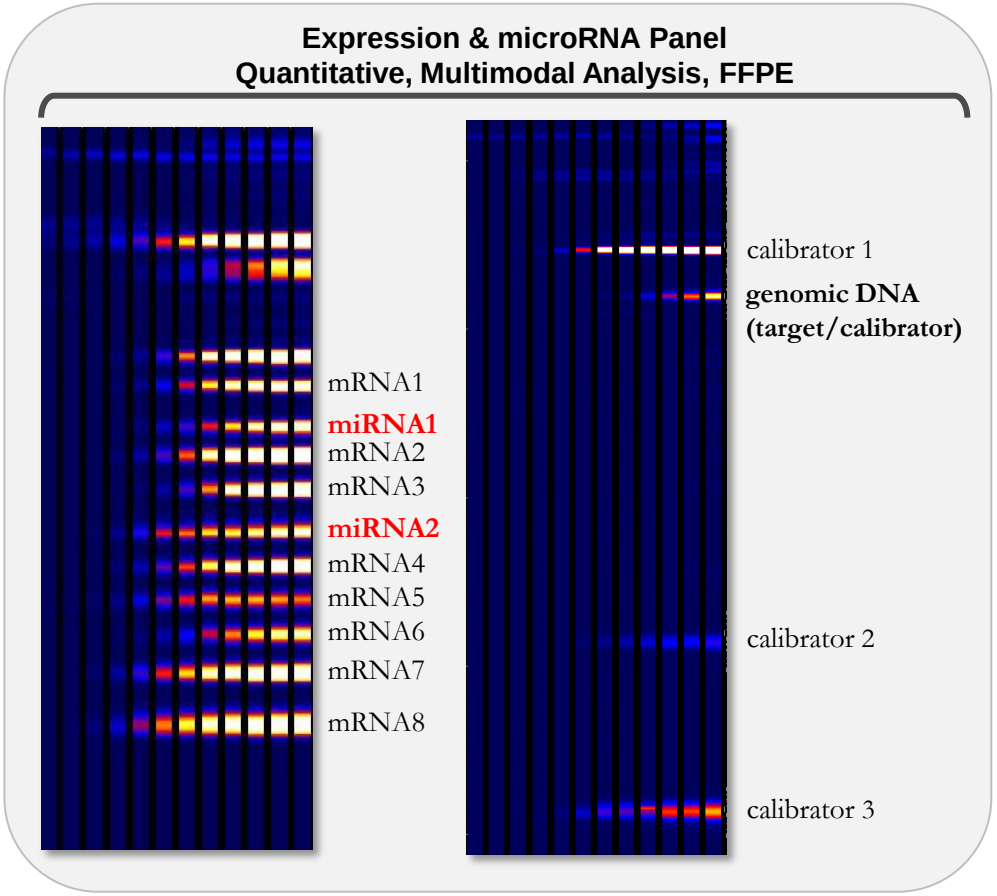
Proof-of-Concept in Oncology

Examples in Infectious Disease, Oncology and Non-Clinical

Quantitative Multiplex Oncology Assays
Multi-modal (mRNA + microRNA + DNA + Calibrators and Controls)
Malignant Melanoma (DNA Methylation Assay)
Colorectal Cancer (KRAS mutations)
Non Small Cell Lung Cancer (Fusion Gene Variants)
Pan-Myeloproliferative Disease (BCR-ABL + JAK2)

Simultaneous Quantification of mRNA and miRNA expression

The First and Only Platform Currently Being Used for Multiple Target Type Detection

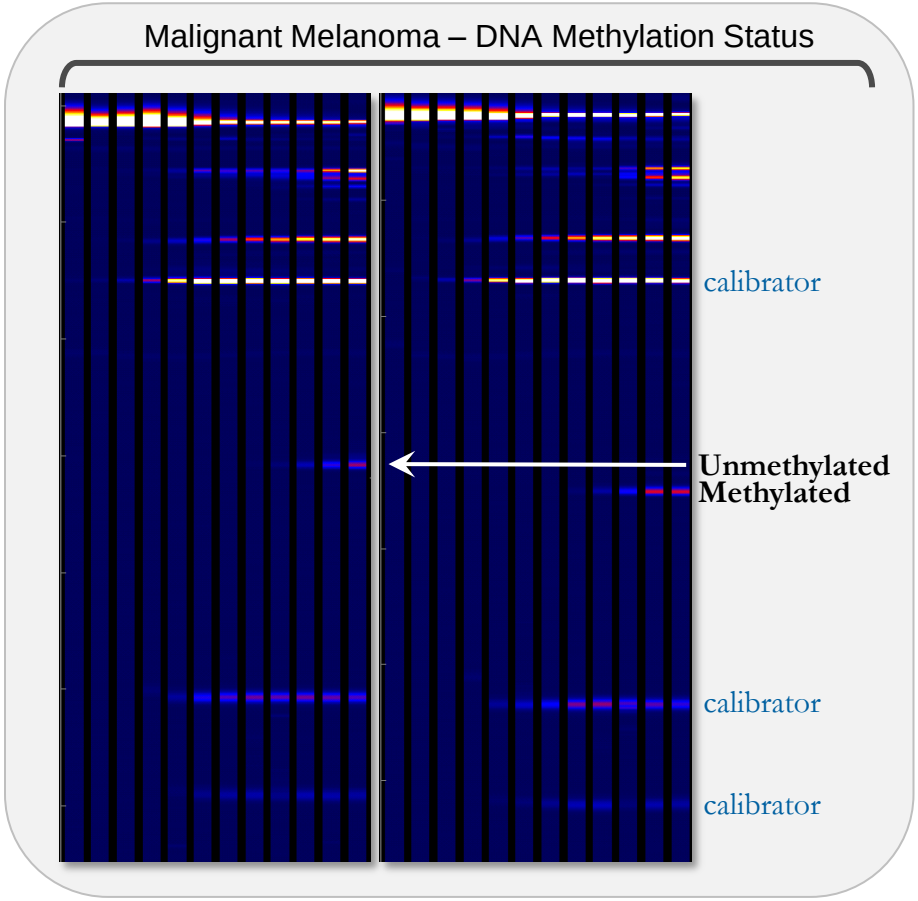


ICE*Plex*:

- ✓ **Companion Diagnostics** will require multi-modality
- ✓ **Simultaneous detection** of multiple target types
- ✓ **Makes complex tests "submit-able" to FDA**

Malignant Melanoma

Detect Methylation in Multiplex

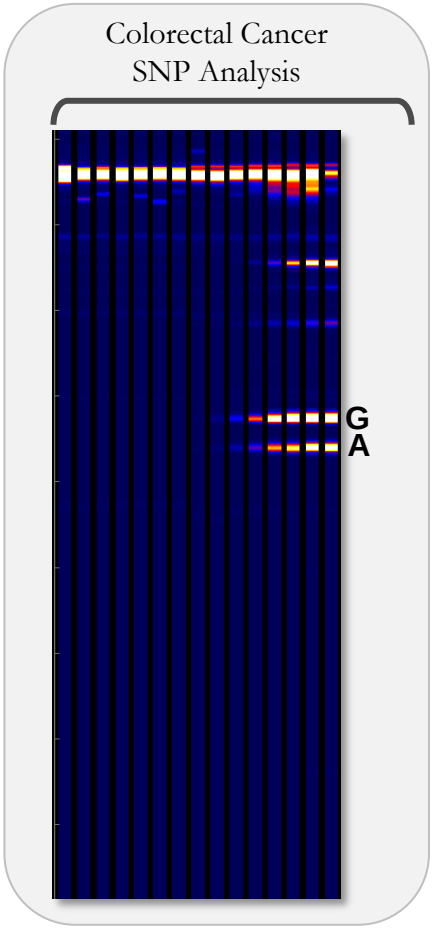


The Methylation state of some genes has been used as a biomarker for tumorigenesis. Here we tested for methylation status of a gene in malignant melanoma tissue.

The ICE*Plex* platform can very easily distinguish between unmethylated and methylated genes. The ability to do this in multiplex will provide a needed tool to clinical labs that are currently finding it difficult to run similar assays.

KRAS Mutation Detection in Colorectal Cancer Tissue

Detect SNPs in Multiplex

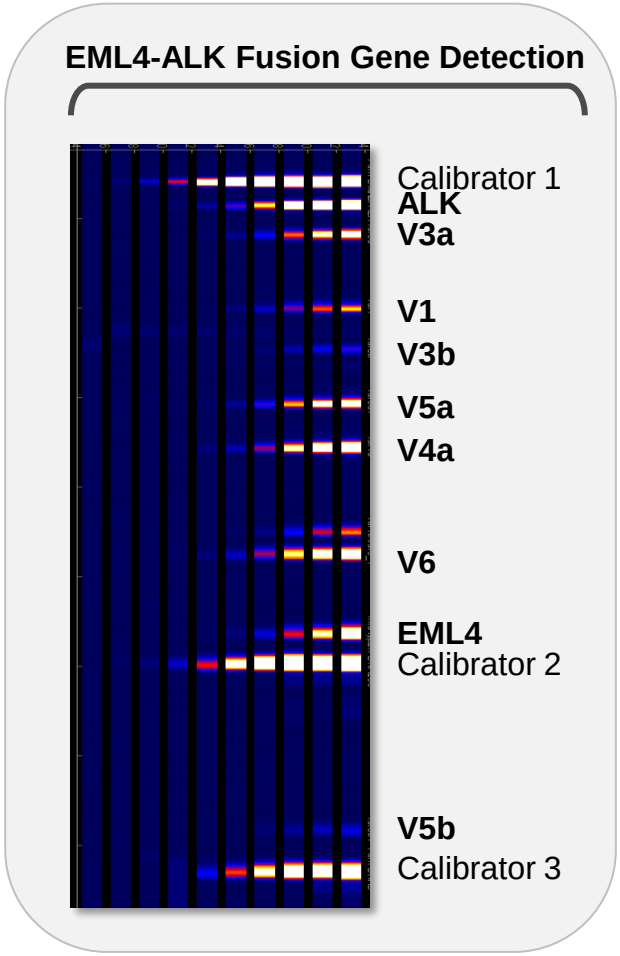


Forty percent of colorectal cancers are associated with mutations in the KRAS gene. At present, the most dependable way to predict whether a colorectal cancer patient will respond to an EGFR-inhibiting drug is to test for mutations in the KRAS gene.

The ICEPlex platform is an easy and inexpensive way to detect multiple point mutations.

Non-Small Cell Lung Cancer Fusion Gene Panel

Detect Fusion Gene Variants in Multiplex



The fusion of the EML4 and ALK genes has been found as a causative agent in ~10,000 new cases of Lung Cancer annually in the United States. Using a multiplex approach, we designed an assay that detects the most common EML4-ALK variants, as well as the EML4 and ALK genes.

Currently, the "gold standard" assay for ALK fusion genes is fluorescence in situ hybridization (FISH). Although FISH is commonly used the results are difficult to interpret. The assay requires specialized technical resources and expertise and, as a result, is not readily available in all pathology laboratories.

The ICEPlex platform provides clinical laboratories with a simple and robust way of detecting all clinically relevant variants.

Pan-Myeloproliferative Disorders Test

BCR-ABL + JAK2

Currently, there are two main mutations that cause most of what have been traditionally been termed the Myeloproliferative Disorders.

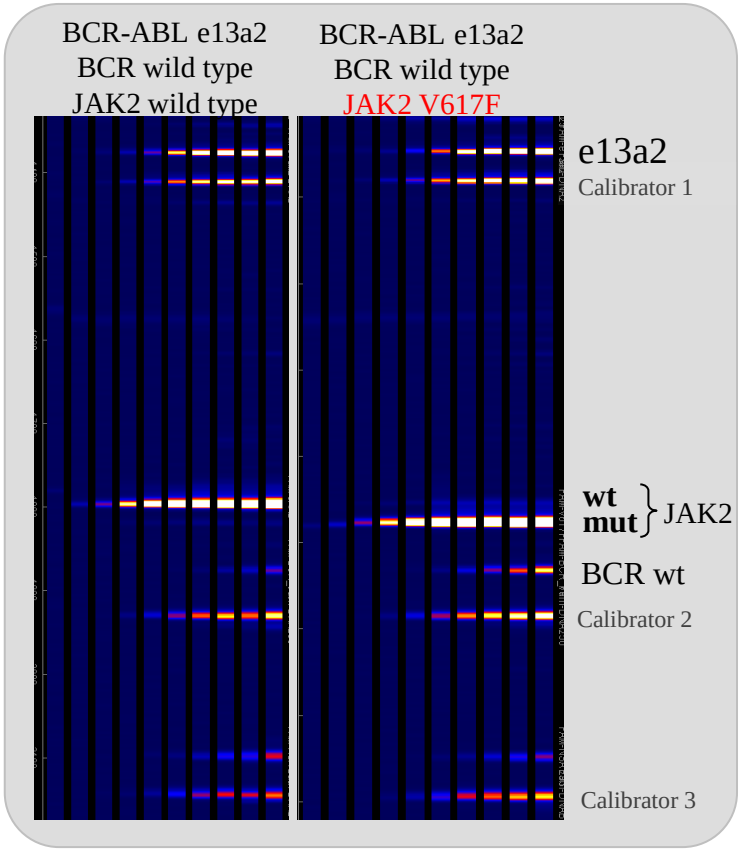
- BCR-ABL fusion
- JAK2 exon 14 V617F

Using the ICEPlex, we are able to simultaneously detect all of the common fusion gene variants as well as the JAK2 exon 14 mutation.

In addition, this test could be expanded to included the recently identified JAK2 exon 12 mutations as well as point mutations conferring resistance to Gleevec, such as ABL T315I

Multi-modal Testing Enables New Ways to Care for Patients

"Single sample, Single slice, Single prep, Single well… Multiple Answers"

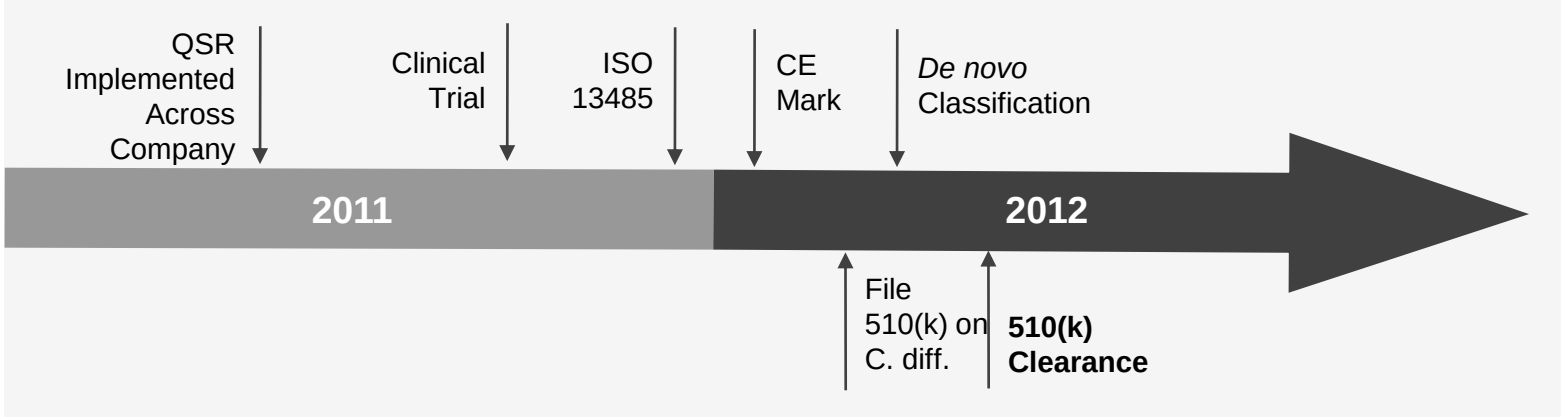


ICE*Plex*:

- ✓ **Simultaneous detection** of all common variants as well as meaningful SNPs
- ✓ **Reduced turnaround time & cost**
- ✓ **Improved disease detection and long-term monitoring**

Achieve FDA Clearance of Platform in 2012

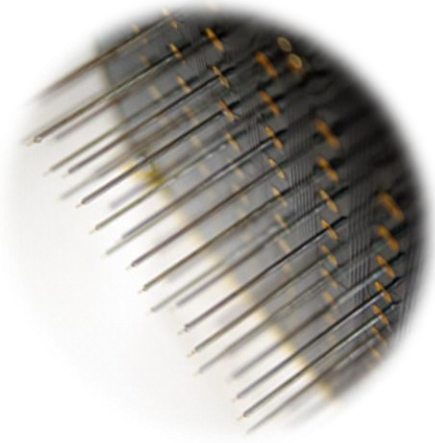
Streamlined Regulatory Strategy – *C. diff*. is well understood



- Technology is **well understood**/accepted by regulators
- PrimeraDx plan **matches recent FDA guidance**
- **510(k) submission:** Q1 2012

The ICE*Plex* Product Line

Instrument and Consumables



PrimeraDx provides customers with everything they need to run their laboratory developed tests or our soon to be cleared *C. difficile* test on the ICE*Plex* instrument.

PrimeraDx provides three cartridge sizes for laboratories with different throughputs.

- 24 well
- 48 well
- 96 well (coming soon)

Last words…

New Paradigm For Multiplex Diagnostics

- Quantitative
- Multi-Modal Testing (mRNA + miRNA + SNP)
- Broad Dynamic Range (what is needed)
- Mid/High Multiplex (the sweet spot)

Breadth of Applications

- Infectious Disease
  - Pathogen Detection
  - Viral Load
- Oncology
  - Cancer Classification
  - Fusion Gene Variant Detection
  - Methylation, SNP, CNV
- Non-Clinical Fields of Use
  - Microbial Detection-Food, Pharma QC

Future Directions

- Expect 510(k) Clearance Q2 2012

PrimeraDx

The Multiplex PCR Company