



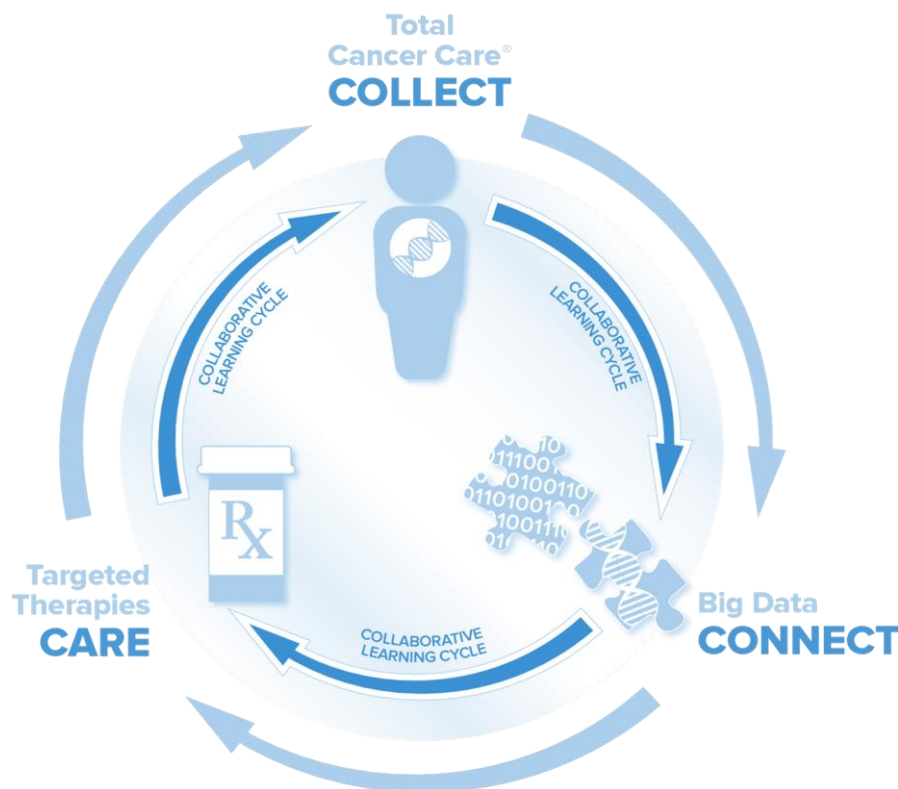
# M2GEN

## ORIEN and ORIEN Avatar

Hongyue Dai  
May 17, 2018  
SITC

# TCC – A Patient-Centric Approach to Research

*The TCC protocol allows M2Gen to follow patients throughout their lifetime enabling the ability to identify patient need, provide evidence to meet need and ultimately predict need*



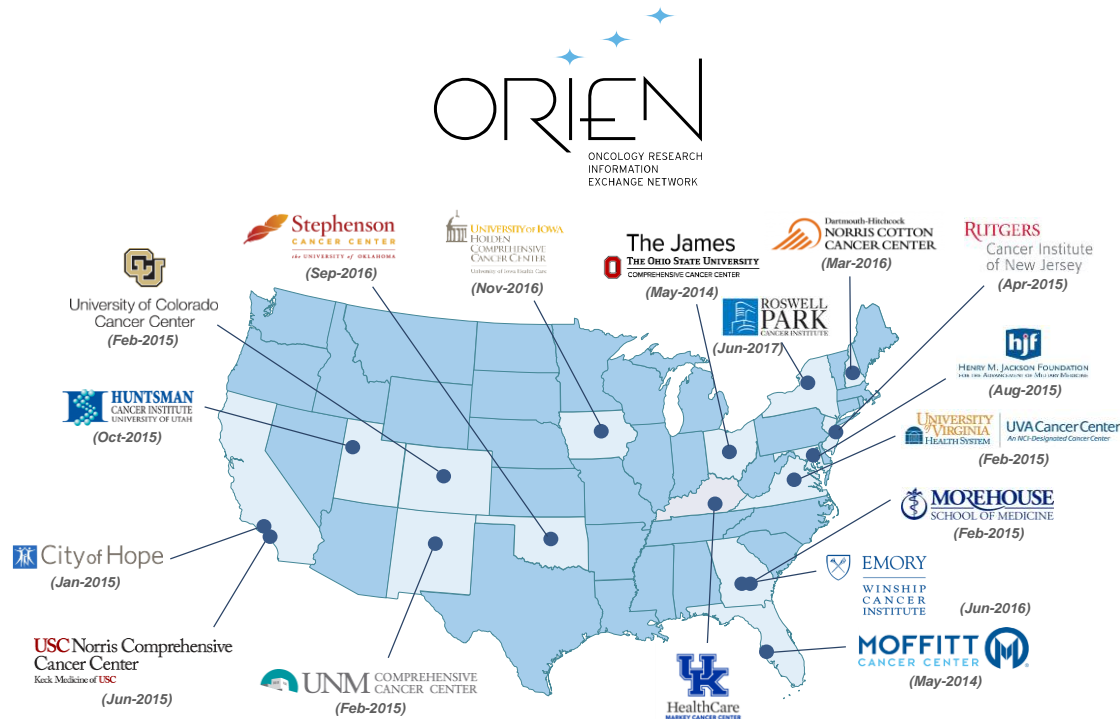
Through TCC, M2Gen is able to:

- Link disparate sources of data, e.g. clinical and molecular
- Engage patients directly for research, including re-contact for clinical trials
- Provide value back to patients, making them proponents of TCC

Using TCC in partnership with pharma collaborators, M2Gen has demonstrated the ability to accelerate discoveries, shorten clinical development timelines and reduce R&D costs

# Oncology Research Information Exchange Network (ORIEN)

*M2Gen currently partners with seventeen of the nation's leading cancer centers to deliver informatics based solutions to accelerate therapy discovery and development via the Oncology Research Information Exchange Network (ORIEN)*



- A National Cancer Center Alliance to integrate “Big Data” and Data Sharing For Cancer Research and Care
- All ORIEN Members agree to operationalize the TCC Protocol, and share the resulting data
- Potential to consent more than 50,000 new patients annually into TCC
- M2Gen maintains exclusive commercialization rights to data shared amongst ORIEN Members from TCC Protocol

# TCC: The Largest Prospective Observational Study of its Kind in Cancer

**10+**

years of operating history

**17**

leading cancer centers

**211,000+**

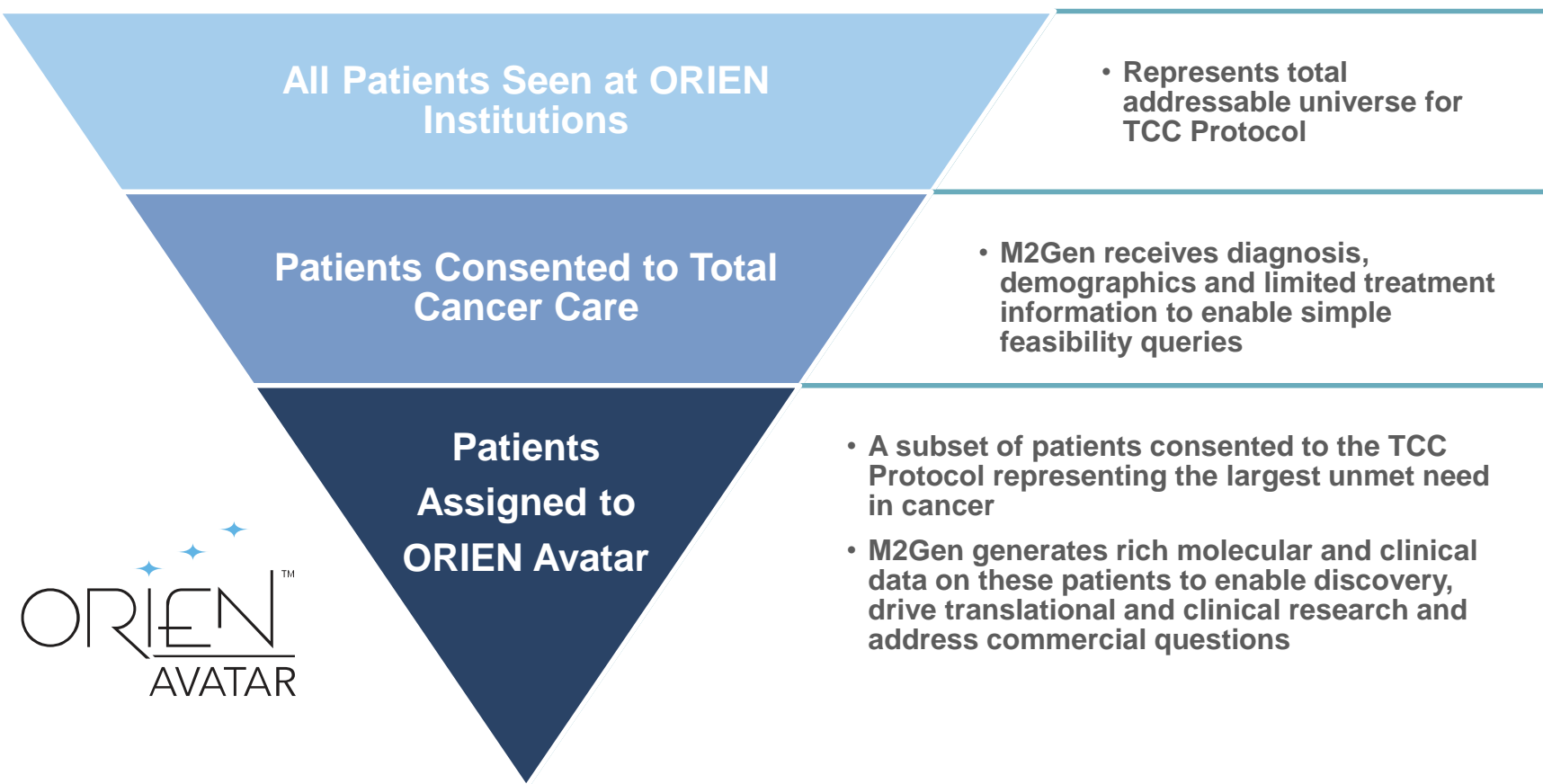
patients consented to date

## *Patients who consent to TCC*

- *Donate all of their clinical data for research purposes*
- *Consent for tissue to be used to generate molecular data*
- *Agree to be re-contacted for future studies, e.g. clinical trials*
- *Agree to allow data to be shared*
- *Become active participants in research*

# ORIEN Avatar – Initial Focus on Unmet Need

*The initial focus of the ORIEN Avatar program is on patients in greatest need*



ORIEN<sup>TM</sup>  
AVATAR

# Patients at High Risk for Disease Progression: Serving an Unmet Need

*In consultation with our pharma sponsors and ORIEN Members, M2Gen has identified cohorts of “high risk” patients, i.e. those with advanced primary or metastatic disease, with limited treatment options, as well as those patients who are likely to develop progressive disease*

- Stage II, III and metastatic lung cancer
- Breast cancer
  - Stage III and Metastatic Breast Cancer, including triple-negative breast cancers
- Stage III and metastatic epithelial ovarian cancers to include serous, clear cell, endometrioid
- Stage III and metastatic melanoma
- Primary brain tumors
  - Astrocytoma
  - Glioblastoma
  - Oligodendroglioma
- GU Cancers: Stage III and IV
  - Renal cell carcinoma
  - Bladder
  - Prostate cancers
- GI cancers:
  - Pancreatic
  - Gastric
  - Esophageal
  - Hepatocellular carcinomas
  - Stage III and metastatic colorectal cancer
- Head and neck cancers (Squamous cell carcinomas)
- Sarcomas
- Heme malignancies including the following diseases, regardless of staging:
  - AML
  - ALL
  - CLL
  - MDS
  - Multiple Myeloma
  - NHL: Follicular Lymphoma (FL), Diffuse Large B-Cell Lymphoma (DLBCL)

# Patient Phenotype: Clinical Data Collection

*M2Gen has developed a robust longitudinal data model and process resulting in a highly curated data set to track patients and understand outcomes as well as the dynamic nature of patients' disease*



## Diagnosis

- Consent
- Cancer site
- Histology
- Staging

## Treatment

- Medications
- Start/stop dates
- Reason for stop/switch

## Outcome/Status

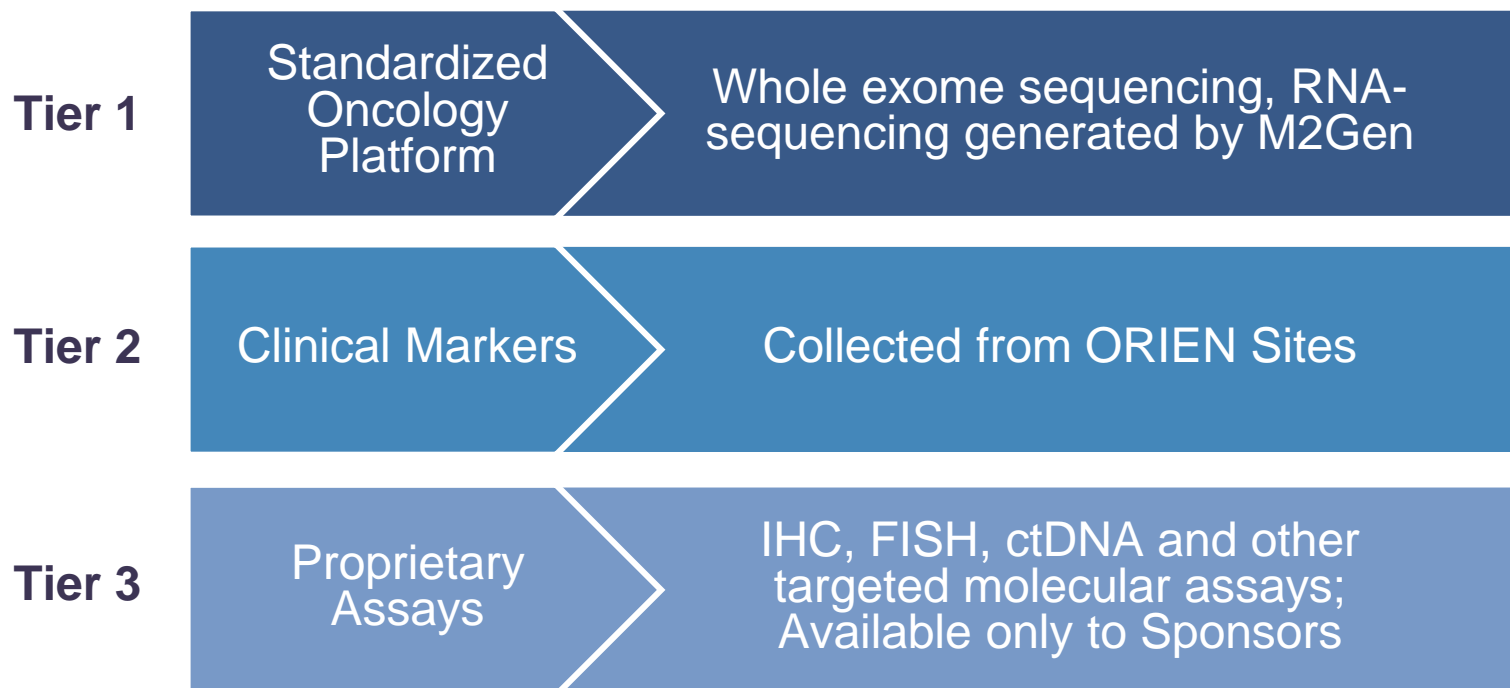
- Vital status
- Disease status
- Last contact
- Cause of death

## Data Updated Over Course of Patient Journey

- Co morbid illnesses
- Tumor markers
- Currently on treatment/trial
- Serum and other markers

# Patient Molecular Data: Standardized Platform Augmented with Flexibility

*M2Gen generates standardized molecular data on patients assigned to the ORIEN Avatar program, while retaining flexibility to examine additional markers of interest, without need to re-consent patient*





# Accelerating Oncology Research

M2Gen has an established track record of accelerating research with biopharmaceutical partners



## Discovery

Biomarker Studies, Target Discovery, Identification of Unmet Need



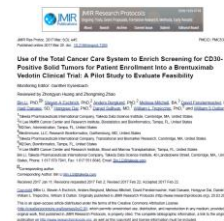
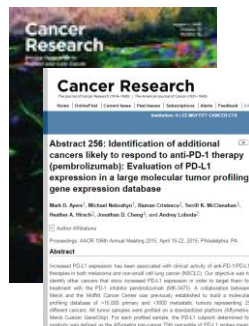
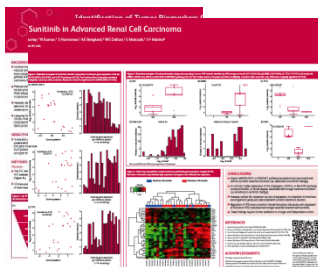
## Clinical Trials

In Silico Trial Design, Combination Strategies, Basket Trial Design



## Post-Market Analysis

Comparative Effectiveness, Pharmacovigilance



# Exploratory Analysis: Validating a published gene signature in Multiple myeloma

*A validated gene expression model of high-risk multiple myeloma is defined by deregulated expression of genes mapping to chromosome 1*

Shaughnessy et al. [Blood 2007 109:2276-2284](#);

## Current Selections

Columns Values  
Diseases\_Type ☒ HEM - Multiple Myeloma  
Signature\_Expression ☒ sig\_MM\_highrisk

<< Back

Clear All

Forward >>

Display & Print Current Selections

K-M analysis

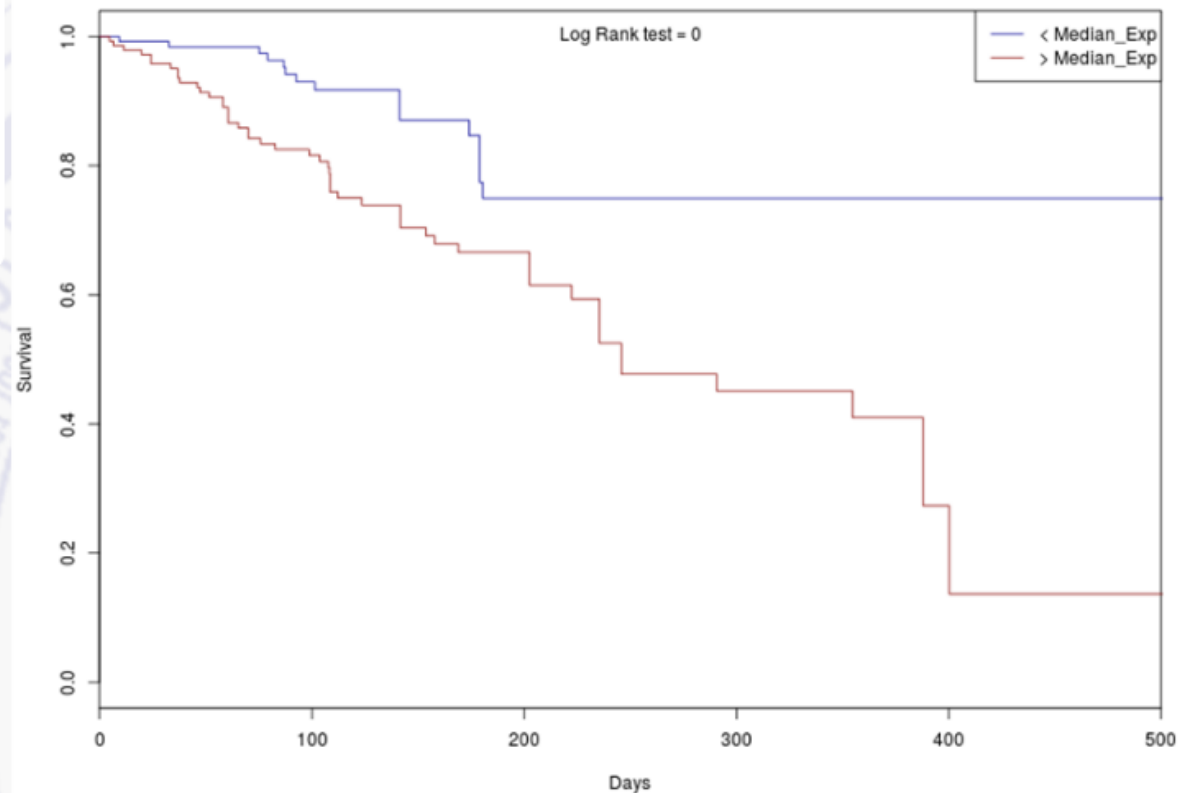
Select a Signature to Analyze

Signature\_Expression ☒ sig\_MM\_highrisk

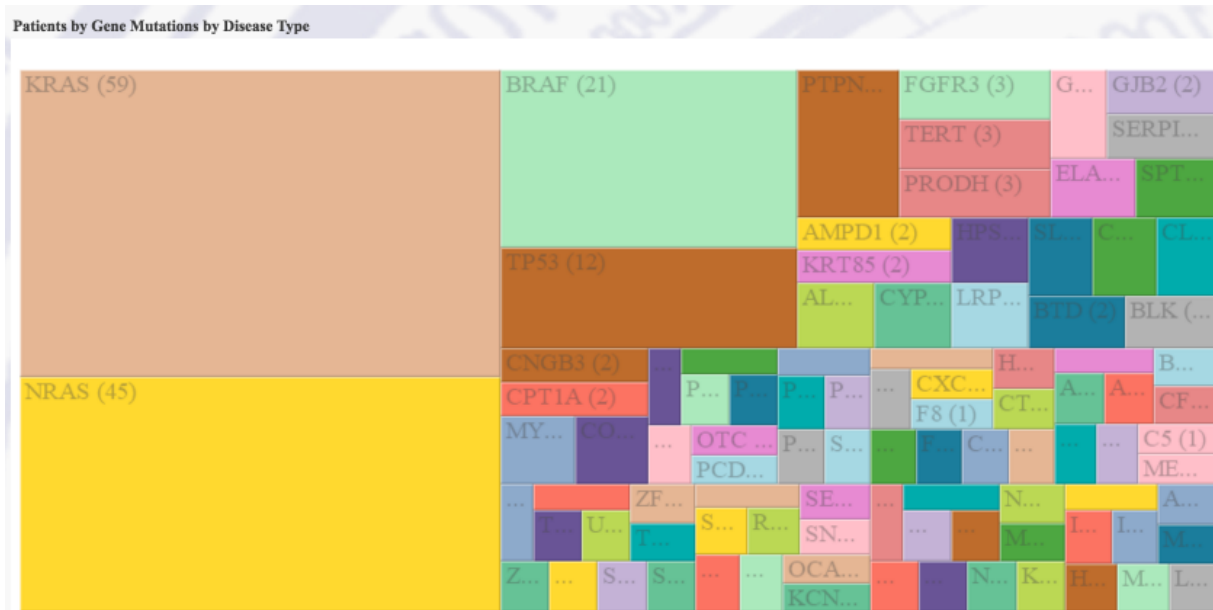
## Data

Deidentified_A...	ExpressionValue	VitalStatus	Overall_Surviv
0BVTUWOREV	0.66	Alive	8.23
0DD55IZ4C1	0.88	Alive	0.78
0EY6BMSGCA	0.87	Alive	5.39
0I09U0FH3E	0.26	Dead	1.09
0L21LYFELV	1.11	Dead	13.34
0L21LYFELV	1.19	Dead	13.34
0L21LYFELV	1.68	Dead	13.34
0TKBAA0R1S	3.51	Alive	0.74
0OT0OSWQIH	0.46	Alive	4.45
1T0W0V77D4	0.62	Alive	1.41

## K-M curve



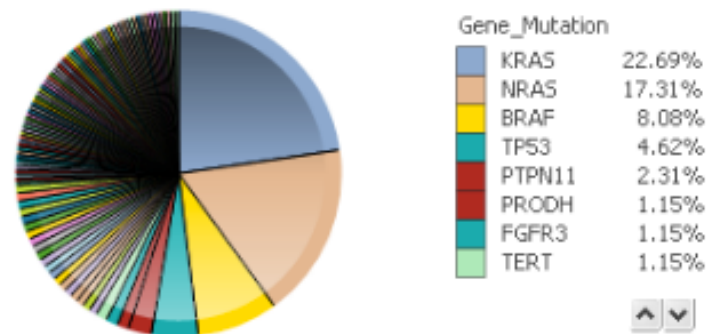
# Exploratory Analysis: Mutation Profile (top genes mutated) in Multiple Myeloma patients



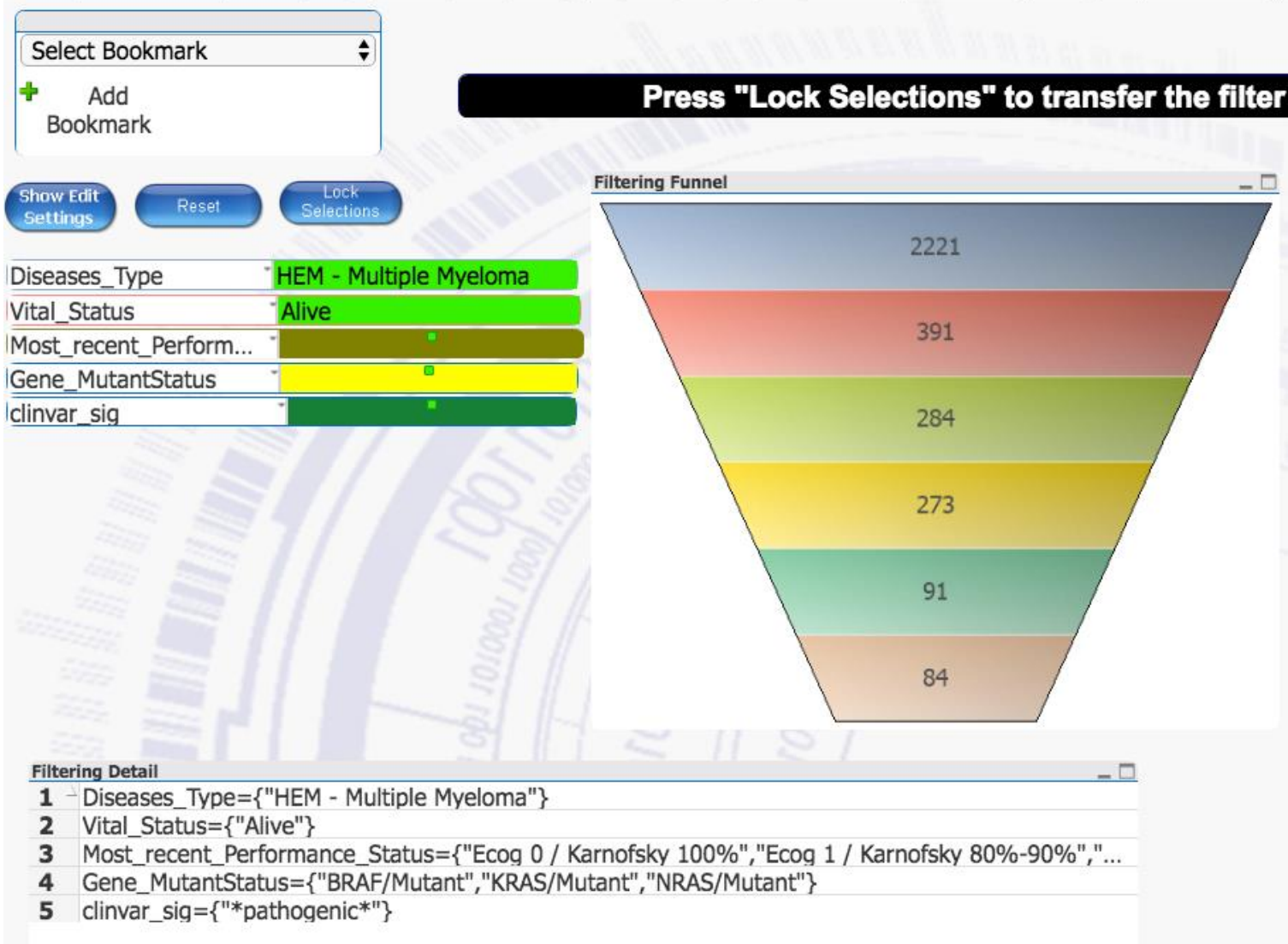
**Mutation Summary: Top mutated genes**

Gene_Mut...	Union of Patients	#Patients with Mutated G...
KRAS	157	59
NRAS	157	45
BRAF	157	21
TP53	157	12
PTPN11	157	6
PROD3	157	3
FGFR3	157	3
TERT	157	3
CPT1A	157	2
CYP17A1	157	2
AMPD1	157	2
CBS	157	2
ALG6	157	2
MYH7	157	2
LRP5	157	2
SERPINA1	157	2
GATA4	157	2
COL18A1	157	2
BLK	157	2

**Pie Chart : Share of Mutations**



# Design and identify patients for clinical trials



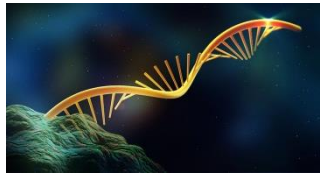
# Patient Molecular Data: Identifying I/O Biomarkers

*The depth and breadth of the ORIEN Avatar molecular data enables study of emerging biomarkers associated with response to immuno-oncology agents*



## Whole Exome Sequencing

*26,000+ genes sequenced at 300x coverage, with matched normal for accurate somatic mutation calling*



## RNA Sequencing

*Characterization of tumor transcriptome, including gene expression, fusion calling and other relevant information*



## I/O Biomarkers

**Microsatellite Instability**

**Presence of Neoantigens**

**Tumor Mutational Burden**

**Tumor Inflammation/T-Cell Infiltration**

**Tumor Microenvironment**

**Acquired Resistance**

# **ORIEN Avatar: Creating an Immuno-oncology Knowledge Base**

*Call to ORIEN members to place special emphasis on I/O-treated patients, building a comprehensive reference dataset which will provide sponsors with the ability to meet the challenges of immuno-oncology drug development and commercialization*



***Collaboration across ORIEN Cancer Center***

***Focus on indications with I/O approvals and clinical trials***

***Comprehensive molecular approach including whole exome and RNA sequencing***

***Ability to analyze pre and post treatment samples***



## **I/O Challenges**

**Response/  
Non-response**

**Acquired  
Resistance**

**Trial Design and  
Enrollment**

**Comparative  
Effectiveness**

**Safety**

# New Funding for ORIEN Member Research

## New Oncologic Visionary Awards (NOVA)



- M2Gen is supporting ORIEN member research by funding Team Science Awards: \$3M over two (2) years
- Team Science Awards are for the purpose of:
  - Promoting team science across the ORIEN members;
  - Supporting the ORIEN mission through collaborative learning;
  - Encouraging the growth of the ORIEN database and promoting data sharing
- Awards will be in two categories:
  - Request for Proposal to address specific challenges
    - Focusing on IO
  - Investigator Initiated Research

# Summary

- ORIEN is a cancer center alliance based on the Total Cancer Care Protocol
- ORIEN promotes collaboration and data sharing among ORIEN members
- ORIEN promotes collaboration between cancer centers and pharma sponsors
- ORIEN Avatar project focuses on patients with unmet medical needs, generates and collects in-depth molecular and clinical data
  - Funding research (NOVA) in Immuno-oncology biomarkers, database and collaboration