

Regulatory & access considerations in mining big data

to advance the development of cancer immune
modulator therapeutics

Ahmad A. Tarhini, MD, PhD

Senior Member, Cutaneous Oncology & Immunology

H. Lee Moffitt Cancer Center & Research Institute

Professor, Oncologic Sciences

University of South Florida Morsani College of Medicine

Chair, ORIEN Scientific Committee & ImmunoOncology Research Subcommittee

DISCLOSURES

- Research support to institution: Bristol Myers Squibb, Genentech-Roche, Regeneron, Sanofi-Genzyme, Nektar, Clinigen, Merck, Acrotech, Pfizer, Checkmate, OncoSec, Scholar Rock, Agenus.
- Consultant role/Advisory board: Bristol Myers Squibb, Merck, Eisai, Instil Bio, Clinigen, Regeneron, Sanofi-Genzyme, Novartis, Partner Therapeutics, Genentech/Roche, BioNTech, AstraZeneca, ConcertAI, InstilBio.

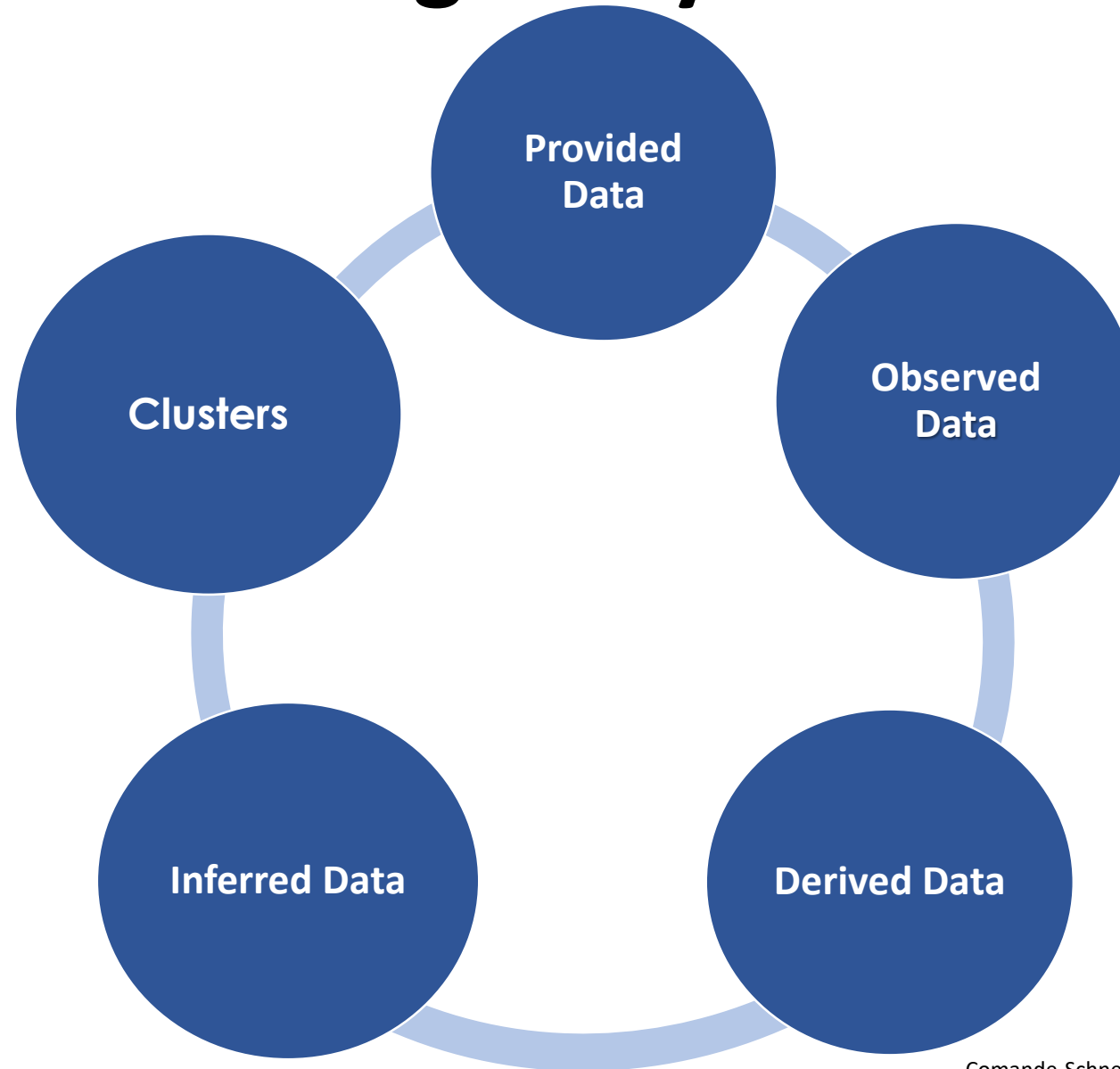
Big Data science increasingly impacts drug development & personalized medicine

Genomics & other biological high throughput data (transcriptomics, epigenomics, proteomics, metabolomics) are expanding at an accelerated pace and are being increasingly integrated with other sources of data

Primarily through new diagnostic and informatics approaches that enrich our understanding of the molecular basis of disease biology and host immunology

- Clinical trial data (Industry-, NCI-, ..., investigator-sponsored)
- EMRs
- Bio-imaging
- Health claims data
- Data from wearable sensors & mobile health applications
- Other ... (Primary & secondary health data sources)

The never-ending lifecycles of health data



Sources of 'omics' data ever expanding ...

- The Cancer Genome Atlas Program (TCGA)
- Gene Expression Omnibus (GEO)
- Dependency Map (DepMap) Consortium
- The database of Genotypes and Phenotypes (dbGaP)
- The Cancer Imaging Archive (TCIA)
- Clinical Proteomic Tumor Analysis Consortium (CPTAC)
- Sequence Read Archive (SRA)
- Single Cell Expression Atlas
- Other sources at NCBI, EBI, others ...

Health Insurance Portability and Accountability Act (HIPAA)

- **Requires** patient authorization to disclose potentially identifying data
- **Or** a decision by an institutional review or privacy board to waive that requirement
- **U.S. federal law that governs the use and disclosure of personal health information**
- **General rule:** Personal health information cannot be disclosed without the patient's authorization
- **Three primary measures:**
 1. **Informed consent**
 2. Study review and approval by **IRBs** and Research Ethics Committees (**RECs**)
 3. Data use limited to **deidentified** information
- **Intent:** Participants are fully aware of the research, and given a clear and accurate account of the potential risks and expected benefits

General Data Protection Regulation (GDPR)

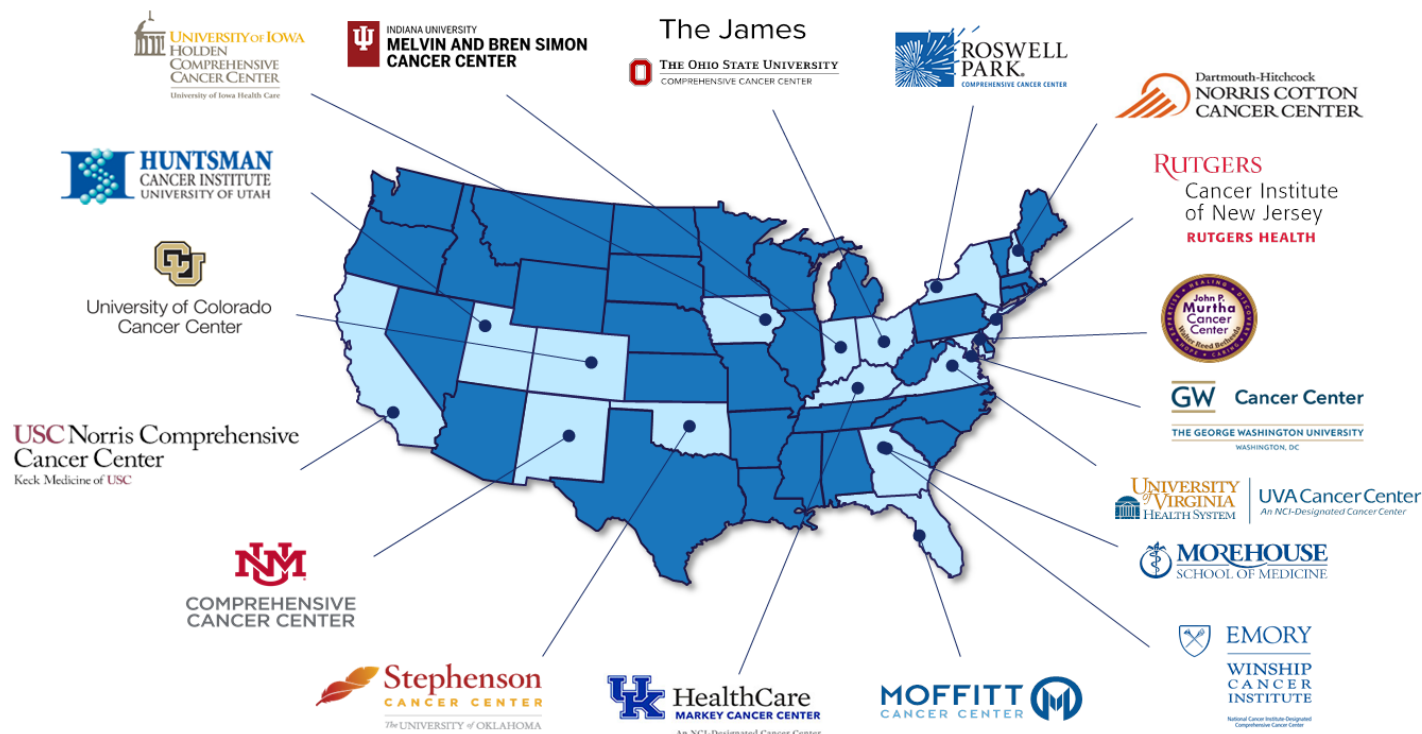
- GDPR (May 2018) applies to all personally identifiable information (PII) related to people in U.K. or E.U. – but covers organizations even if they operate outside of those jurisdictions
- Health Data covered under ‘Special Categories’ of Art. 9 of GDPR
- Organizations must appoint a Data Protection Officer (DPO) to oversee the implementation of GDPR & HIPAA

Key Elements in Maximizing Privacy in Big Data Research

- Ensuring HIPAA and GDPR organizational compliance
- Thoughtful governance of Big Data Sharing
- Improve EHR systems
- Patients given the information and opportunity to ask questions needed to give meaningful informed consent to future uses of their data
- Particular attention to racial and ethnic minorities
- Engagement of patients/patient representatives
- Whether to further regulate patient data sharing, who should regulate it, and how it should be regulated ...



An alliance of 18 U.S. cancer centers, which have implemented a common longitudinal protocol (Total Cancer Care; NCT03977402)



14+ years of data collection and research

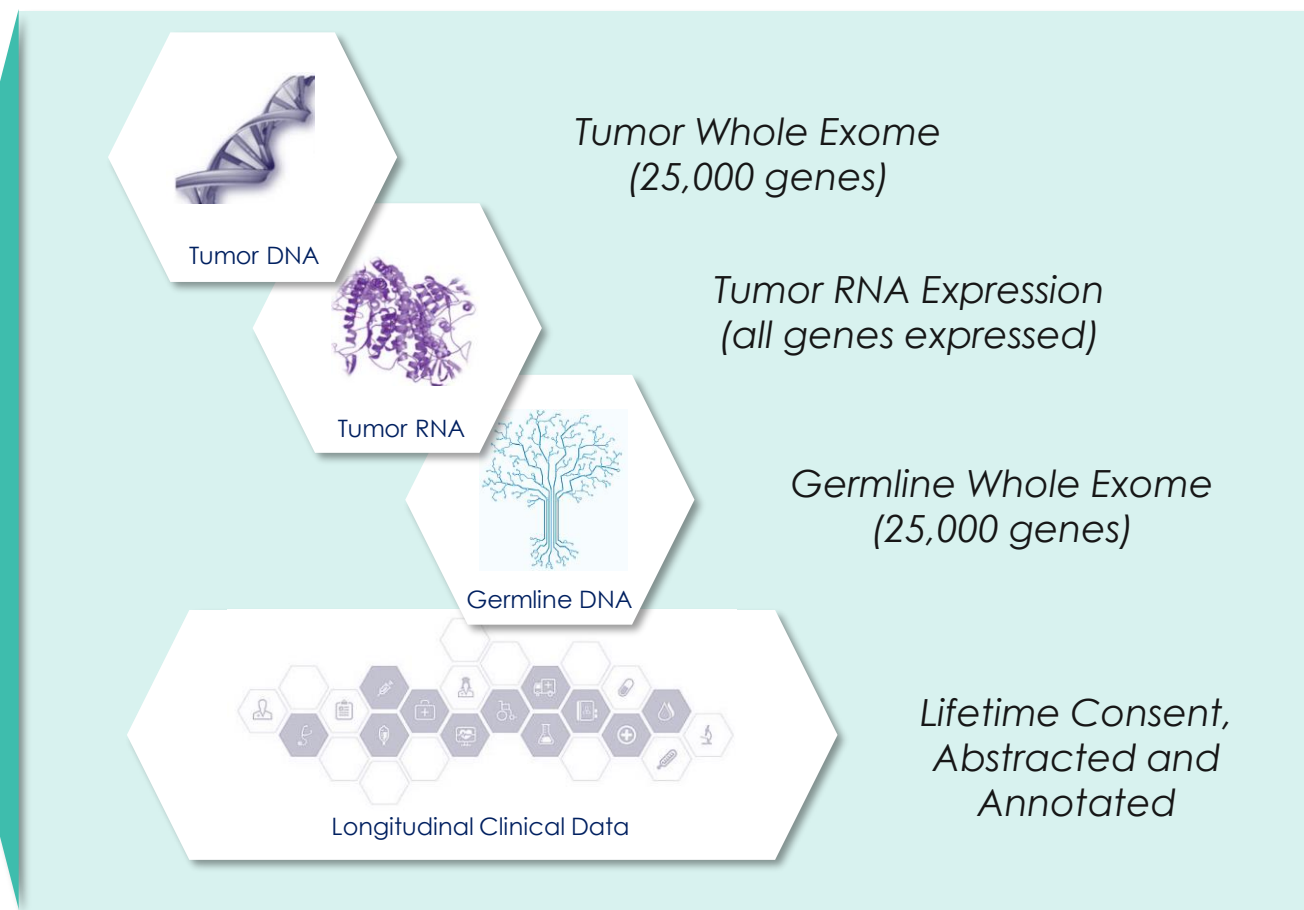
325,000+ cancer patients enrolled

18 leading cancer centers sharing data

Mission: Accelerating cancer discovery and delivering hope through collaborative learning and partnerships

ORIEN AVATAR

Oncology database with **whole exome, whole transcriptome and germline sequencing** data coupled with **longitudinal clinical profiles** from **consented patients**





ORIEN Guiding Principles

Collaboration

Commit to using a common protocol to ensure data quality and promote partnerships in research

Total Cancer Care (TCC) Protocol

- **IRB Review and Approval:** Institutional IRB of record
- **Consent:** Patients individually consented at their respective institutions
- **One central honest broker:** M2GEN where data is de-identified
- **Governing Body:** Representatives from the 18-member cancer centers, Patient Advisory Council & M2GEN

Patient Demographics Across ORIEN

Collaborative

African American

Morehouse, EMO,
CINJ, UVA & GW

Rural & Frontier

HCI, SIM & OSU

Appalachian

MAR & OSU

Inclusiveness

American Indian

UNM, SCC, HCI

Active Military & Veterans

MURTHA

Adolescents, Young Adults & Pediatrics

RPC, UCC,
MAR & MCC

Asian and Pacific Island

USC

Hispanic

MCC & USC

Notes:

- NCI defined race and ethnicity criteria
- NCI / NIH demographic taxonomy



Operations

M2GEN has developed and operates the informatics platform to link data from ORION members

Disease	Response Deadline	Status	MCC	OSU	UVA	UCC	UNM	CINJ	USC
Brain, Pancreatic, M	01/24/20	Active							
Solid Tumors	01/24/20	Active							
Pan-Cancer	12/11/19	Active							
Pan-Cancer	12/11/19	Active							
Ovarian	12/11/19	Active							
Endometrial	12/11/19	Active							
Solid Tumors	12/11/19	Active							
Solid Tumors	01/24/20	Active							
Pan-cancer	11/12/19	Active							
Melanoma	10/11/19	Active							
Sarcoma	10/11/19	Active							
Adenocarcinoma	12/16/19	Active							
Colorectal	08/30/19	Active							
Urothelial	08/10/17	Active							
Colorectal	08/30/19	Active							
Renal Cell	08/30/19	Active							
Sarcoma	07/18/18	Active Self-N							
Pan-cancer	N/A	Ongoing							
I/O Treated	N/A	Ongoing							
I/O Treated	N/A	Ongoing							
Leukemia	09/28/18	Active Self-N							
NHL	09/28/18	Active							
Pancreatic	09/28/18	Active Self-N							
Pan-Cancer	09/28/18	Active							
I/O Treated	09/28/18	Active Self-N							
Pan-Cancer	09/28/18	Active							
I/O Treated	05/12/20	Active Self-N							
Pan-cancer	06/16/21	Active							
Pan-cancer	Active	Active							

Projects

Network



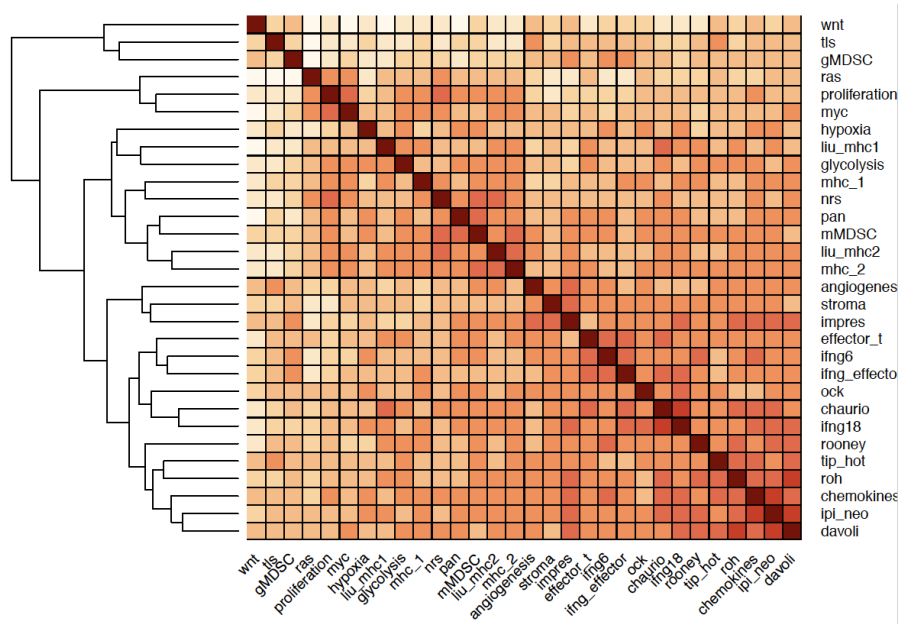
ORION

Can ORION
ag

ORION INTERMEMBER PROJECT ID:	PI Name	Project Title
38	19PRJ049USC	Zada, Gabriel
39	19PRJ048UVA	Rutkowski, Melanie
40	19PRJ046OSU	Roychowdhury, Sameek
41	19PRJ045OSU	Roychowdhury, Sameek
42	19PRJ044MAR	Gorski, Justin
43	19PRJ041MAR	Kolesar, J. / Riggs, McKayla
44	19PRJ039CINJ	Khiabani, Hossein
45	19PRJ038MAR	Kolesar, Jill
46	19PRJ036HCI	Gupta, Sumati
47	19PRJ035HCI	Holmen, Sheri
48	19PRJ024RIG-SAR	Andy Brohl
49	19PRJ016RPC	Mukherjee, Sarbajit
50	19PRJ015HCI	Ulrich, Neli
51	19PRJ012HCI	Gupta, Sumati
52	19PRJ003CINJ	Hochster, Howard
53	18PRJ023MCC	Manley, Brandon
54	RIGs	Chairs: Andrew Brohl & David L
55	SARCOMA RIG	Chairs: Wendy Kohlmann & Par
56	RIGIR	Chairs: Ahmad Tarhini & George
57	RIG - I/O	
58	NOVA	
59	19PRJNOVA001MC	Bejanyan, Nelli
60	19PRJNOVA002WC	Cohen, Jonathon
61	19PRJNOVA003MC	Permeth, Jennifer
62	19PRJNOVA004HC	Dai, Donghai
63	19PRJNOVA006CII	Ganesan, Shridar
64	20PRJNOVA008MA	Kolesar, Jill
65	21PRJNOVA009MC	Tarhini, Ahmad
66	21PRJNOVA010US	Craig, David Wesley

Predictors of immunotherapeutic benefits in patients with melanoma

- Pearson's correlation of 28 predictive gene signatures in melanoma based on AUROC
- Heatmap illustrates 2 main clusters: **"immune active"** (right/lower) & **"immune suppressive"** (left/upper)



Top 7 GE signatures & correlation with survival (>24 vs. <24 months) in cutaneous melanoma (n=123 pts)

Gene Signature	Description	Reference	AUROC	U-test (P-value)
IFNg-6	6-gene IFNg associated	Ayers 2017	0.670	0.0013
IFNg-18	18-gene IFNg	Ayers 2017	0.661	0.0024
Effector T cell	Effector T cell gene set	Bolen 2011	0.676	0.0009
IFNg/Effector T cell	IFNg & effector T cell gene set	Fehrenbacher 2016	0.679	0.0007
Chemokine	Chemokine gene set	Coppola 2011 Mule 2012	0.644	0.0067
MHC II	13 MHC-II genes	Liu 2021	0.629	0.0152
Cytotoxic/Helper T cell & B cell interplay	T & B cell interplay	Tarhini 2017	0.642	0.0075

- Signatures related to IFNg, effector T cells, chemokines, MHC II & Tertiary Lymphoid Structures were significantly predictive of ICI benefits in advanced melanoma
- Ongoing analyses are investigating these signatures in other malignancies and integrating the GE data with data related to TMB, somatic mutations and germline genetic variations



ORIEN Guiding Principles

Collaboration

Commit to using a common protocol to ensure data quality and promote partnerships in research

Inclusiveness

Participation by Cancer Centers, Community Providers and Patients in their respective communities with **representation of diverse and underserved populations**

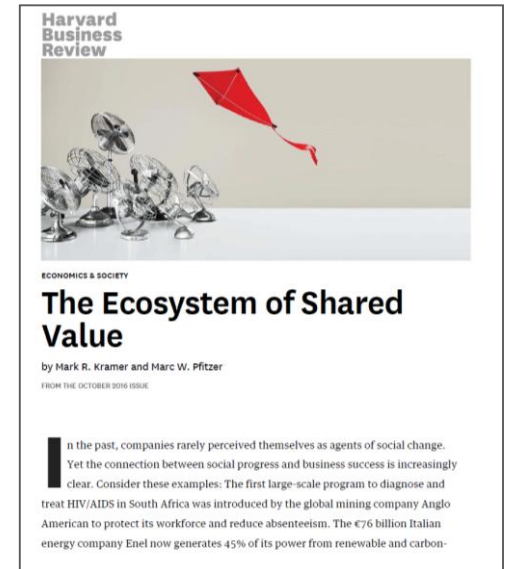
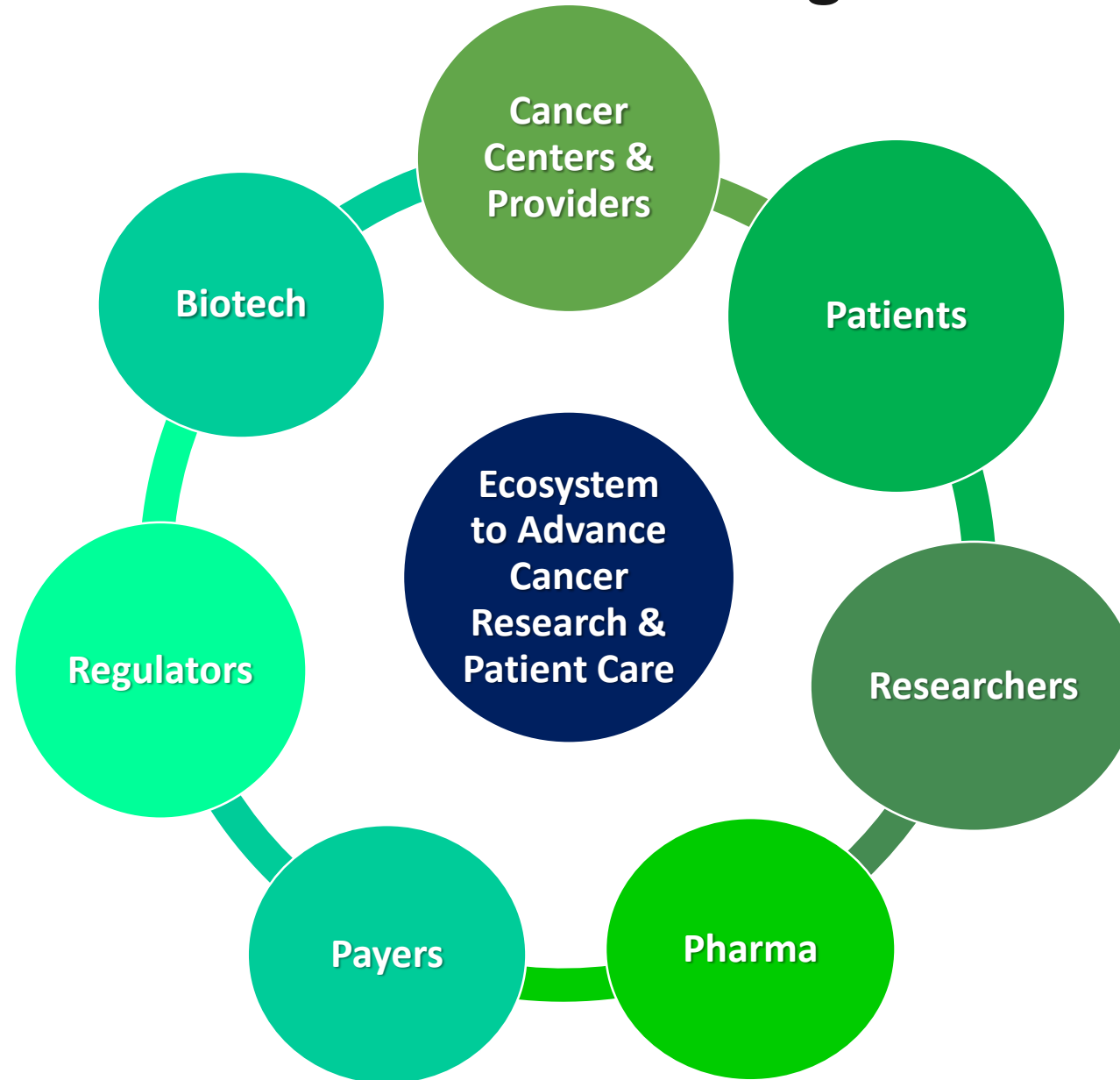
Accessibility of Data

Access to aggregated, harmonized research data; **centrally processed and maintained** by M2GEN

Partnerships

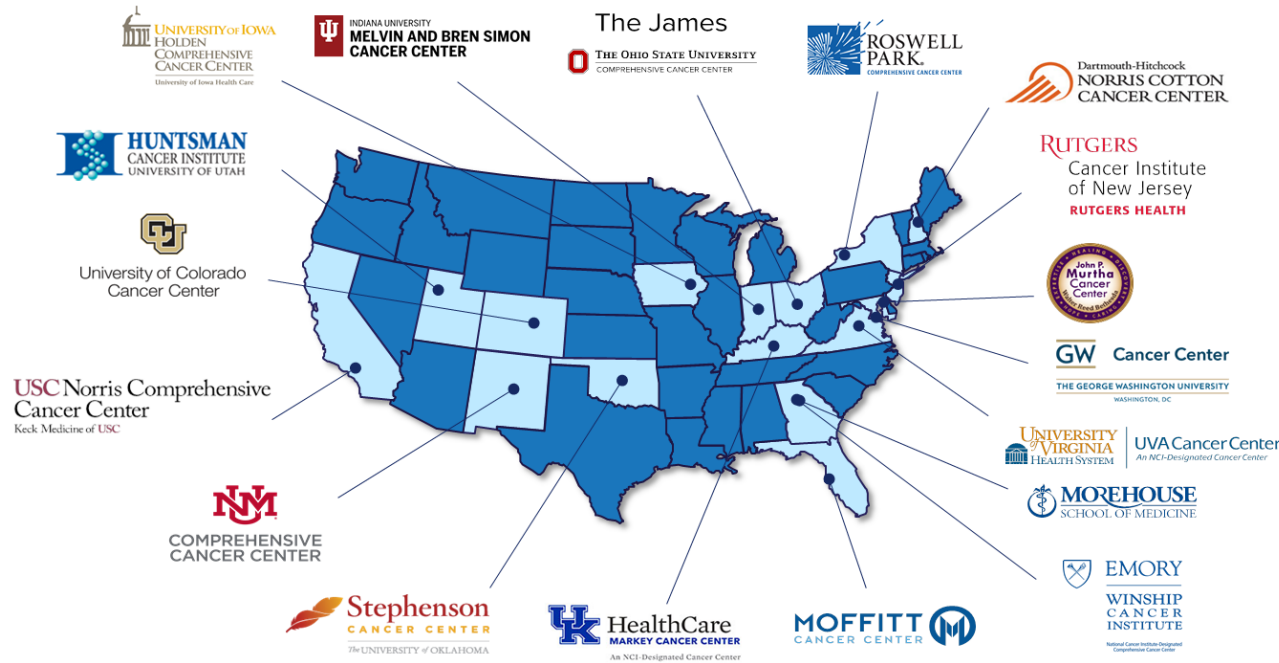
Establish trusted business relationships within and across sectors to achieve long-term program sustainability

An Ecosystem of Shared Values With the Primary Goal of Advancing Cancer Research while Serving & Protecting the Patient



Acknowledgements

ORIEN & M2GEN



Member Name	City	State
Rutgers Cancer Institute of New Jersey	New Brunswick	NJ
Emory Winship Cancer Institute	Atlanta	GA
George Washington Cancer Center	Washington	DC
Holden Comprehensive Cancer Center	Iowa City	IA
Huntsman Cancer Institute	Salt Lake City	UT
UK Markey Cancer Center	Lexington	KY
H. Lee Moffitt Cancer Center & Research Institute	Tampa	FL
Morehouse School of Medicine	Atlanta	GA
Murtha Cancer Center	Bethesda	MD
Norris Cotton Cancer Center	Lebanon	NH
The James Cancer Hospital	Columbus	OH
Roswell Park Comprehensive Cancer Center	Buffalo	NY
Stephenson Cancer Center	Oklahoma City	OK
IU Health Simon Cancer Center	Indianapolis	IN
UHealth Cancer Care-Anschutz Medical Campus-University of Colorado Cancer Center	Aurora	CO
UNM Comprehensive Cancer Center	Albuquerque	NM
USC Norris Comprehensive Cancer Center	Los Angeles	CA
UVA Emily Couric Clinical Cancer Center	Charlottesville	VA



Thank you!