HIMSS18 The leading health information and technology conference

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Conference & Exhibition | March 5–9, 2018

Las Vegas | Venetian – Palazzo – Sands Expo Center

OPENING KEYNOTE: PRECISION MEDICINE AT THE INFLECTION POINT

Session PM1, March 5, 2018

Damon Hostin, CEO, Precision Medicine Alliance, LLC

Catholic Health Initiatives. | Dignity Health.

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Conflicts of Interest

Damon Hostin

Has no real or apparent conflicts of interest to report.

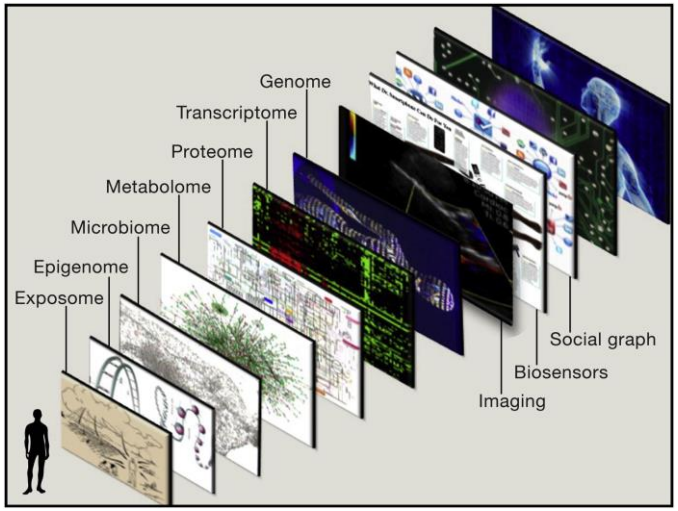
Agenda

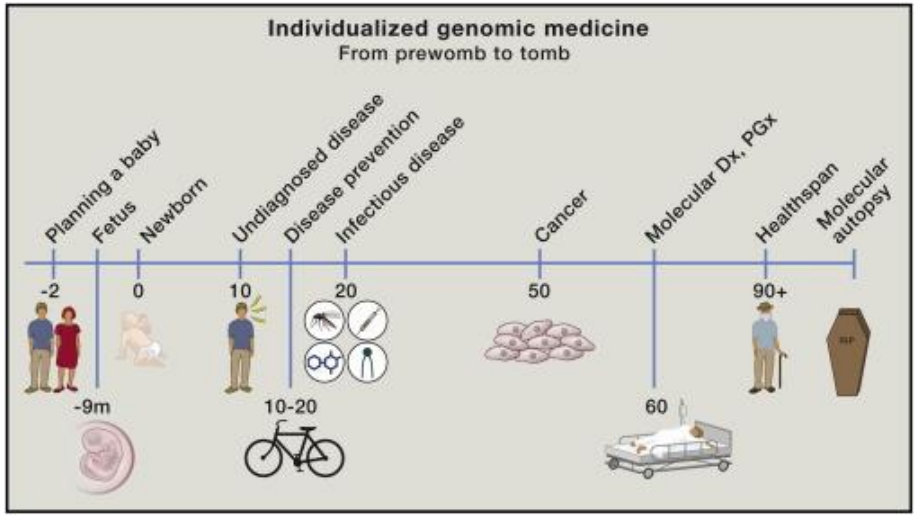
- Precision Medicine- Scope and Definition of Terms
- The Ecosystem and Dynamics
- Data Matters, Context and Value in Workflow
- Decision Support and Resources
- State of Reimbursement
- Closing Thoughts

Learning Objectives

- Describe the current state of precision medicine
- Discuss the precision medicine ecosystem, drivers, emerging technologies, and C&BI tools required for the journey
- Explain the need for data interoperability, integration into the provider workflow, and data sharing across the care continuum
- Assess clinical decision support tools for selecting the best targeted therapy and pre-screening of patients for clinical trials
- Outline the reimbursement strategies for precision medicine treatments

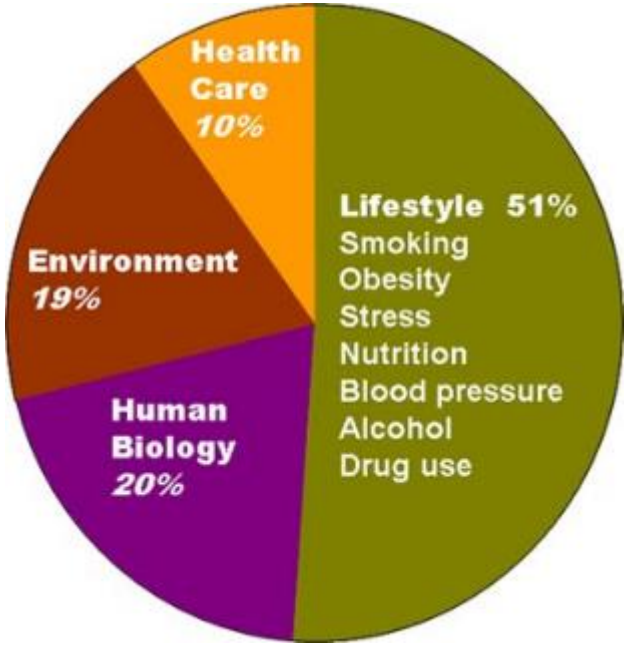
Precision Medicine- Scope and Definition of Terms





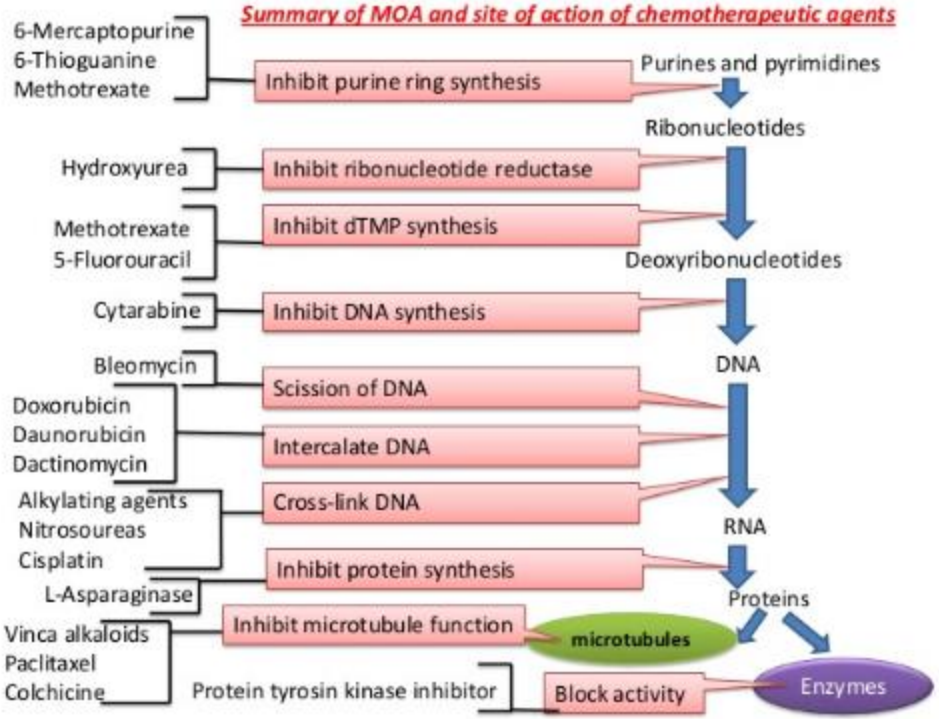
Cell PRESS
Individualized Medicine from Prewomb to Tomb
Topol, Eric J.
Cell , Volume 157 , Issue 1 , 241 - 253

Contribution of Human Diversity to Health

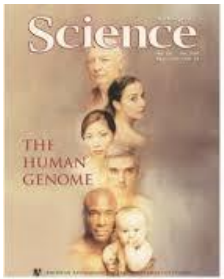


Traditional Cancer Therapy

- Destabilize cell division/ kill all fast growing cells = collateral damage
- Block growth hormones- incomplete story
- Ablate root cells (e.g. rituximab anti-CD20) – hard to get them all
- Still a foundation of treatment



Human Genome Project (HGP) to the Modern Dawn of Precision Medicine



	HGP Begins	HGP Ends	10 Years after HGP	14 Years after HGP
	1990	2003	2013	2017
Genome Sequencing				
Cost to Generate a Human Genome Sequence	~$1 billion	~$10-50 million	~$3-5 thousand	~$1,000
Time to Generate a Human Genome Sequence	~6-8 years	~3-4 months	~1-2 days	~1 day
Human genome Sequences	0	1	Thousands	~500,000
Human Genetics				
No. Genes with Known Phenotype/Disease-Causing Mutation	53	1474	2972	3755
No. Phoenotypes/Disorders with Known Molecular Basis	61	2264	4847	6005
No. Published Genome-Wide Assocation Studies (GWAS)	0	0	1542	2982
Replicated Disease-Associated Genetic Variants	0	6	~2900	~3700
Genomic Medicine				
Drugs with Pharmacogenomics Information on Label	4	46	106	238




References:
1. https://www.genome.gov/sequencingcosts/
2. Miller NA et al., "A 26-hour system of highly sensitive whole genome sequencing for emergency management of genetic diseases." *Genome Medicine*. 2015 September 30; 7:100
3. https://www.forbes.com/sites/matthewherper/2017/01/09/illumina-promises-to-sequence-human-genome-for-100-but-not-quite-yet/#7285fea6386d
4. "The NHGRI-EBI Catalog of published genome-wide association studies." Available at: https://www.ebi.ac.uk/gwas. Accessed 20 Jun, 2017.
5. Chakravarty D et al., "OncoKB: A Precision Oncology Knowledge Base." *JCO Precision Oncology*. 2017 May 2017; DOI: 10.1200/PO.17.00011. http://oncokb.org/#/
6. https://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm

Definition of Personalized (Precision?) Medicine

Personalized medicine is an evolving field in which care givers use molecular diagnostic tests to determine which medical treatments will work best for the patients.

By combining the data from those tests with an individual's medical history, circumstances, and values, health care providers and patients can develop targeted treatment and prevention plans.

Adapted from:

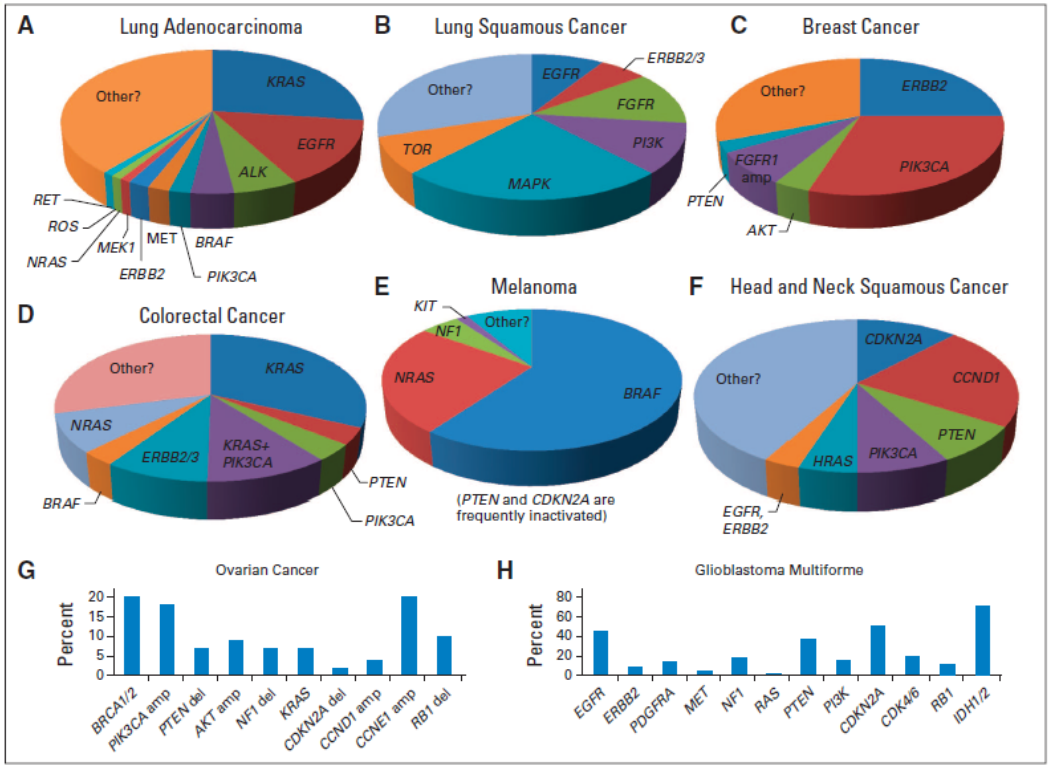
PMC
PERSONALIZED MEDICINE COALITION

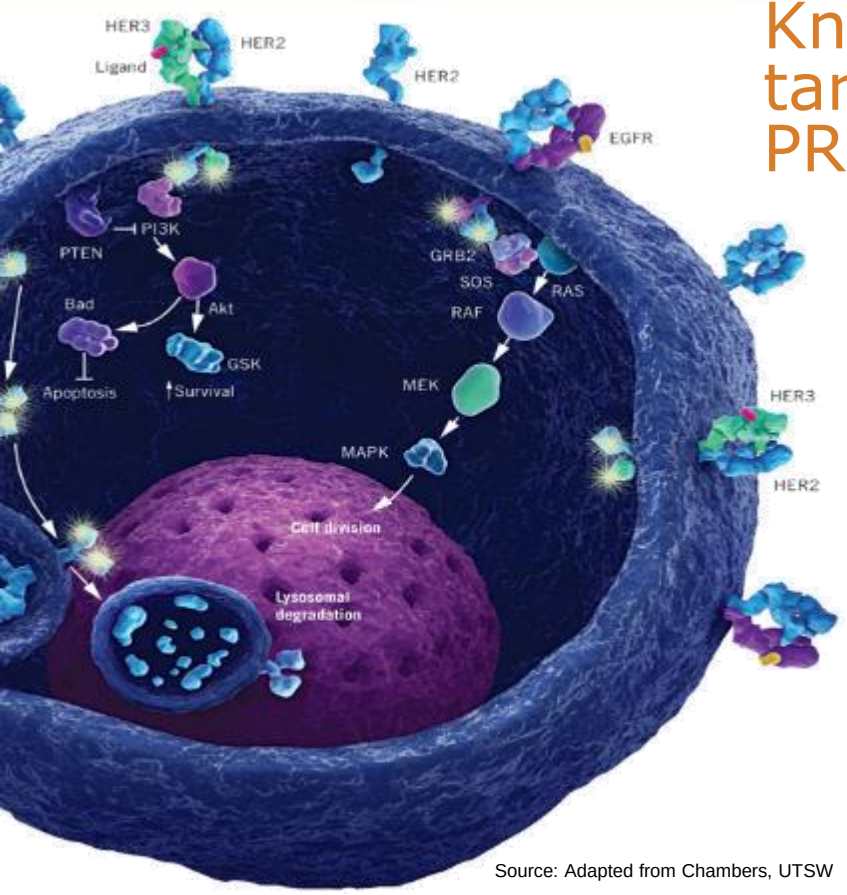
VOLUME 31 · NUMBER 15 · MAY 20 2013

JOURNAL OF CLINICAL ONCOLOGY

Genomics-Driven Oncology: Framework for an Emerging Paradigm

Levi A. Garraway





Source: Adapted from Chambers, UTSW

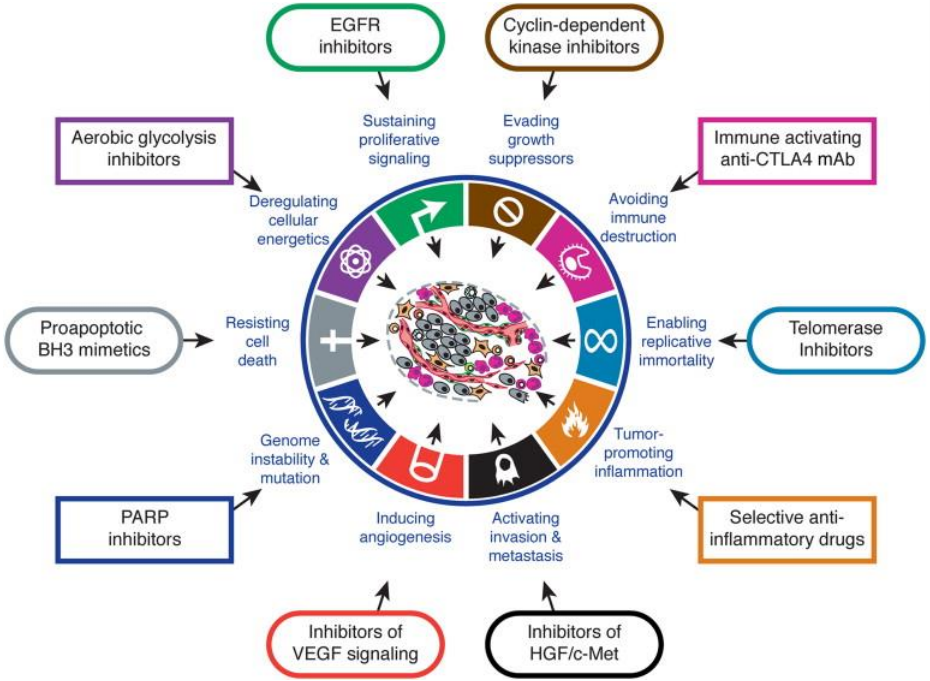
Knowledge of tumor biology targets and Mechanism of Action= PRECISION ONCOLOGY

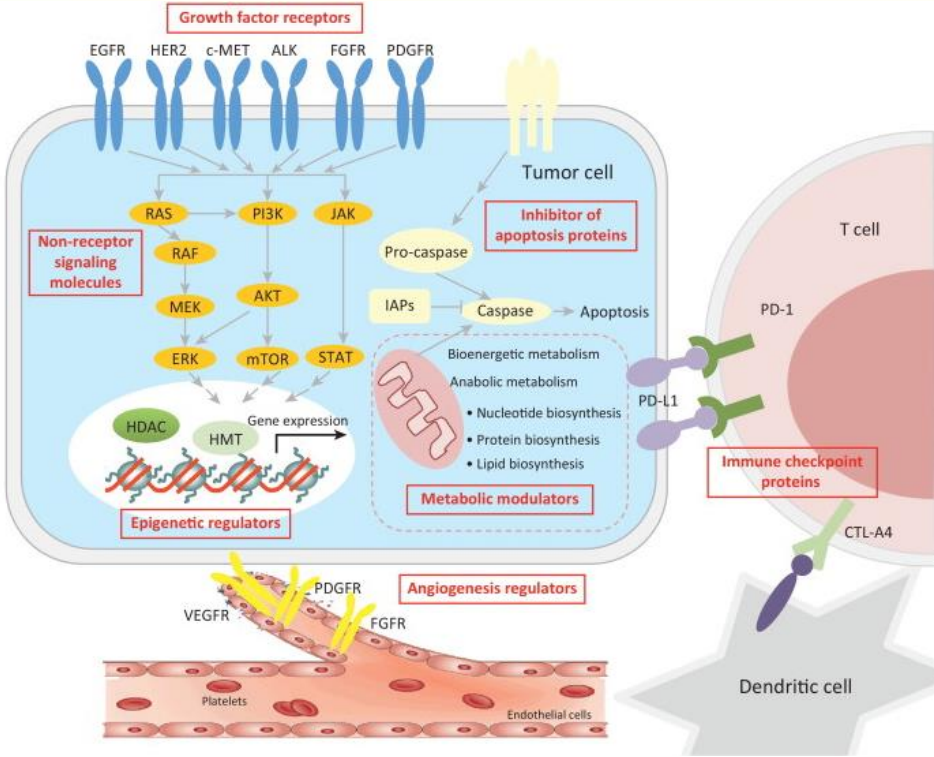
Targeted therapeutics disrupt growth signals, induce cancer cell death, and/or make target cells visible to the immune system

Some targets have variants that may convey resistance to drugs- therefore more information on the patient's tumor is needed

Tumor profiles inform the clinicians of each patient's tumor armor and weakness

Also- epigenetics, proteomics, RNA…

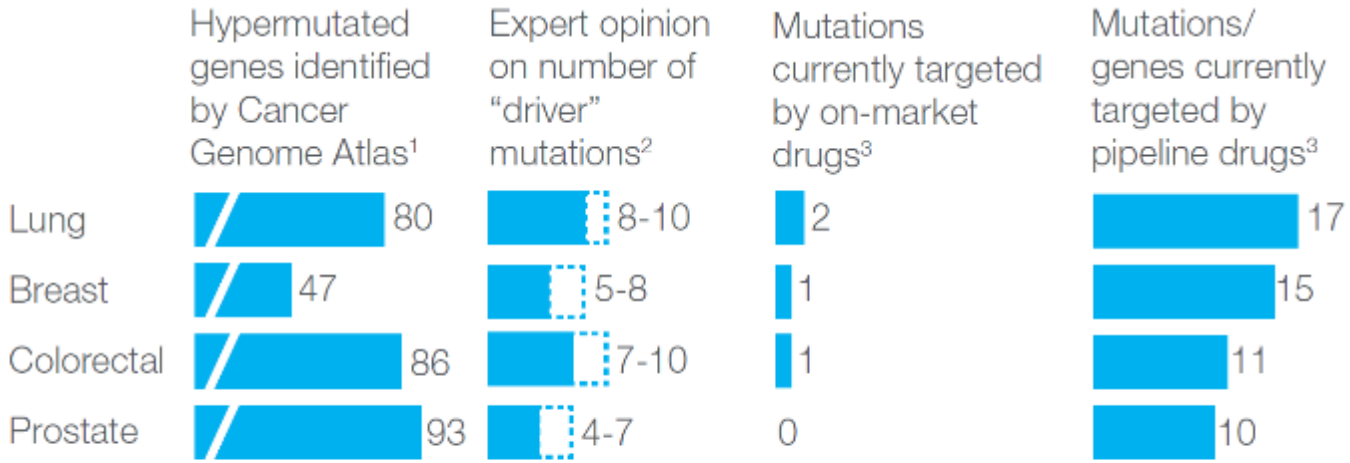




Hallmarks of Cancer: The Next Generation
Hanahan, Douglas et al.
Cell , Volume 144 , Issue 5 , 646 - 674

Molecularly targeted cancer therapy: some lessons from the past decade
Huang, Shen, Ding, Geng; Shanghai Institute of Materia Medica, Chinese Academy of Sciences

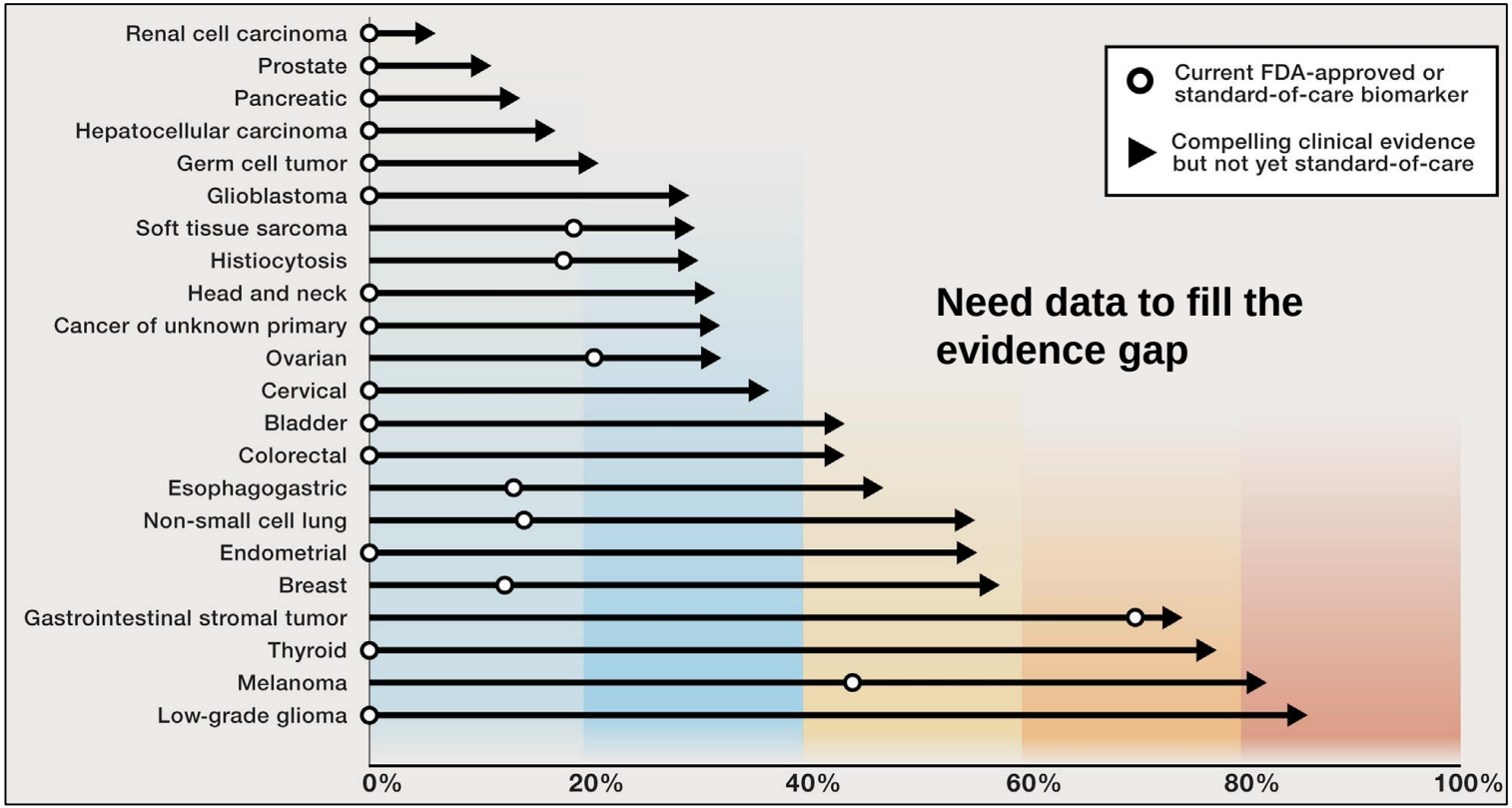
2013: Novel Therapeutics = Broader Tumor Sequencing



1 Based on q-value analysis using MutSig software from the Broad Institute
2 Based on expert interviews
3 Based on Evaluate Pharmaceuticals database; for pipeline, includes Phase 1 and above only

Personalized Medicine, McKinsey & Co. 2013

2017: Moving from Molecular Plausibility to STD of Care



Implementing Genome-Driven Oncology

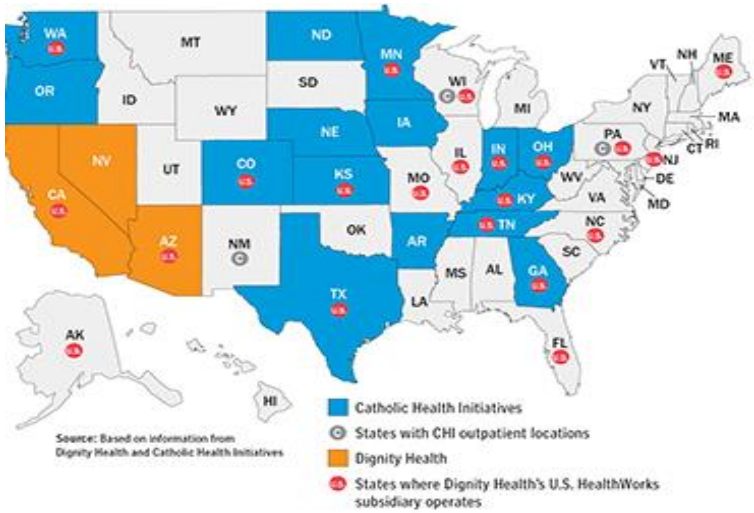
Cell 168, February 9, 2017

David M. Hyman,1,5 Barry S. Taylor,2,3,4 and Jose´ Baselga1,2,5,*
1Department of Medicine
2Human Oncology and Pathogenesis Program
3Department of Epidemiology and Biostatistics
for Molecular Oncology
Memorial Sloan Kettering Cancer Center, 5Weill Cornell Medical College

The Precision Medicine Ecosystem and Dynamics

Together CHI and Dignity Impact:

- ~25% of United States Population (~95 Million lives)
- At least 70,000 new analytic cancer cases/ year
- Patients through:
  - Acute Care facilities in 15 states
  - Non-acute facilities in 25 states
- Dozens of underserved communities by providing charitable care and services (~$3.8 Billion 2016)



- The combined system would have more than $28 billion in operating revenues, more than 700 care sites, about 159,000 employees and more than 25,000 physicians and other advanced practitioners.

Precision Medicine Alliance Program Elements and Applications

Elements

- Clinician Education, Support and Tools
- Clinical Workflow and Decision Support
- Healthcare-centric Diagnostic Tests
- Clinical Trial Portfolio Access
- Data Management for Quality/Outcome Research

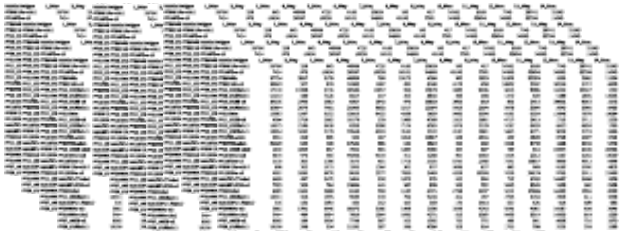
Applications

- Cancer treatment (tumor profiling)/ risk
- Pharmacogenomics
  - Cardiovascular (w/ constitutional risks)
  - Pain management
  - Behavioral health
- Population wellness

Precision Medicine Alliance Strategy

- Post-Modern approach to diagnostics
- Fast Follower/ Shoulders of giants
- Eschew urges to vertically integrate
- Highly partnered -Industry friendly
- Data-centric and Research integrated
- Sustain a bridge to Precision Medicine Standard of Care
- Access is Key- avoid ROI diminishing returns
- Share where appropriate for the common good

Harmonized Dataset and Workflow – Ecosystem Considerations



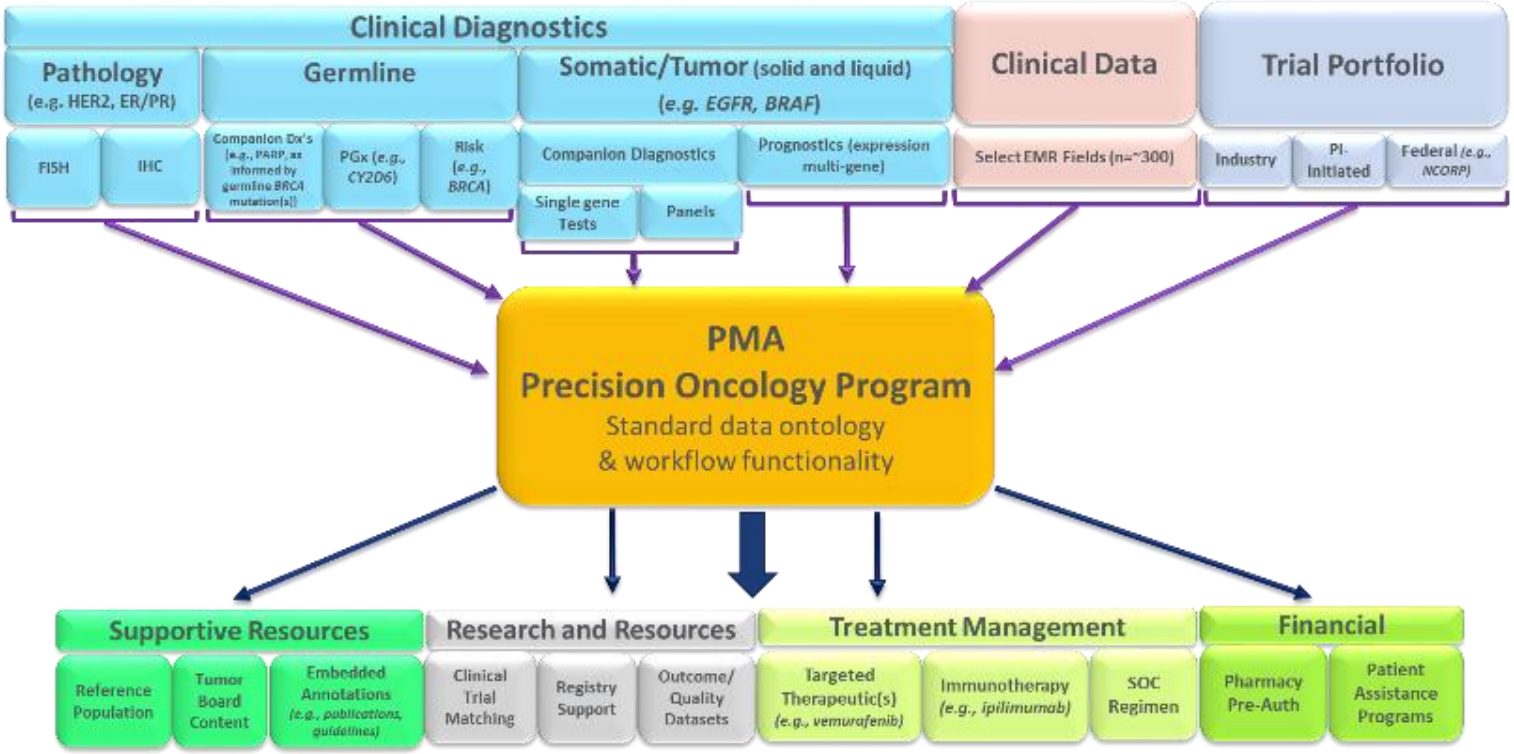
Clinical and Operational

- Clinical case queries
- Reference Population
- Payer evidence
- Outcomes research
- Quality improvement
- Moonshot applications

Business Opportunities

- Real World Evidence
- Clinical Trial Optimization and Enrollment
- Value-based Care
- Biomarker Testing Surveillance,
- Decision Support
- Patient Connectivity (RWO…)

Data Matters, Context and Value in Workflow



Anatomy of a Pan-Tumor NGS MDx Test

Number of Markers and Cost

Discovery Research

Non-validated mutations in known oncogenes

Putative markers or genes

Clinical Trial Inclusion and Off-Label Access

Novel Therapeutic Inclusion/ Exclusion Markers

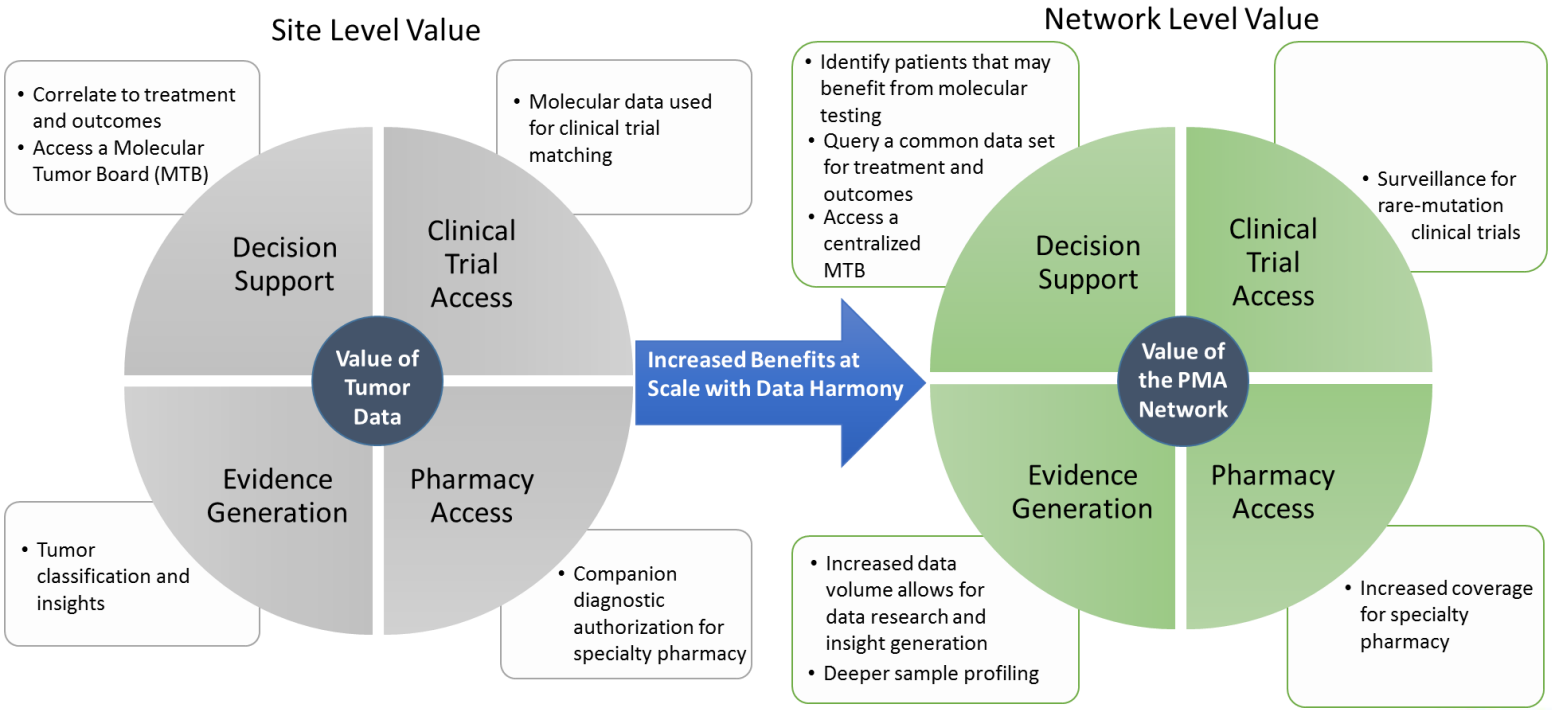
Off-Label Approved Therapeutic Markers

Indicated Cancer Markers

"Companion" Diagnostics

Clinical Evidence and Payer Coverage

Extracting Value from Tumor Data in Workflows



Decision Support and Resources

Gene n=64

SMARCB1	VHL
RB1	MPL
TP53	NTRK
ERBB4	FLT3
FBXW7	FGFR3
BRAF	CDH1
KIT	KDR
GNAS	HNF1A
HRAS	MLH1
EGFR	ALK
PDGFRA	IDH1
PIK3CA	GNAQ
CDKN2A	AKT1
ERBB2	JAK3
ABL1	FGFR2
JAK2	GNA11
KRAS	MET
NRAS	CSF1R
NOTCH1	ROS-1
ATM	PIK3
FGFR1	AKT
STK11	BRAFR
PTPN11	DDR2
APC	HER2
SMAD4	BCR/ABL
PTEN	TPMT
SMO	c-KIT
CTNNB1	PML/RAR
RET	PDGFR
IDH2	MYCN
SRC	MS4A1
EZH2	CD274

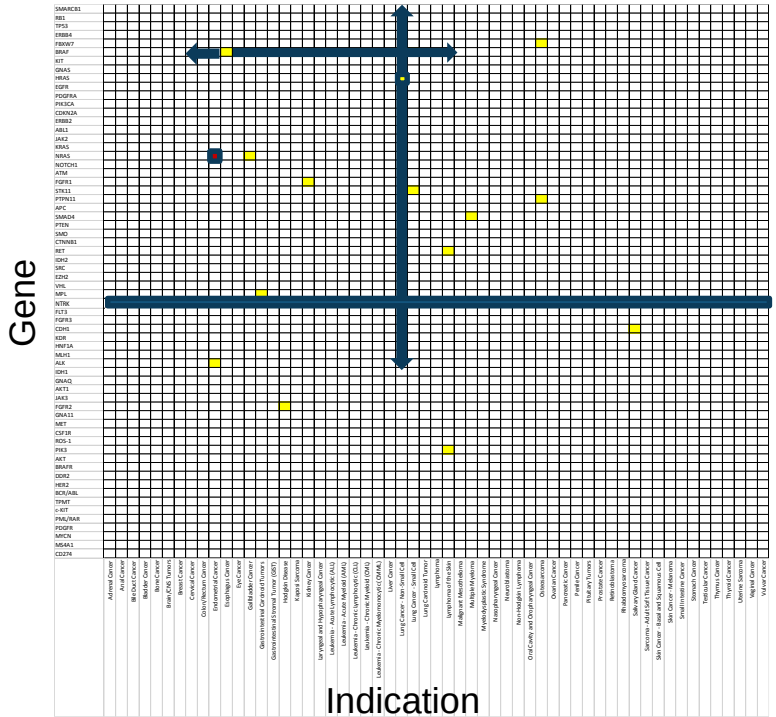
Indication n=58

Lymphoma of the Skin	Adrenal Cancer
Malignant Mesothelioma	Anal Cancer
Multiple Myeloma	Bile Duct Cancer
Myelodysplastic Syndrome	Bladder Cancer
Nasal Cavity and Paranasal Sinus Cancer	Bone Cancer
Nasopharyngeal Cancer	Brain/CNS Tumors
Neuroblastoma	Breast Cancer
Non-Hodgkin Lymphoma	Cervical Cancer
Oral Cavity and Oropharyngeal Cancer	Colon/Rectum Cancer
Osteosarcoma	Endometrial Cancer
Ovarian Cancer	Esophagus Cancer
Pancreatic Cancer	Eye Cancer
Penile Cancer	Gallbladder Cancer
Pituitary Tumors	Gastrointestinal Carcinoid Tumors
Prostate Cancer	Gastrointestinal Stromal Tumor (GIST)
Retinoblastoma	Hodgkin Disease
Rhabdomyosarcoma	Kaposi Sarcoma
Salivary Gland Cancer	Kidney Cancer
Sarcoma - Adult Soft Tissue Cancer	Laryngeal and Hypopharyngeal Cancer
Skin Cancer - Basal and Squamous Cell	Leukemia - Acute Lymphocytic (ALL)
Skin Cancer - Melanoma	Leukemia - Acute Myeloid (AML)
Small Intestine Cancer	Leukemia - Chronic Lymphocytic (CLL)
Stomach Cancer	Leukemia - Chronic Myeloid (CML)
Testicular Cancer	Leukemia - Chronic Myelomonocytic (CMML)
Thymus Cancer	Liver Cancer
Thyroid Cancer	Lung Cancer - Non-Small Cell
Uterine Sarcoma	Lung Cancer - Small Cell
Vaginal Cancer	Lung Carcinoid Tumor
Vulvar Cancer	Lymphoma

Gene - Indication – Drug Relationship Complexity

Drug n=93

abiraterone acetate (Zytiga®)	dinutuximab (Unituxin™)	panobinostat (Farydak®)
ado-trastuzumab emtansine (Kadcy	durvalumab (Imfinzi™)	pazopanib (Votrient®)
afatinib dimaleate (Gilotrif®)	elotuzumab (Empliciti™)	pembrolizumab (Keytruda®)
alectinib (Alecensa®)	enzalutamide (Xtandi®)	pertuzumab (Perjeta®)
alemtuzumab (Campath®)	erlotinib (Tarceva®)	ponatinib hydrochloride (Iclusig®)
alitretinoin (Panretin®)	everolimus (Afinitor®)	pralatrexate (Folotyn®)
anastrozole (Arimidex®)	exemestane (Aromasin®)	radium 223 dichloride (Xofigo®)
atezolizumab (Tecentriq™)	fulvestrant (Faslodex®)	ramucirumab (Cyramza®)
avelumab (Bavencio®)	gefitinib (Iressa®)	regorafenib (Stivarga®)
axitinib (Inlyta®)	Ibritumomab tiuxetan (Zevalin®)	ribociclib (Kisqali®)
belinostat (Beleodaq®)	ibrutinib (Imbruvica®)	rituximab (Rituxan®)
bevacizumab (Avastin®)	idelalisib (Zydelig®)	romidepsin (Istodax®)
bexarotene (Targretin®)	Imatinib mesylate (Gleevec®)	rucaparib camsylate (Rubraca™)
blinatumomab (Blincyto®)	ipilimumab (Yervoy®)	ruxolitinib phosphate (Jakafi®)
bortezomib (Velcade®)	ixazomib citrate (Ninlaro®)	siltuximab (Sylvant®)
bosutinib (Bosulif®)	Lanreotide acetate (Somatuline® De	sonidegib (Odomzo®)
brentuximab vedotin (Adcetris®)	lapatinib (Tykerb®)	sorafenib (Nexavar®)
brigatinib (Alunbrig™)	lenvatinib mesylate (Lenvima®)	sunitinib (Sutent®)
cabazitaxel (Jevtana®)	letrozole (Femara®)	tamoxifen (Nolvadex)
cabozantinib (Cabometyx™)	midostaurin (Rydapt®)	temsirolimus (Torisel®)
cabozantinib (Cometriq®)	necitumumab (Portrazza™)	toremifene (Fareston®)
carfilzomib (Kyprolis®)	neratinib maleate (Nerlynx™)	trametinib (Mekinist®)
ceritinib (LDK378/Zykadia™)	nilotinib (Tasigna®)	trastuzumab (Herceptin®)
cetuximab (Erbitux®)	niraparib tosylate monohydrate (Ze	Tretinoin (Vesanoid®)
cobimetinib (Cotellic™)	nivolumab (Opdivo®)	vandetanib (Caprelsa®)
crizotinib (Xalkori®)	obinutuzumab (Gazyva®)	vemurafenib (Zelboraf®)
dabrafenib (Tafinlar®)	ofatumumab (Arzerra®)	venetoclax (Venclexta™)
daratumumab (Darzalex™)	olaparib (Lynparza™)	vismodegib (Erivedge®)
dasatinib (Sprycel®)	olaratumab (Lartruvo™)	vorinostat (Zolinza®)
denileukin diftitox (Ontak®)	osimertinib (Tagrisso™)	aflibercept (Zaltrap®)
Denosumab (Xgeva®)	palbociclib (Ibrance®)	



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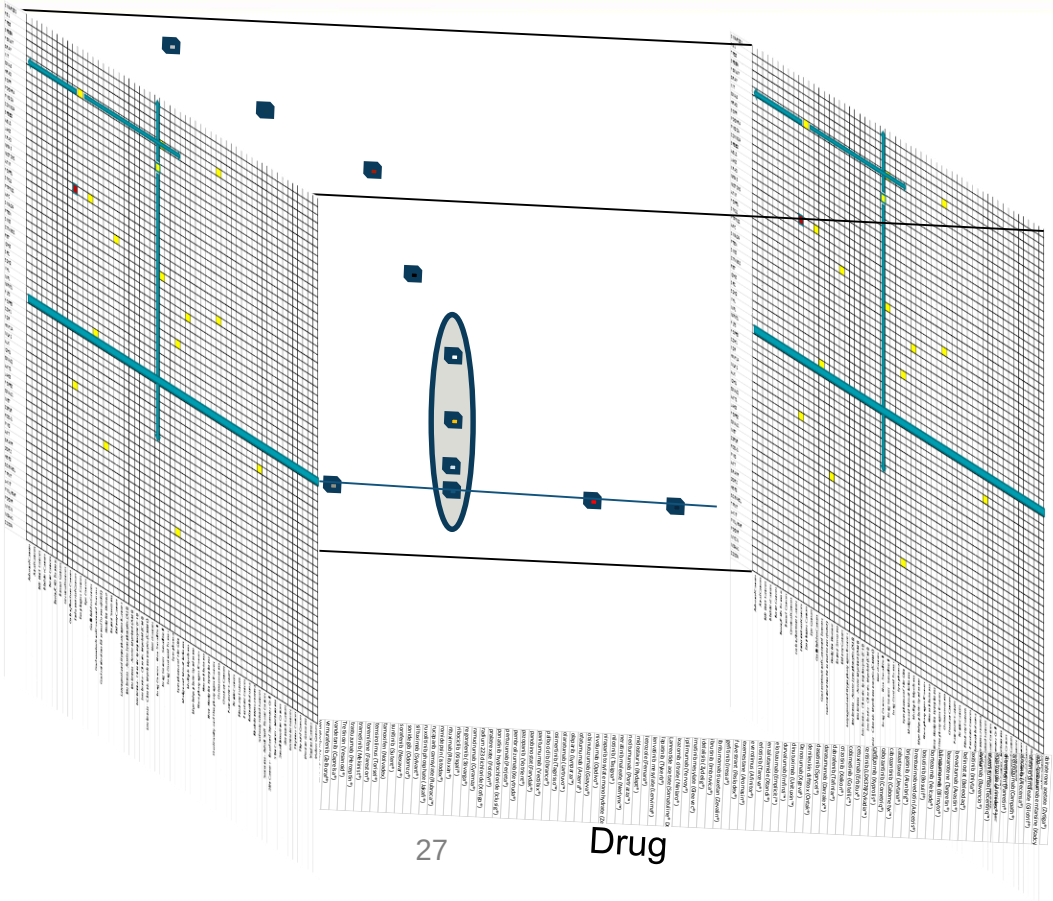
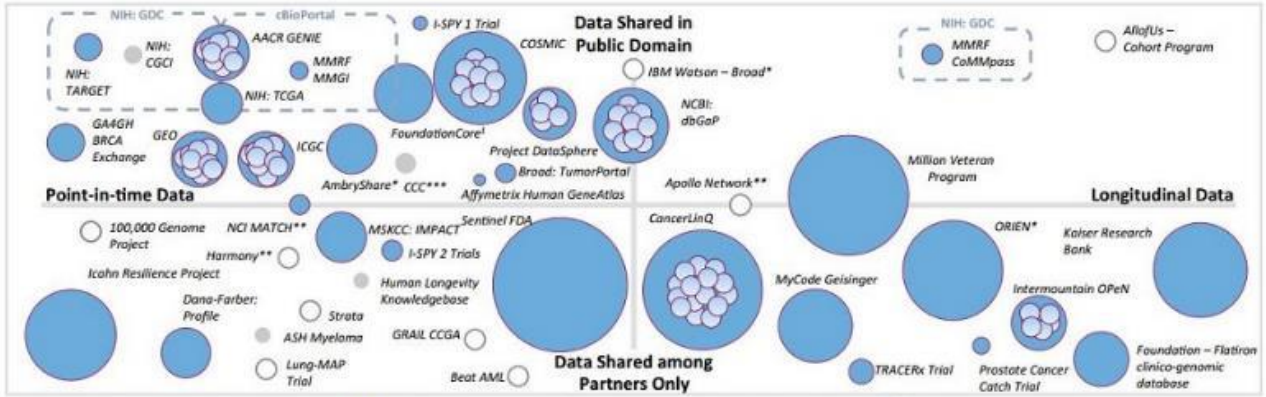


Oncology Precision Medicine Dataset Snapshot (2016)



Opportunity exists to generate publicly available longitudinal data to drive understanding of genetic mutations and find Precision Medicine cures

*Datasets have potential to include longitudinal data in the future
**Public/private information not available
***Serves as a portal also, has potential to include longitudinal data in the future

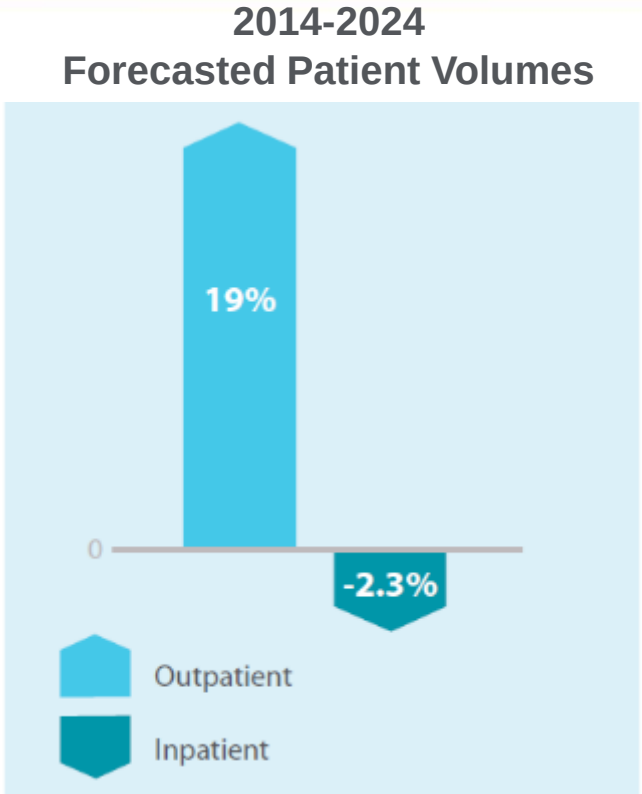
1. FoundationCore's pediatric cancer data has been made public

HARVARD BUSINESS SCHOOL
Kraft Precision Medicine Accelerator

State of Reimbursement

A Revolution in Health Care

- Shifting incentives
- Payment pressures/innovations
- New competitors
- Technology advancements
- Consumer expectations
- Cost shifting- risk bearing models



Sources: *Sg2 Impact of Change® v14.0; NIS; PharMetrics; CMS; Sg2 Analysis*

Pan-gene MDx Testing

COVERAGE RATIONALE

Molecular profiling using multiplex or next generation sequencing proven and medically necessary to guide systemic chemotherapy i metastatic stage IV non-small cell lung cancer (NSCLC) when both are met:

- **Molecular profiling using multiplex or NGS technology is us epidermal growth factor receptor (*EGFR*) mutations, human factor receptor 2 (*HER2*) mutations, *RET* rearrangements, a lymphoma kinase (*ALK*) gene arrangements;**

  (Note: See the National Comprehensive Cancer Network (NCCN Guideline for Non-Small Cell Lung Cancer, available at: www.nc regarding oncogenes used in molecular profile testing for NSCL

- **The laboratory providing molecular profiling testing service the New York State Department of Health for performing the**

  (Note: See the following Web Site for clinical laboratories holdin Department of Health permit in the category of oncology molecu markers:
  http://www.wadsworth.org/labcert/clep/CategoryPermitLinks/Cat
  (Accessed June 3, 2015)

Molecular profiling using multiplex or NGS technology is unproven and not medically necessary when the above criteria are not met.
There is insufficient evidence in the clinical literature demonstrating that molecular profiling has a role in clinical decision-making or has a beneficial effect on health outcomes for other indications. Further studies are needed to determine the analytic validity, clinical validity and/or clinical utility of molecular profiling using multiplex or NGS technology for other indications.

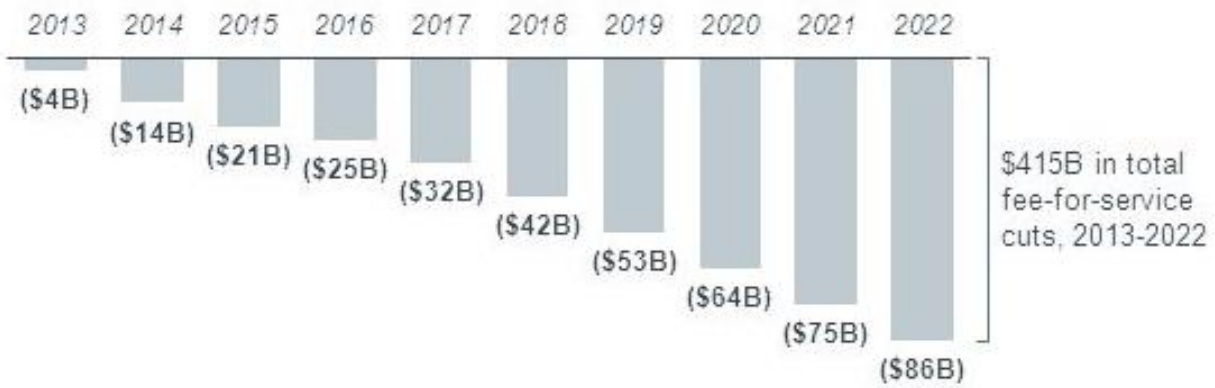
Other Cancers

Molecular profiling has many theoretical clinical applications in the field of oncology. Published clinical studies have addressed the use of molecular profiling for the following:

- Adrenocortical cancer (Ross et al., 2014a)
- Breast cancer (Ganesan et al., 2014; Wheler et al., 2014)
- Gastric and gastrointestinal cancer (Vignot et al., 2015; Miura et al., 2014)
- Head and neck cancer (Chung et al., 2015)
- Melanoma (Wheler et al., 2015; Hutchinson et al., 2013)
- Ovarian cancer (Ross et al., 2013)
- Pancreatic cancer (Chmielecki et al., 2014; Chantrill et al., 2015)
- Prostate cancer (Beltran et al., 2013)
- Unknown primary cancer site (Ross et al., 2015; Gatalica et al., 2014)
- Urothelial carcinoma (Ross et al., 2014b; Millis et al., 2015)

There is insufficient published evidence to support the use of molecular profiling for these cancers. The main evidence deficiencies for molecular profiling for these cancers are insufficient data on analytical validity, clinical validity, and clinical utility. Published studies evaluating molecular profiling for these conditions are mainly case reports or case series with a limited number of patients.

Medicare FFS Payment Cuts



$260B
Hospital payment rate cuts, 2013-2022

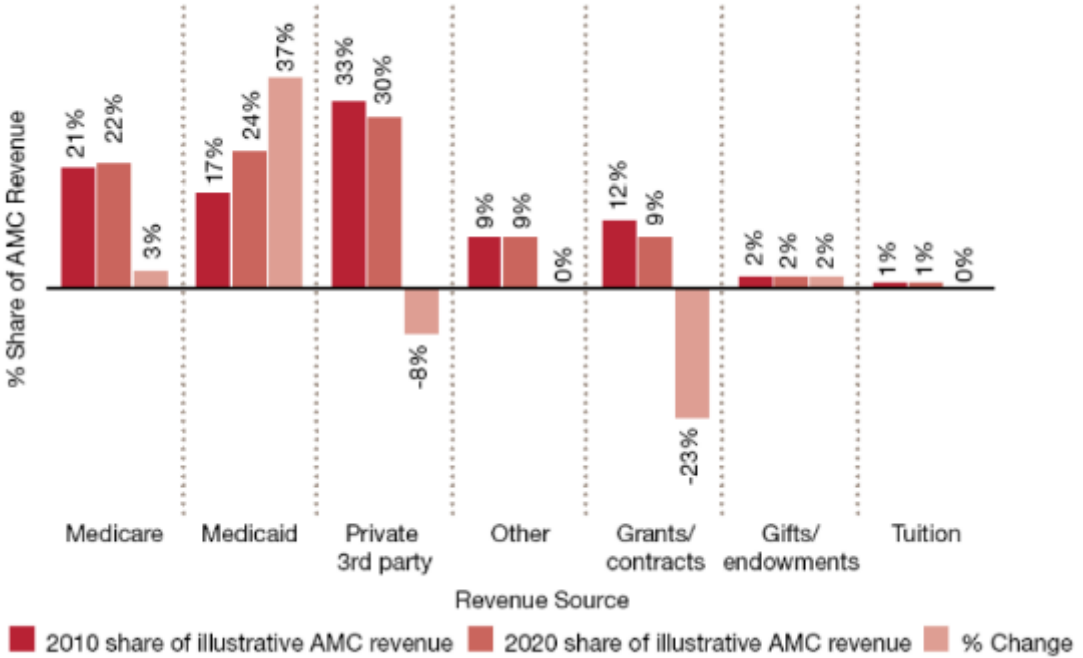
$56B
Reduced Medicare and Medicaid DSH[2] payments, 2013-2022

Source: The Advisory Board 2017

PwC Health Research Institute

The future of the academic medical center:

Strategies to avoid a margin meltdown



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Source: PwC Health Research Institute Analysis

The **Medicare Access and CHIP Reauthorization Act** of 2015 (MACRA) is a bipartisan legislation signed into law on April 16, 2015

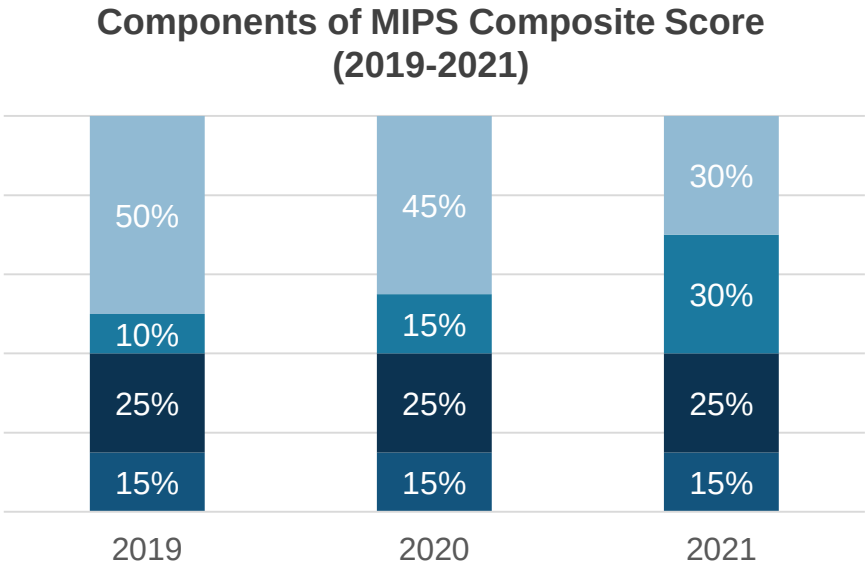
Repeals the Sustainable Growth Rate formula for physician payments

Establishes a path toward a new payment system more closely aligned to quality and outcomes

Offers significant financial incentives for health care professionals to participate in risk-bearing, coordinated care models

Adapted from Deloitte Advisory Regulatory Services for Life Sciences and Health Care

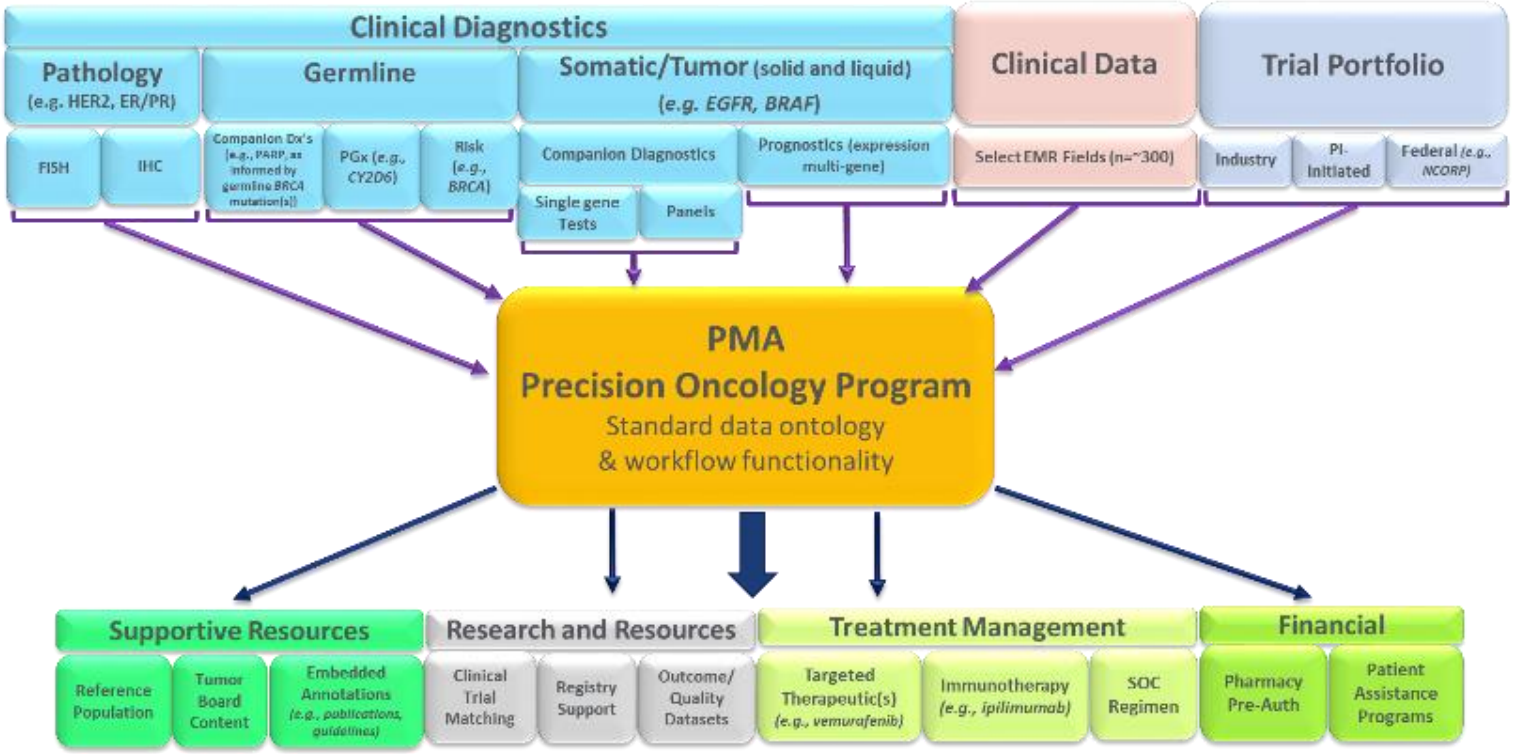
Merit-based Incentive Payment Systems (MIPS)



- **Quality**: PQRS
- **Resource Use**: Value-based Payment Modifier measures
- **Meaningful Use of EHRs**: EHR Incentive Payment measure
- **Clinical Improvement Activities**: Expanded access, population management, care coordination, beneficiary engagement, patient safety, and alternative payment models

Existing incentive programs end 2018, and performance consolidated into a new composite score MIPS payment starting 2019

Source: Public Law 114-10 (April 16, 2015;)
Adapted from Deloitte Advisory Regulatory Services for Life Sciences and Health Care



Providing Opportunities for Scalable Impact: An approximate trajectory of value

Phase 1 (~ 3 Years)	
Clinical Workflow/Value	Incremental Operation Improvement
Clinical Trial Management	Limited sponsor-led trials
Payment Environment	Low coverage and lagging behind observed clinical outcomes
Business Opportunities	Increased clinical trial accrual

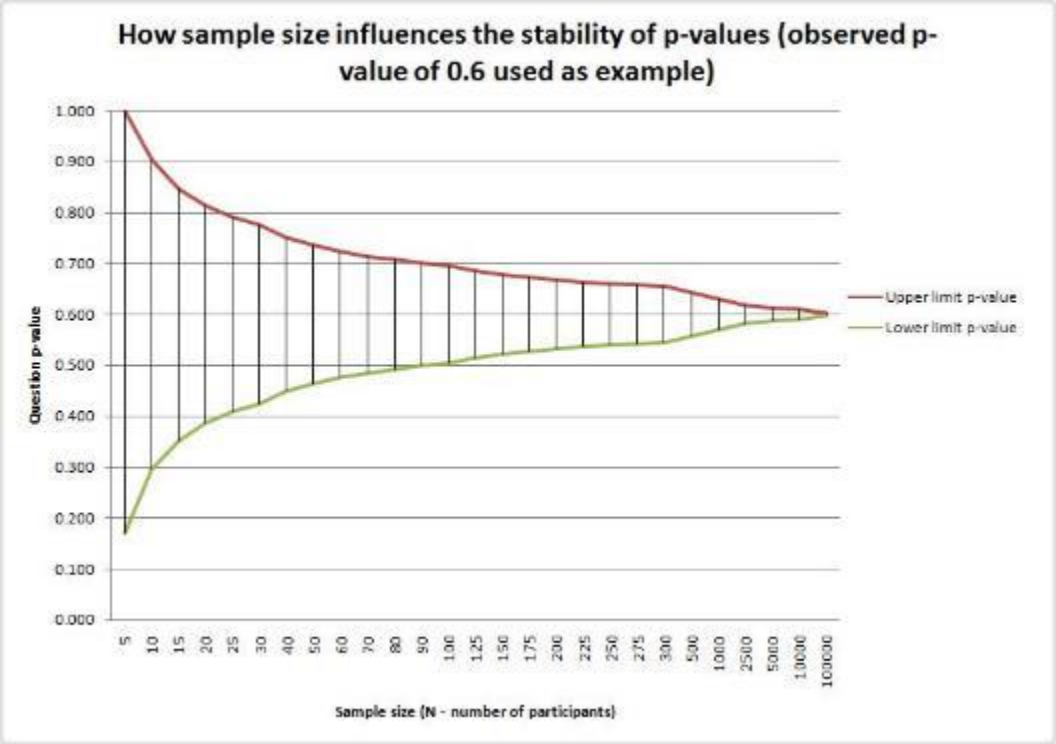
Phase 2 (~ 6 Years)	
Clinical Workflow/Value	Increased data management & data support
Clinical Trial Management	Ecosystem demand for additional trials allows for portfolio expansion opportunities
Payment Environment	Reimbursement established for firmer core pathways
Business Opportunities	Continued increase in trial accrual and increase in overall patient volume and retention

Phase 3 (~ 10 Years)	
Clinical Workflow/Value	Requisite decision support
Clinical Trial Management	Robust national portfolio, including long-tail (rare mutation) trials
Payment Environment	Evidence-based medicine / In Vitro Diagnostics
Business Opportunities	Reduction in total cost of care across the healthcare networks

Closing Thoughts

- Central vs. local program – management strategy
- Testing strategy – Dx business?
  - Compete with artificial economies and secondary usage markets subsidizing testing?
- Research strategy?
- Data readiness (also governance, ownership, operations, policy)
- Are other capabilities built and prepared to derive value?
- Is the program an investment or operational upgrade?
- Can the team be a service company?
- Is your organization ready for a challenge?
- Can you stay focused? Avoid envy?

Need for Good Data (Evidence)



Respect the Complexity of Biology= Fight the urge to be reductionist, but go forward

Questions?

Damon Hostin, CEO

Precision Medicine Alliance, LLC

Dignity Health/Catholic Health Initiatives

Please complete session evaluation!

Presentation thanks to:
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