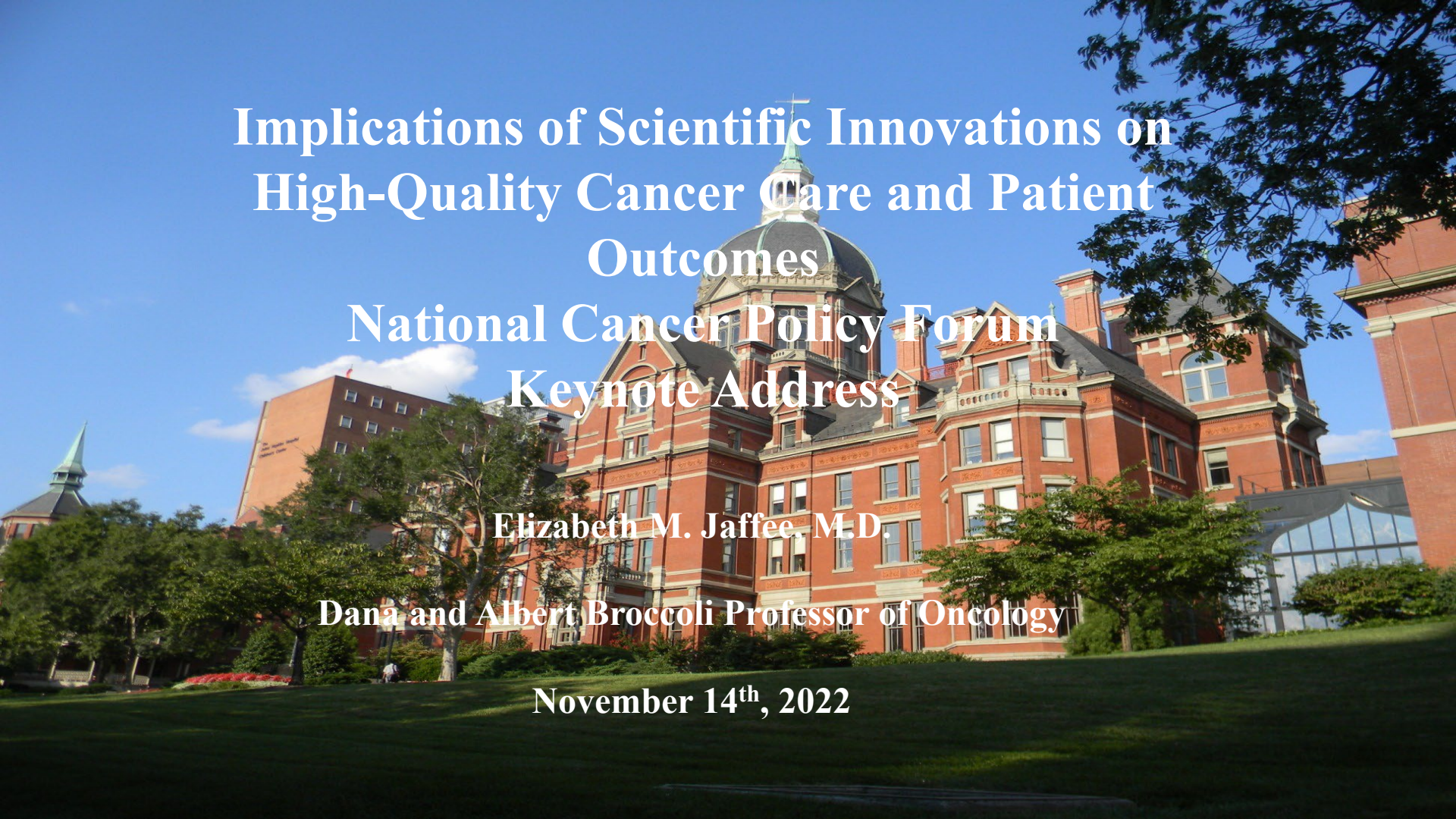




Implications of Scientific Innovations on High-Quality Cancer Care and Patient Outcomes National Cancer Policy Forum Keynote Address

Elizabeth M. Jaffee, M.D.

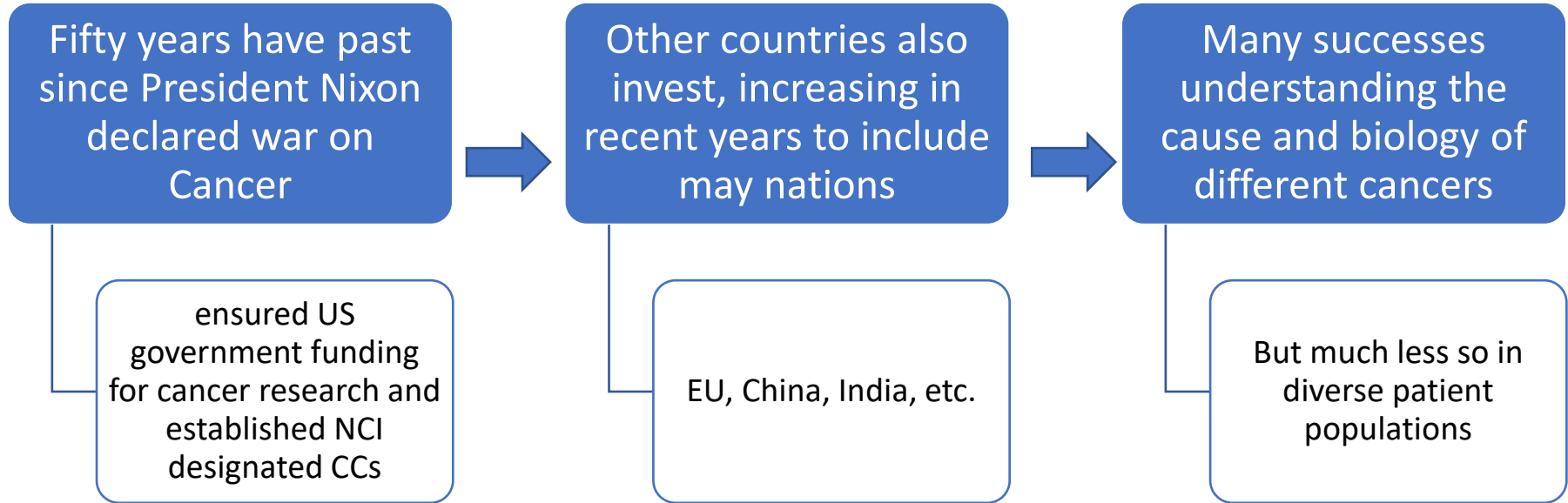
Dana and Albert Broccoli Professor of Oncology

November 14th, 2022

We are at a pivotal time in cancer research and care!

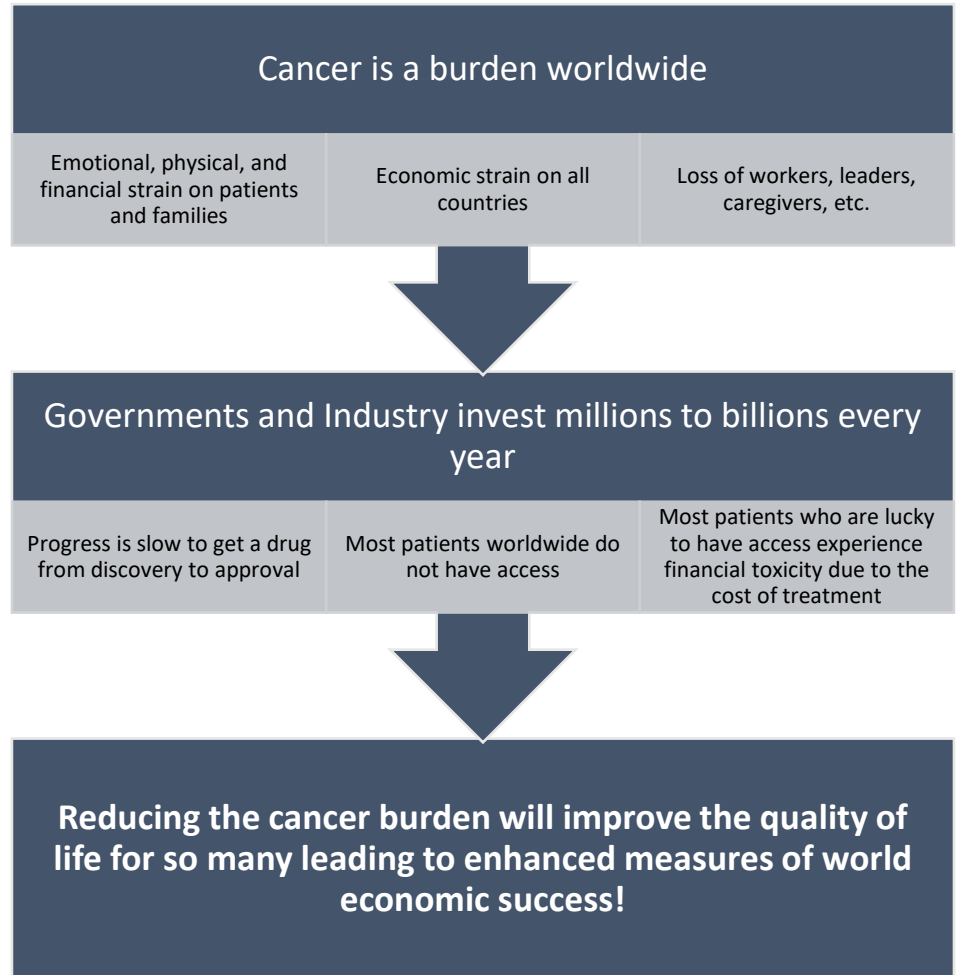
- Cancer has become an urgent problem worldwide
 - Second leading cause of death in most countries
 - Health inequality in most countries are amplifying the problem
- Governments and Industry are investing more today than ever before
- We are seeing more rapid successes today due to progress in basic science, innovations in technology, and development of more targeted drugs
- We are in a technologic revolution providing the opportunity to expedite drug development

How did we arrive at today's opportunities?



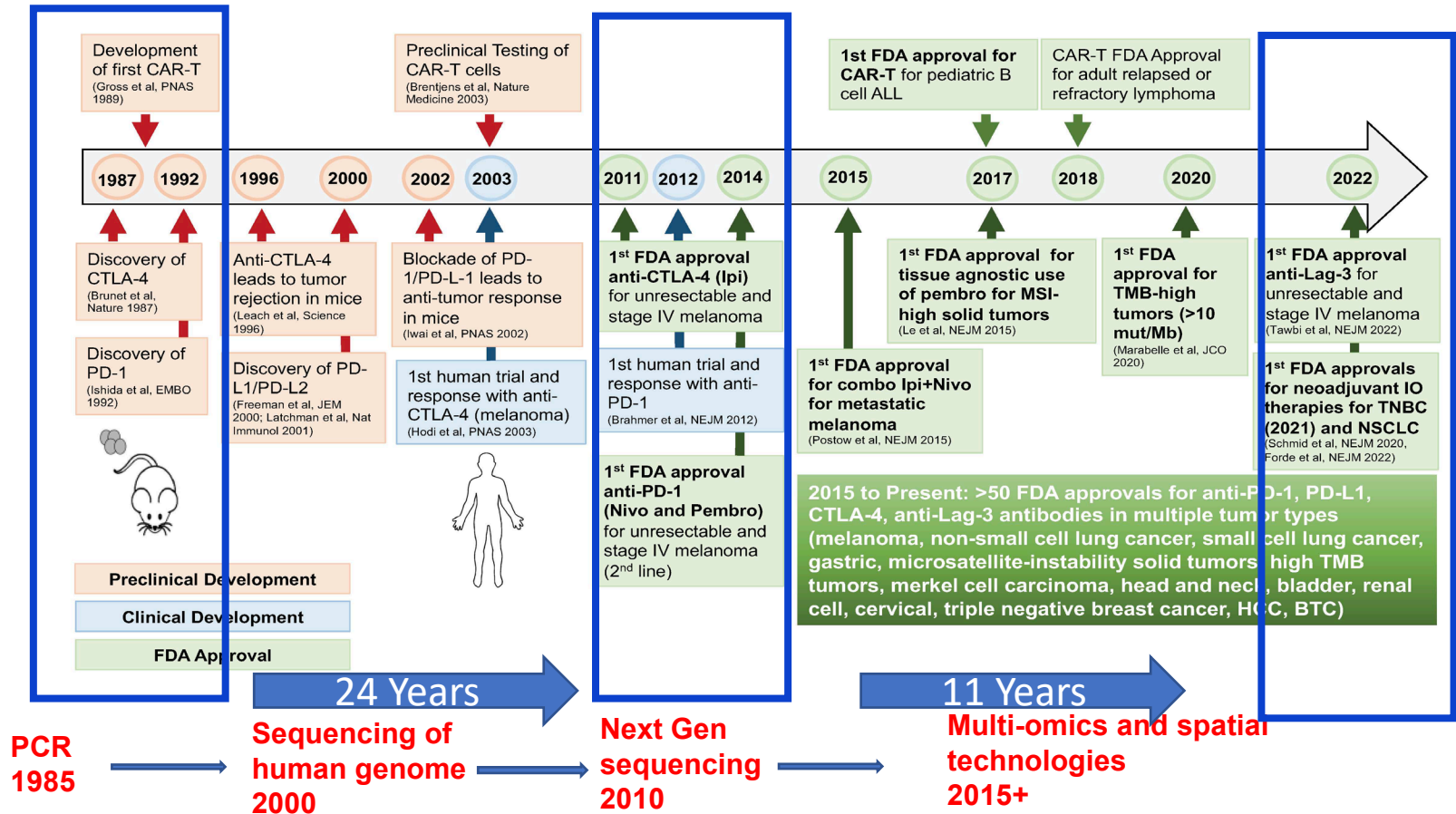
It is time to leverage these unprecedented opportunities into more rapid and improved patient outcomes for all cancer patients!

What is it worth
to all of us to
prevent and cure
cancer?



Developments in Technology Parallel Development of Combination Immunotherapies

T Cell Therapy: From Development to Approval



More rapid development of combination immunotherapies requires solving "BIG" challenges

New clinical trial designs

- To optimize combination dose and schedule
- Easily adaptable to facilitate rapid testing of multiple combinations
- Multi-center/clinic to improve access

Open access platforms for clinical trial data sharing accessible to government, industry and academia

- To identify pathways of resistance to PD-1 therapy for new drug development
- To identify sub-populations responsive and resistant to PD-1 therapy
- To develop biomarkers that can be used to optimize combinations

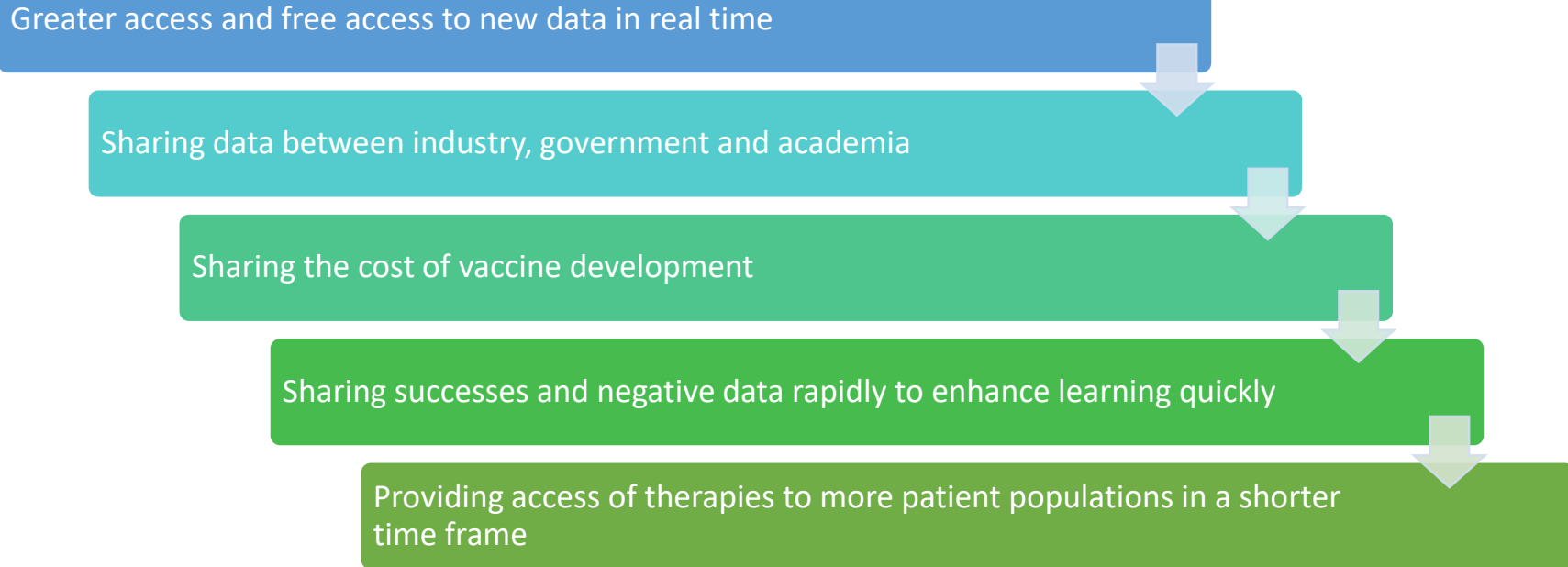
New approaches to improve access to clinical trials

- Patient driven national registration trials
- Digital technologies for adverse event monitoring/education/communication

These challenges will require close collaborations between government, industry, academia, patient advocacy groups, foundations, and the public!

Collaborative approach to data and cost sharing produced multiple covid vaccines in the first year of the pandemic!

Greater access and free access to new data in real time



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graph TD; A[Greater access and free access to new data in real time] --> B[Sharing data between industry, government and academia]; B --> C[Sharing the cost of vaccine development]; C --> D[Sharing successes and negative data rapidly to enhance learning quickly]; D --> E[Providing access of therapies to more patient populations in a shorter time frame];
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Sharing data between industry, government and academia

Sharing the cost of vaccine development

Sharing successes and negative data rapidly to enhance learning quickly

Providing access of therapies to more patient populations in a shorter time frame

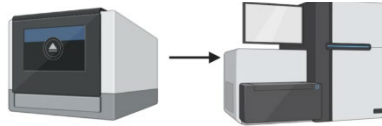


Recent Technologies are Quickly Uncovering Pathways of Sensitivity and Resistance to PD-1 Blockade

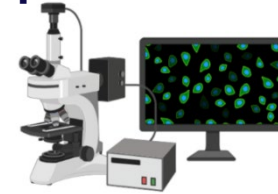
CyTOF and Imaging Mass Cytometry



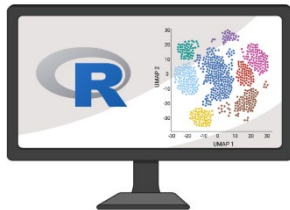
Single cell/Spatial RNA/TCR sequencing



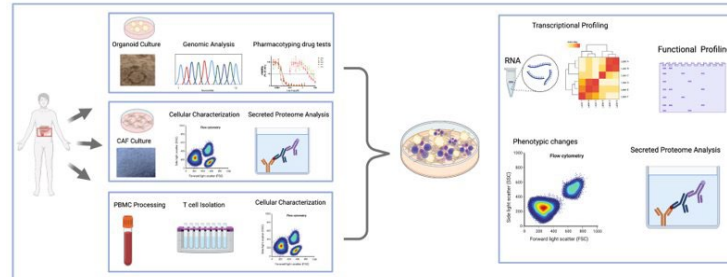
Multiplex/Spatial proteomics



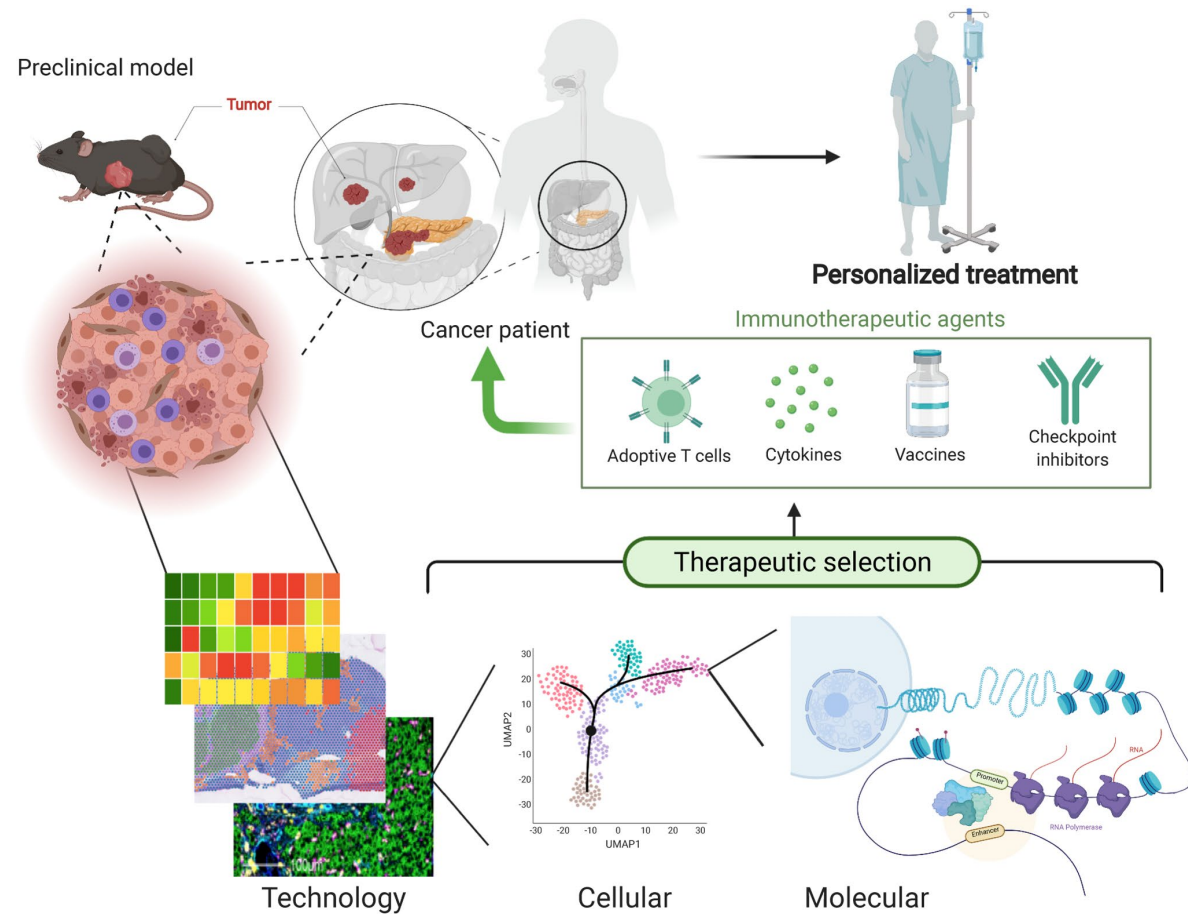
Data Science Platforms and Artificial Intelligence Modeling



New Technologies to Model Human Cancers Organoid/3-D Models



BUT! We need new analytical tools to integrate technology-driven human and preclinical model datasets to inform selection of new immunotherapy combinations



We are behind in training experts in data science! This has created a data bottleneck!



New Clinical Trial Designs

Innovative adaptive and biology rich trial designs are generating more rapid data for combination selection

Seamless phase I-III biomarker driven trials

- PD-L1+, TMB high, MSI-high companion biomarkers
- high PR/CRs with single agent led to accelerated approvals
- Did not require randomization

Adaptive trial design used in I-SPY-2

- Serial studies to predict therapeutic response through imaging and molecular analysis
- This design randomized locally advanced breast cancer patients to one of several arms in the neo-adjuvant setting
- Included exploratory biomarker and imaging studies
- Graduated 6 regimens over 10 years to successful Phase III

Multistage multiarm (MAMS) design used in STAMPEDE Trial

- Evaluated drug efficacy in advanced prostate cancer
- Simultaneously compared multiple treatment arms
- All against 1 control arm
- Added and dropped arms based on early readout
- Successful arm became control arm

Adaptive Trial Designs Based on Big Data and Real-World Evidence (RWE) Are Needed to Accelerate Progress

Randomized controlled trials are less feasible for cancer drug development

- targeted drugs and combinations work best in smaller groups of selected patients
- New drugs and combinations are available off study reducing control arm participants

External control arms (EMR and Claims Information) are potential surrogates

- Large commercial Databases (Flatiron, Acorn AI) have demonstrated value of aggregating diverse sources for generating RWE and drug approvals
- Need standardizations among elements and systems including EMRs, data generating labs, etc.

Consortiums have shown success with genetic data

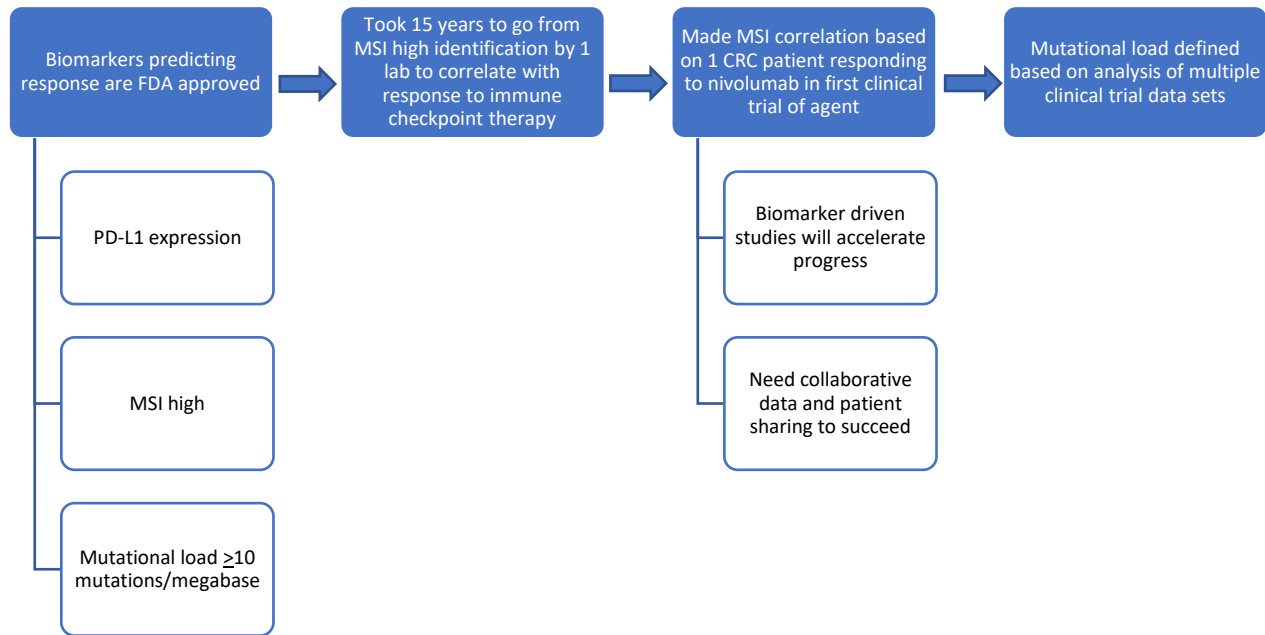
- Need to expand to include all cancer patients
- Need to adapt platforms for emerging datasets

What should be next?

Integration of novel multidimensional biomarkers to select patients and combination treatments!

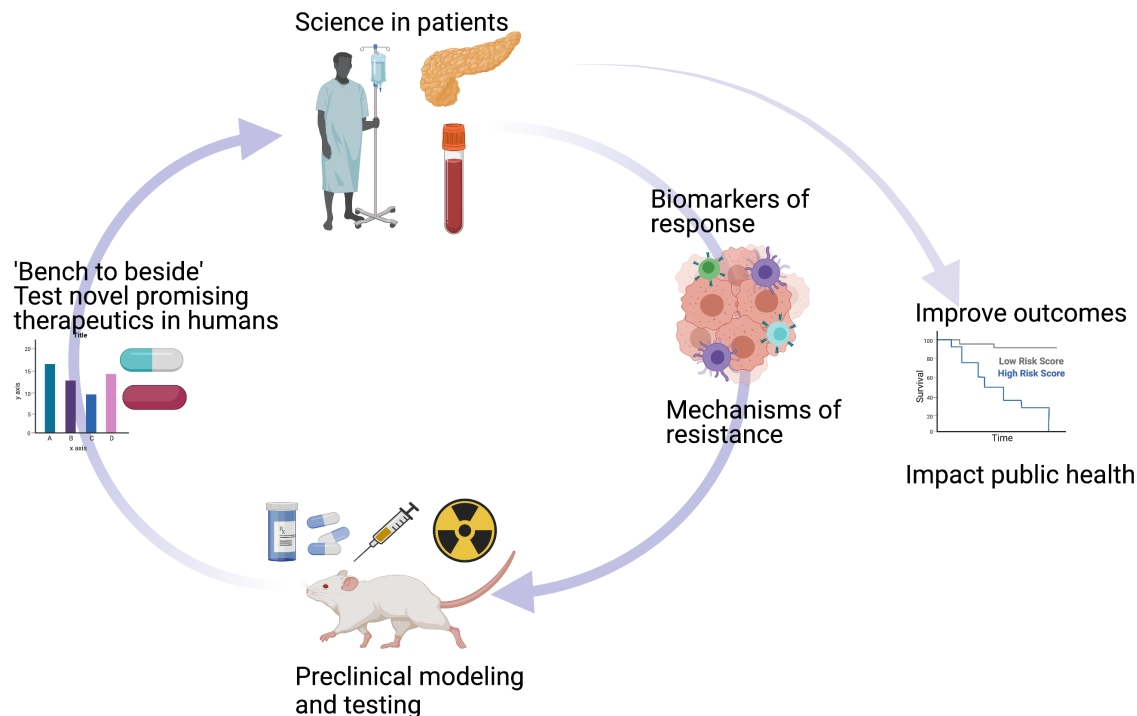
- Whole exome or genome-based mutation signatures
- Digital spatial transcriptomic and proteomic profiling of TME
- Quantitative features extracted from standard of care imaging
- Molecular target imaging
- Clonal tracking dynamics using circulating tumor DNA
- Baseline immune health features
- Machine learning and artificial intelligence to assist with combination selection

But it took many years to identify and validate these biomarkers!



Collaborations in data and biobank sharing will accelerate biomarker driven therapies!

'Bench-to-Bedside' Bidirectional Translational Research Can Drive Progress in Cancer Therapeutics



Iterative integration of data from rapidly evolving technologies applied to science driven human and preclinical models needed to identify the best combination to move into approval studies

High Tech
health revolution

DIGITAL HEALTH

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0110 0110
1001 1001000
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Wearables

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graph TD
    A[Government agencies] --- B(( ))
    B --- C[Patient portals]
    C --- D[Research studies]
    D --- E[Generic databases]
    E --- F[Electronic health records (EHR)]
    F --- G[Public records]
    G --- H[Search engine data]
    H --- I[Wearable devices]
    I --- J[Smart phones]
    J --- K[Payer records]
    K --- A
    K --- B
  
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AI Drug Discovery

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Open Access Platforms and Data Sharing

Data sharing benefits all stakeholders!

All sectors have access to large data sets to ask the most patient relevant questions in larger defined populations

Reduces waste in research

Increases research opportunities

Government and industry co-investments go further!

Pharma has access to large data sets to identify new druggable pathways and biomarkers

Patients get cures through precision medicine!

How do we
more
rapidly
share data
to make
progress?



We need to accelerate and facilitate clinical trial data sharing

A few regulations mandate registration and disclosure of clinical trial results

- Clinicaltrials.gov; EudraCT
- Both positive and negative results
- These databases fall short on ease of data sharing and integration to identify resistance mechanisms

Scientific journals mandate depositing raw data into in public repositories for easy use

- Omics; cytometry and imaging; mathematical/modeling resources
- *Scientific Data - Nature: Data Repository Guidance*
- *Recommended Repositories – PLOS One*
- *sharing.nih.gov/data-management-and-policy*

A national effort to exploit current opportunities in emerging technologic and big data advances to accelerate drug development

- New trial designs for rapid identification of drug combinations
- New approaches to give access to all cancer patients
- Modernizing regulations around PHI and data sharing
- Reinventing data acquisition processes to facilitate data sharing

Moonshot Encouraged Collaborative Projects!



10/18/16: Blood Profiling Atlas Face 2 Face

We need to rapidly adopt new technologies
to model drug development!

Can we accelerate drug development through Digital Twins and improve cancer outcomes through Digital medicine technologies?

Imagine integrating large data sets to predict response to new drugs/combinations?

Defining a Digital Twin



Represents assets in the physical world with a digital model



Is NOT just a data model. It must include relational interaction



Looks and feels like the real environment



Connects with relevant time data to ensure the model mirrors reality



Simulates models forward with varying degrees of fidelity





New Approaches to Improve Access to Clinical Trials

Digital Medicine
Opportunities can
eventually improve
access and health
of more patients
with cancers!

- Digital tools to increase access to screening, diagnosis, etc.
- Wearables to improve symptom management
- Reduce patient time in medical facilities - improve quality of life
- Integrate with machine learning to improve diagnosis, treatment choice, and longitudinal management
- National databases –
 - patient entering their own data
 - National registration for clinical trials
 - Identify high risk populations for early interventions reducing morbidity and cost of health care

Policy Issues Identified as Barriers by the BRP to Drug Development

- Medical coverage and reimbursement
 - Costs of screening and preventive care not currently covered, including follow-up colonoscopy; reimbursement for referral, home-based care, clinical trials and non-physician health care providers
- Enhanced patient engagement
 - Design uniform informed consent, increase patient access to data
- Delivery of cancer care in the community
 - Reduce economic burden of clinical trial enrollment on community practitioner, sharing of electronic medical record data, best practices for state vaccine registries
- Improve clinical trials system
 - Central IRB, data sharing among federal agencies, improve clinical trial site evaluation
- Improve the outcome for children with cancer
 - Incentives for pediatric cancer drug development, especially molecularly targeted agents
- Develop data sharing mechanisms and incentives
 - Common ontologies, data standardization, umbrella licensing, private sector sharing

A CALL TO ACTION!

We need strong and innovative leaders among all stakeholders to collaborate. To make big changes for the good of all!



THANK YOU!