

# DOE-NCI pilots

## Collaborations across the national labs

*Warren Kibbe, PhD*

*NCI Center for Biomedical Informatics*

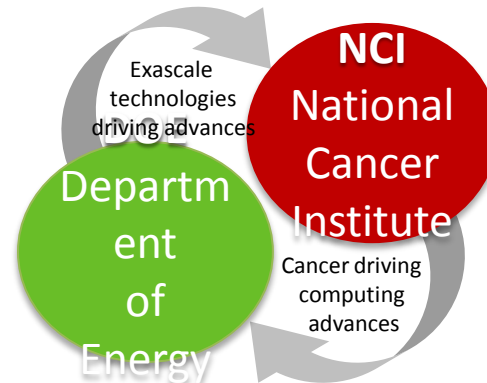
*warren.kibbe@nih.gov*



@wakibbe

# Joint Design of Advanced Computing Solutions for Cancer

*DOE-NCI partnership to advance exascale development through cancer research*



Warren Kibbe (NCI) & Dimitri Kusnezov (DOE)



U.S. DEPARTMENT OF  
**ENERGY**



**NATIONAL CANCER INSTITUTE**

# National Strategic Computing Initiative (NSCI)

*Executive Order, July 30, 2015*

It is the policy of the United States to sustain and enhance its scientific, technological, and economic leadership position in HPC research, development, and deployment through a coordinated Federal strategy guided by four principles:

- 1) The United States must deploy and apply new HPC technologies broadly for economic competitiveness and scientific discovery.
- 2) The United States must foster **public-private collaboration**, relying on the respective strengths of government, industry, and academia to maximize the benefits of HPC.
- 3) The United States must adopt a "whole-of government" approach that draws upon the strengths of and seek cooperation among all Federal departments and agencies with significant expertise or equities in HPC in concert with industry.
- 4) The United States must develop a comprehensive technical and scientific approach to efficiently transition HPC research on hardware, system software, development tools, and applications into development and, ultimately, operations.

**This order establishes the NSCI to implement this whole-of-government strategy, in collaboration with industry and academia, for HPC research, development, and deployment.**

DOE is a Lead Agency for NSCI

NIH/NCI is a Broad Deployment Agency for NSCI

# President Obama's Precision Medicine Initiative (PMI)

January 30, 2015

## Objectives of the Precision Medicine Initiative:

- 1. More and better treatments for cancer** *NCI will accelerate the design and testing of effective, tailored treatments for cancer by expanding genetically based clinical cancer trials, exploring fundamental aspects of cancer biology, and establishing a national "cancer knowledge network" that will generate and share new knowledge to fuel scientific discovery and guide treatment decisions.*
- 2.** Creation of a voluntary national research cohort
- 3.** Commitment to protecting privacy
- 4.** Regulatory modernization
- 5. Public-private partnerships** *The Obama Administration will forge strong partnerships with existing research cohorts, patient groups, and the private sector to develop the infrastructure that will be needed to expand cancer genomics, and to launch a voluntary million-person cohort. The Administration will call on academic medical centers, researchers, foundations, privacy experts, medical ethicists, and medical product innovators to lay the foundation for this effort, including developing new approaches to patient participation and empowerment. The Administration will carefully consider and develop an approach to precision medicine, including appropriate regulatory frameworks, that ensures consumers have access to their own health data – and to the applications and services that can safely and accurately analyze it – so that in addition to treating disease, we can empower individuals and families to invest in and manage their health.*

# Vice President Biden's Cancer Initiative

January 2016

## Scientific Objectives of the Vice President's Cancer Initiative Blue Ribbon Panel

- Prevention and Cancer Vaccine Development
- Early Cancer Detection
- Cancer Immunotherapy and Combination Therapy
- **Genomic Analysis of Tumor and Surrounding Cells**
- Enhanced Data Sharing
- Oncology Center of Excellence
- Pediatric Cancer
- Exceptional Scientific Opportunities in Cancer Research

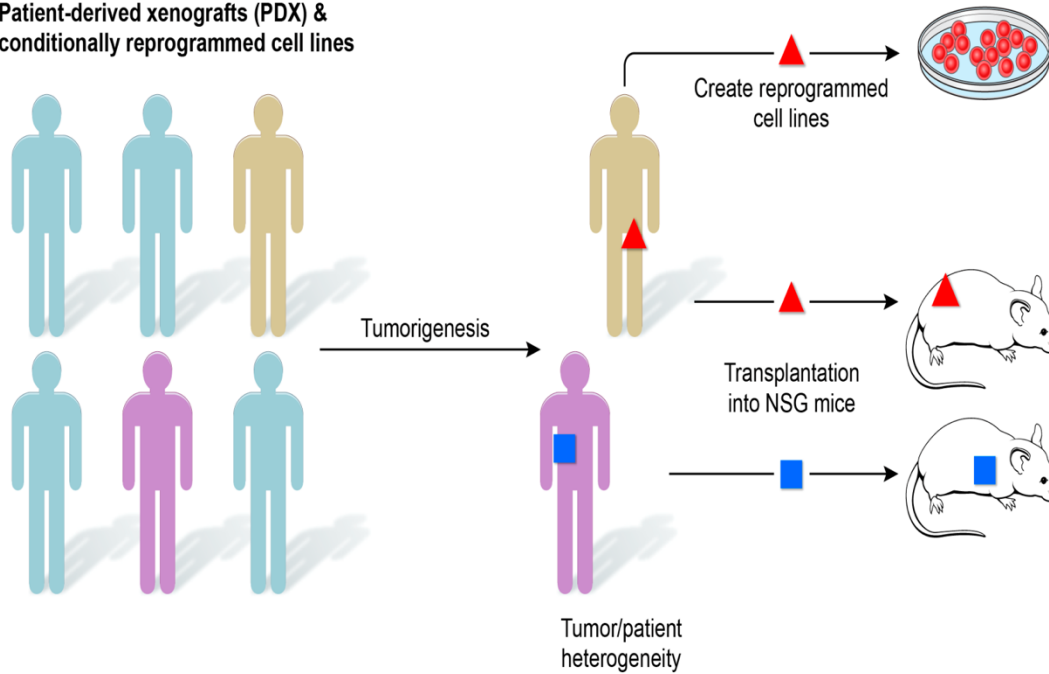
# Three Pilot projects – data types

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- **Molecular/atomistic scale data – RAS initiative data**
- **Genomic+clinical diagnostic+pathology data – PMI pre-clinical models**
- **Population level cancer incidence and outcomes data – SEER registry**

# Predictive algorithm for cancer therapy

Patient-derived xenografts (PDX) & conditionally reprogrammed cell lines

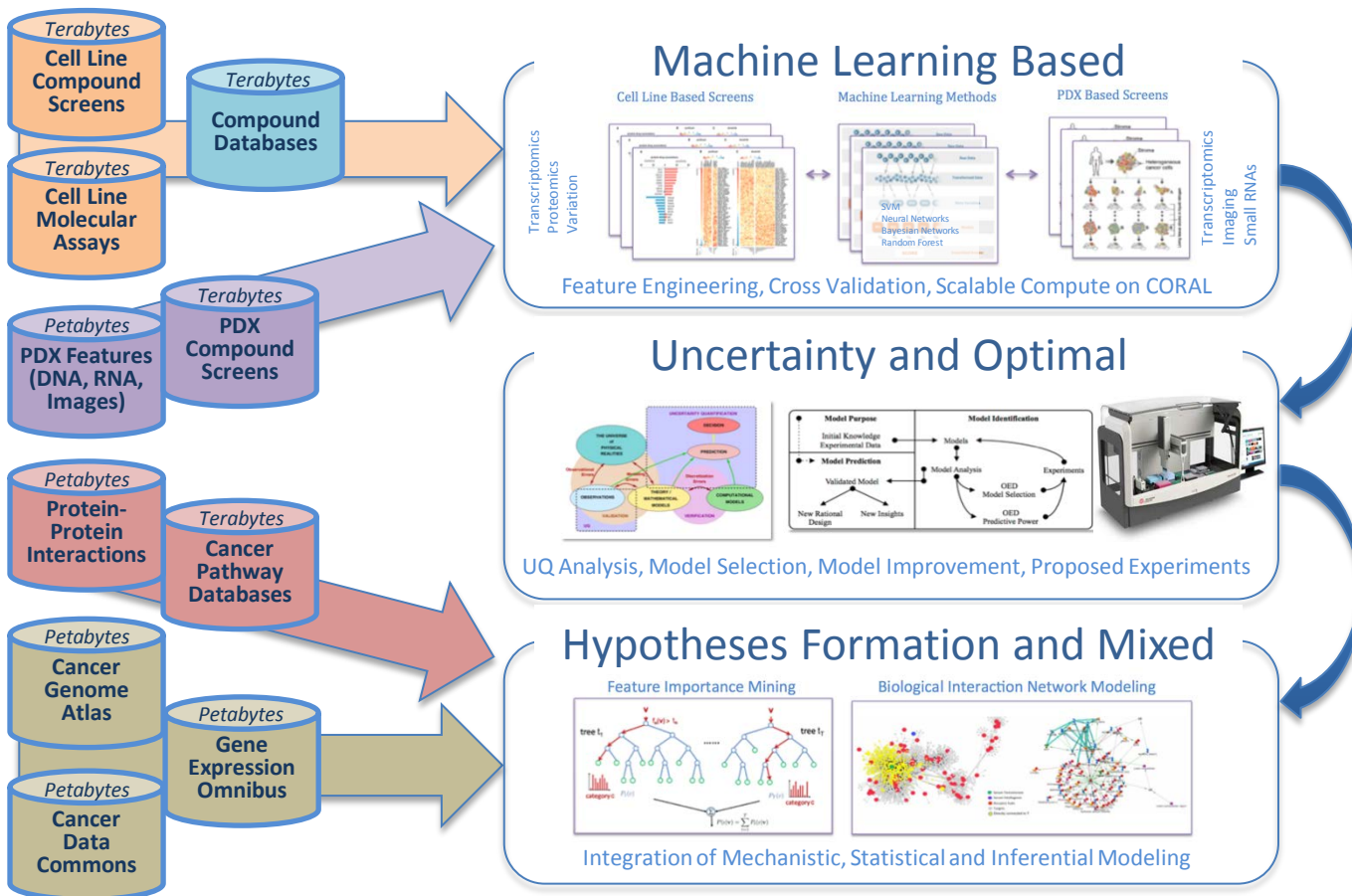


Molecularly characterize, treat/screen mice bearing transplants & cells with relevant drugs.

“Pre-clinical clinical trials”

Nature Rev. Clin. Oncol. 11: 649-662, 2014.

# Predictive Models for Pre-Clinical Screening

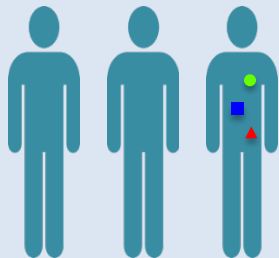




# Predict novel therapeutic targets for RAS drug discovery

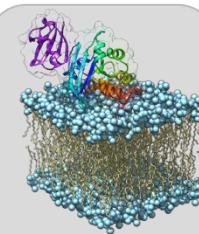
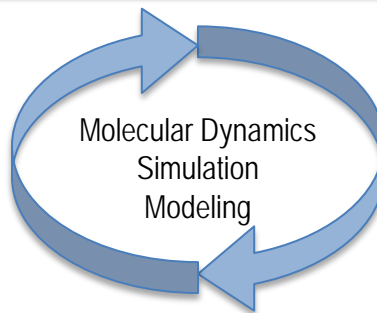
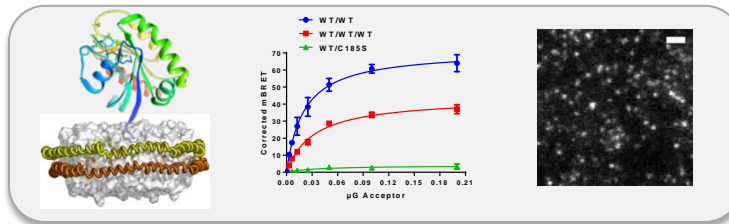
30% of cancers have mutated RAS

~1M deaths/year

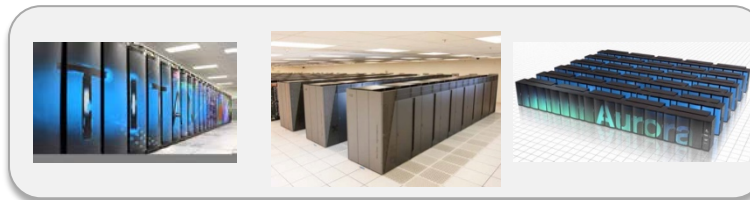


Current therapies ineffective against RAS-driven cancer

Facilitate discovery and development of novel therapeutics

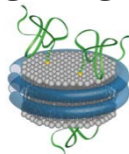


RAS biology  
ID targets  
New inhibitors

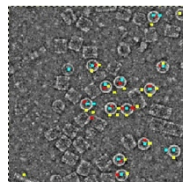


# RAS proteins in membranes

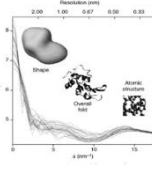
## RAS activation experiments at



Experiments on nanodisc



CryoEM imaging



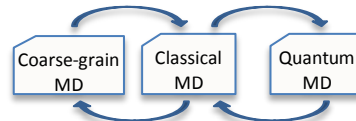
X-ray/neutron scattering

Multi-modal experimental data, image reconstruction, analytics

Protein structure databases

## New adaptive sampling molecular dynamics simulation codes

Adaptive time stepping



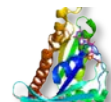
Adaptive spatial resolution

High-fidelity subgrid modeling

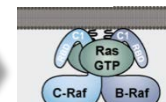
## Predictive simulation and analysis of RAS activation



Granular RAS membrane interaction simulations

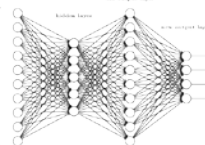


Atomic resolution sim of RAS-RAF interaction



Inhibitor target discovery

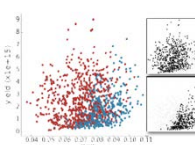
## Machine learning guided dynamic validation



Unsupervised deep feature learning



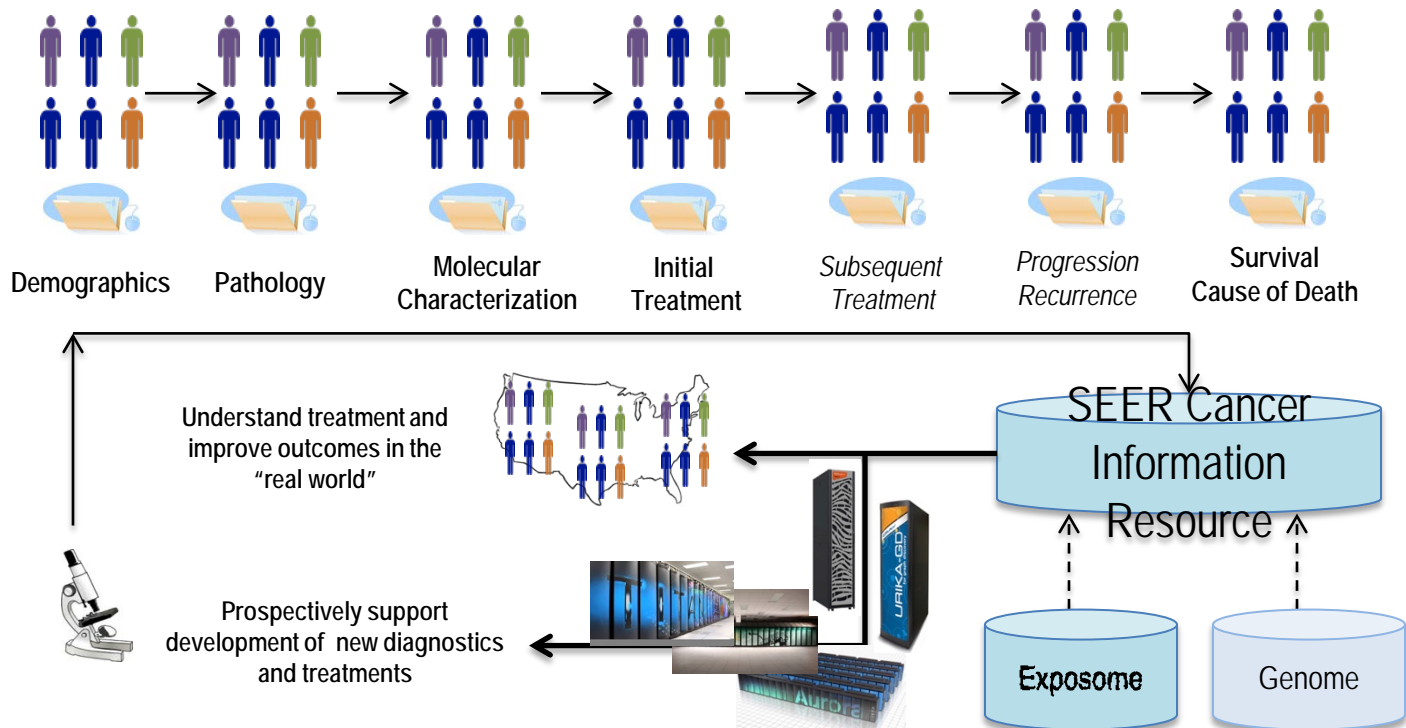
Mechanistic network models



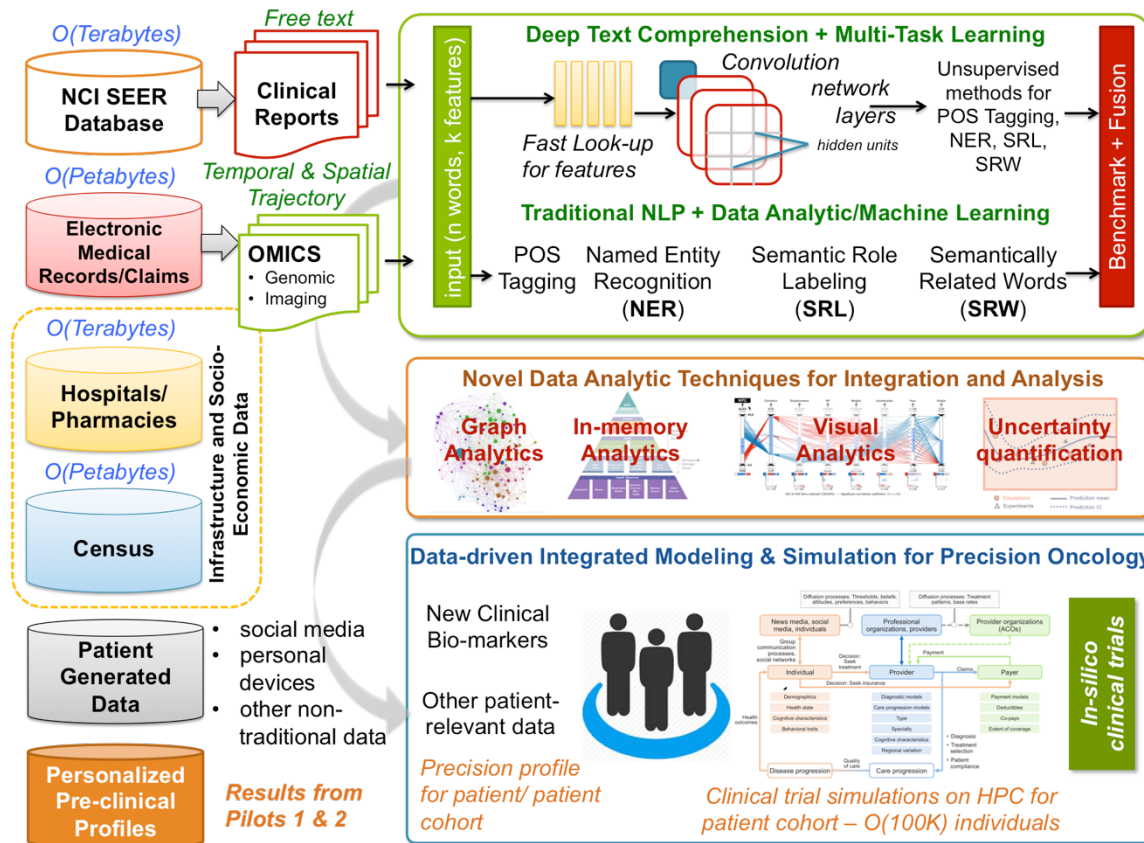
Uncertainty quantification

# Improve the effectiveness of cancer treatment in the “real world” through automation of cancer surveillance

Surveillance data captured on each cancer patient for the entire population



# Population Information Integration, Analysis and Modeling



# Milestones for 3-year pilots

- Pilot 1:** Framework for predictive models for preclinical screening. Initial integration of machine learning functionality into CORAL nodes
- Pilot 2** Extended RAS-complex interaction model  
Adaptive time and length scaling in dynamic multi-scale simulations  
Development of machine learning for dynamic validation of models
- Pilot 3** Modeling framework for predictive simulations of patient health trajectories.  
Integration of big data analytics with data-driven modeling and simulation for CORAL architectures

# NCI Precision Oncology – Extending the Frontiers

- Identify promising new treatment options through the use of advanced computation to rapidly develop, test and validate predictive pre-clinical models for precision oncology.
- Deepen understanding of cancer biology and identify new drugs through the integrated development and use of new simulations, predictive models and cutting-edge information spanning the range from molecular biophysical properties to patient outcomes.
- Transform cancer care by applying advanced computational capabilities to population-based cancer data to understand the impact of new diagnostics, treatments and patient factors in real world patients.

## What these pilots offer:

- **Jointly supported efforts**
- **Jointly managed and planned**
- **Three 3-year pilots**
- **Four DOE Labs, one NCI Lab**
- **Builds on CORAL**
- **Pushes the frontiers in Oncology and Exascale simultaneously**
- **Supports all 4 policy goals of the NSCI and 4 of 5 objectives**
- **Supports 2 of 4 objectives of the PMI**
- **Aligns and leans into two 2015 Presidential Initiatives**
- **Draws in private sector interests**



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[www.cancer.gov](http://www.cancer.gov)

[www.cancer.gov/espanol](http://www.cancer.gov/espanol)