



Digital twins across scales: Informing cancer drug discovery and development

Bissan Al-Lazikani

THE UNIVERSITY OF TEXAS
MDAnderson
Cancer Center
Making Cancer History®

Disclosures



Research Funding:

Cancer Prevention and Research Institute of Texas • Cancer Research UK • Lyda Hill Foundation • Wellcome Trust • UKRI:Medical Research Council • Children with Cancer UK • Prostate Cancer UK • National Institute of Health Research

Financial Conflicts:

Drug Hunter • Exscientia AI • Recursion Bio • AstraZeneca

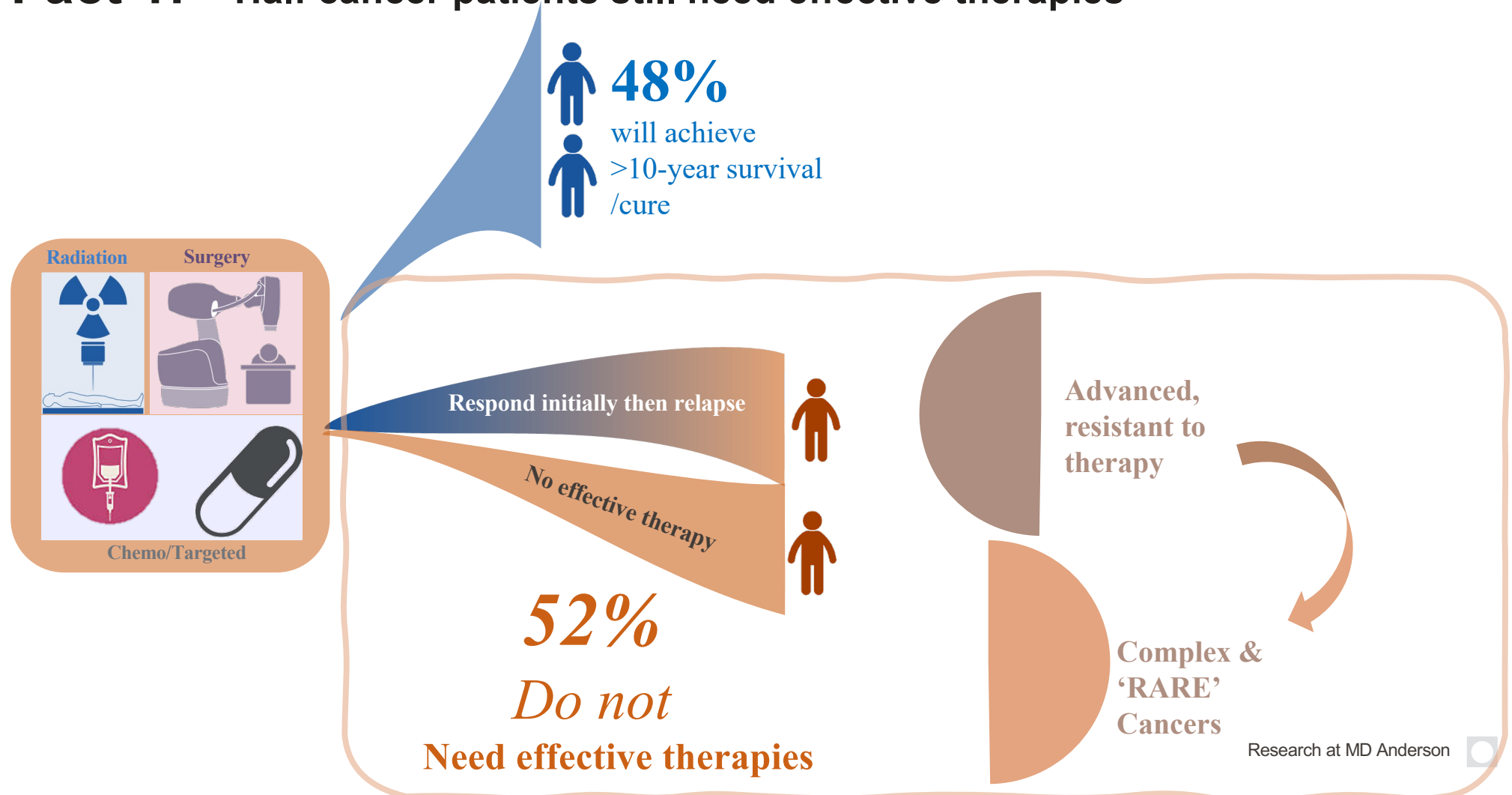
MD Anderson Cancer Center and The Institute of Cancer Research—reward to inventors programs

Consultant/Scientific Advisory Board member for:

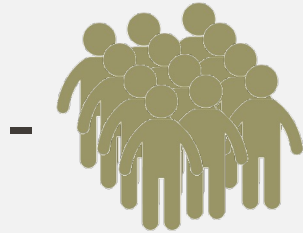
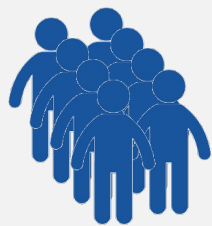
Commercial: Astex Pharmaceuticals • Santé Ventures • GSK • Astelas Pharma • AstraZeneca • Novodordisk • Cancer Research UK Commercial Partnerships

Public Bodies: US National Academies of Science, Engineering and Medicine • Cancer Research UK – Member of Scientific Advisory Board and Chair of Data Research Strategy Board • Fight Kids Cancer • UK Science and Parliamentary Committee • Wellcome Trust • New York Genome Center • City of Vienna Fund • Nordic Digital Life Fund •

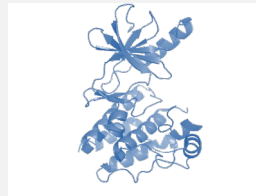
Fact 1: > Half cancer patients still need effective therapies



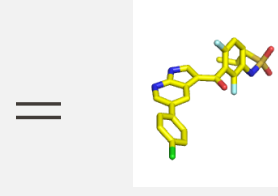
Fact 2: Complex cancers do not have clear molecular signals – too much noise



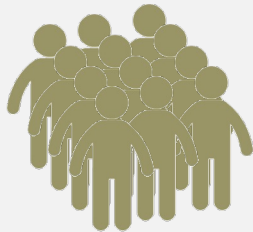
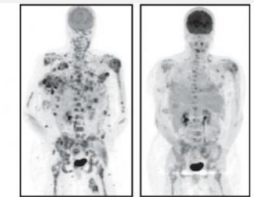
=



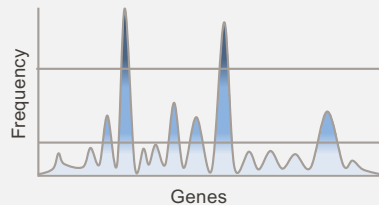
V600E



=

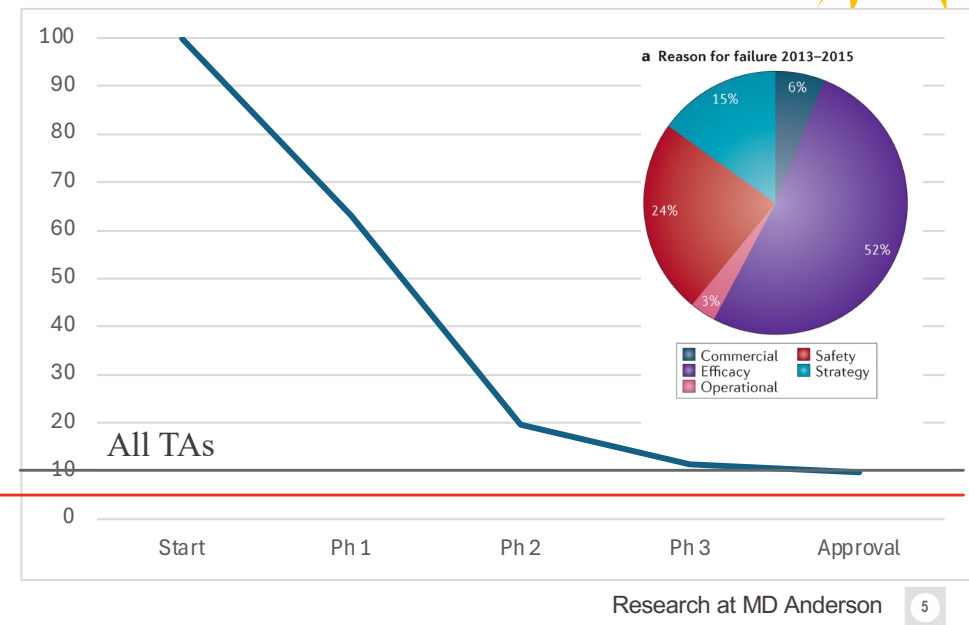


=



Workman & Al-Lazikani, (2013) Nat. Rev. Drug Discovery

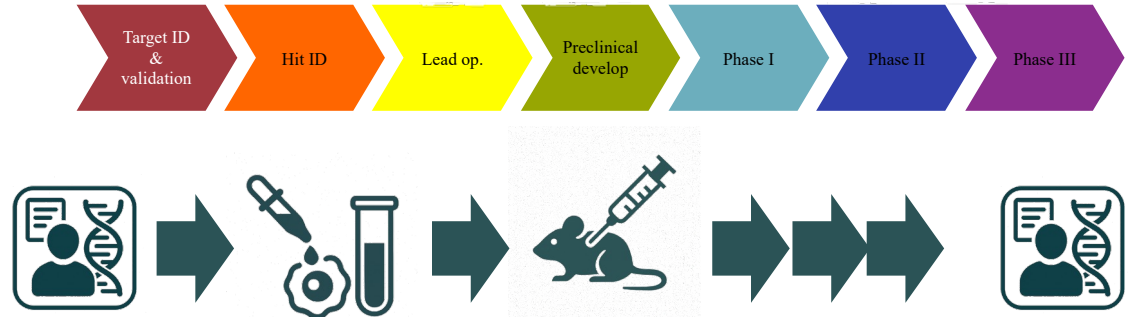
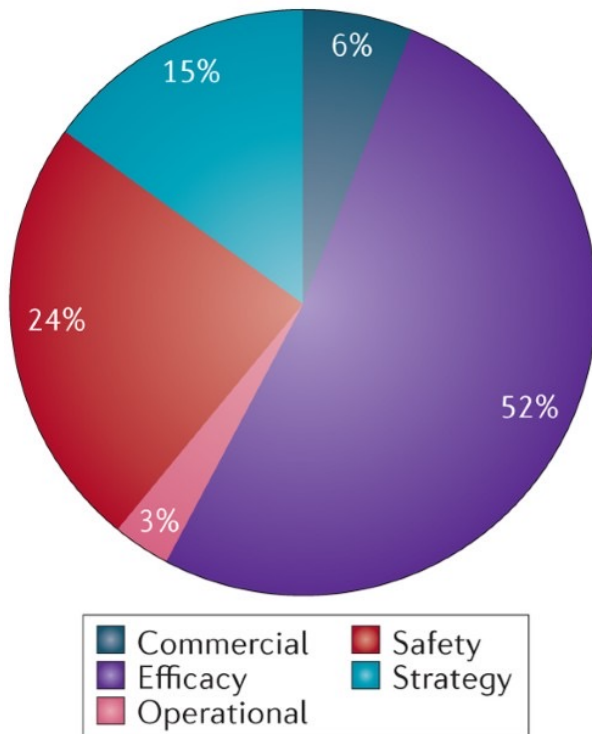
Fact 3: Standard process for drug discovery and development is a *'Patient Capital'* investment



- 95% of oncology drugs fail in clinical trials

Lack of efficacy!

a Reason for failure 2013–2015

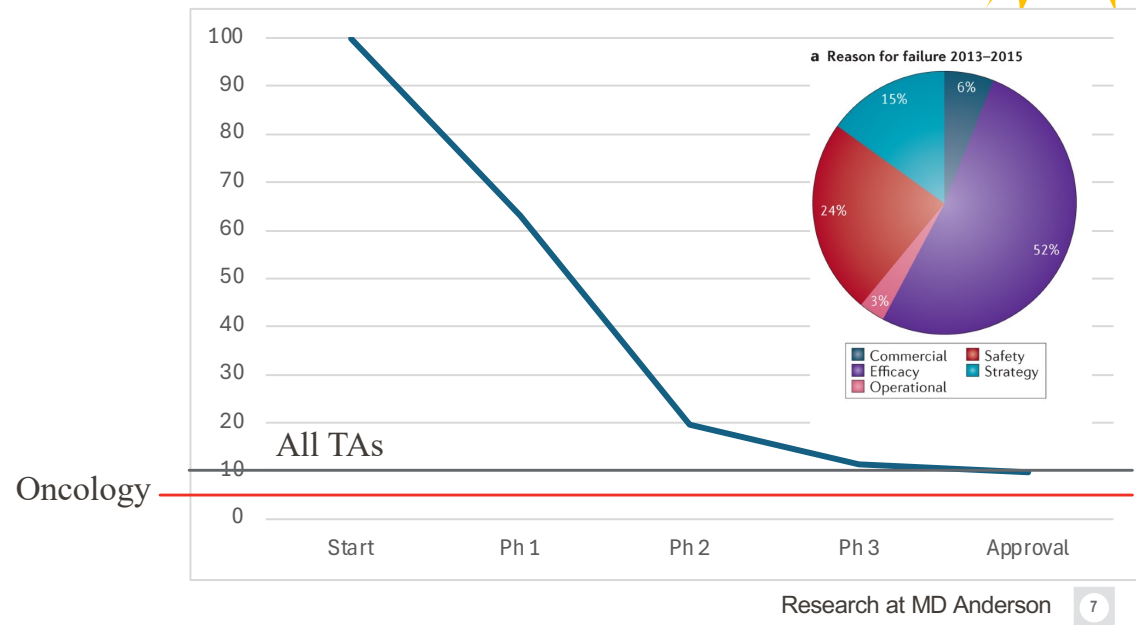


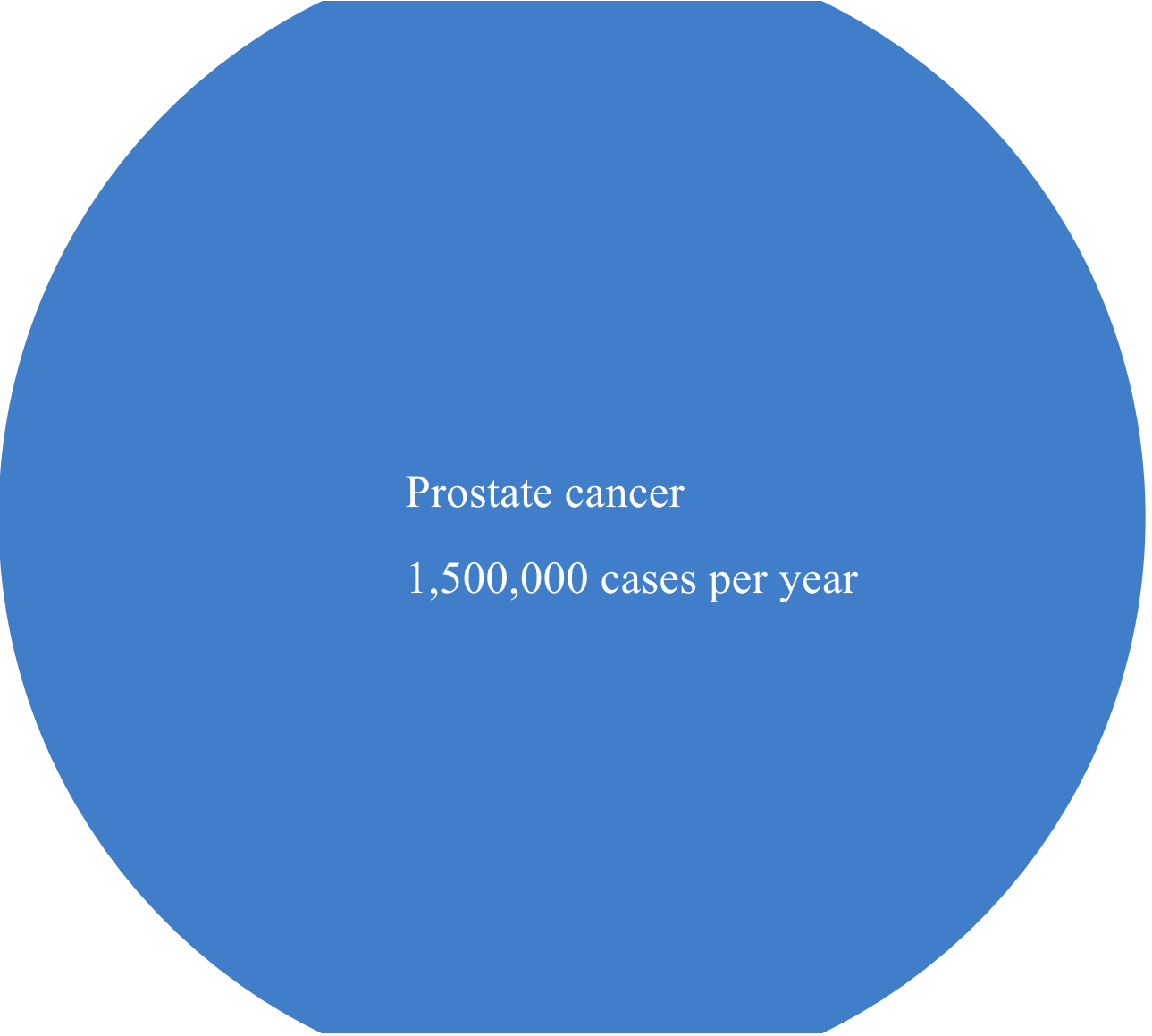
- While original biological hypothesis may be wrong
- Much more likely patient stratification in trials was insufficient to reach efficacy without tox

Fact 3: Standard process for drug discovery and development is a *'Patient Capital'* investment

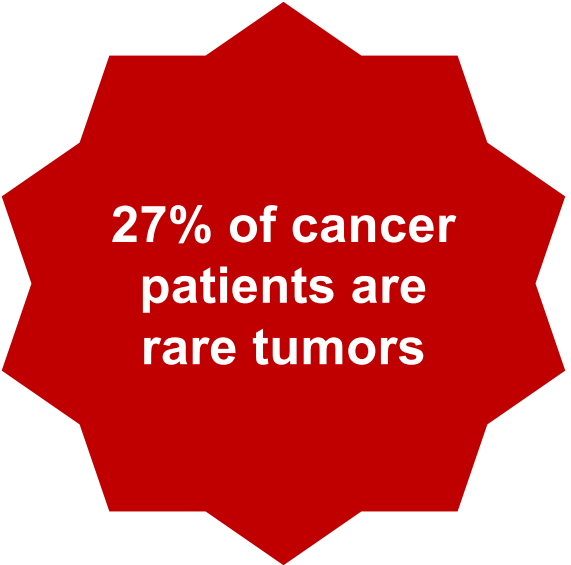


- ~\$2Bn
- ~15 years
- 95% FAILURE rate
- The winners win big





Prostate cancer
1,500,000 cases per year



**27% of cancer
patients are
rare tumors**

Lyomyosarcoma

1,200 cases per year

‘Patient Capital’ model not fit for purpose here

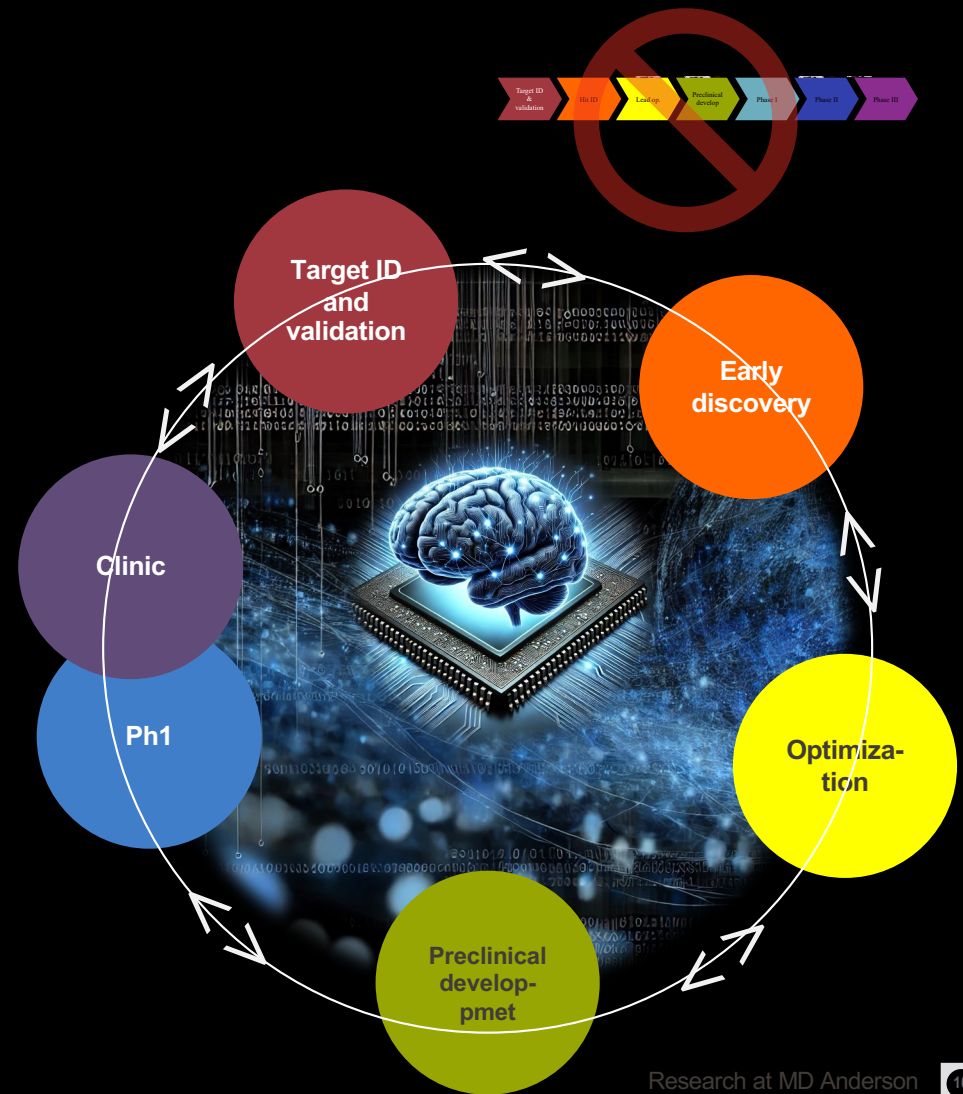
**Need rapid,
effective way
to turn
patient data
into PoC for
drug
development**

**Need smarter
ways to stay
on track for
patient
selection**

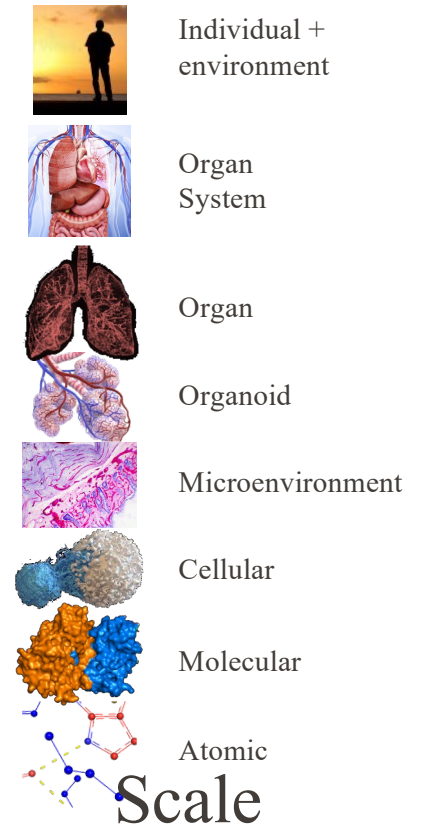
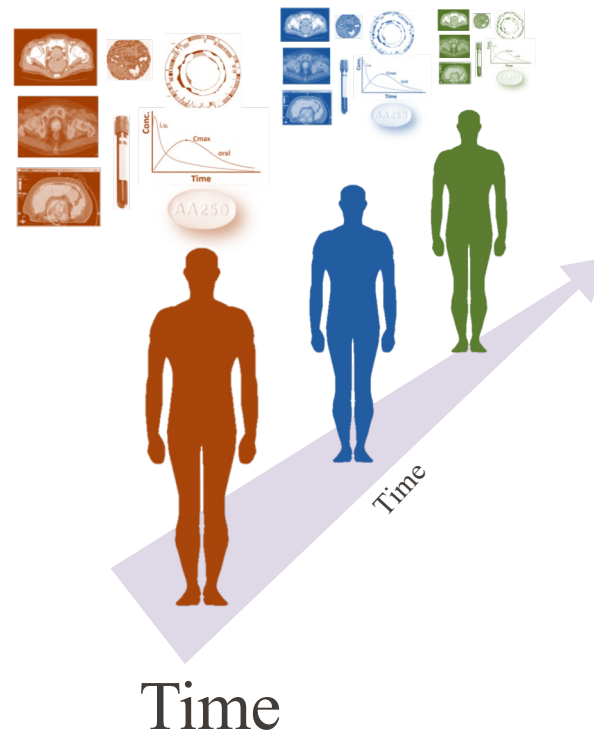
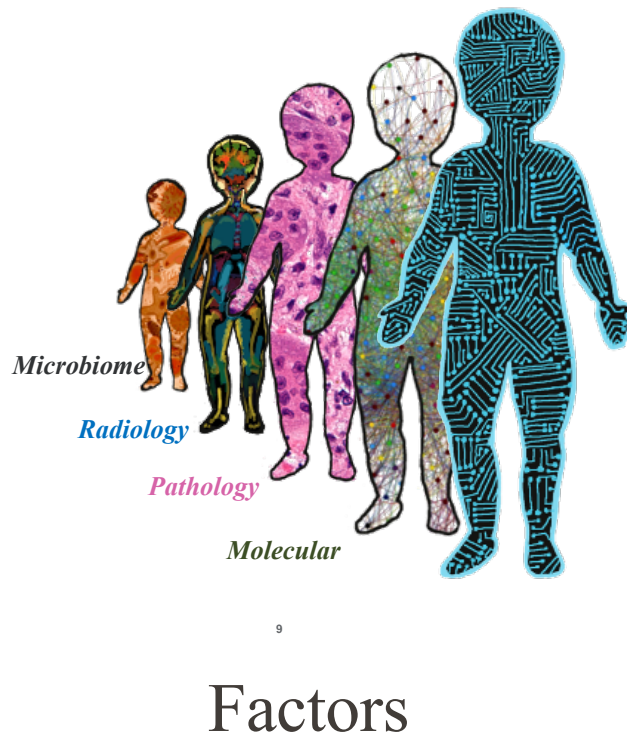
**Forecast
forward;
identify risks,
FAIL FAST**

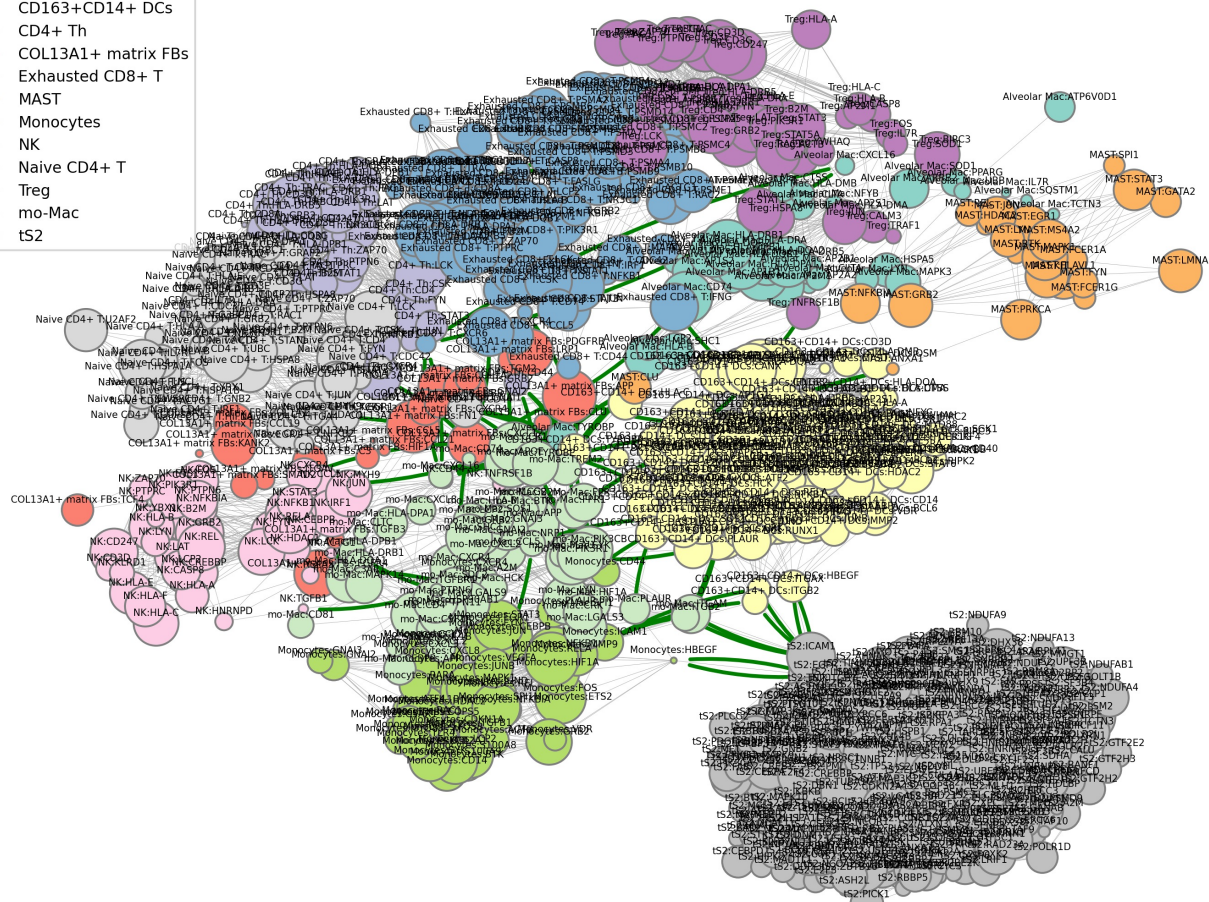
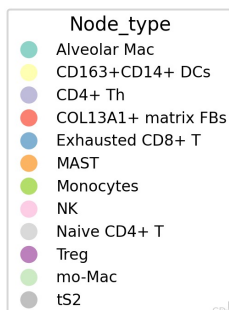
New AI-enabled paradigm

- Patient-centric
- Iterative information flow
- Data and AI-enabled
- Objective, every decision enabled by data and predictive modelling
- Use AI to forecast each program
 - Identify risk trajectories
 - Recommend order of steps
 - Load odds in favor of success



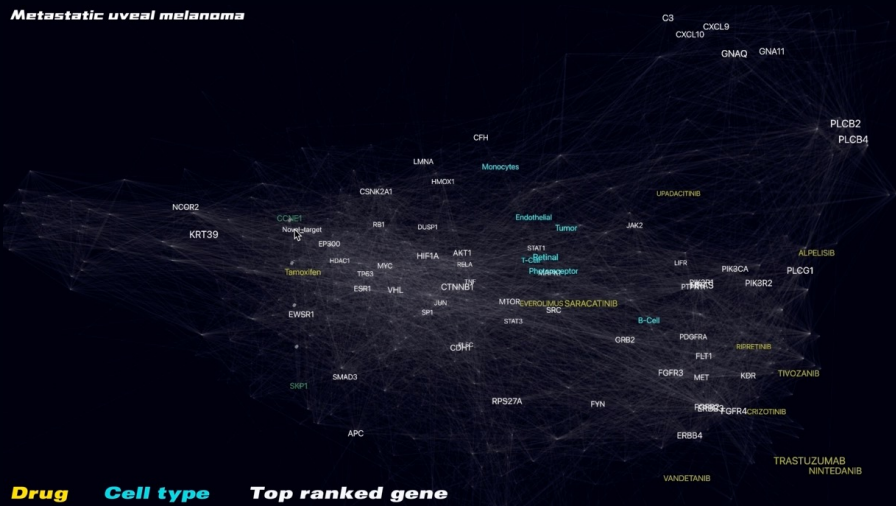
Across modalities, scales and Time



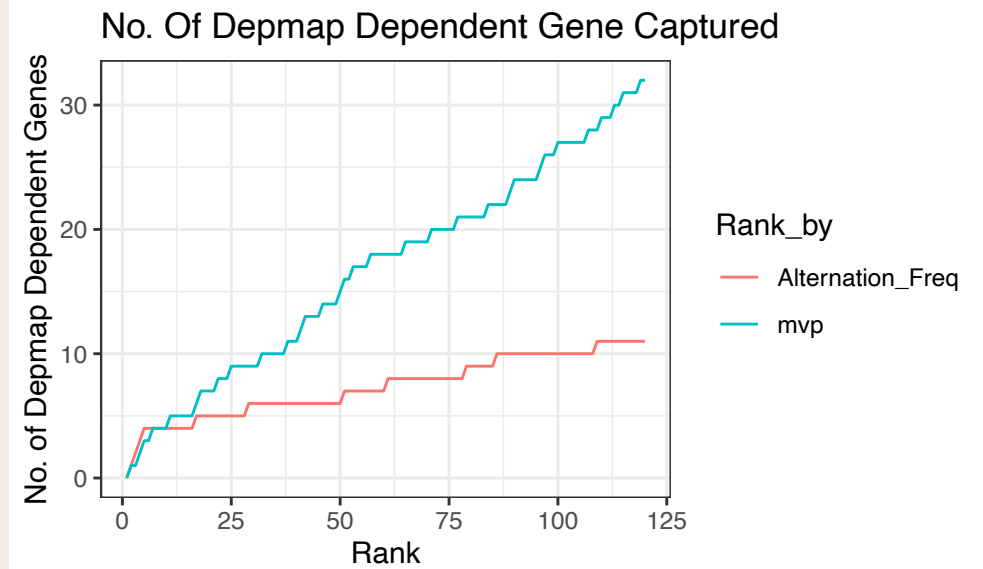


Signal from noise

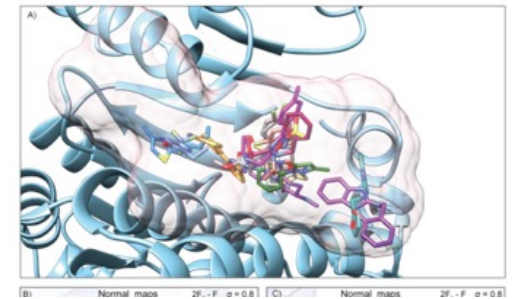
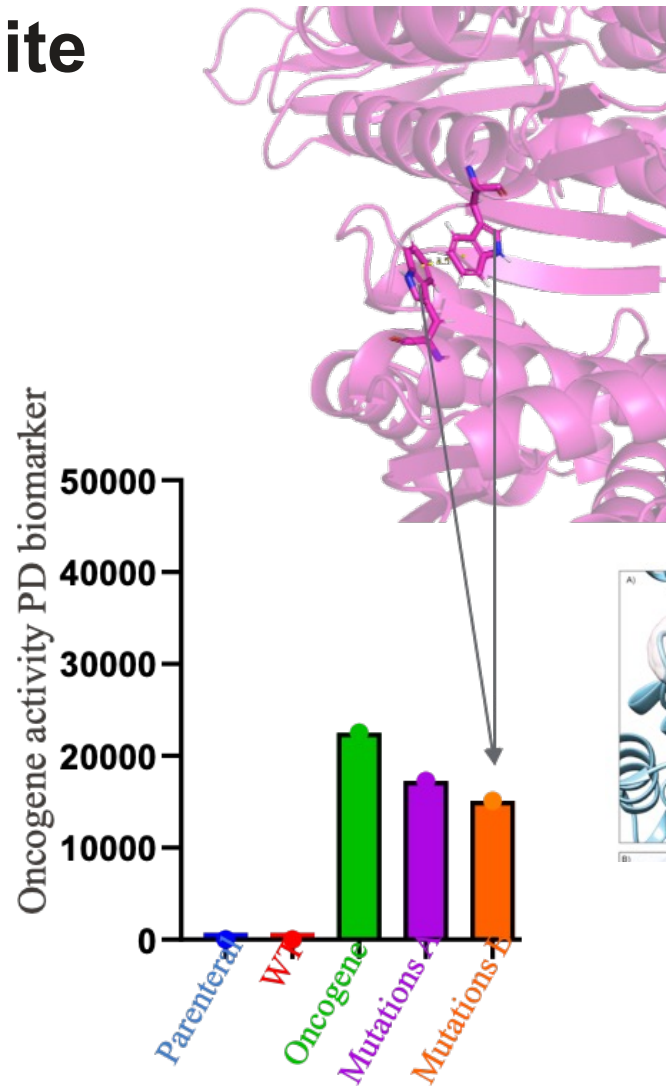
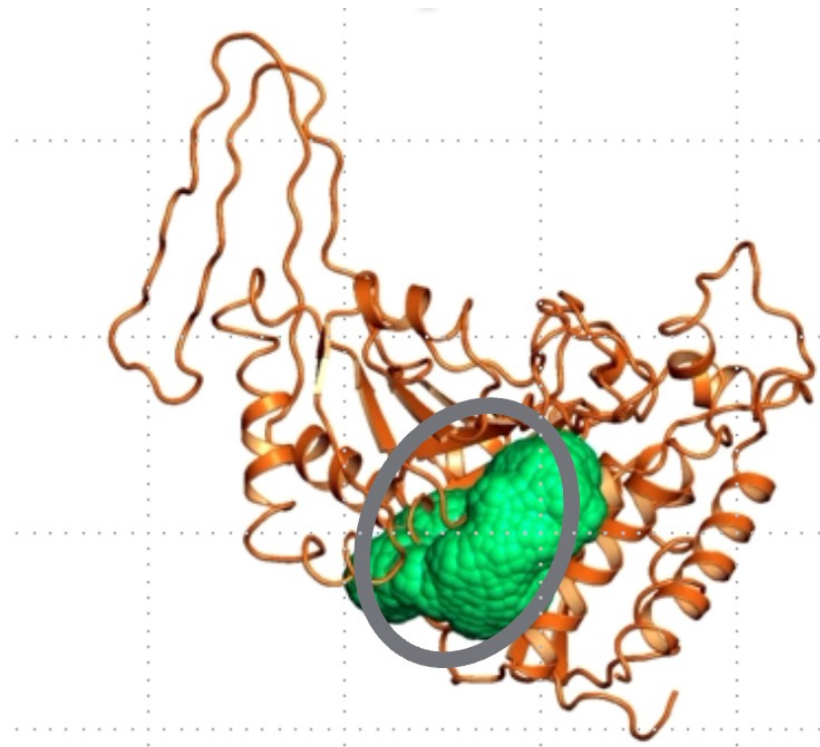
Uveal Melanoma



Pediatric medulloblastoma

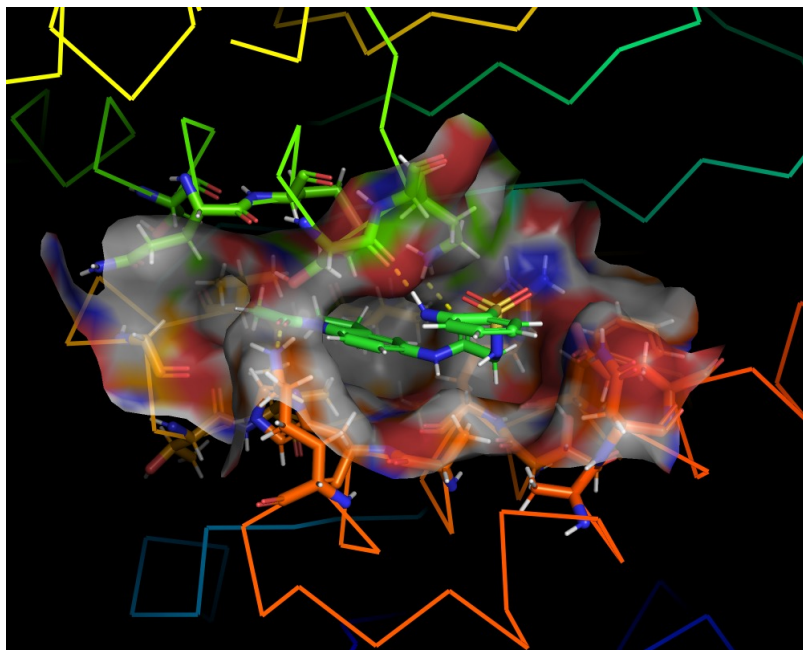


Novel, cryptic allosteric site

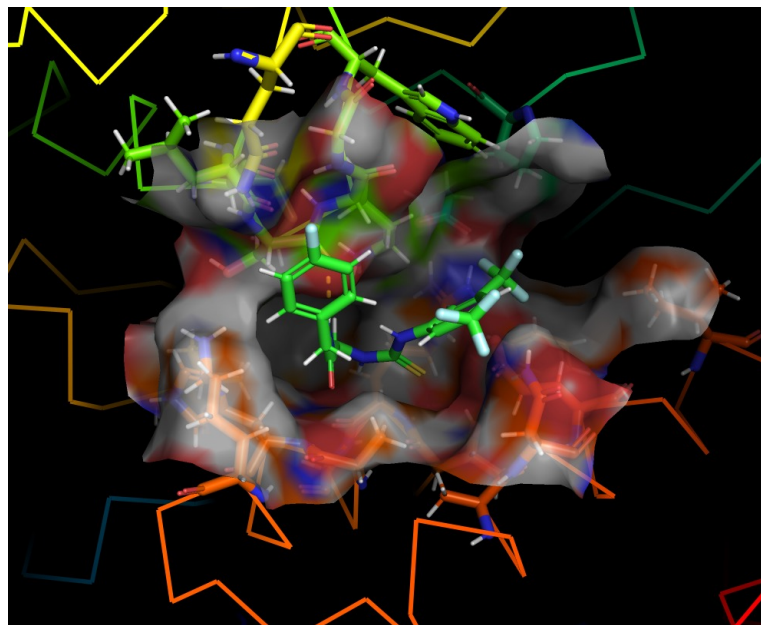


AI augments and significantly improves on physics-based methods

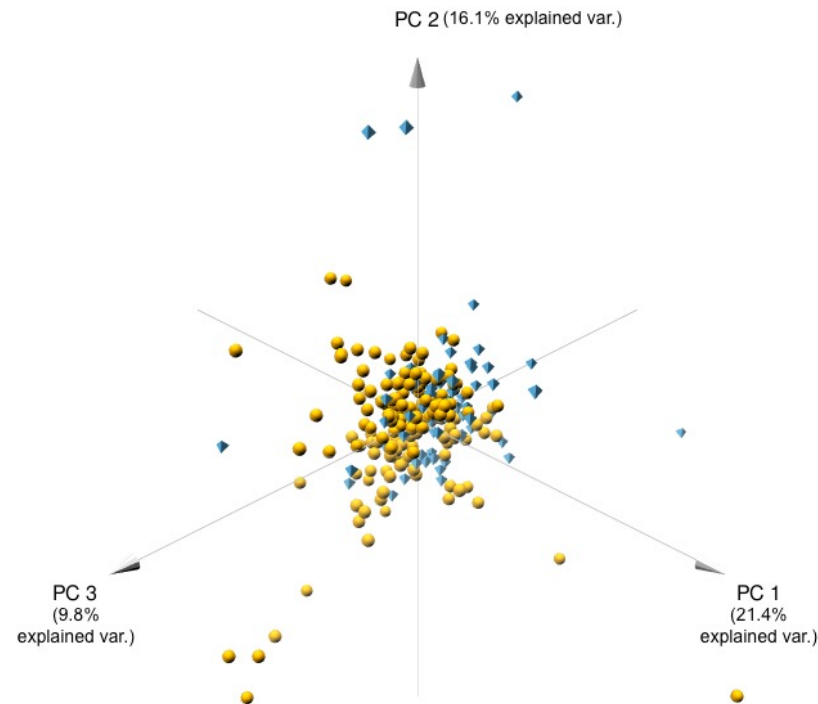
A 9th ranked positively classified (0.91) pose



A 1st ranked negatively classified (0.02) pose



A machine-augmented tool for the clinician



Preclin- training sample ●

◆ New Patient sample (unseen by model)

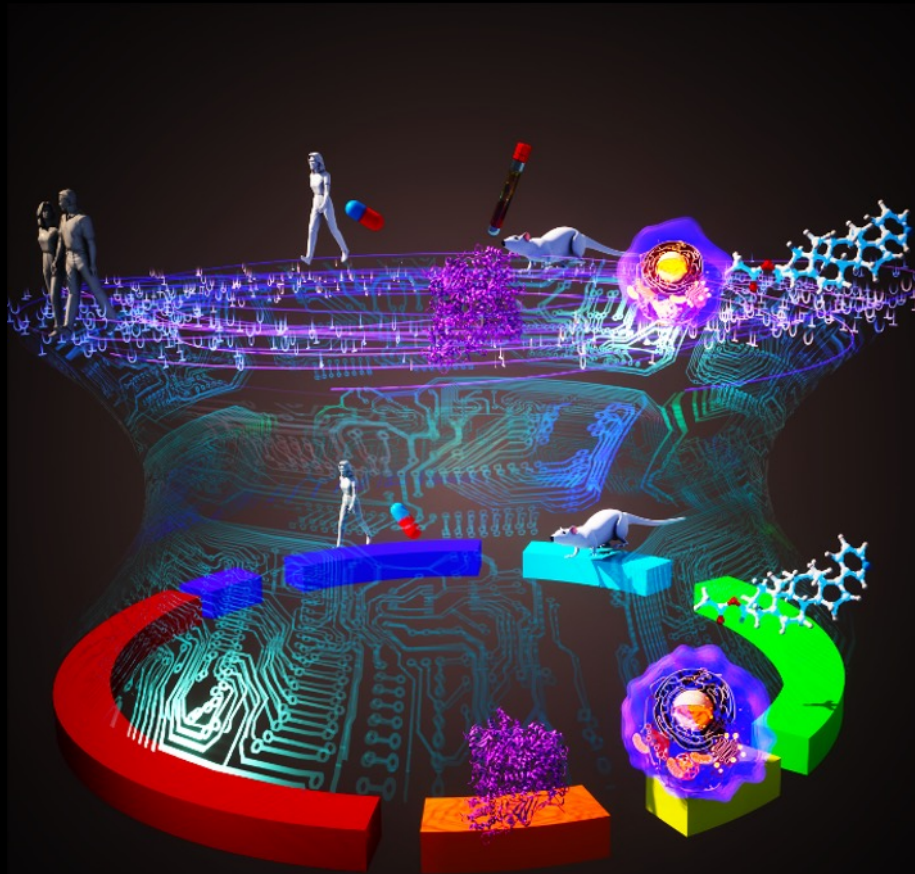
Coker et al, MCT, 2022

Research at MD Anderson

16

© Al-Lazikani – do not share without explicit permission

What the (very near) future looks like



Research at MD Anderson

17

© Al-Lazikani – do not share without explicit permission