THE UNIVERSITY OF CHICAGO
CENTER FOR COMPUTATIONAL MEDICINE & CLINICAL ARTIFICIAL INTELLIGENCE

Artificial Intelligence to Determine Actionable Cancer States

Alexander T. Pearson MD PhD

DISCLOSURES

Advisory boards: Prelude Therapeutics, Ayala, Elevar Therapeutics

Research funds: Kura Oncology, Abbvie, Merck

Travel: Caris

Consulting: Abbvie, ThermoFisher, Breakthrough Cancer

IP: University of Chicago pursuing patents related to this work

OUTLINE

- My background and interest in AI for Medicine
- Applying computer vision to digital pathology for Oncology applications
- Methods extensions to improve AI for physicians
- Future applications of AI in Medicine

AI IN MEDICAL PRACTICE

MY TRAINING PATH AS A COMPUTATIONAL PHYSICIAN

Cornell University

BS, Biometry and Statistics

Pre-med coursework
Agricultural Statistics

University of Rochester

MD + PhD (Statistics)

Medicine
Computational and Graphical Statistics

University of Michigan

Physician Scientist Training Program
Medicine + Hematology/Oncology Fellowship

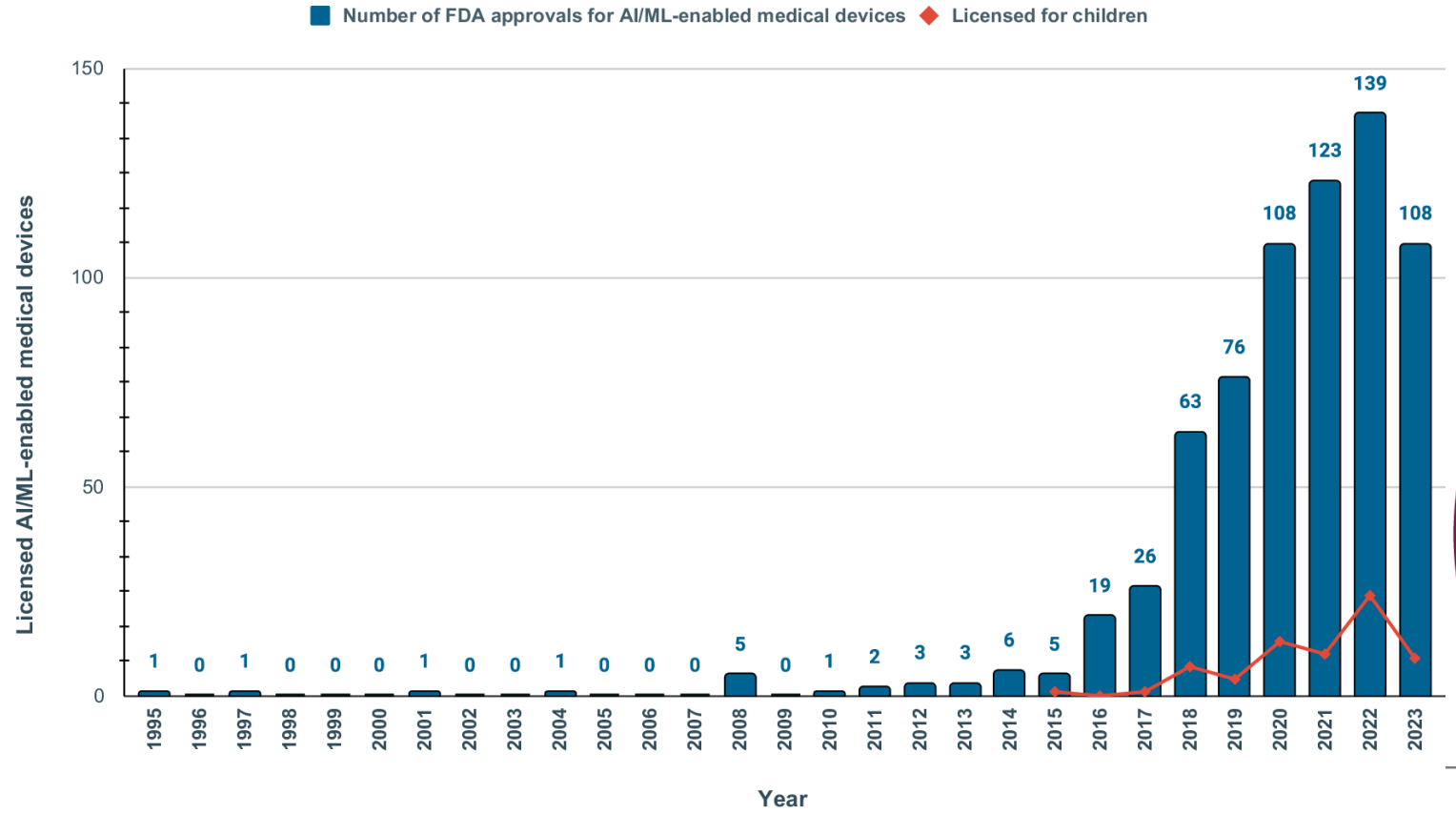
Subspecialty Cancer care
Postdoc in cancer stem cell biology (wet lab) + Applied Math

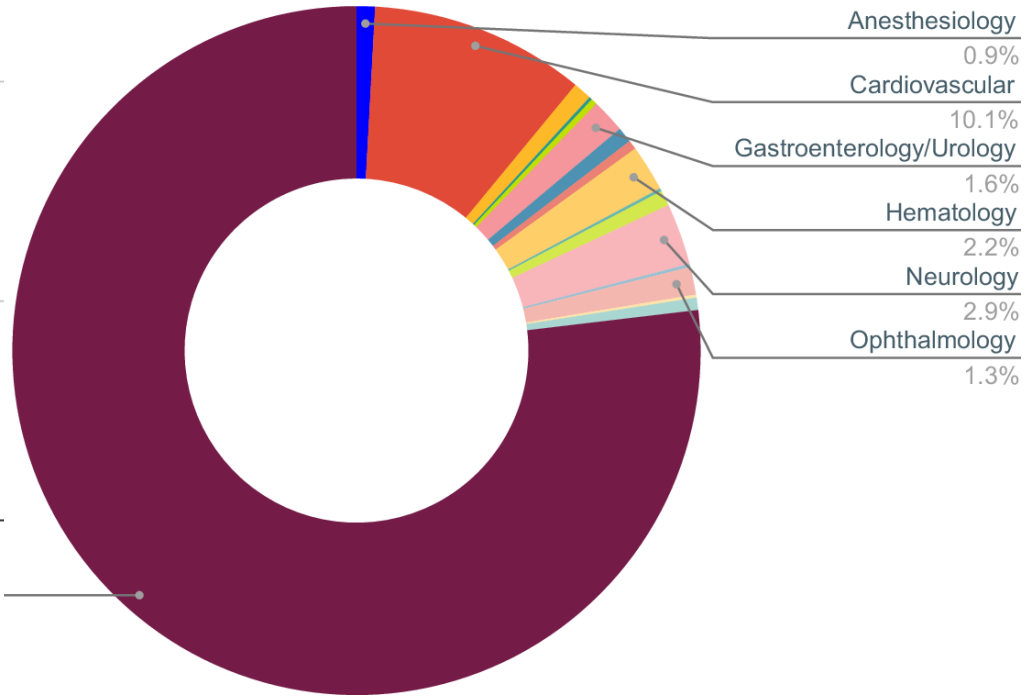
University of Chicago

Associate Professor of Medicine

Director, Head and Neck Cancer Program in Medical Oncology
Director, Center for Computational Medicine and Clinical AI

AI Medical Devices: FDA-Approved AI Devices Have Grown Rapidly

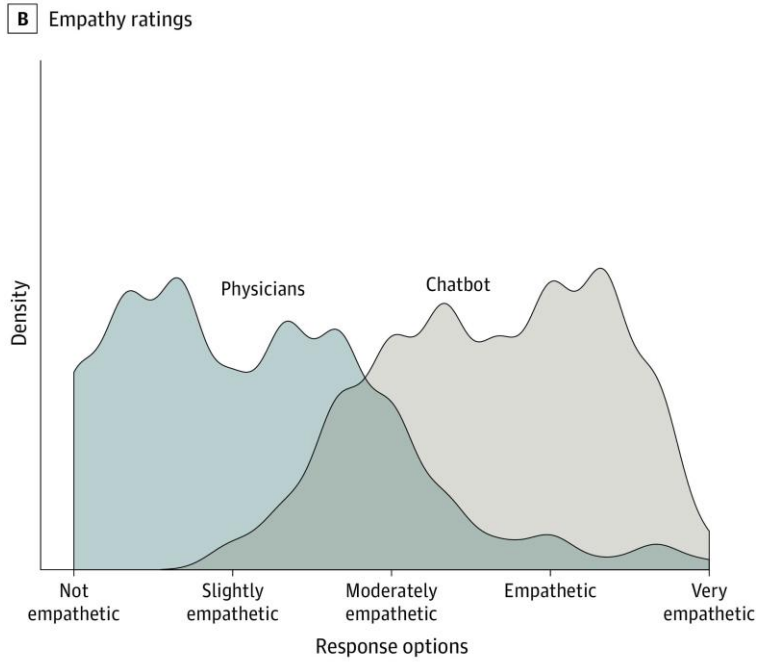


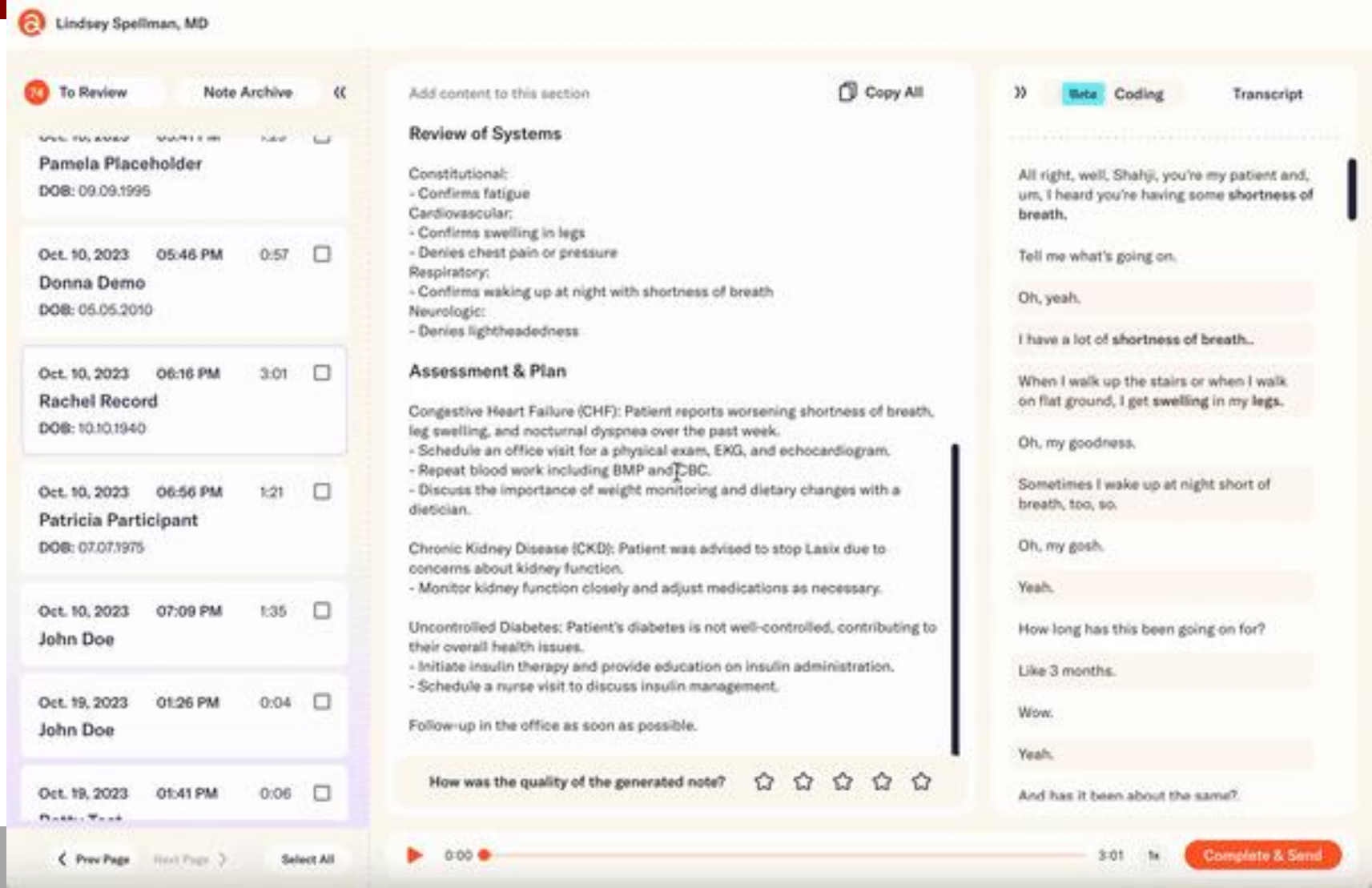


AI MEDICAL DEVICES: FDA-DESIGNATED TROP2 COMPANION DIAGNOSTIC

- Granted FDA Breakthrough Designation **4/28/2025**
- Required for the device:
  - TROP2 algorithm
  - Navify Digital Pathology Image Management System
  - Roche Digital Pathology scanners (DP 200, DP 600)
  - VENTANA TROP2 (EPR20043) RxDx Assay used with OptiView DAB Detection Kit for staining on a BenchMark ULTRA IHC/ISH staining instrument

AI MEDICAL DEVICES: LLM-BASED AMBIENT DICTATION FOR ROUTINE USE





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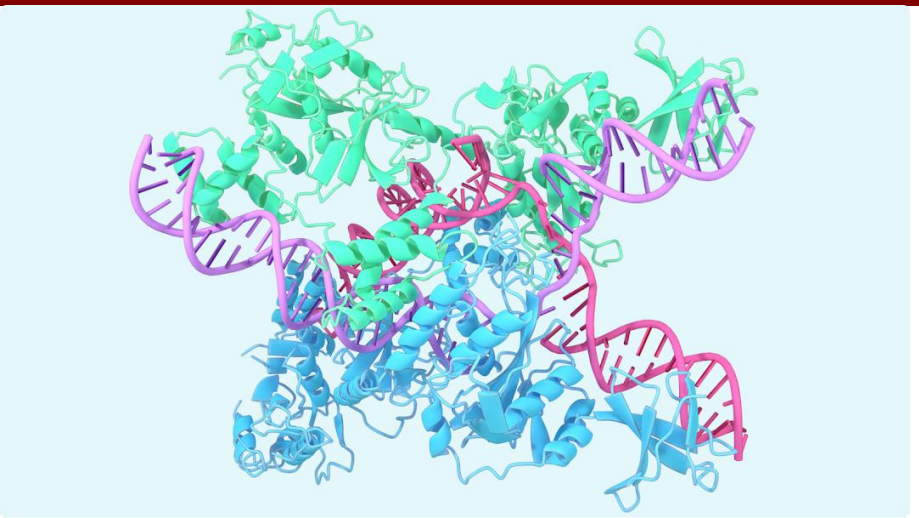
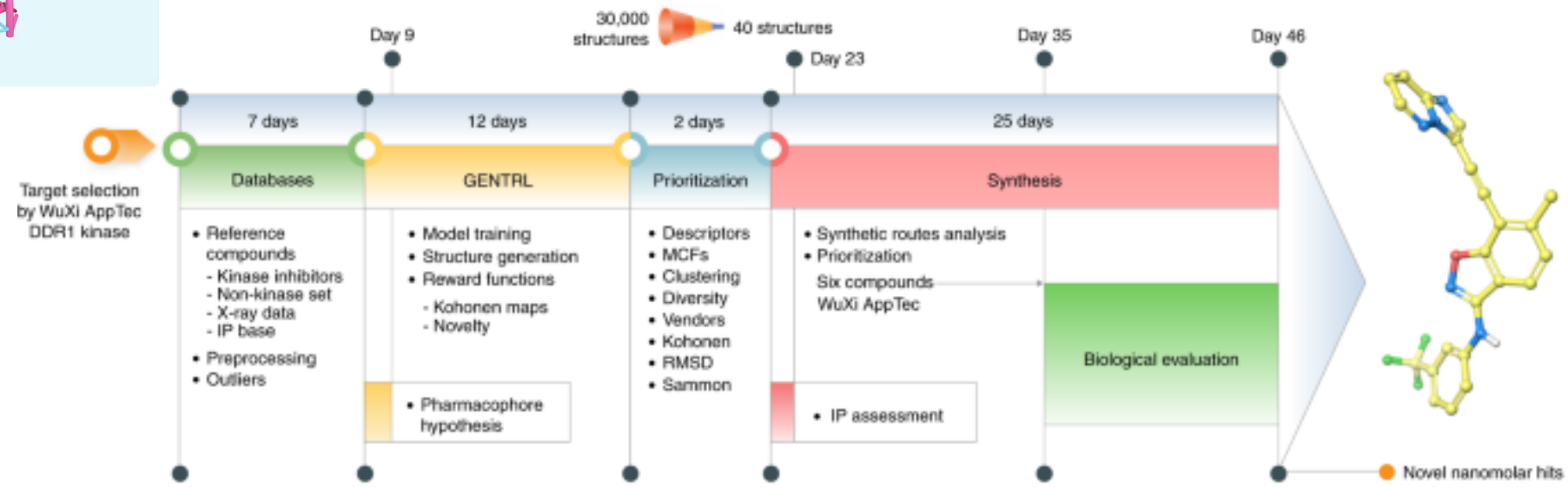
AI MEDICAL DEVICES: GENERATED MOLECULES IN TRIALS



- Interstitial lung disease targeting AI generated molecule met it's primary endpoint in Phase II clinical trial

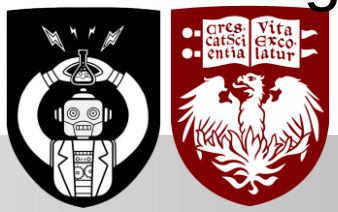


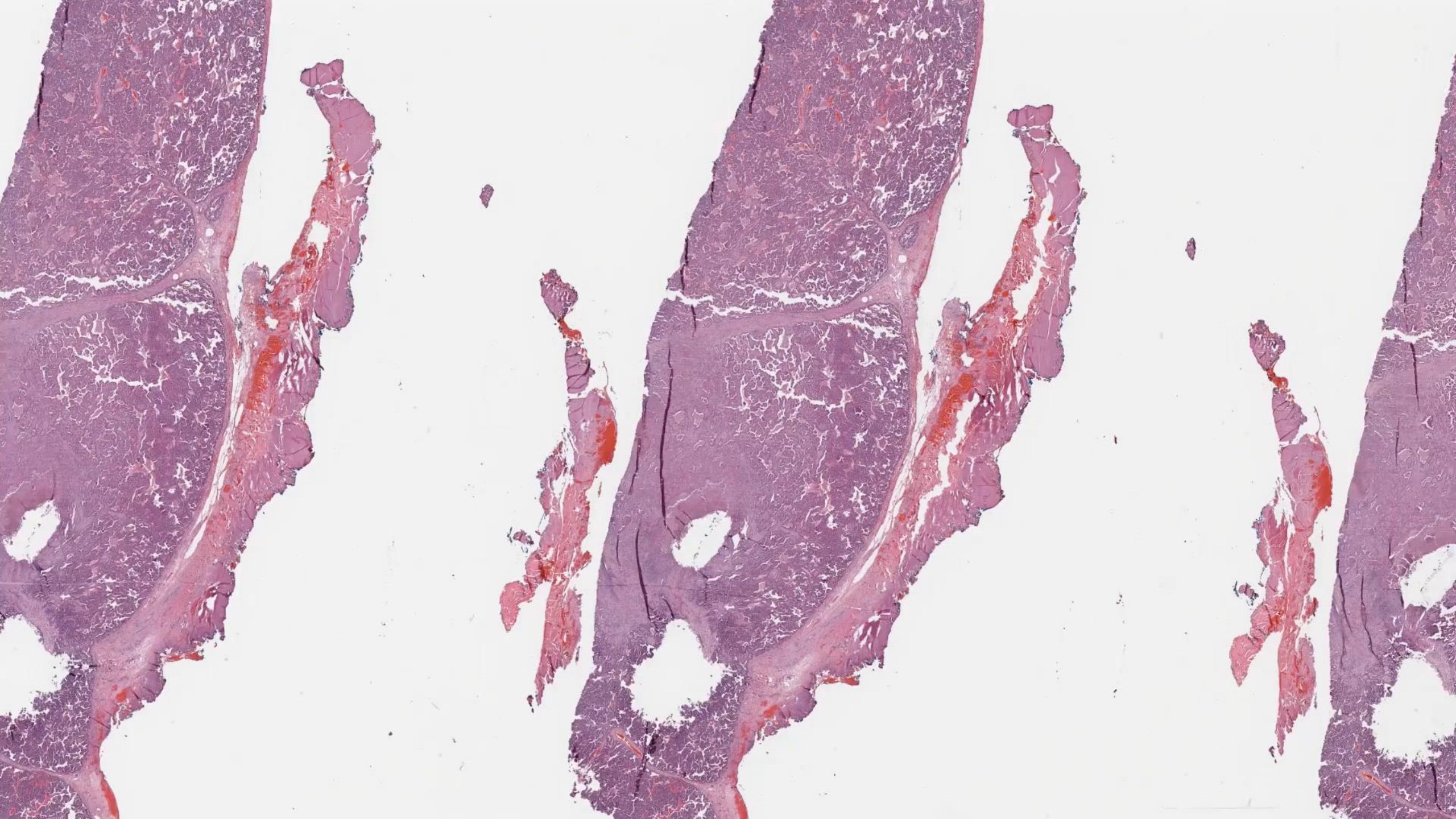
Google Alphafold; Zhavoronkov *Nature Biotech* 2019

DEEP LEARNING FOR DIGITAL PATHOLOGY

DIGITAL PATHOLOGY FOR CANCER: RATIONALE FOR USE

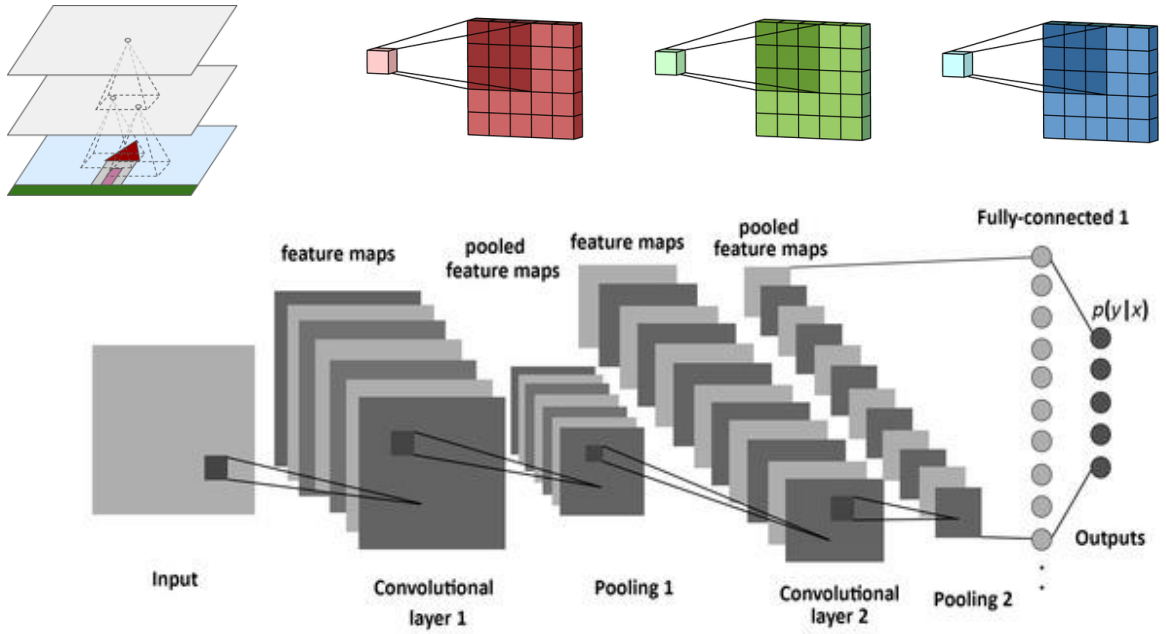
- Manual examination of human tissue is the global cornerstone for cancer diagnosis
- Preserved, fixed on glass Hematoxylin and Eosin (H&E) stained tissue is evaluated by trained Pathologist physicians to render a diagnosis from a tissue sample
- This process has remained largely unchanged for ~100 years
- In medicine, H&E pathology slides are:
  - Ubiquitous and globally consistent
  - Low cost
  - Information rich
- A good place to try applying computer vision!





ARTIFICIAL INTELLIGENCE ARCHITECTURES LEARN TO INTERPRET IMAGES

Convolutional Neural Network



Vision Transformer

Géron, A. (2017). Hands-on machine learning with Scikit-Learn and TensorFlow : O'Reilly Media; Albelwi, S., & Mahmood, A. (2017). A framework for designing the architectures of deep convolutional neural networks. *Entropy*, *19*(6), 242; Looking inside neural nets. Retrieved September 2019, from https://ml4a.github.io/ml4a/looking_inside_neural_nets/; Satish Kumar, Analytics Vidhya

PEARSON LAB RESEARCH PIPELINE

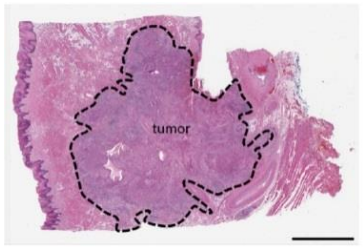
Digital slide scanner image capture of tumor regions

Automated digital slide image partitioning and rotation

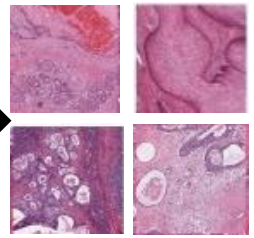
Deep neural network texture analysis and feature creation

High dimensional statistical analysis of derived features

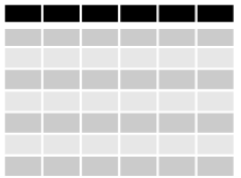
1) H&E Stained Slides



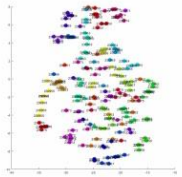
2) Tumor ROI virtual slide



3) “digestable” digital slide tiles



4) High-dimensional spreadsheet of derived features



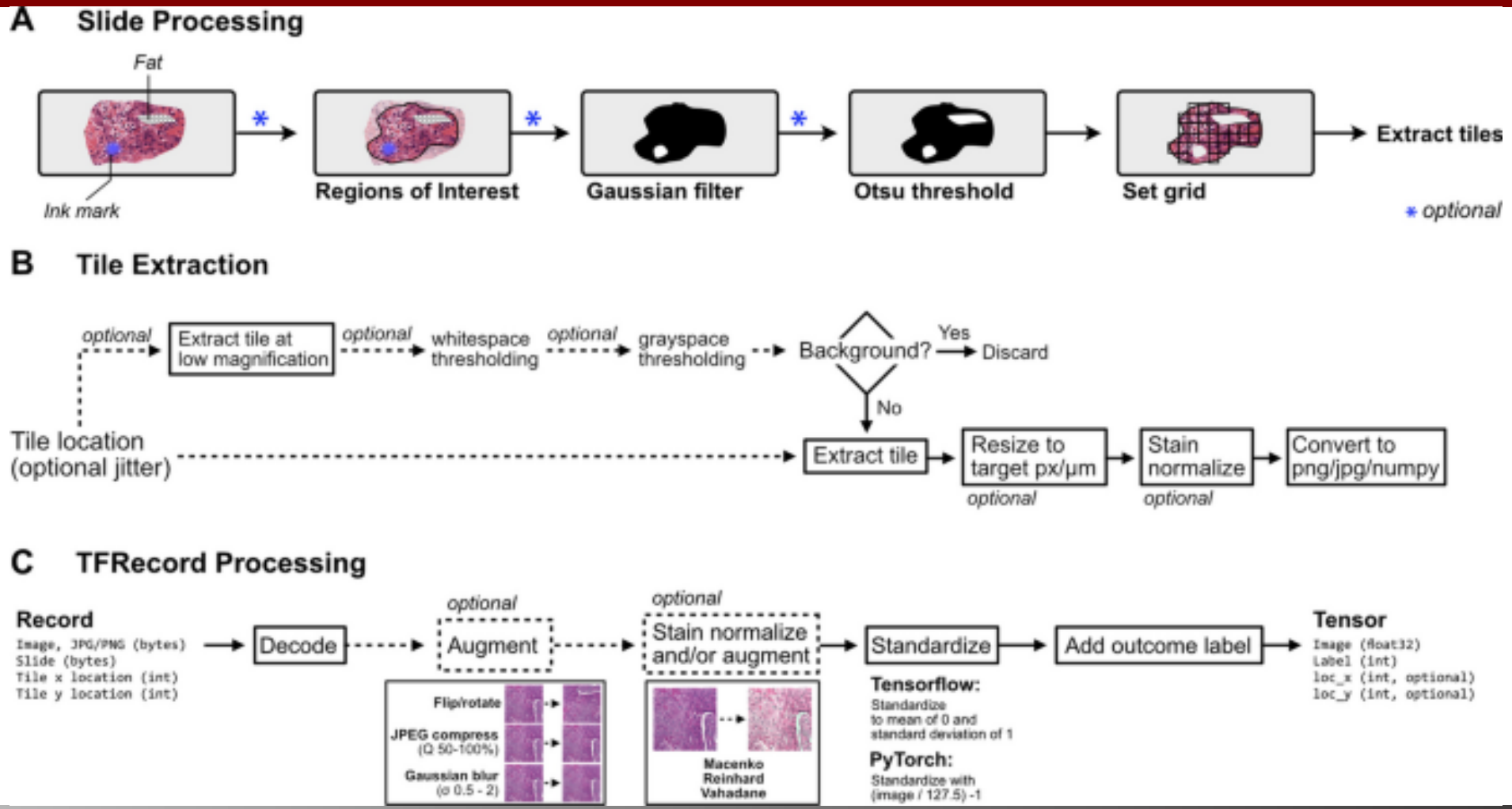
5) Statistical analysis output

- **>100TB of imaging data with paired clinical and genomic annotations**
- **Genetic alterations sorted by “actionability” via OncoKB**

PROCESSING DIGITAL PATHOLOGY SAMPLES

Slideflow

www.slideflow.dev

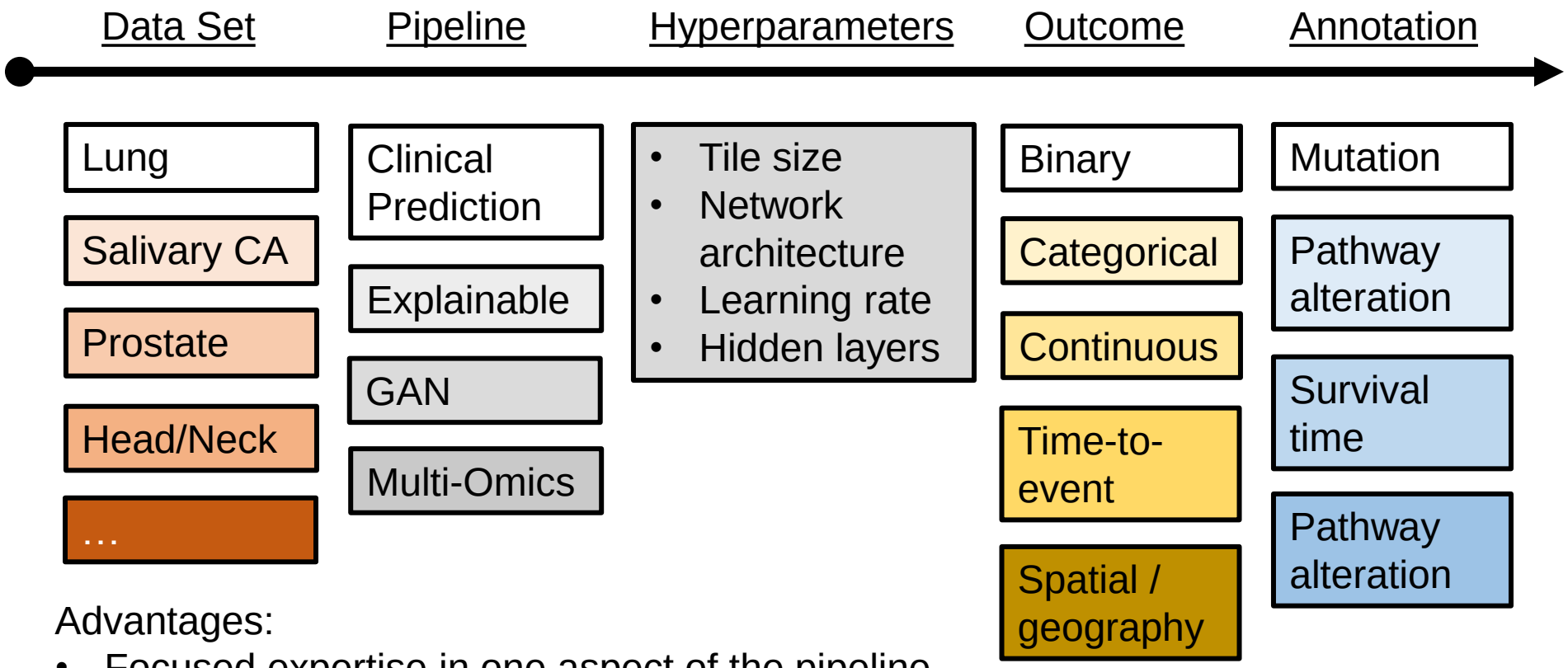


@Lab_Pearson

www.slideflow.dev

arXiv: 2304.04142

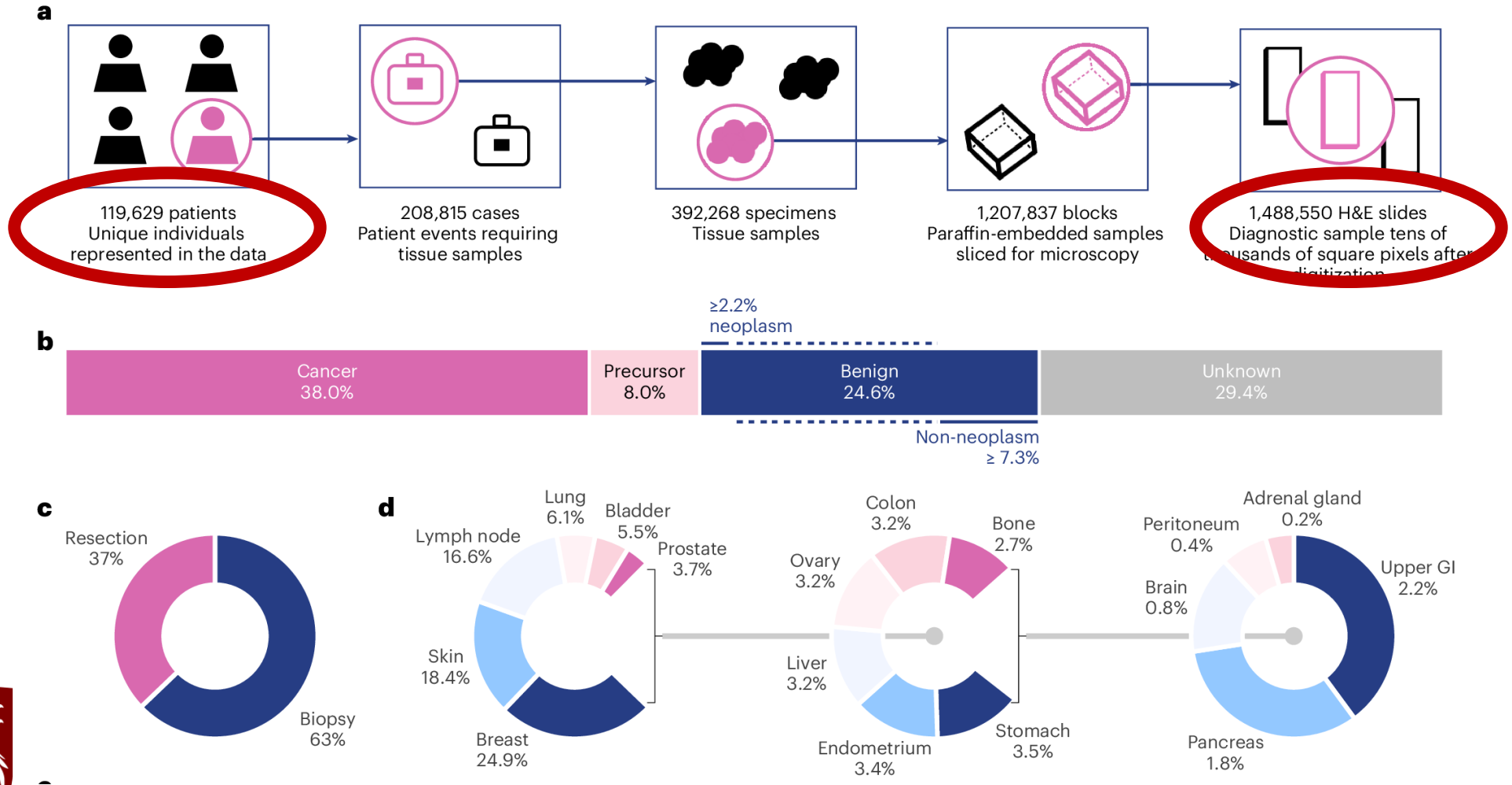
ADAPTABLE PIPELINE FOR CLINICAL APPLICATIONS



Advantages:

- Focused expertise in one aspect of the pipeline
- Allows for parallel, modular development
- Customize the analysis for the appropriate clinical need

FOUNDATION MODELS REFLECT VAST COMPUTATIONAL EXPOSURE



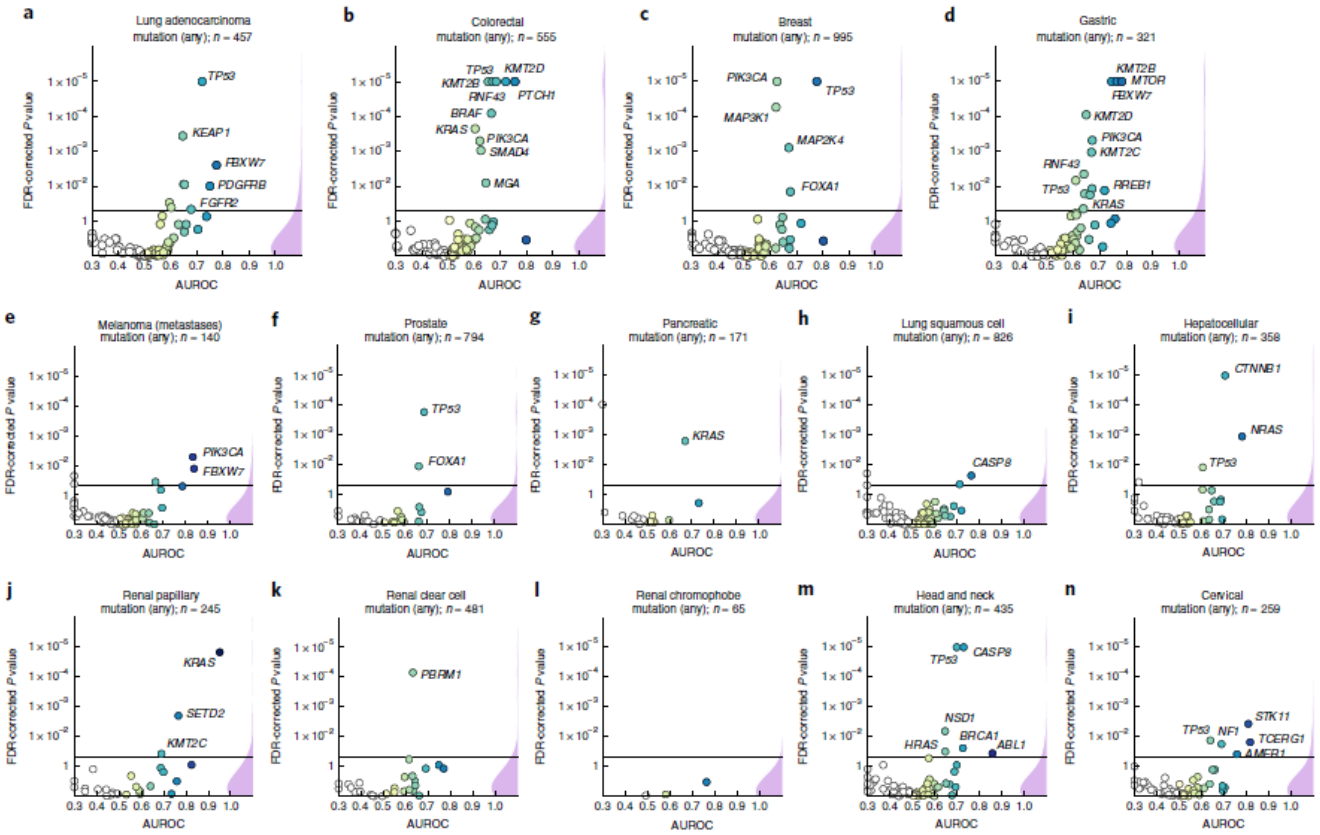
AI IN DIGITAL PATHOLOGY USE CASES

PRECISION MEDICINE: Background

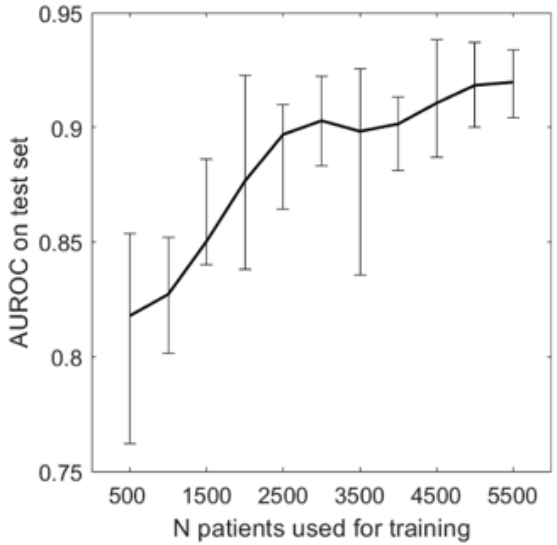
- Goal to increase effectiveness and minimize unnecessary treatment side effects:
  - “The right drug for the right patient at the right time”
- Matching drug to patient in cancer might use diverse information:
  - Pathological subtype
  - Mutation status
  - Gene expression profile
  - Clinical risk factors
  - New types of data or AI models?

CLINICAL APPLICATION #1: Pan-Cancer "Digital NGS" from digital histopathology

- Next generation sequencing (NGS) is costly and time consuming?
- Can we predict actionable mutations directly from pathology?
- Trained models of every OncoKB actionable cancer alteration in >4000 pts.

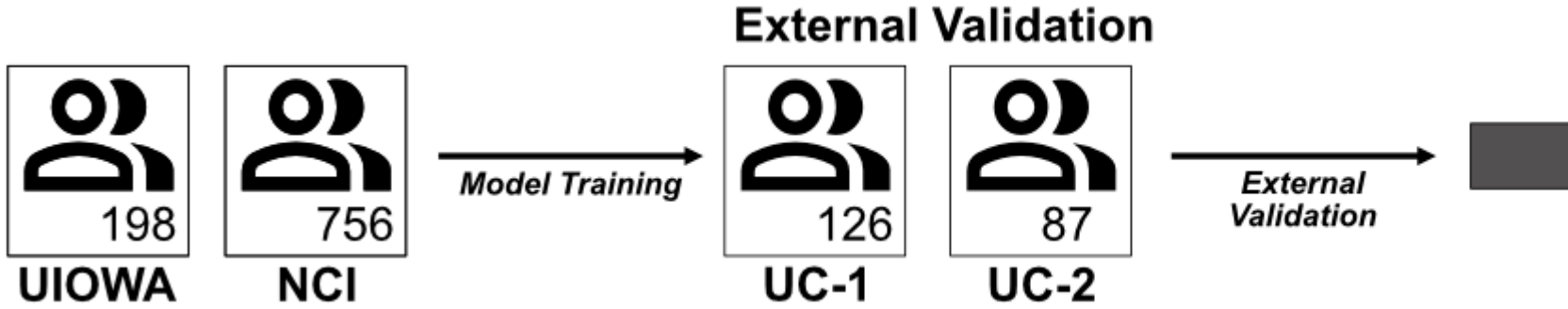


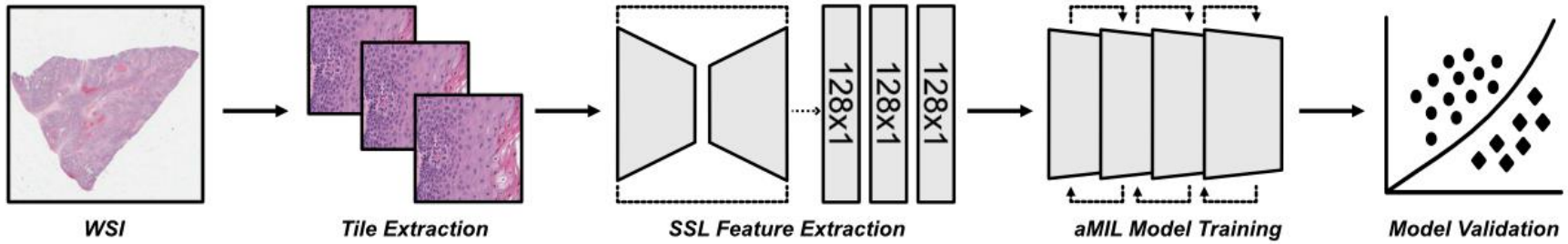
- Model performance improves with access to more data:

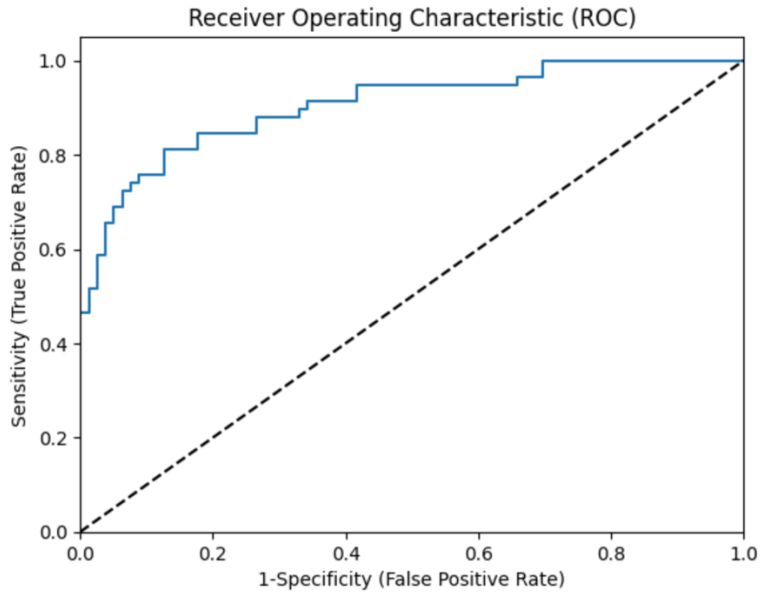


3/21/2019: Conceptualized *pan-cancer* deep learning for actionable alterations
11/8/2019: Posted BioRXiv Pre-print
4/17/2020: Manuscript Accepted in *Nature Cancer* DOI: 10.1101/833756

CLINICAL APPLICATION #2:
Cancer progression prediction in OPL





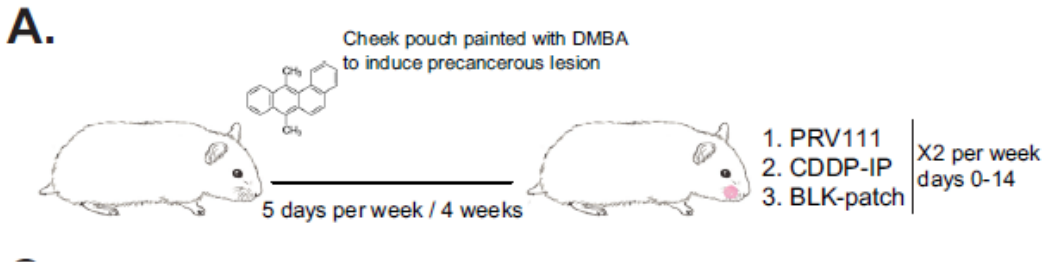


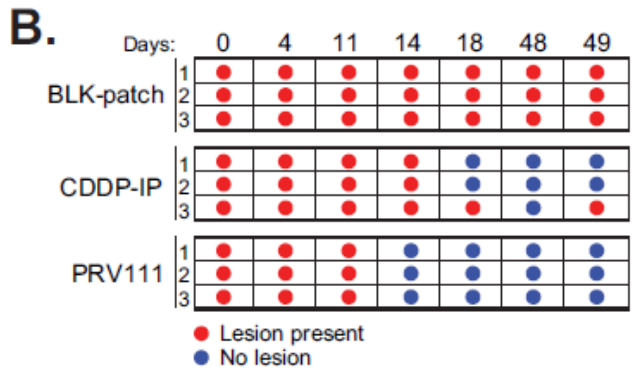
EXTERNAL VALIDATION
AUROC = 0.905, a Highly specific rule-in test?
Performance exceeds human grading

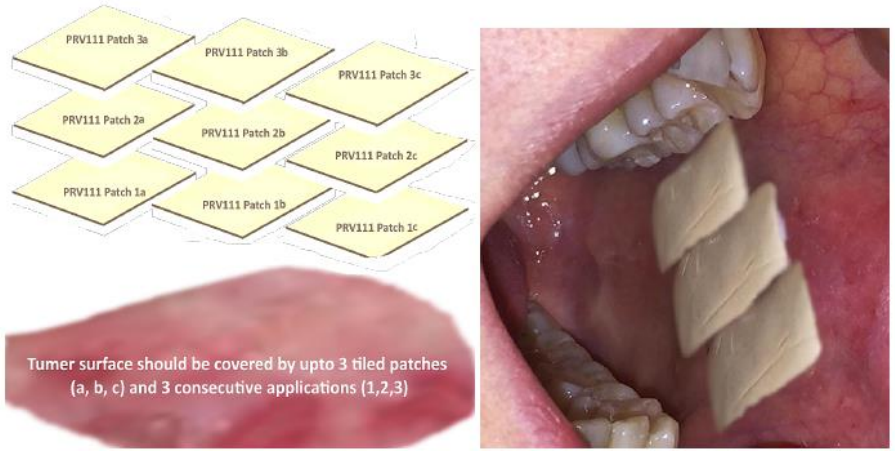
Ramesh S et. al. *JCO Global Oncology* 2023 DOI: 10.1200/GO.2023.9.Supplement_1.90

CLINCIAL APPLICTAION #2: Selecting Topical Chemo Candidates

- PRV111 is a cisplatin-embedded nanoparticle emitting patch
- Reverses dysplasia in 4NQO murine models
- Now in active Phase 1/2 trial at UChicago for CIS







NCT05893888; Goldberg M *Nature Communications* 2022

EXTENSIONS FOR COMPUTER VISION TO AID COMPUTATIONAL ONCOLOGISTS

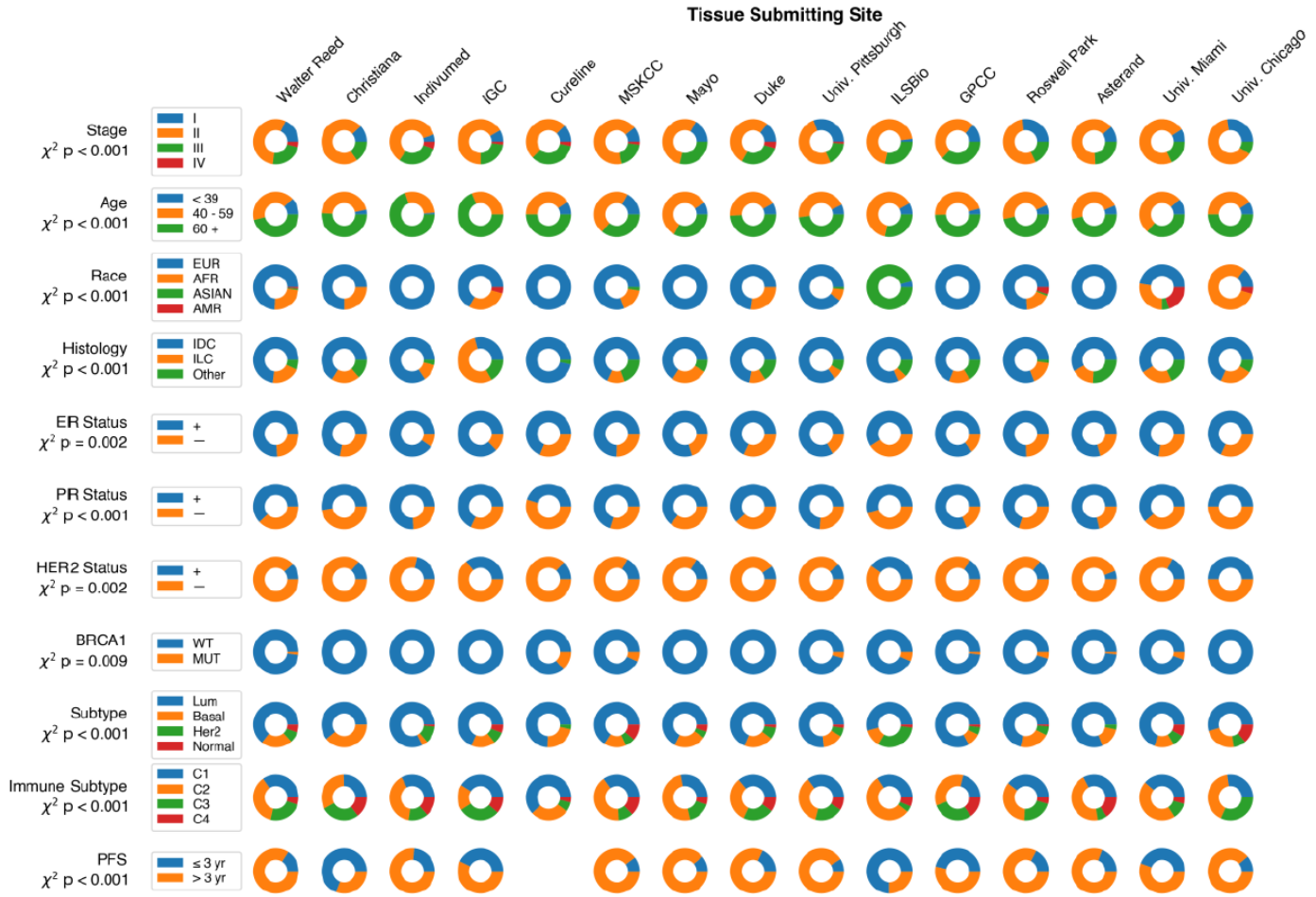
TRUSTWORTHY DIAGNOSTICS: Explainable AI

- Many neural networks are not inherently explainable
- Can we trust the results of an algorithm enough to make an important clinical decision for patient care?

(a) Husky classified as wolf

(b) Explanation

MULTI-SITE DL MODELS ARE SUSCEPTIBLE TO IMBALANCE BIAS

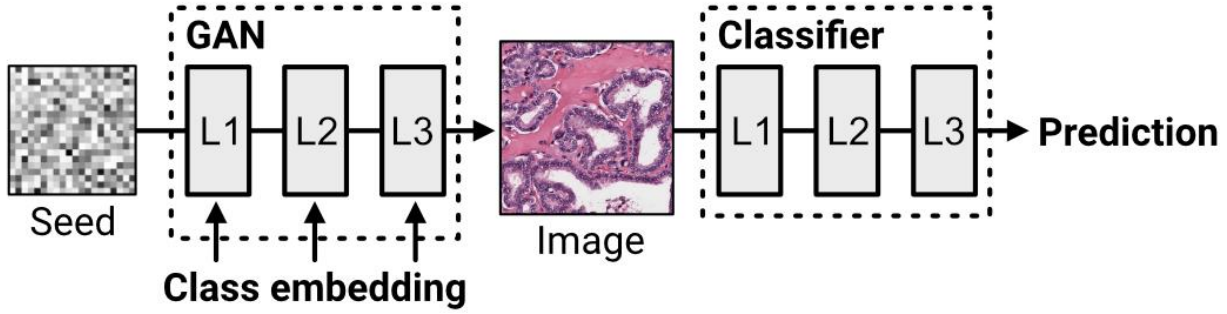


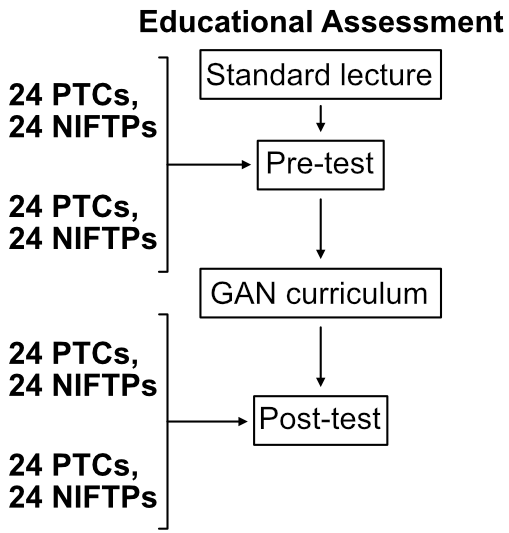
- AI models for cancer require the underlying data to be accurate reflections of reality.

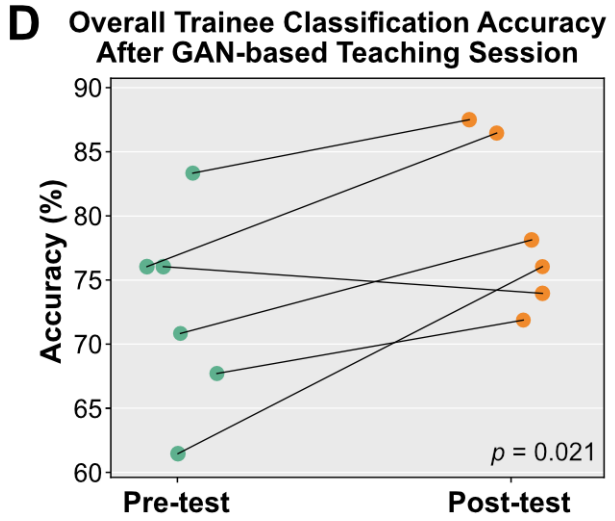
Howard et. al. *Nature Communications* 2022

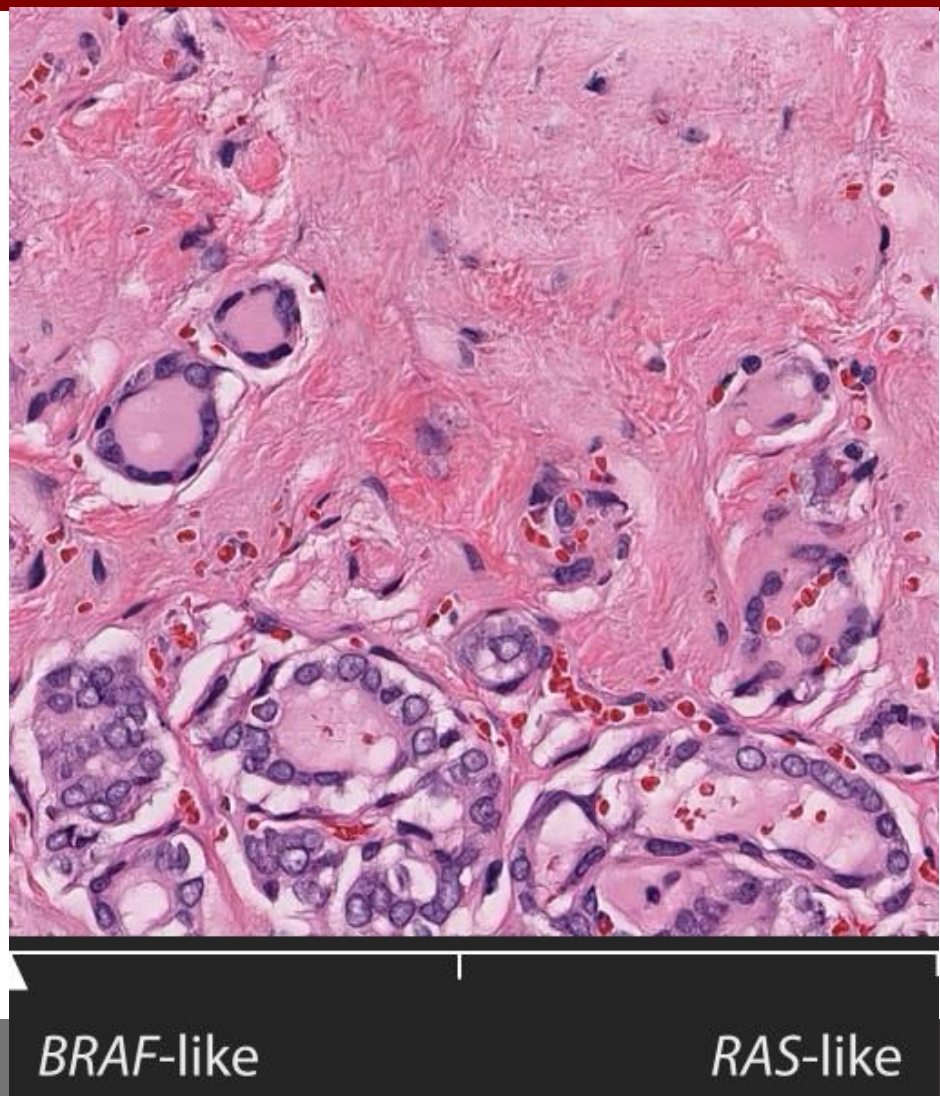
TRUSTWORTHY DIAGNOSTICS: Generative AI Explanations

AI based generative imaging can create images with enough information to train human pathologists



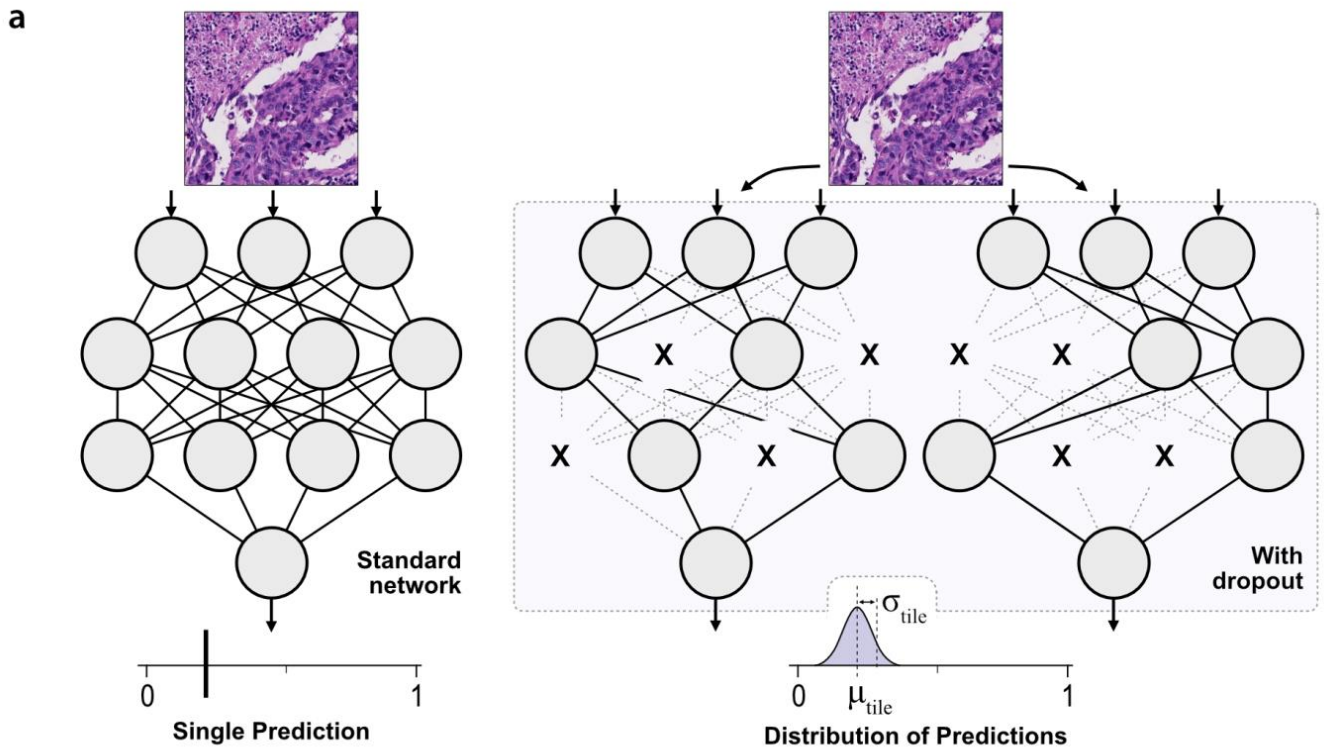


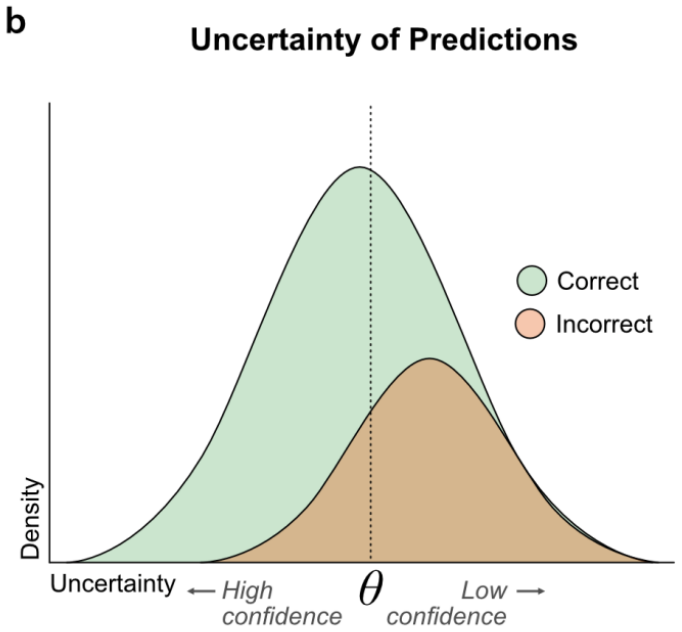




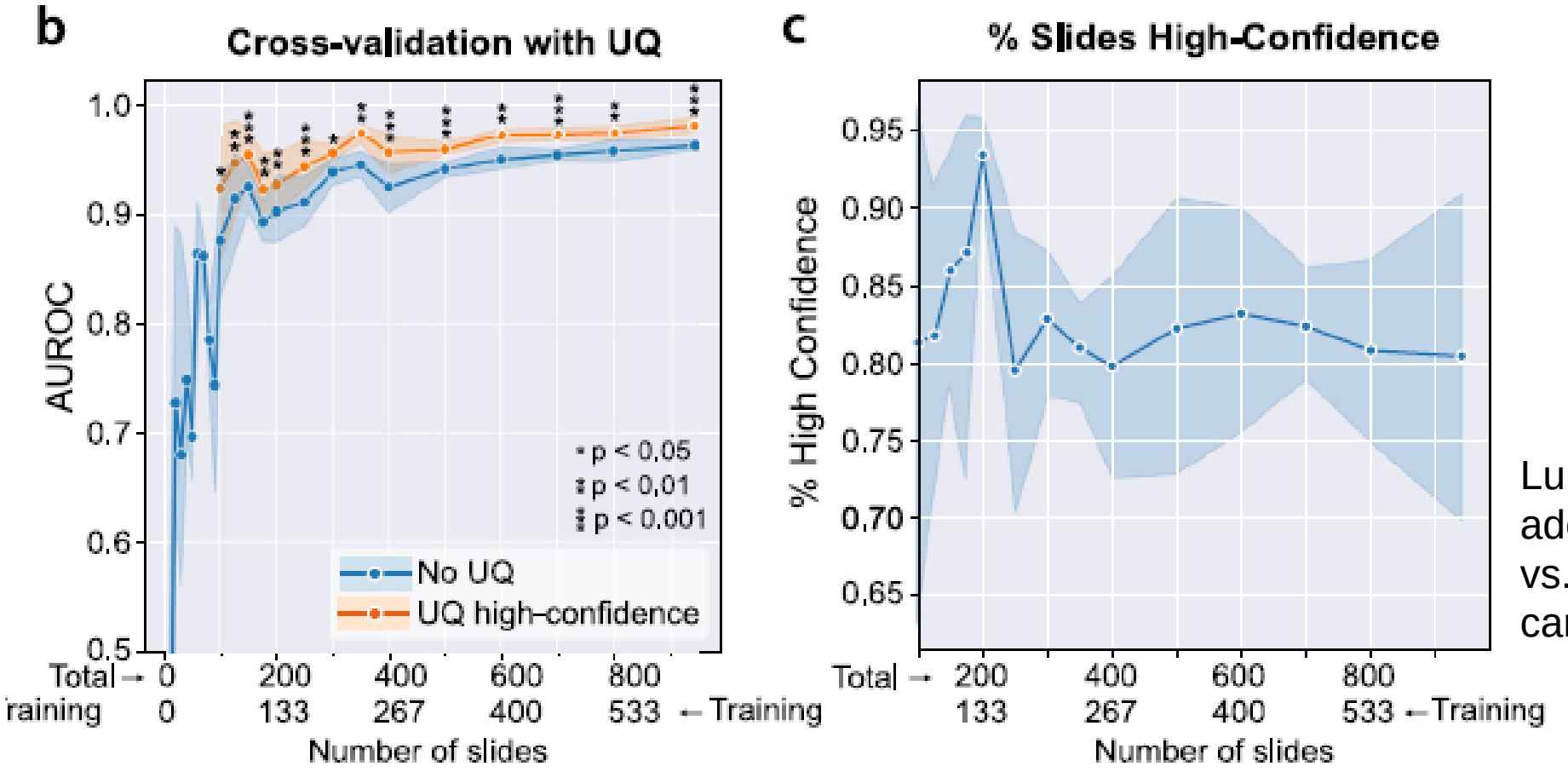
Dolezal et. Al., *npj Precision Oncology* 2023

TRUSTWORTHY DIAGNOSTICS: Excluding Non-Trustworthy Predictions



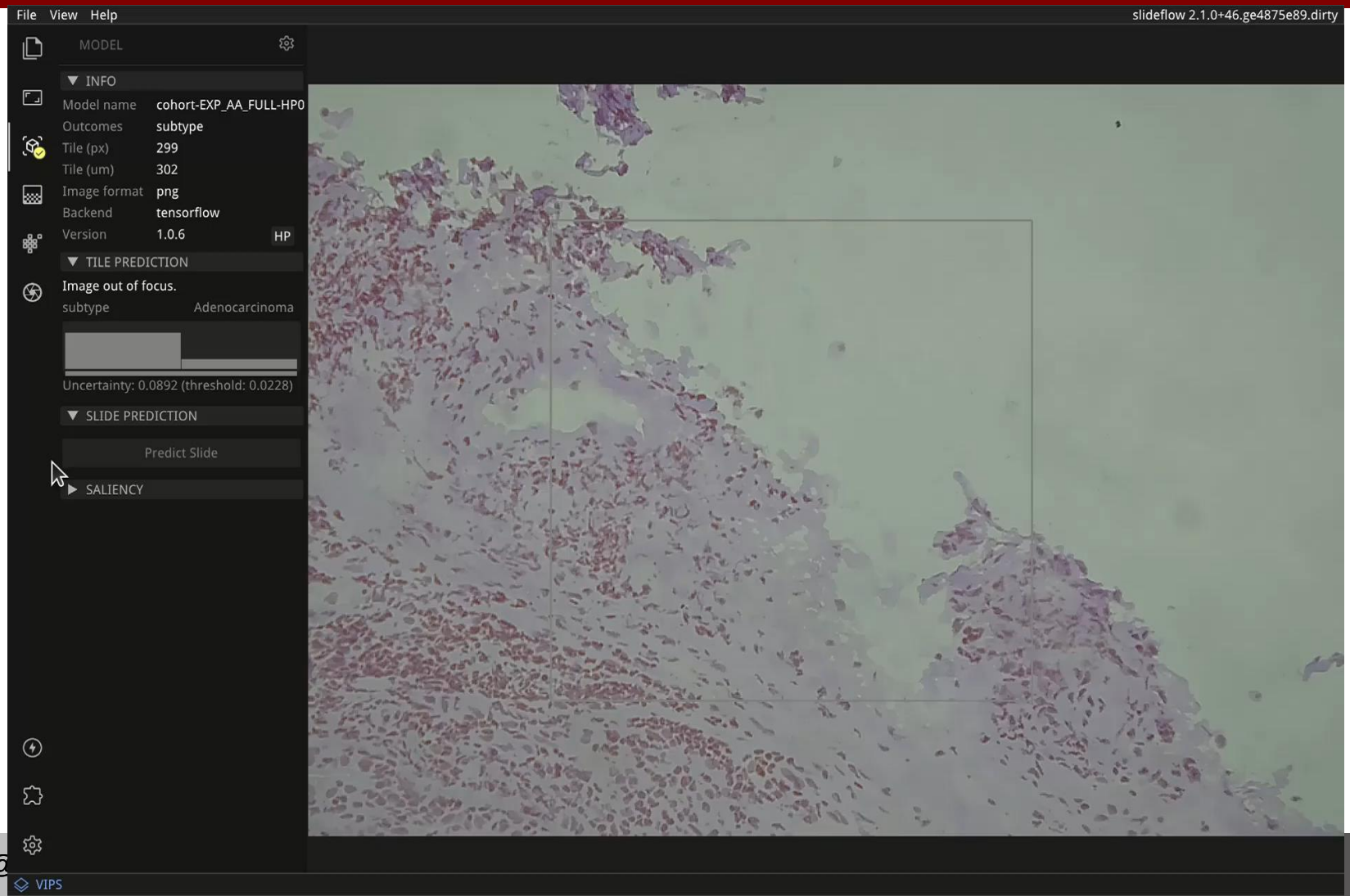


TRUSTWORTHY DIAGNOSTICS: Excluding Non-Trustworthy Predictions



Lung cancer adenocarcinoma vs. squamous cell carcinoma

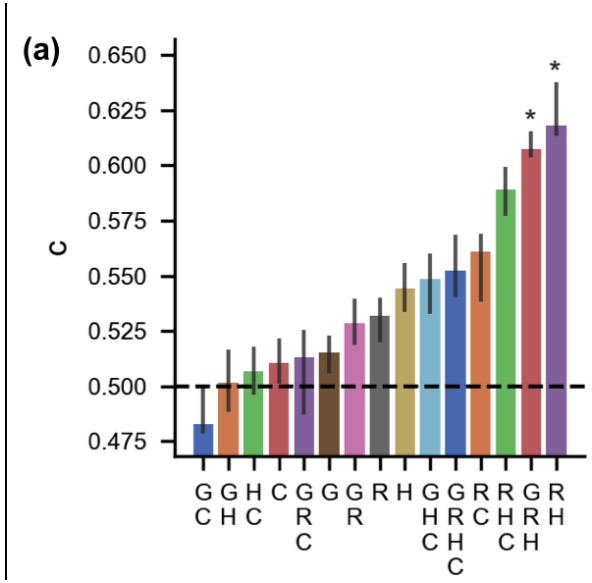
TRUSTWORTHY DIAGNOSTICS: Uncertainty Quantification in Real Time



MULTI-MODAL DATA: Improving Clinical Utility

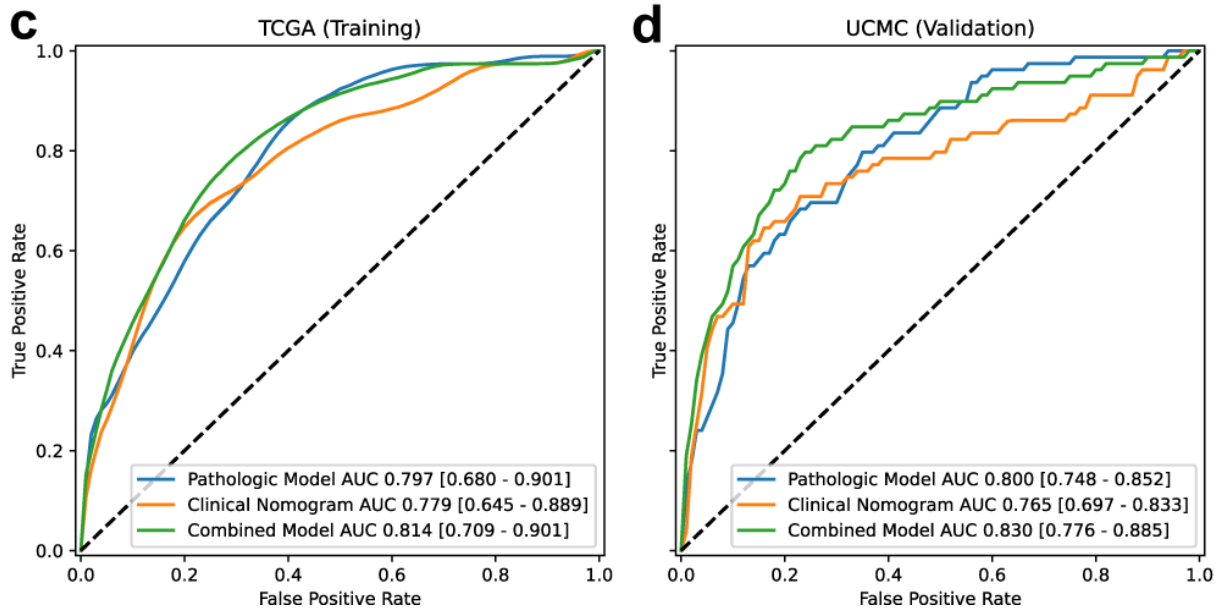
- The promise of multi-modal data:
  - A single clinical tool that obtains higher performance using two data types is more valuable than 2 clinical tools each using a single data type

…but only if the cost and time of the tool are not worse in the real world



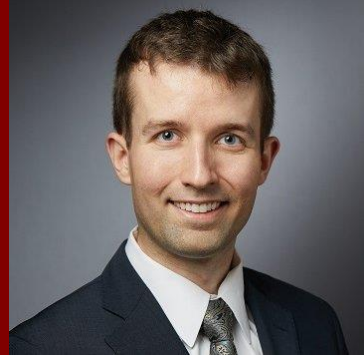
Serous Ovarian Cancer Risk stratification is improved with more data modes

Breast Cancer recurrence prediction is improved with more data modes

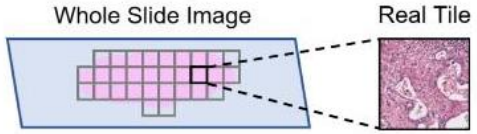


Boehm K et. al. *Nature Cancer* 2022; . Howard F et. al. *NPJ Breast Cancer* 2023

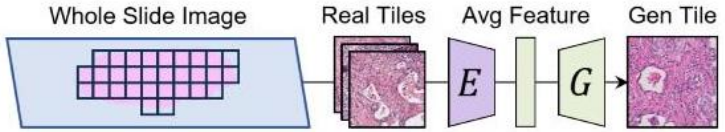
MULTI-MODAL DATA:
Jointly Embedding Multiple Data Types



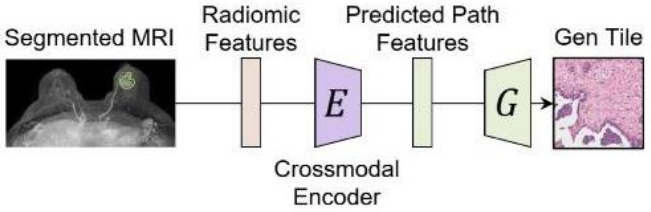
Original Digital Slides

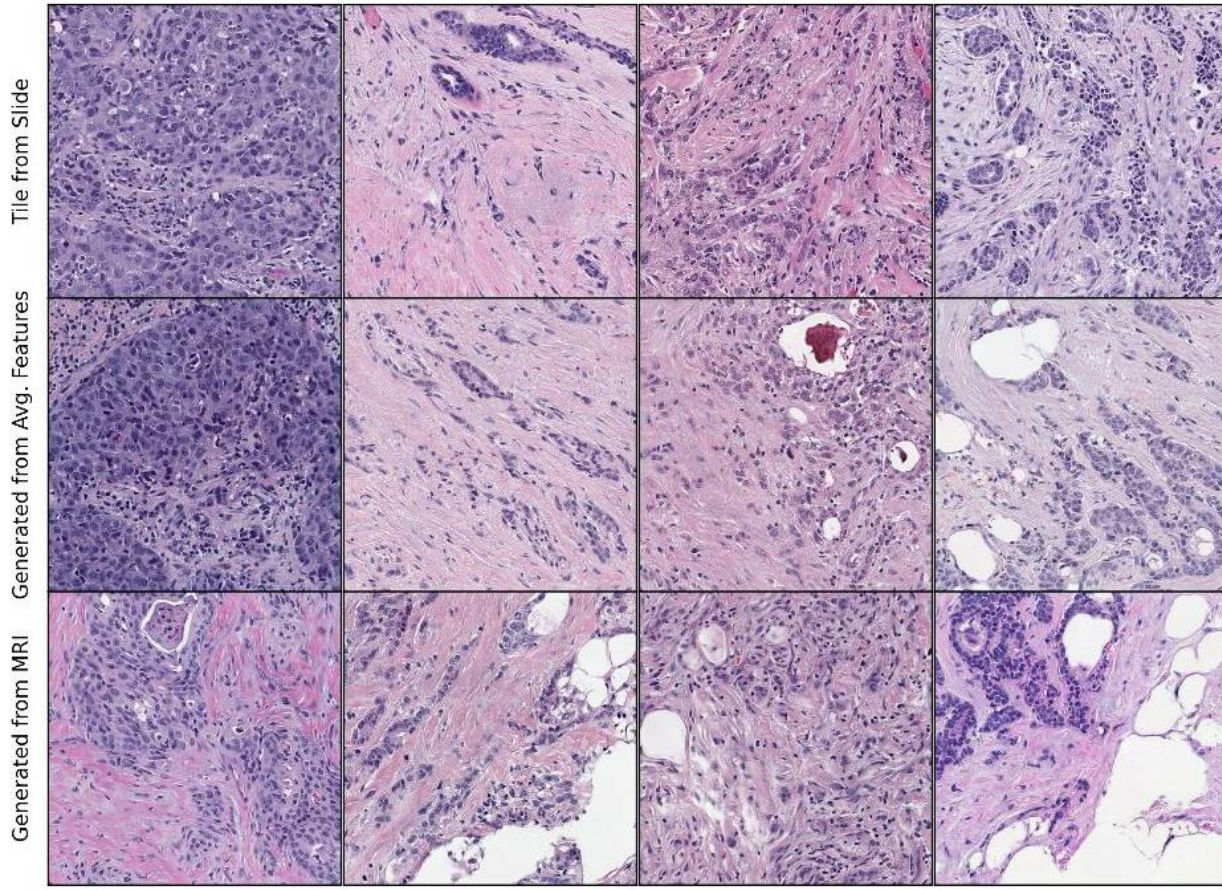


Synthetic Digital Slides
Built from *Pathology*
FM Features



Synthetic Digital Slides
Built from *Radiology*
FM Features





In Press at *Science Advances*; BioRXiv: 10.1101/2024.03.22.586306

LOCALLY-PRODUCED OPEN-SOURCE LOW-COST DEPLOYMENT

HNSCC

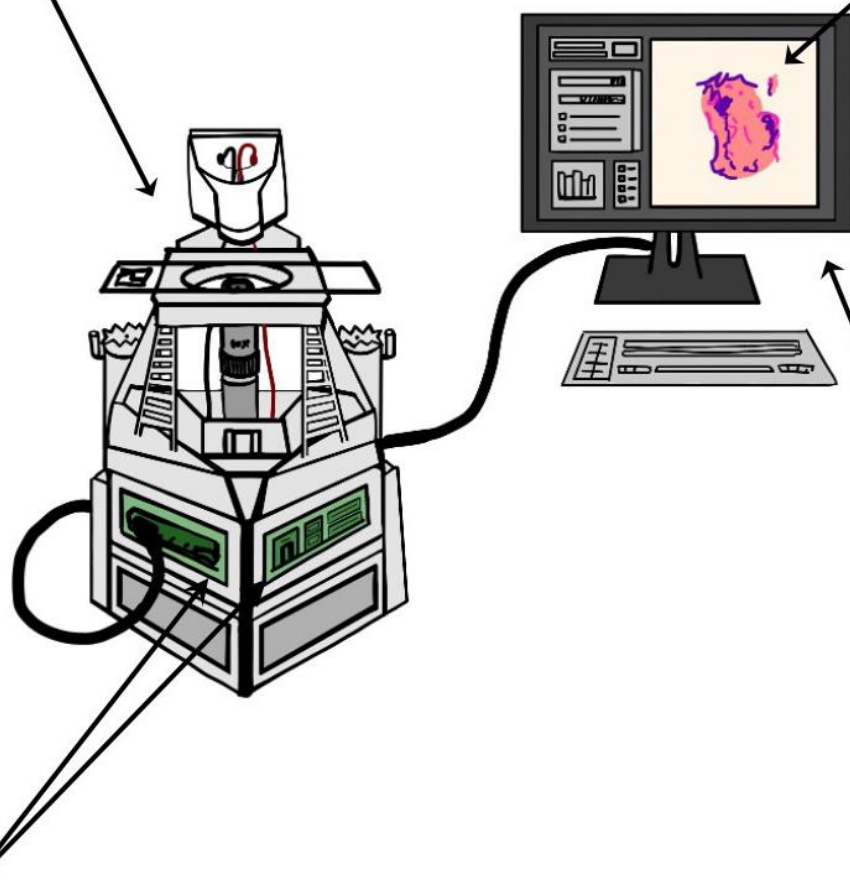
OpenFlexure Microscope
Cost: $100
License: Creative Commons Attribution 4.0 International License (CC BY 4.0)

Raspbian-OpenFlexure OS (OpenFlexure Connect)
Cost: Free
License: GNU General Public License (v3)

Raspberry Pi 4 Model B
Cost: $35
License: Creative Commons Attribution-NoDerivatives 4.0 International (CC BY-ND)

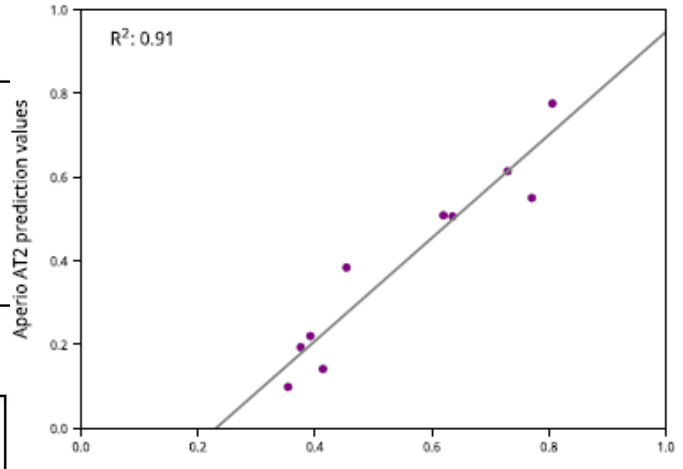
Raspberry Pi Camera Module
Cost: $65
License: Creative Commons Attribution-NoDerivatives 4.0 International (CC BY-ND)

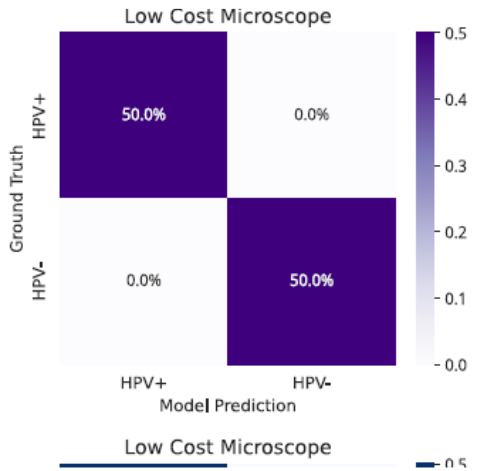
Raspberry Pi OS
Cost: Free
License: The 3-Clause BSD License



Slideflow and Slideflow Studio GUI
Cost: Free
License: GNU General Public License v3.0

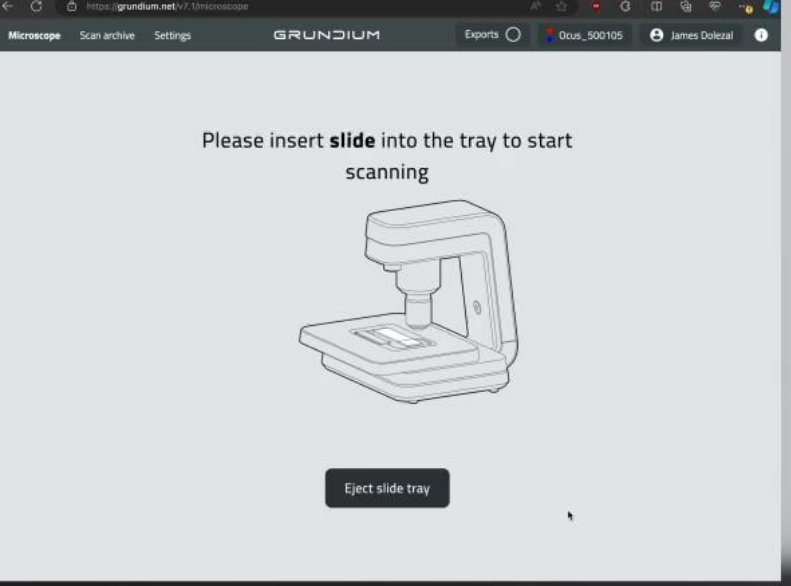
Monitor
Monitor connects to OpenFlexure microscope
Cost: <$100
License: Variable





Low Cost Microscope

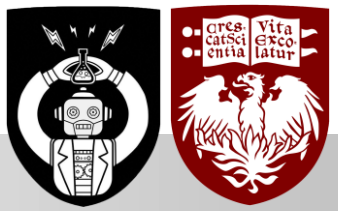
Choudhury D, *eBioMedicine* 2024



(Near) Real-Time AI Deployment

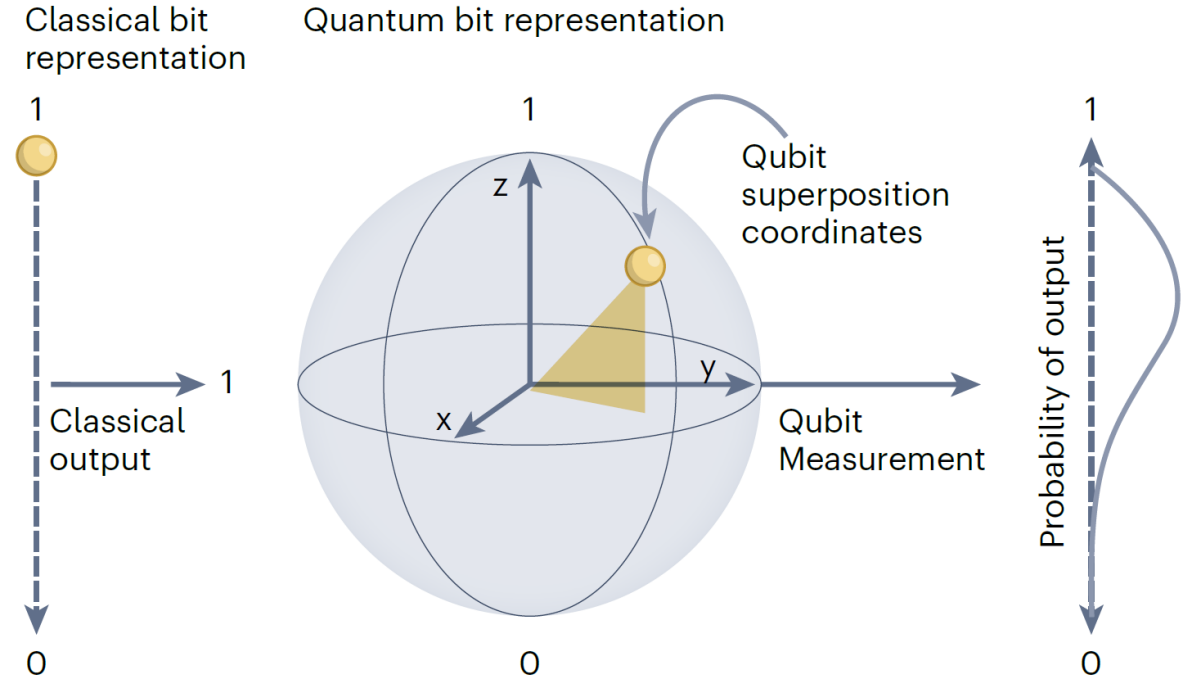
- Hardware: Grundium
- Software: Grundium API, SlideFlow Studio (OS)
  - Dolezal J, *BMC Bioinformatics* 2024
- Model: Vision Transformer MSI prediction (OS)
  - Wagner SJ, *Cancer Cell* 2023

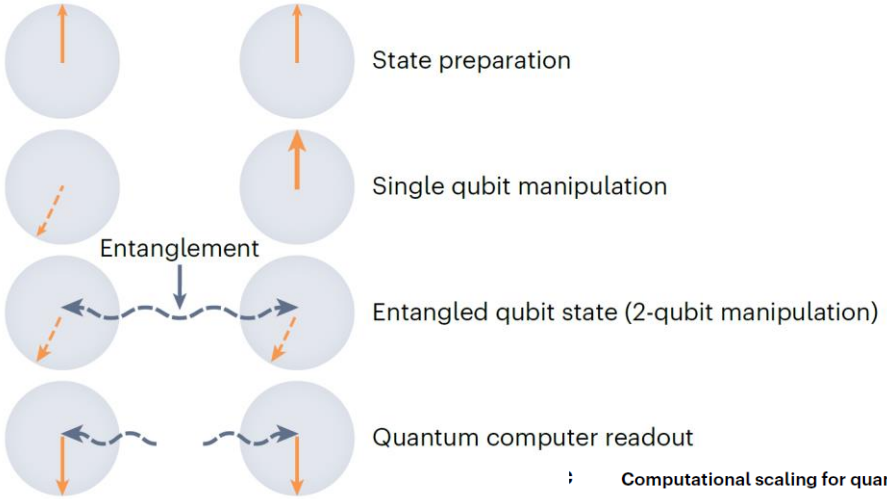
FUTURE AI: QML FOR MEDICINE

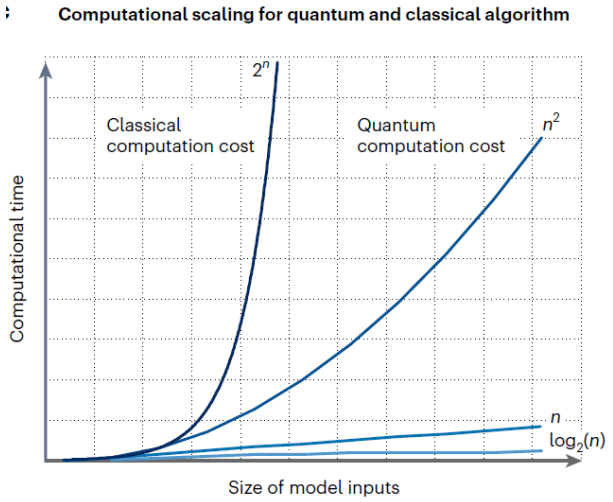


QUANTUM COMPUTING ADVANATGES AND DISADVANTAGES

- Quantum properties can lead to exponential gains in computing efficiency for some applications



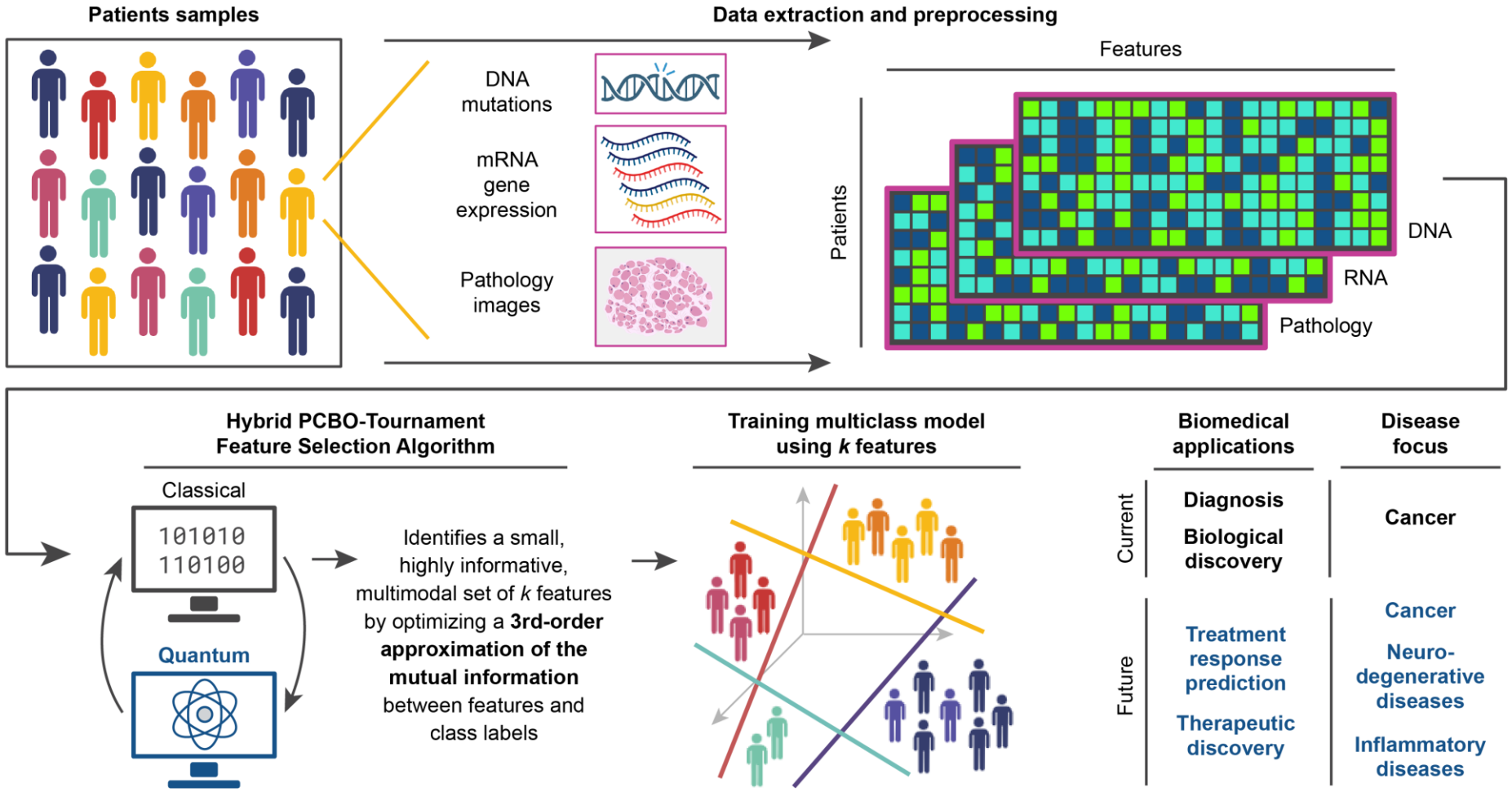




Ramesh S et. al., *Nature Cancer* (2024)

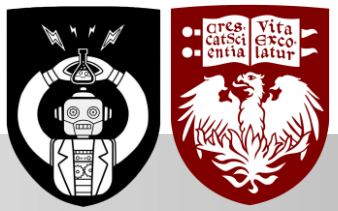
QUANTUM COMPUTING EXAMPLE: Q4Bio Phase 3 Grant Concept

- Multi-modal cancer data is:
  - Expensive
  - Complexly correlated
  - Benefitted if sparce explanations can be generated



Ramesh S et. al. *AACR Annual Meeting* 2025, Abstract 5020

AI-COMPATIBLE MEDICAL CARE: UCHICAGO APPROACH TO CLINICAL AI



CENTER FOR CLINICAL AI: Mission and Vision

- Mission: Consolidate medical AI expertise and resources to promote collaboration, research development, and AI-informed patient care
- Vision: The University of Chicago Medical Center and Biological Sciences Division fully leverages the world class AI and Data Science resources of the University to provide cutting edge clinical care and pursue transformative research

THE UNIVERSITY OF CHICAGO
CENTER FOR COMPUTATIONAL MEDICINE & CLINICAL ARTIFICIAL INTELLIGENCE

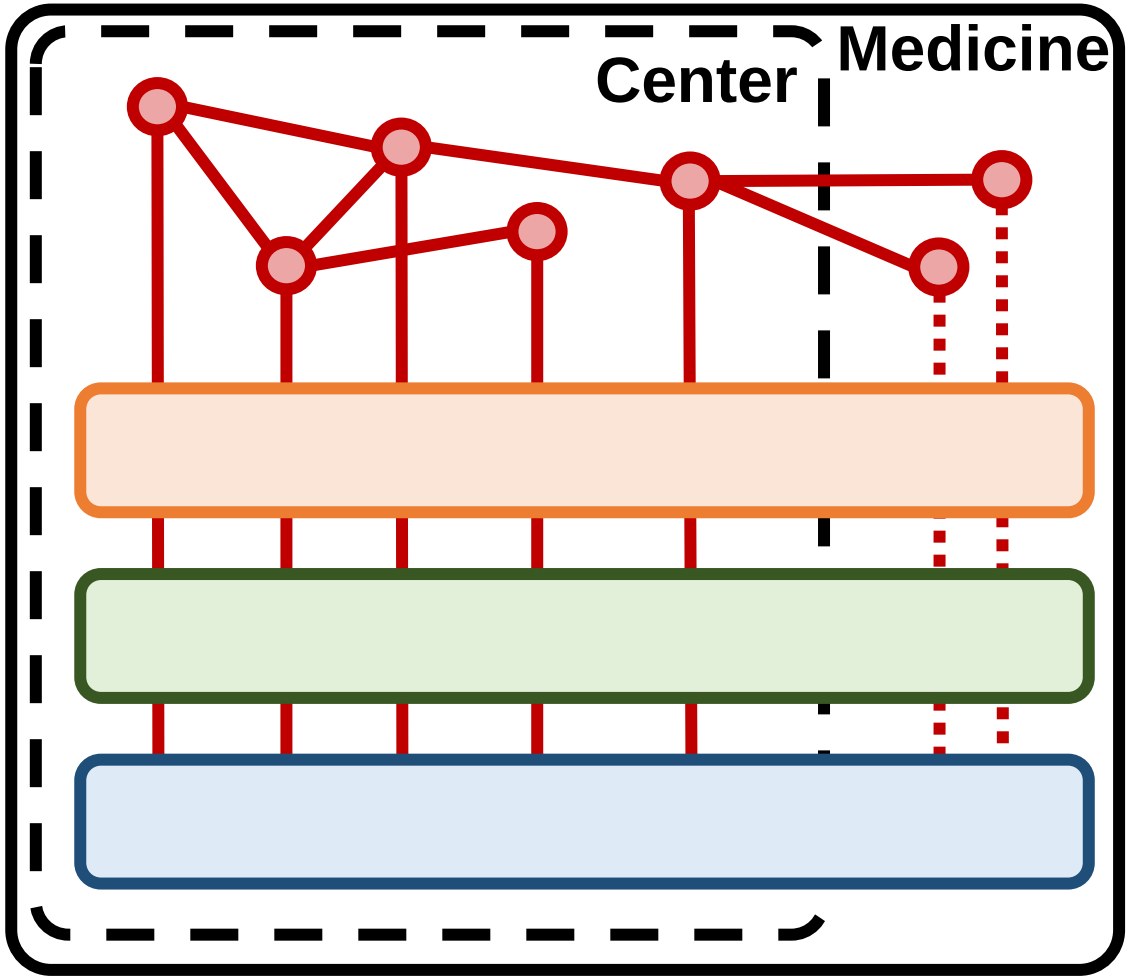
ORGANIZATIONAL DESIGN

Human Resources (Faculty, Staff, and Collaborators)

Hardware Resources

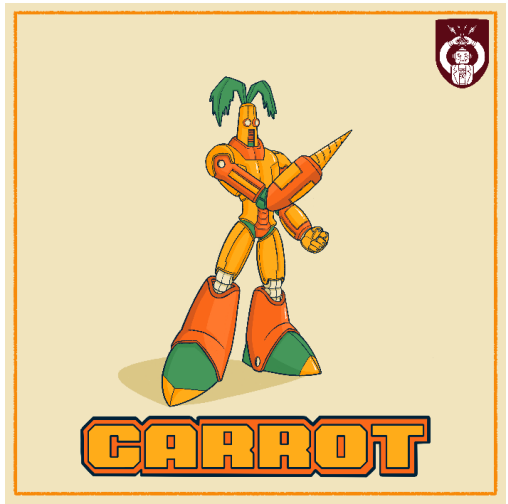
Expertise and Training Resources

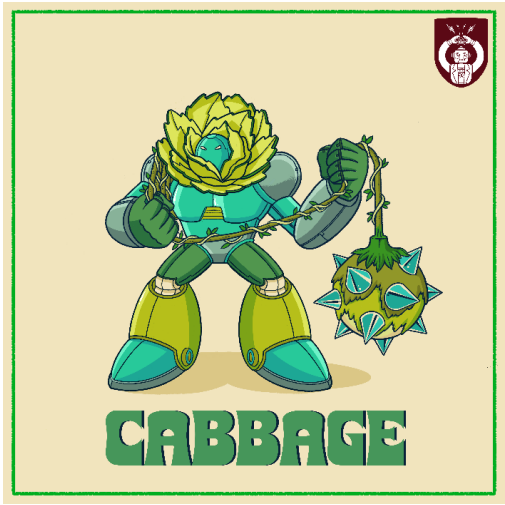
Software and Data Resources

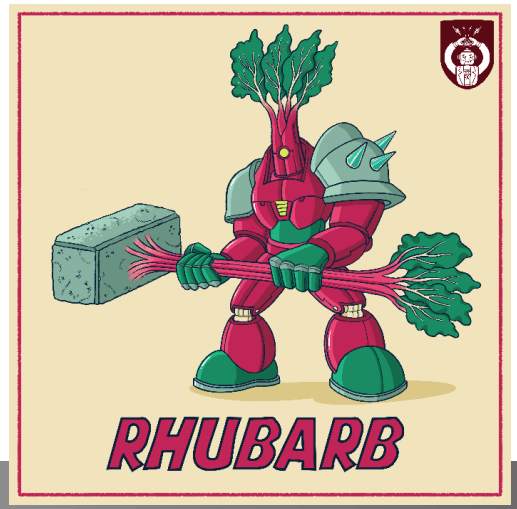


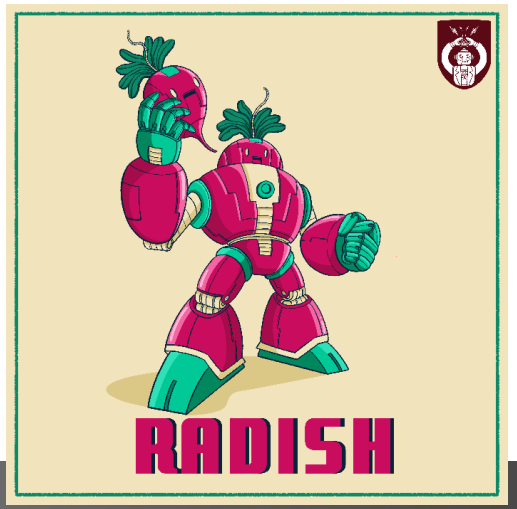
HARDWARE RESOURCES

- 4 desktop development workstations
- 12x A100s in 2 nodes
- Liquid cooled 8x GH200
- 250TB super-fast storage server



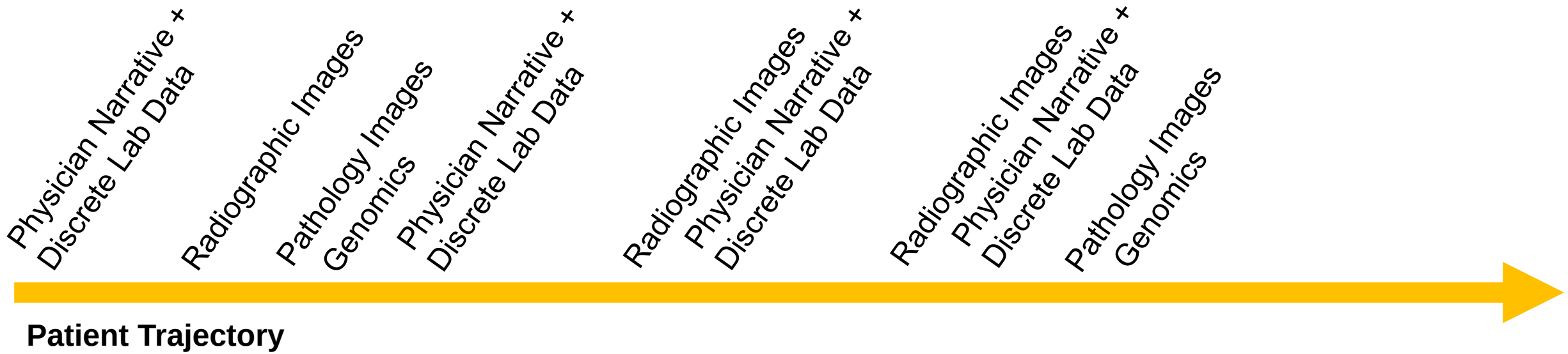




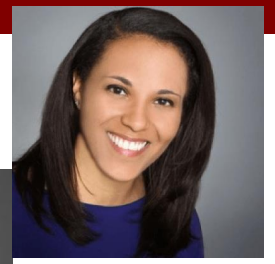


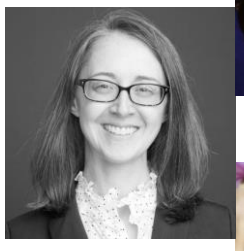
DIGITAL DATA ON PATIENT MEDICAL JOURNEY

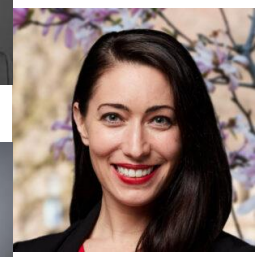
- **A patient's medical journey through time generates significant and varied digital health data**
- **The CCMCAI has brought together experts in each of these data domains to better process and understand human health trajectories**

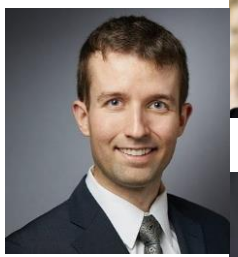


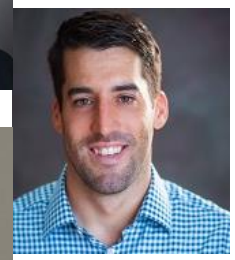
MODE-SPECIFIC INFORMATION EXTRACTION FOR HEALTH DATA











Loren Saulsberry, PhD — Demographics and Spatial Data

Heather Whitney, PhD — Deep Learning Radiomics

Madeleine Torcasso, PhD — Digital Omics

Fred Howard, MD — Deep Learning Pathomics

Brett Beaulieu-Jones, PhD
Will Parker, MD PhD — LLM Context

Nabil Mir, MBBS — Biometric Wearables Data

Multi-Modal AI

Samantha Riesenfeld, PhD

HEAD NECK PROGRAM: VISION FOR DIGITAL MEDICINE

Models:
Agentic AI Tumor Board with Automated Documentation

- Radiology — 1-2.
- Pathology — 2-9.
- EHR Data — 10-11.
- Other Modes — 12-18.
- Ambient Summary

Clinical Interventions & Trials:
Adaptive Clinical Trials and AI-Optimized Surveillance

- Radiology-Adaptive — 19-22.
- ct-DNA Adaptive — 23-24.
- Surveillance-Adaptive — 25-26.

Commons:
Multi-Modal Data Capture for Future AI-Based Analysis

- Hybrid Physical-Digital Biomarker Data Repository — 27.

Publications/Preprints:

1. Meneghetti AR et al, *BMC AI* 2025
2. Howard FM et al, *Breast Can Res Treat* 2022
3. Kather JN et al, *Nature Cancer* 2020
4. Dolezal J et al, *BMC Bioinformatics* 2024
5. Dolezal J et al, *Modern Pathology* 2021
6. Kather JN et al, *BioRxiv* 2019
7. Hieromnimon H et al, *Oral Oncology* 2025
8. Ramesh S et al, *JCO Global Oncology* 2023
9. Dolezal et al, *NPJ PO* 2023
10. Woo EG et al, *NPJ DM* 2025
11. Burkhart MC, *arXiv* 2025
12. Hieromnimon H et al, *Genome Medicine* 2025
13. Howard FM et al, *JAMA NO* 2020
14. He L et al, *Fall Voice Conference* 2025
15. Ghantous Y et al, *IJC* 2021
16. Nazari F et al, *PLOS Comp Bio* 2018
17. Viet C et al, *NPJ PO* 2024
18. Sannigrahi MK et al, *JNCI* 2025
19. Rosenberg AJ et al, *Oral Oncology* 2021
20. Rosenberg AJ et al, *BMC Cancer* 2022
21. Rosenberg AJ et al, *JAMA Onc* 2024
22. Rosenberg AJ et al, *JAMA Onc* 2025
23. NCT 05420948
24. Rosenberg AJ et al, *Clinical Cancer Research* 2025
25. Nair V et al, *JAMA NO* 2022
26. Mihammadi N, *medRxiv* 2025
27. Grossman RL, *arXiv* 2025

TRAINING RESOURCES

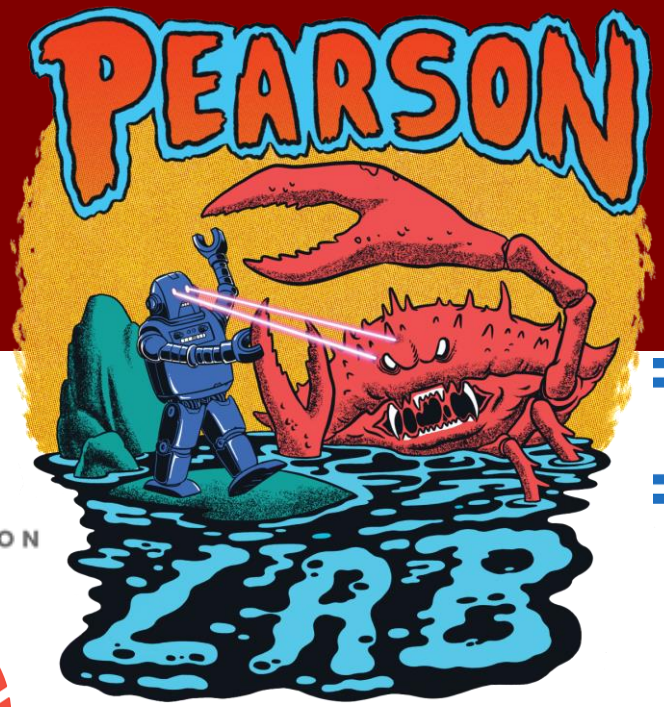
- AI in BioMedicine Journal Club
  - Weekly open journal club for methods and applications
  - Thursdays 1-2PM in W632
- Facilitate DSI, Argonne, TTIC collaboration
  - Working to expand training opportunities
- Multiple AI for healthcare data courses available or in development

https://biomedai.bsd.uchicago.edu/journalclub/

TRAINING RESOURCES: International Dissemination

- NIH Sponsored “Train the Trainer” UE5 grant for building AI for Medicine readiness in Africa
- 1st Cohort now completed training

THANKS!



- Sara Kochanny
- Matteo Sacco
- Lilly Li
- Erik Wolf
- Anran Li
- Hanna Hieromnimon
- Sid Ramesh, MD
- Grace Li
- Frank Wen, MD PhD
- Meghan Hutch, PhD
- Emma Dyer
- Dmitry Karpyev, PhD
- Divya Choudhury
- Caroline Montag
- Lawrence He
- Juliana Byanyima