Integrated Diagnostics Workshop

Kojo S. J. Elenitoba-Johnson, M.D.

03-06-2023

An Overview of the Current State and Vision for Integrated Diagnostics in Cancer Care

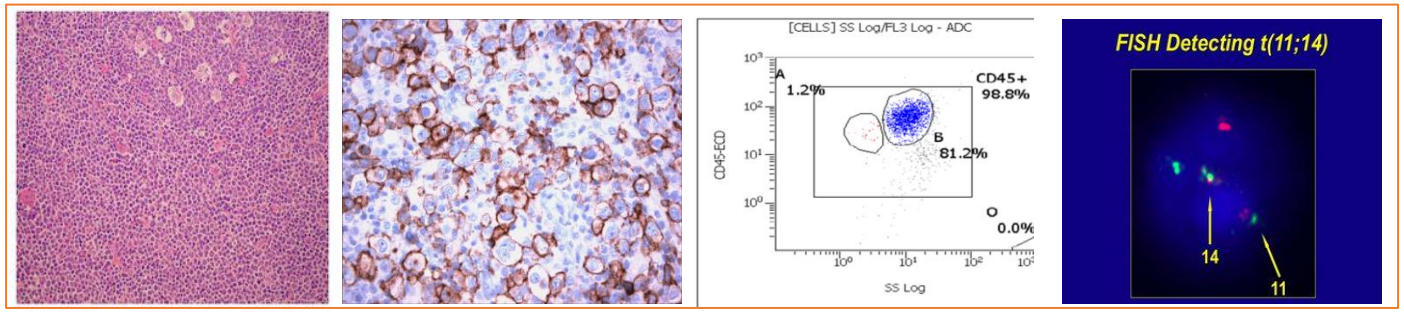
- Definition(s) and critical areas that will be addressed by the workshop
- Essential elements for optimal implementation
- Improving Evidence Generation Models
- Operationalization
- Oversight and Coverage
- Considerations for maximal patient access participation
- Models (Academic Centers, Industry, Private Public **Partnerships**)
- Opportunity costs for enhancing patient outcomes
- Opportunity costs

Definition(s)

Integrated diagnostics refers to the concept of the convergence of imaging, pathology, and laboratory tests with advanced information technology, and it has enormous potential for revolutionising the diagnosis and therapeutic management of many diseases, including cancer

Hedvig Hricak
January 2022

Fundamental patient-driven goals for Integrated Diagnostics



1) **What disease does the patient have? (diagnosis)**

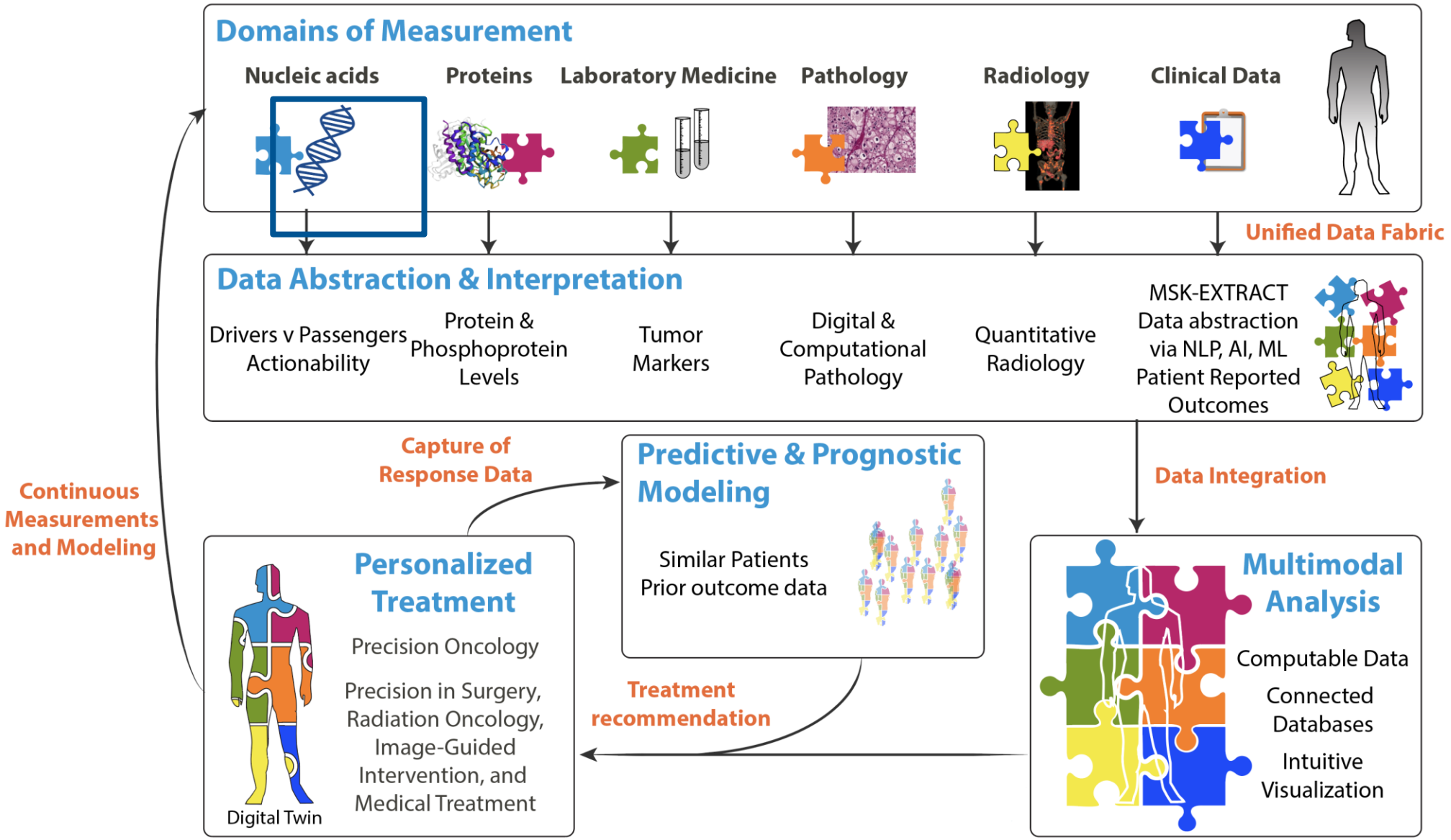
2) **How much of the disease is there? (residual disease)**

3) **Who needs treatment? (prognosis)**

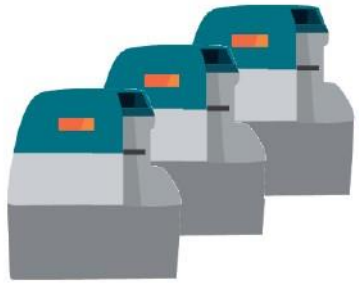
4) **What is the best treatment for this patient? (therapy)**

5) **What dose? (pharmacogenomics, dynamics)**

Integrated Data Science



Nikolaus Schultz
Integrated Diagnostics Initiative



Scanner

Leica (11x GT450, 10x AT2, 1x CS2)
Philips (3x UFS)
3DHistech (1x P1000)

IMS

IMS

meta data

molecular pathology data

pathology reports

image files

Pathology DB

MPath

CoPath

IDB

image files

HoBBIT

Data Warehouse

Redactor

Image de-id

pathology reports

molecular pathology data

image meta data

image files

HPC Cluster

7x DGX-1 (56 V100)
6x 4U (12 CTX 1080, 12 Titan X)

MSK Viewer

Viewing and Annotating

Visualization

Annotation

Organization

WSI Storage Cluster

9 PB for clinical, research and archive

Legend

identified

de-id

Path report

WSI

pathology report data

molecular pathology data

image meta data

image files

Hospital Apps

Education

Research

cBioPortal

PPBC

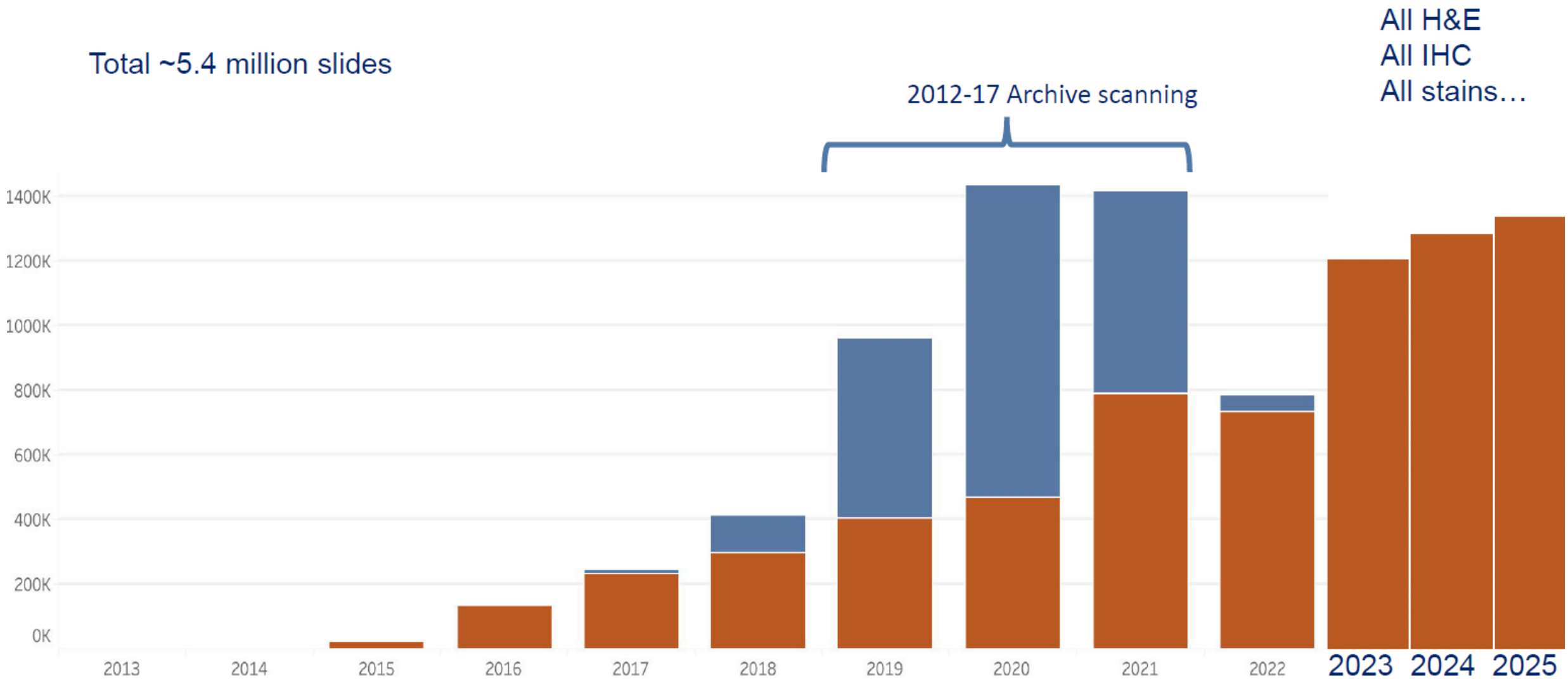
MPath

CoPath

Annual Slide Scan Volumes

Total ~5.4 million slides

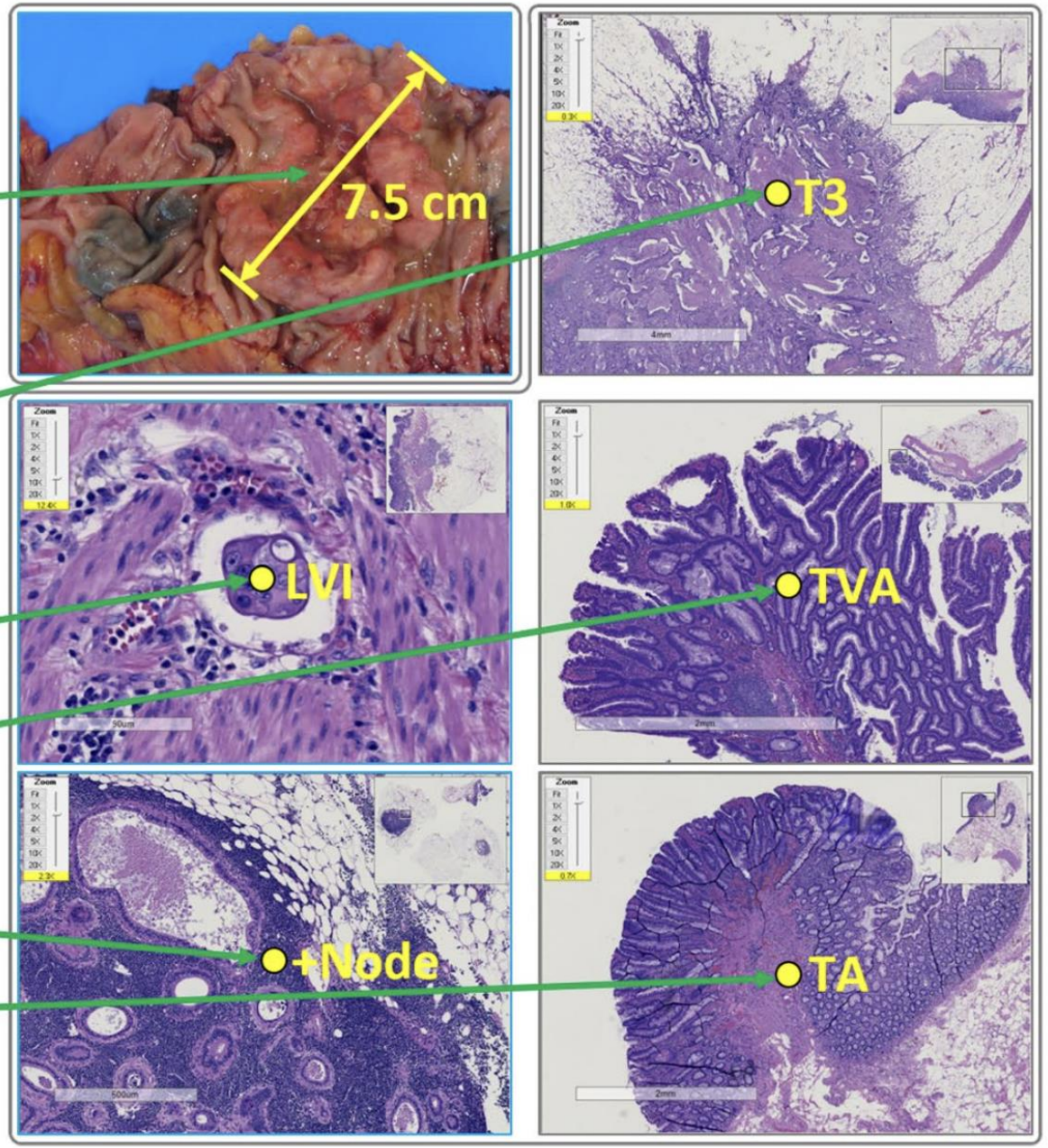
All H&E
All IHC
All stains…



Detailed Digital Annotation Promotes Enhanced Reporting

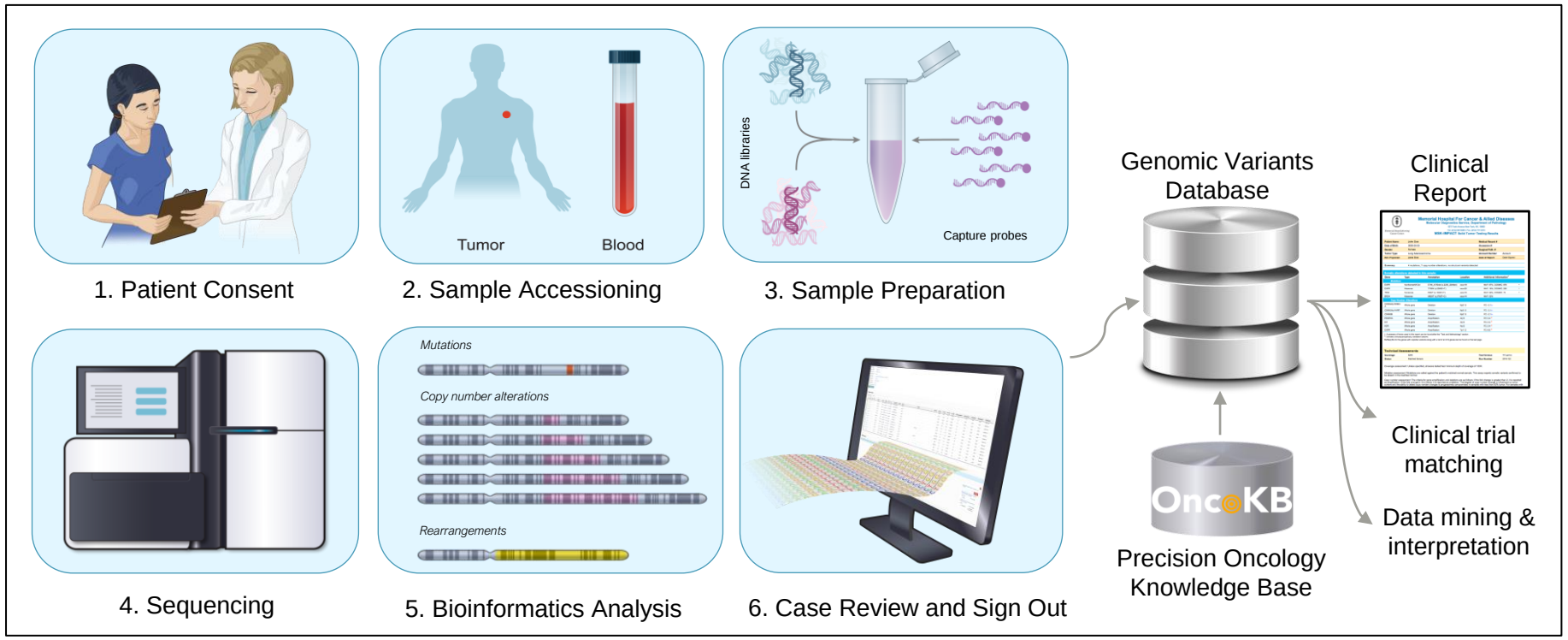
Anatomic Pathology: Colon Resection Synoptic Report

Procedure:	Low anterior resection
Tumor Site:	Sigmoid colon
Tumor Location:	Entirely above the anterior peritoneal reflection
Tumor Size:	Greatest dimension: 7.5 cm
Macroscopic Tumor Perforation:	Not identified
Macroscopic Intactness of Mesorectum:	Complete
Histologic Type:	Adenocarcinoma
Histologic Grade:	G2: Moderately differentiated
Tumor Extension:	Tumor invades through the muscularis propria into pericolorectal tissue
Margins:	All margins are uninvolved
Margins examined:	Proximal, distal, radial
Distance of invasive carcinoma from closest margin:	4.5 cm
Specify closest margin:	Radial
Distance of tumor from distal margin:	5.0 cm
Lymph-Vascular Invasion:	Present
Perineural Invasion:	Present
Type of Polyp in Which Invasive Carcinoma Arose:	Tubulovillous adenoma
Tumor Deposits:	Not identified
Lymph Node Examination:	
Number of Lymph Nodes Involved:	1
Number of Lymph Nodes Examined:	15
Pathologic Stage Classification (pTNM, AJCC 8th):	pT3 N1a
Additional Pathologic Findings:	Tubular adenoma



Roth et al. Journal of Digital Imaging (2021) 34:495–522

MSK-IMPACT for Tumor Tissue Profiling



- Matched tumor/normal deep sequencing of **505 genes** to guide treatment

2011: Established as research assay

2013: Validation in Molecular Diagnostics

2014: Approved for clinical use by NYS DOH

2015: Opt-in clinical germline analysis

2017: Authorized by US FDA as class II tumor profiling assay

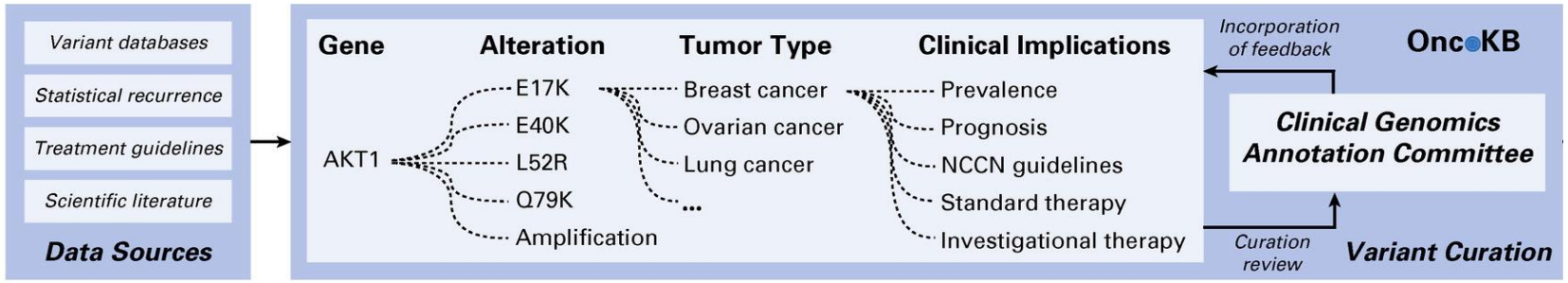
2020: Surpassed 50,000 patients profiled

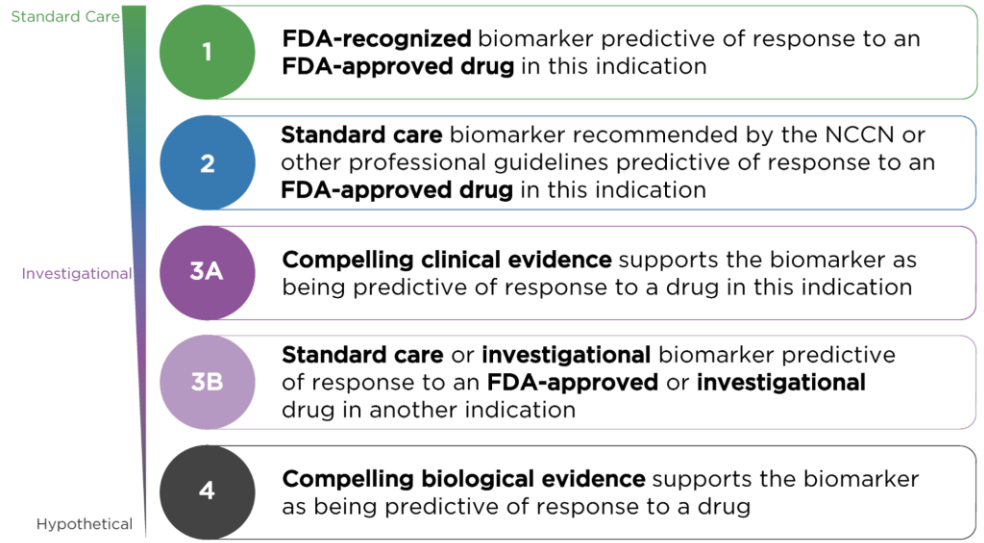
Zehir, Benayed, *et al.*, *Nature Medicine*, 2017

Slide Courtesy of Mike Berger

Key Component : Clinical Knowledge Base

OncoKB
Precision Oncology Knowledge Base
oncokb.org



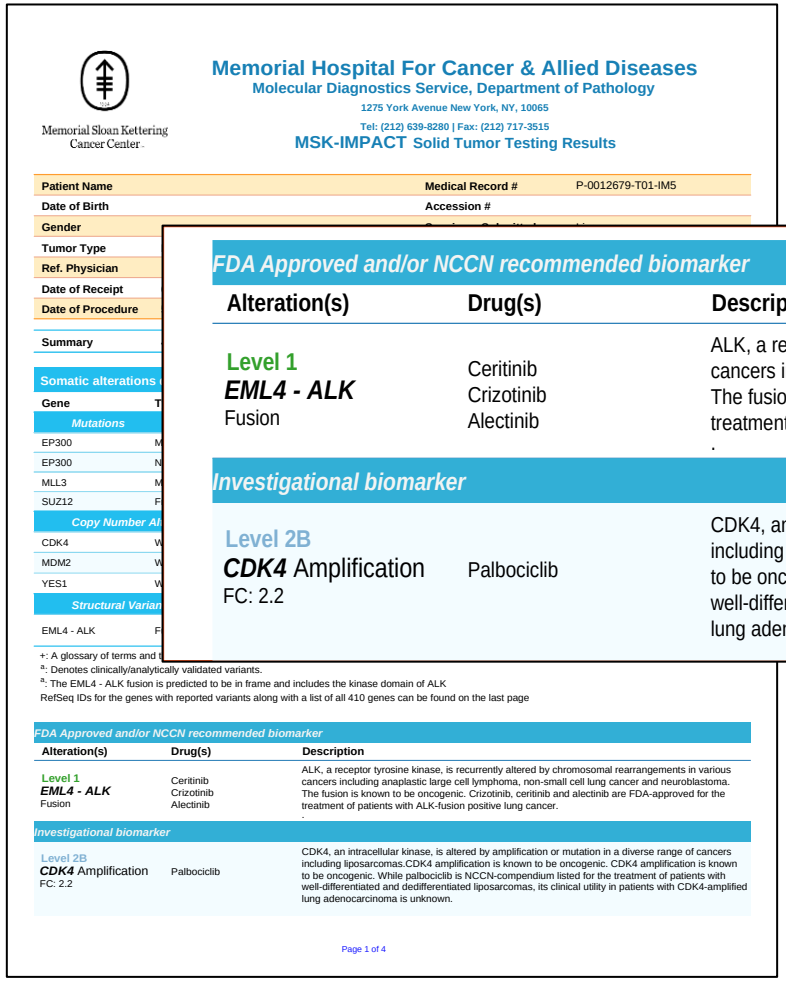


Debyani Chakravarty, JJ Gao, Niki Schultz, David Solit
Chakravarty *et al*., *JCO Precision Oncology*, 2017

Comprehensive Diagnostic Assessment for Every Patient

Personalized MSK-IMPACT Report

- Mutations
- Gene Amplifications
- Gene Deletions
- Chromosomal Rearrangements
- Tumor Mutation Burden (TMB)
- Microsatellite Instability (MSI)
- OncoKB annotations



Memorial Sloan Kettering Cancer Center

Memorial Hospital For Cancer & Allied Diseases
Molecular Diagnostics Service, Department of Pathology
1275 York Avenue New York, NY, 10065
Tel: (212) 639-8280 | Fax: (212) 717-3515
MSK-IMPACT Solid Tumor Testing Results

Patient Name		**Medical Record #**	P-0012679-T01-IM5
Date of Birth		**Accession #**	
Gender			
Tumor Type			
Ref. Physician			
Date of Receipt			
Date of Procedure			

Summary

Somatic alterations

Gene	T
Mutations	
EP300	M
EP300	N
MLL3	M
SUZ12	F
Copy Number Al	
CDK4	W
MDM2	W
YES1	W
Structural Varian	
EML4 - ALK	F

+: A glossary of terms and t
[a]: Denotes clinically/analytically validated variants.
[a]: The EML4 - ALK fusion is predicted to be in frame and includes the kinase domain of ALK
RefSeq IDs for the genes with reported variants along with a list of all 410 genes can be found on the last page

FDA Approved and/or NCCN recommended biomarker

Alteration(s)	Drug(s)	Description
Level 1 ***EML4 - ALK*** Fusion	Ceritinib Crizotinib Alectinib	ALK, a receptor tyrosine kinase, is recurrently altered by chromosomal rearrangements in various cancers including anaplastic large cell lymphoma, non-small cell lung cancer and neuroblastoma. The fusion is known to be oncogenic. Crizotinib, ceritinib and alectinib are FDA-approved for the treatment of patients with ALK-fusion positive lung cancer.

Investigational biomarker

Level 2B ***CDK4*** Amplification FC: 2.2	Palbociclib	CDK4, an intracellular kinase, is altered by amplification or mutation in a diverse range of cancers including liposarcomas.CDK4 amplification is known to be oncogenic. CDK4 amplification is known to be oncogenic. While palbociclib is NCCN-compendium listed for the treatment of patients with well-differentiated and dedifferentiated liposarcomas, its clinical utility in patients with CDK4-amplified lung adenocarcinoma is unknown.

Page 1 of 4

FDA Approved and/or NCCN recommended biomarker

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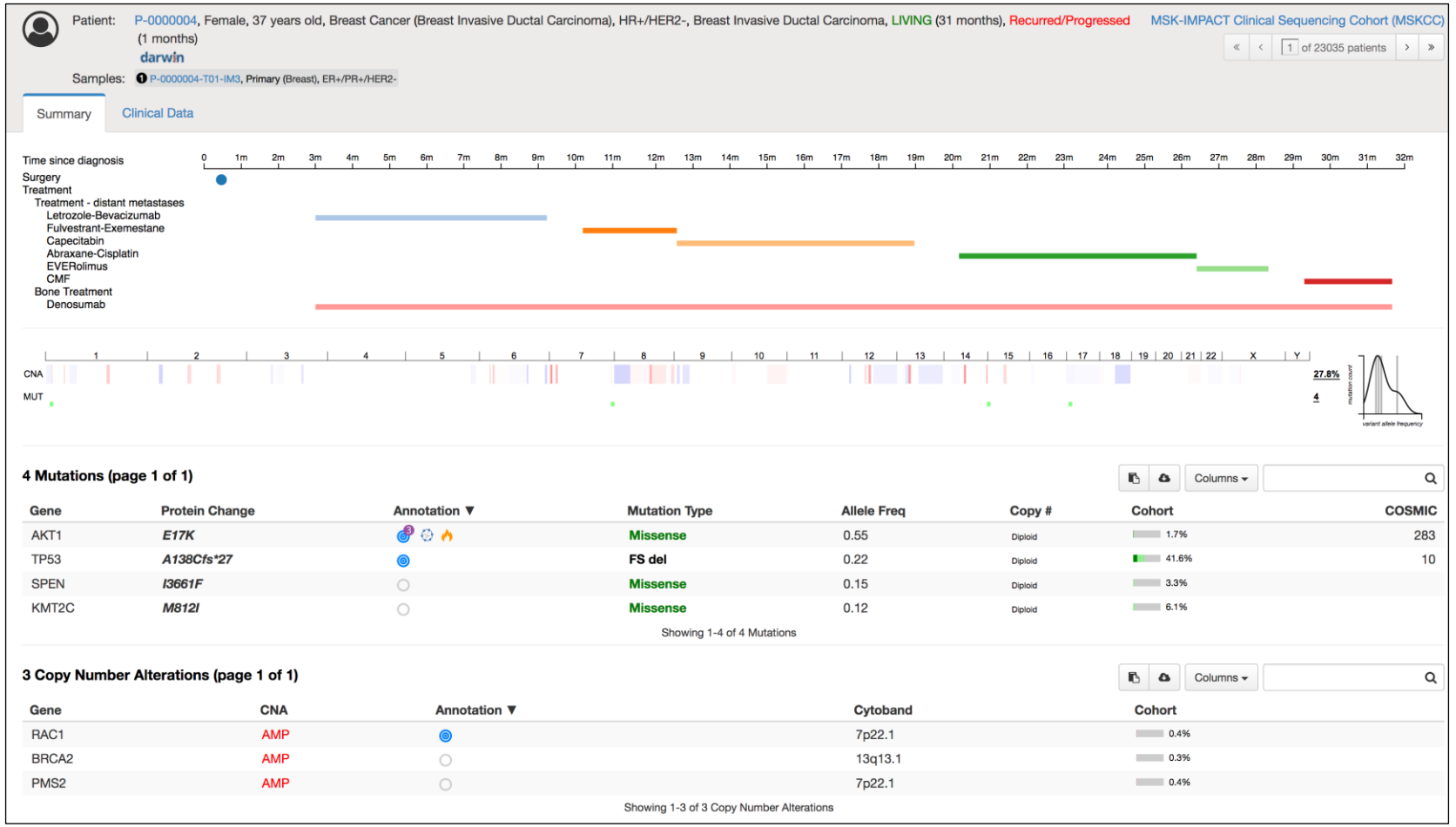
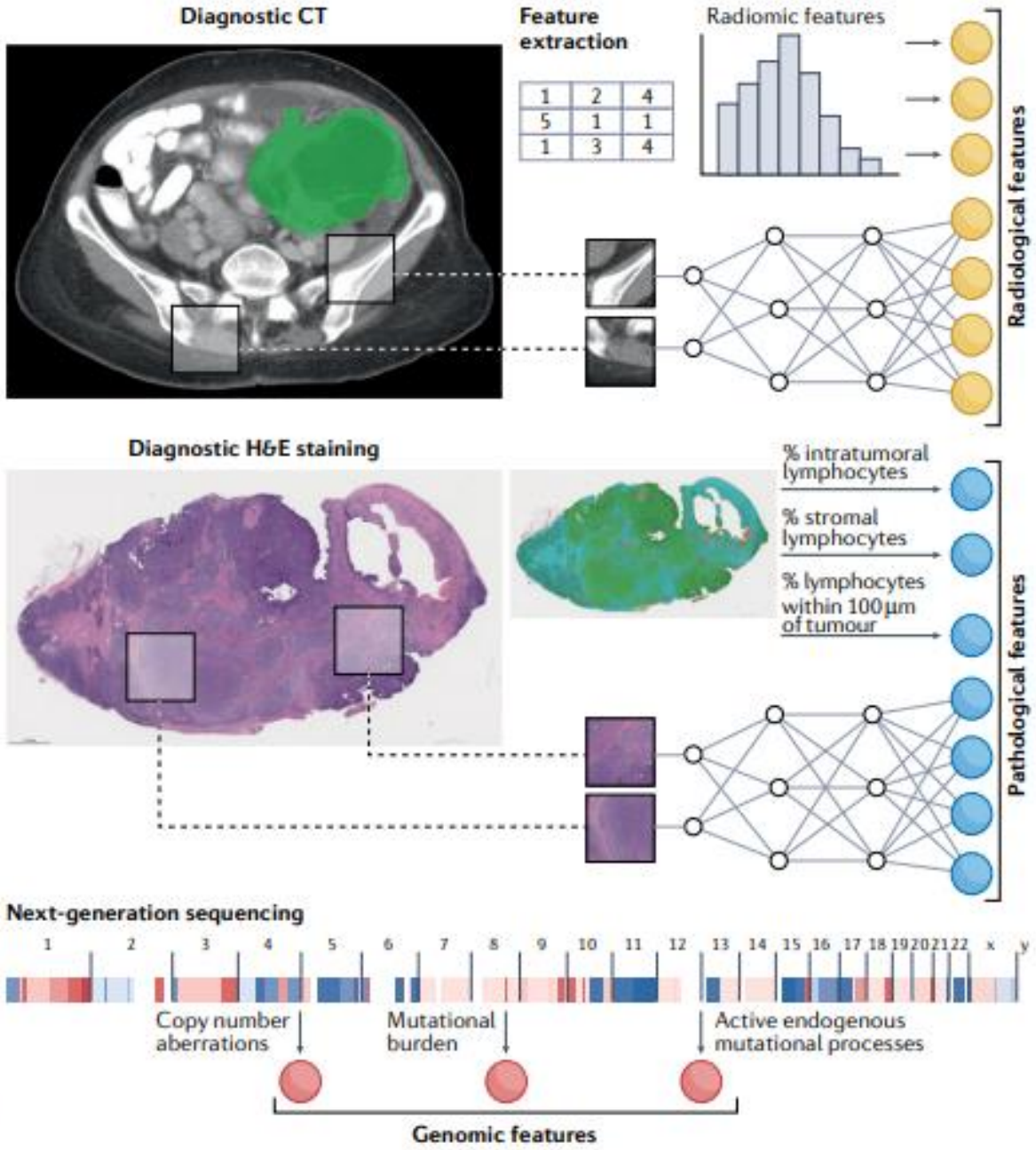
MSK-IMPACT Data Sharing Paradigm (+ Clinical Data)

cBioPortal FOR CANCER GENOMICS



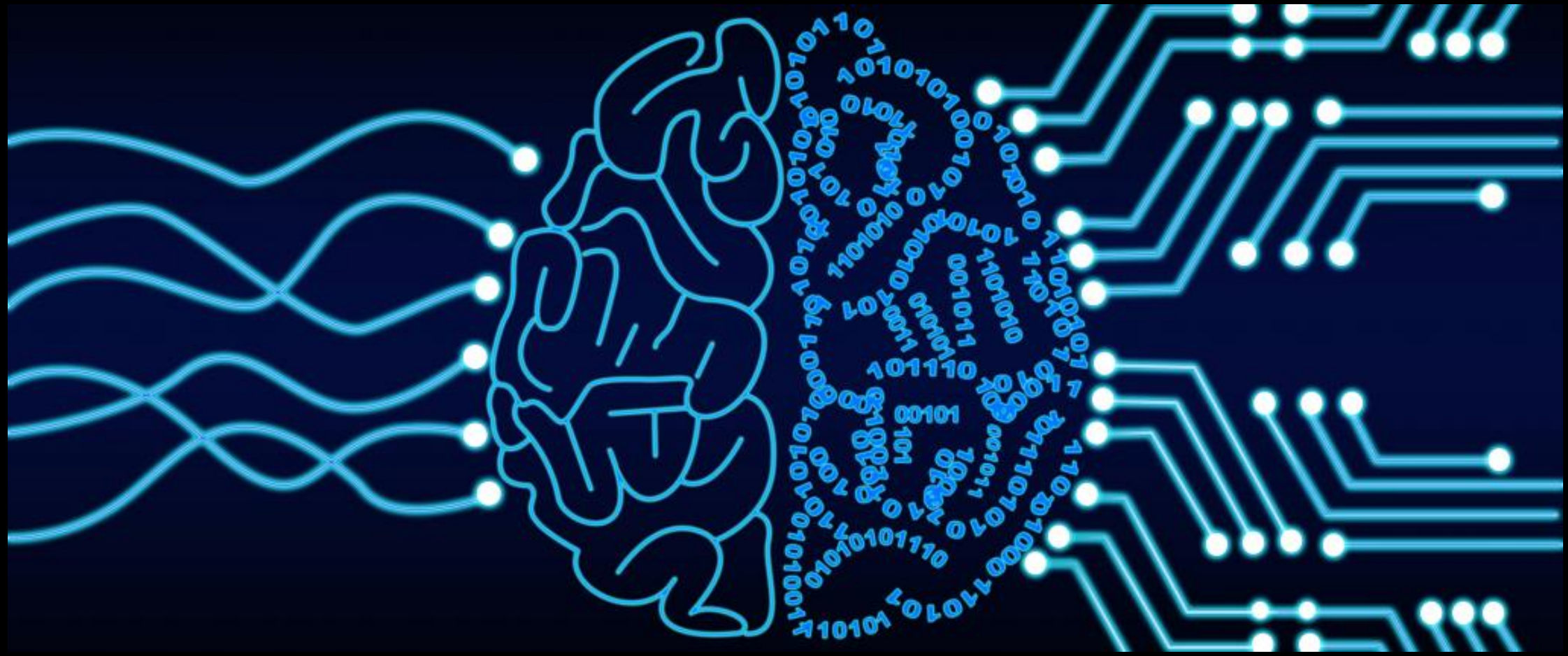
cbioportal.mskcc.org

Harnessing multimodal data integration to advance patient outcomes

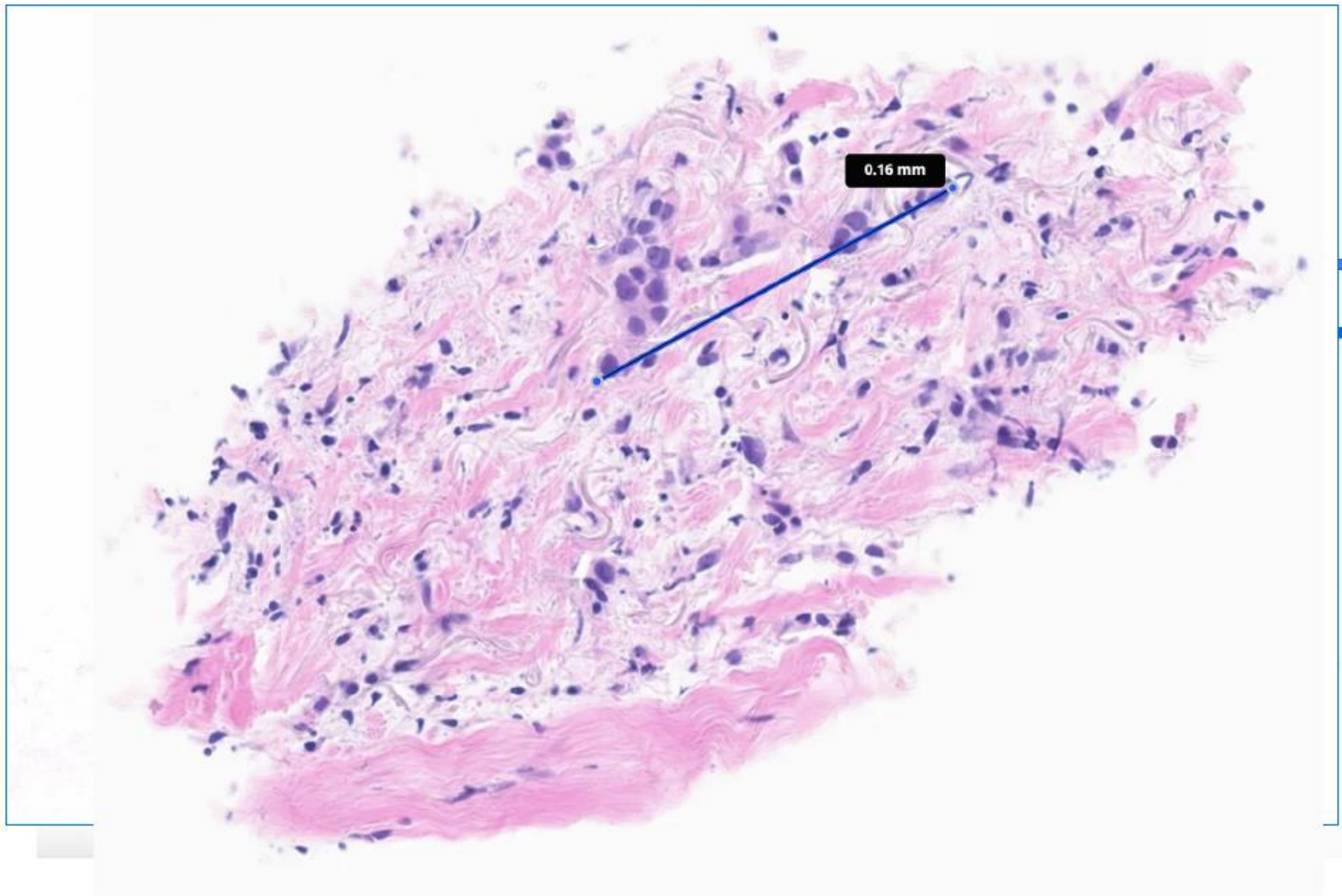


Boehm K et al. 2022

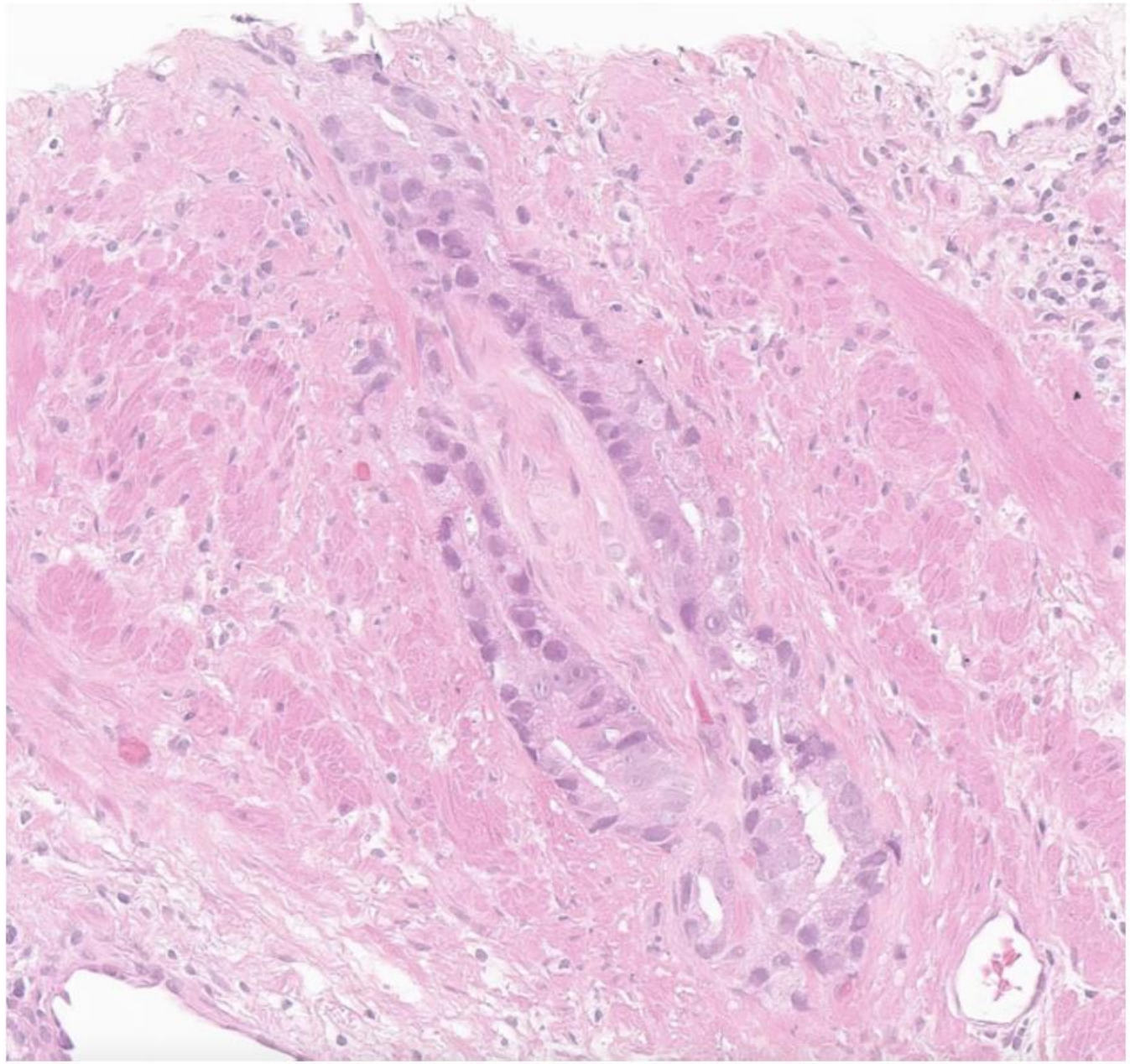
Machine learning



AI-based detection of tiny focus of breast carcinoma Impact on Patient safety



Quantitative assessment of prostate cancer for Gleason scoring



Detection	Analysis
Invasive Carcinoma	22.95 %
Invasive Carcinoma Length	3.76 mm
Pattern 3	45.15 %
Pattern 4	41.76 %
Pattern 5	13.09 %
Gleason Score	3 + 5 = 8
Perineural Invasion	

Slide courtesy of Matthew Hanna

nature cancer

ARTICLES

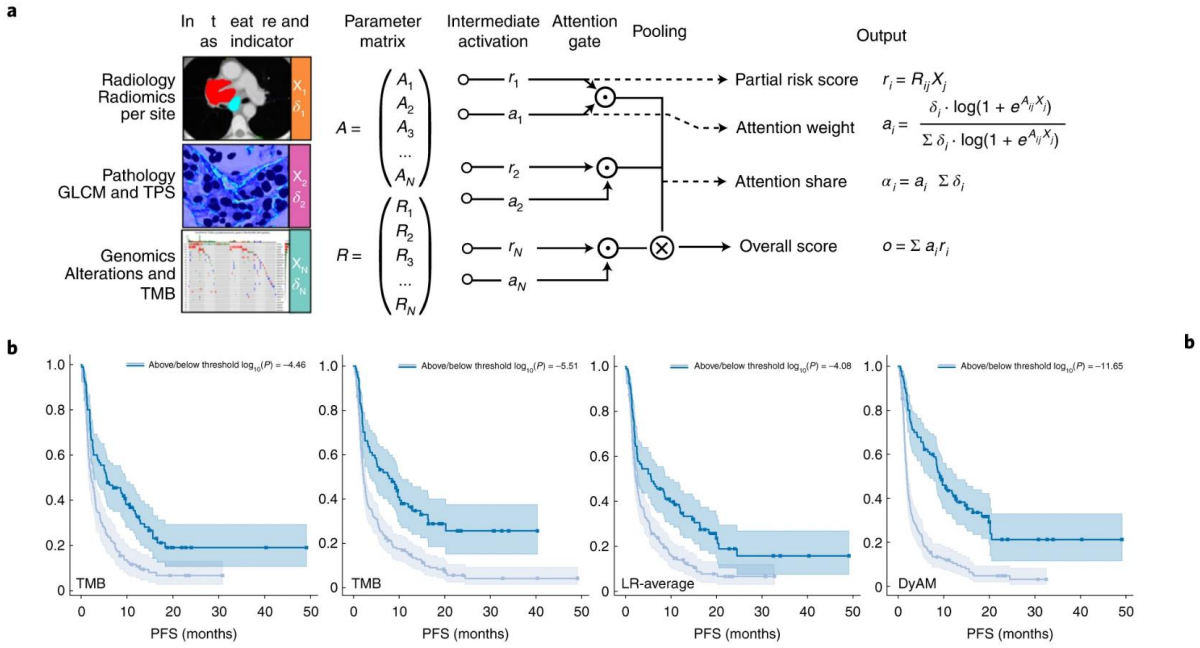
https://doi.org/10.1038/s43018-022-00388-9

Check for updates

OPEN

Multimodal data integration using machine learning improves risk stratification of high-grade serous ovarian cancer

Kevin M. Boehm[1,2], Emily A. Aherne[3], Lora Ellenson[4], Ines Nikolovski[3], Mohammed Alghamdi[4], Ignacio Vázquez-García[1,5], Dmitriy Zamarin[6,7], Kara Long Roche[8], Ying Liu[6,7], Druv Patel[1], Andrew Aukerman[1], Arfath Pasha[1], Doori Rose[1], Pier Selenica[9], Pamela I. Causa Andrieu[3], Chris Fong[1], Marinela Capanu[10], Jorge S. Reis-Filho[9], Rami Vanguri[1], Harini Veeraraghavan[11], Natalie Gangai[3], Ramon Sosa[3], Samantha Leung[1], Andrew McPherson[1], JianJiong Gao[1,12], MSK MIND Consortium*, Yulia Lakhman[3,13] ✉ and Sohrab P. Shah[1,13] ✉



nature cancer

ARTICLES

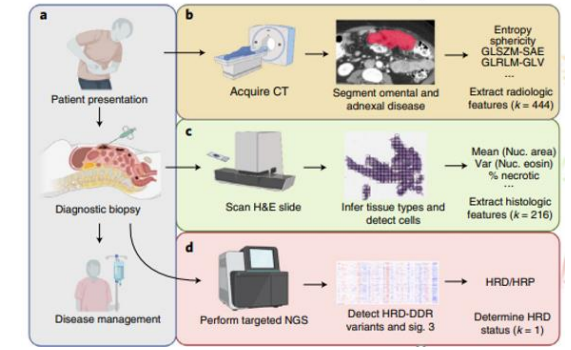
https://doi.org/10.1038/s43018-022-00416-8

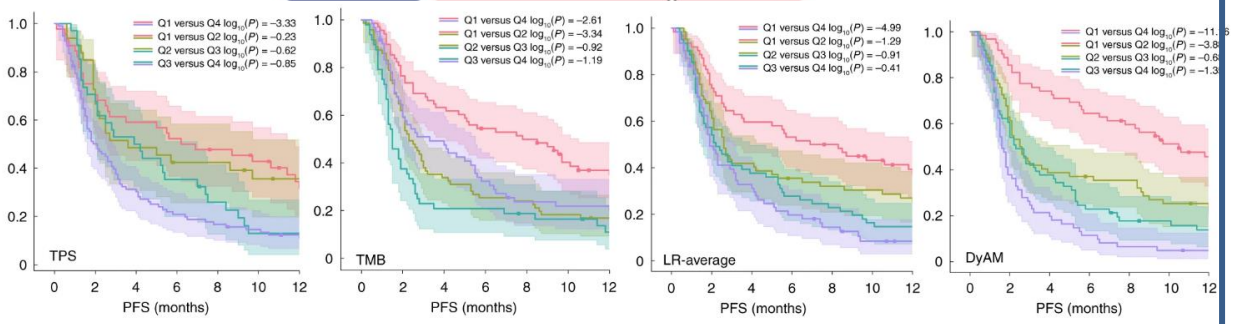
Check for updates

OPEN

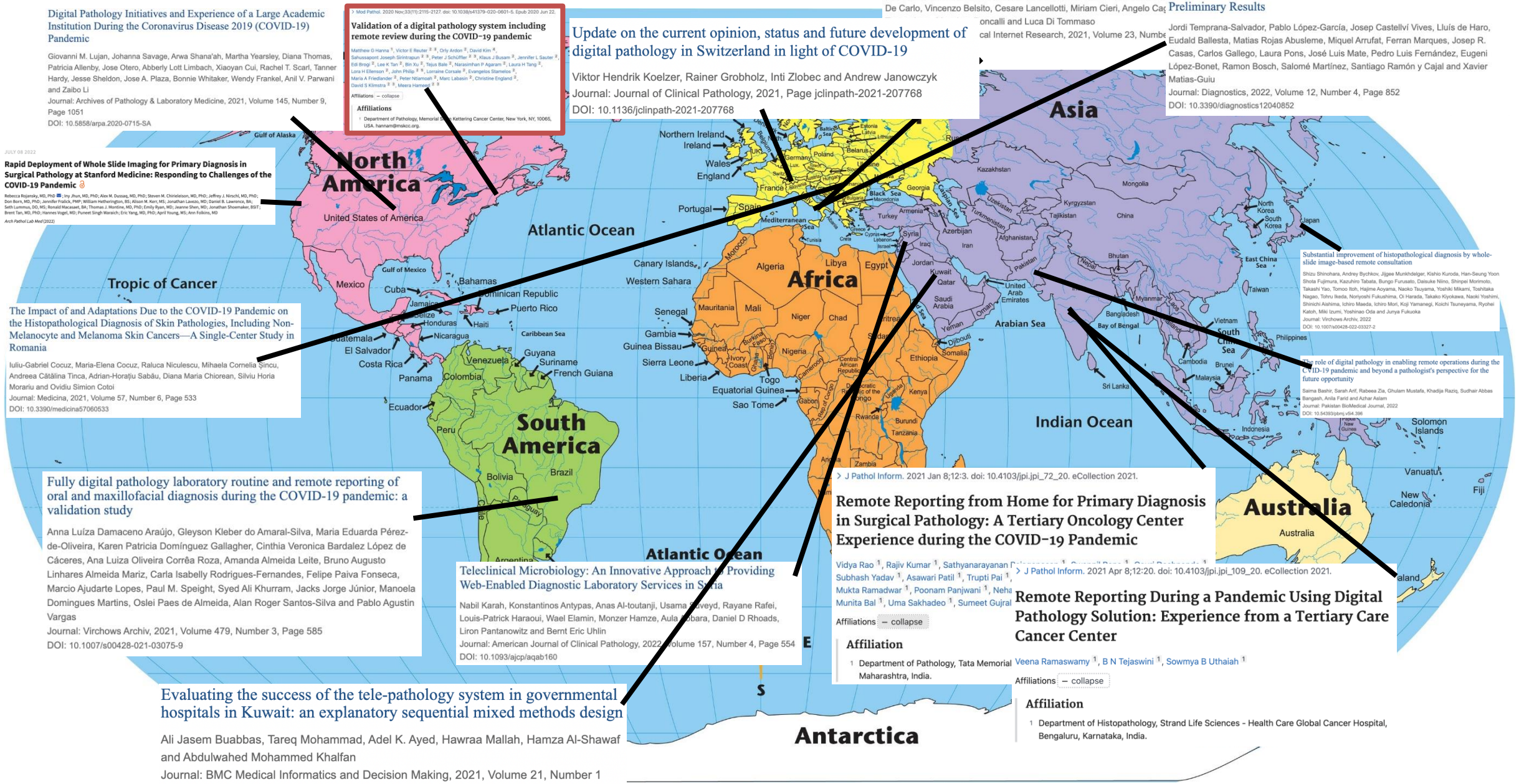
Multimodal integration of radiology, pathology and genomics for prediction of response to PD-(L)1 blockade in patients with non-small cell lung cancer

Rami S. Vanguri[1,9], Jia Luo[2,9], Andrew T. Aukerman[1,9], Jacklynn V. Egger[3,9], Christopher J. Fong[1], Natally Horvat[4], Andrew Pagano[4], Jose de Arimateia Batista Araujo-Filho[4], Luke Geneslaw[5], Hira Rizvi[2], Ramon Sosa[4], Kevin M. Boehm[1,6], Soo-Ryum Yang[5], Francis M. Bodd[5], Katia Ventura[5], Travis J. Hollmann[5,7], Michelle S. Ginsberg[4], Jianjiong Gao[1,8], MSK MIND Consortium*, Matthew D. Hellmann[2,7,10], Jennifer L. Sauter[5,10] ✉ and Sohrab P. Shah[1,10] ✉





Remote Diagnostics at Scale



Digital Pathology Initiatives and Experience of a Large Academic Institution During the Coronavirus Disease 2019 (COVID-19) Pandemic

Giovanni M. Lujan, Johanna Savage, Arwa Shana'ah, Martha Yearsley, Diana Thomas, Patricia Allenby, Jose Otero, Abberly Lott Limbach, Xiaoyan Cui, Rachel T. Scarl, Tanner Hardy, Jesse Sheldon, Jose A. Plaza, Bonnie Whitaker, Wendy Frankel, Anil V. Parwani and Zaibo Li

Journal: Archives of Pathology & Laboratory Medicine, 2021, Volume 145, Number 9, Page 1051

DOI: 10.5858/arpa.2020-0715-SA

Validation of a digital pathology system including remote review during the COVID-19 pandemic

Affiliations — collapse

Affiliations

Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, 10065, USA. hannam@mskcc.org.

Digital Pathology During the COVID-19 Outbreak in Italy: Survey Study

Simone Giaretto, Salvatore Lorenzo Renne, Daoud Rahal, Paola Bossi, Pierguiseppe Colombo, Paola Spaggiari, Sofia Manara, Mauro Sollai, Barbara Fiamer Brambilla, Bethania Fernandes, Stefania Rao, Abubaker Elamin, Marina De Carlo, Vincenzo Belsito, Cesare Lancellotti, Miriam Cieri, Angelo Cag oncalli and Luca Di Tommaso

cal Internet Research, 2021, Volume 23, Numbe

DigiPatICS: Digital Pathology Transformation of the Catalan Health Institute Network of 8 Hospitals—Planification, Implementation, and Preliminary Results

Jordi Temprana-Salvador, Pablo López-García, Josep Castellví Vives, Lluís de Haro, Eudald Ballesta, Matias Rojas Abusleme, Miquel Arrufat, Ferran Marques, Josep R. Casas, Carlos Gallego, Laura Pons, José Luis Mate, Pedro Luis Fernández, Eugeni López-Bonet, Ramon Bosch, Salomé Martínez, Santiago Ramón y Cajal and Xavier Matias-Guiu

Journal: Diagnostics, 2022, Volume 12, Number 4, Page 852

DOI: 10.3390/diagnostics12040852

Update on the current opinion, status and future development of digital pathology in Switzerland in light of COVID-19

Viktor Hendrik Koelzer, Rainer Grobholz, Inti Zlobec and Andrew Janowczyk

Journal: Journal of Clinical Pathology, 2021, Page jclinpath-2021-207768

DOI: 10.1136/jclinpath-2021-207768

JULY 08 2022

Rapid Deployment of Whole Slide Imaging for Primary Diagnosis in Surgical Pathology at Stanford Medicine: Responding to Challenges of the COVID-19 Pandemic

Arch Pathol Lab Med (2022)

The Impact of and Adaptations Due to the COVID-19 Pandemic on the Histopathological Diagnosis of Skin Pathologies, Including Non-Melanocyte and Melanoma Skin Cancers—A Single-Center Study in Romania

Iuliu-Gabriel Cocuz, Maria-Elena Cocuz, Raluca Niculescu, Mihaela Cornelia Sincu, Andreea Cătălina Tinca, Adrian-Horaţiu Sabău, Diana Maria Chiorean, Silviu Horia Morariu and Ovidiu Simion Cotoi

Journal: Medicina, 2021, Volume 57, Number 6, Page 533

DOI: 10.3390/medicina57060533

Substantial improvement of histopathological diagnosis by whole-slide image-based remote consultation

Shizu Shinohara, Andrey Bychkov, Jijgee Munkhdelger, Kishio Kuroda, Han-Seung Yoon Shota Fujimura, Kazuhiro Tabata, Bungo Furusato, Daisuke Niino, Shinpei Morimoto, Takashi Yao, Tomoo Itoh, Hajime Aoyama, Naoko Tsuyama, Yoshiki Mikami, Toshitaka Nagao, Tohru Ikeda, Noriyoshi Fukushima, Oi Harada, Takako Kiyokawa, Naoki Yoshimi, Shinichi Aishima, Ichiro Maeda, Ichiro Mori, Koji Yamanegi, Koichi Tsuneyama, Ryohei Katoh, Miki Izumi, Yoshinao Oda and Junya Fukuoka

Journal: Virchows Archiv, 2022

DOI: 10.1007/s00428-022-03327-2

The role of digital pathology in enabling remote operations during the COVID-19 pandemic and beyond a pathologist's perspective for the future opportunity

Saima Bashir, Sarah Arif, Rabeea Zia, Ghulam Mustafa, Khadija Raziq, Sudhair Abbas Bangash, Anila Farid and Azhar Aslam

Journal: Pakistan BioMedical Journal, 2022

DOI: 10.54393/pbmj.v5i4.396

Fully digital pathology laboratory routine and remote reporting of oral and maxillofacial diagnosis during the COVID-19 pandemic: a validation study

Anna Luíza Damaceno Araújo, Gleyson Kleber do Amaral-Silva, Maria Eduarda Pérez-de-Oliveira, Karen Patricia Domínguez Gallagher, Cinthia Veronica Bardalez López de Cáceres, Ana Luiza Oliveira Corrêa Roza, Amanda Almeida Leite, Bruno Augusto Linhares Almeida Mariz, Carla Isabelly Rodrigues-Fernandes, Felipe Paiva Fonseca, Marcio Ajudarte Lopes, Paul M. Speight, Syed Ali Khurram, Jacks Jorge Júnior, Manoela Domingues Martins, Oslei Paes de Almeida, Alan Roger Santos-Silva and Pablo Agustin Vargas

Journal: Virchows Archiv, 2021, Volume 479, Number 3, Page 585

DOI: 10.1007/s00428-021-03075-9

Teleclinical Microbiology: An Innovative Approach to Providing Web-Enabled Diagnostic Laboratory Services in Syria

Nabil Karah, Konstantinos Antypas, Anas Al-toutanji, Usama Dabbagh, Rayane Rafei, Louis-Patrick Haraoui, Wael Elamin, Monzer Hamze, Aula Abbara, Daniel D Rhoads, Liron Pantanowitz and Bernt Eric Uhlin

Journal: American Journal of Clinical Pathology, 2022, Volume 157, Number 4, Page 554

DOI: 10.1093/ajcp/aqab160

J Pathol Inform. 2021 Jan 8;12:3. doi: 10.4103/jpi.jpi_72_20. eCollection 2021.

Remote Reporting from Home for Primary Diagnosis in Surgical Pathology: A Tertiary Oncology Center Experience during the COVID-19 Pandemic

Vidya Rao [1], Rajiv Kumar [1], Sathyanarayanan [illegible], Subhash Yadav [1], Asawari Patil [1], Trupti Pai [1], Mukta Ramadwar [1], Poonam Panjwani [1], Neha Munita Bal [1], Uma Sakhadeo [1], Sumeet Gujral

Affiliations — collapse

Affiliation

1 Department of Pathology, Tata Memorial Maharashtra, India.

J Pathol Inform. 2021 Apr 8;12:20. doi: 10.4103/jpi.jpi_109_20. eCollection 2021.

Remote Reporting During a Pandemic Using Digital Pathology Solution: Experience from a Tertiary Care Cancer Center

Veena Ramaswamy [1], B N Tejaswini [1], Sowmya B Uthaiah [1]

Affiliations — collapse

Affiliation

1 Department of Histopathology, Strand Life Sciences - Health Care Global Cancer Hospital, Bengaluru, Karnataka, India.

Evaluating the success of the tele-pathology system in governmental hospitals in Kuwait: an explanatory sequential mixed methods design

Ali Jasem Buabbas, Tareq Mohammad, Adel K. Ayed, Hawraa Mallah, Hamza Al-Shawaf and Abdulwahed Mohammed Khalfan

Journal: BMC Medical Informatics and Decision Making, 2021, Volume 21, Number 1

DOI: 10.1186/s12911-021-01567-x

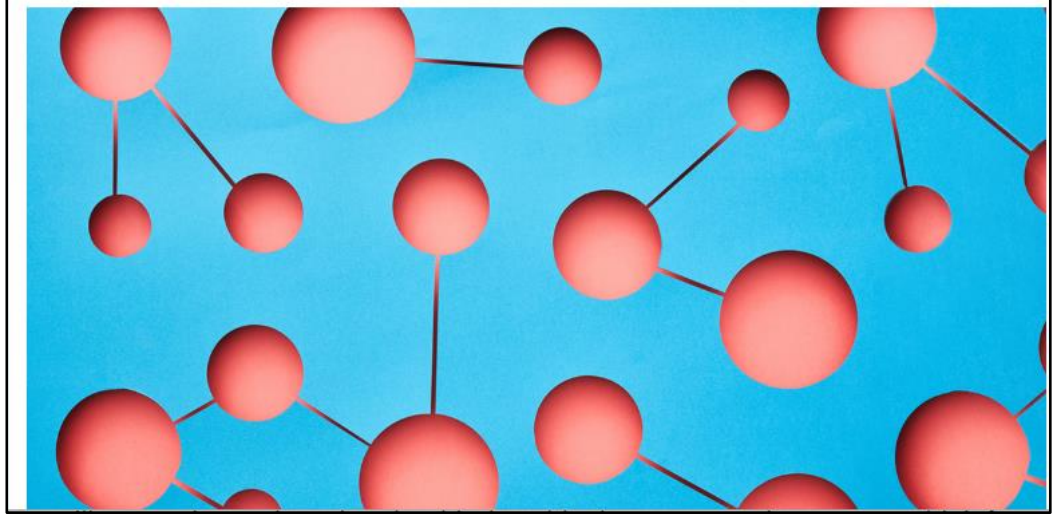
Artificial intelligence is not infallible intelligence

Analytics And Data Science

Why AI Failed to Live Up to Its Potential During the Pandemic

by Bhaskar Chakravorti

March 17, 2022

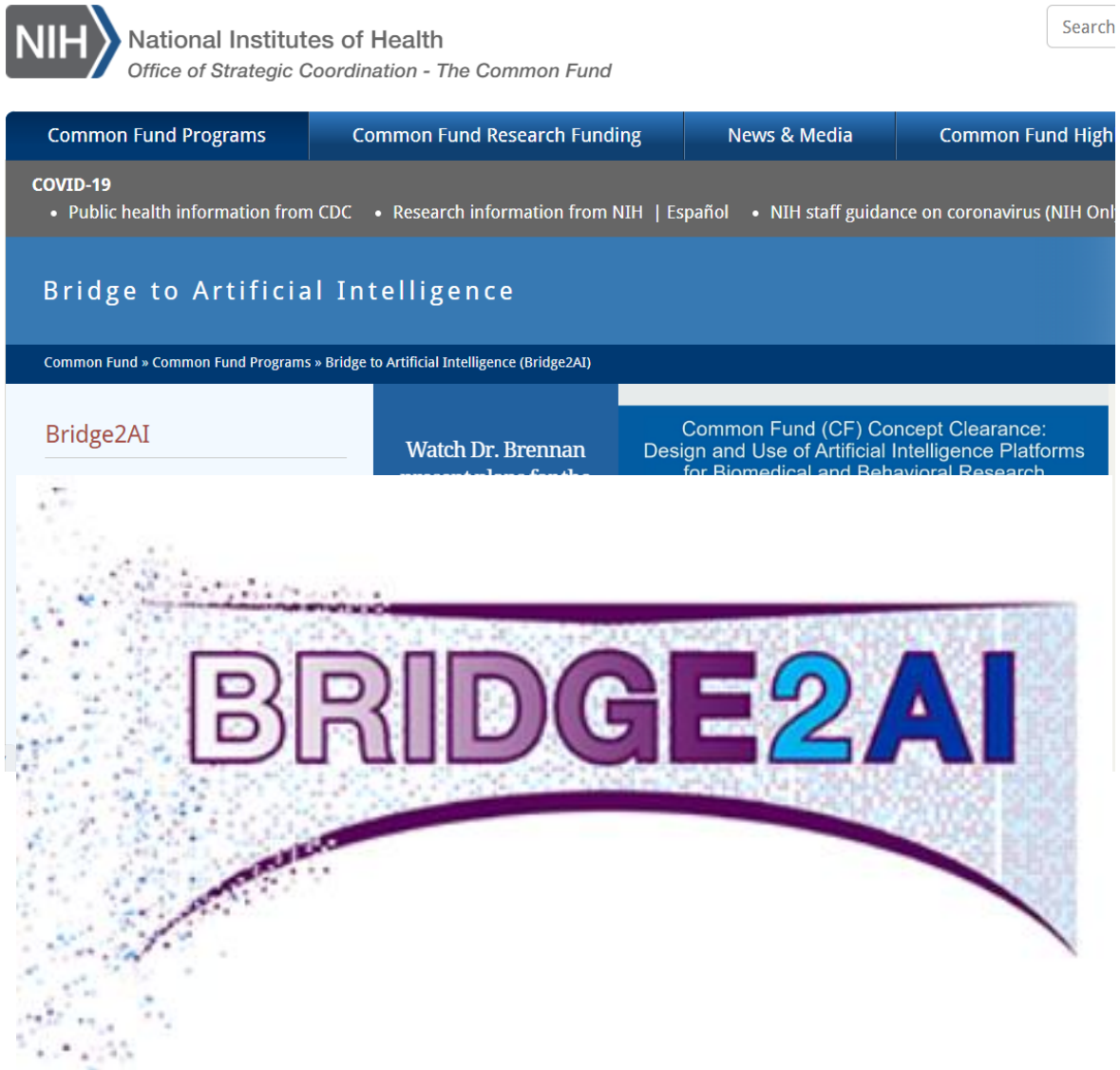


- **The Danger of Bad Datasets**
- **Automated Discrimination**
- **Human Error**
- **Complex and Uneven Global Context**

How to get it right

- **Find better ways to assemble comprehensive datasets and merge data from multiple sources.**
- **There needs to be a diversity of data sources.**
- **Incentives must be aligned to ensure greater cooperation across teams and systems.**
- **Write international rules for data sharing.**

The NIH Common Fund's Bridge to Artificial Intelligence (Bridge2AI) program



- **Propel biomedical research**
- Tackles complex biomedical challenges **beyond human intuition**
- Generating new "flagship" data sets and **best practices**
- FAIR (**F**indable, **A**ccessible, **I**nteroperable, and **R**eusable)
- **E**thically sourced data sets

Predicting the Future — Big Data, Machine Learning, and Clinical Medicine

Ziad Obermeyer, M.D., and Ezekiel J. Emanuel, M.D., Ph.D.

N ENGL J MED 375;13 NEJM.ORG SEPTEMBER 29, 2016

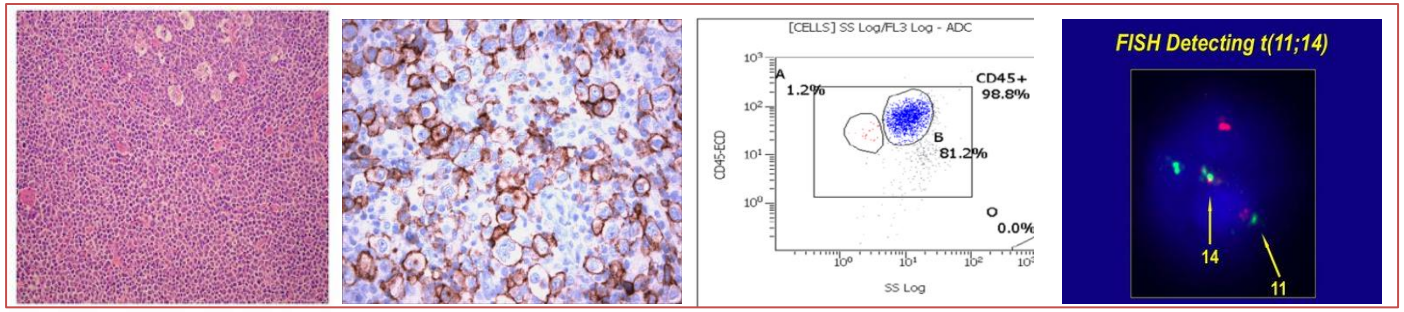
The New England Journal of Medicine

"Machine learning has become ubiquitous and indispensable for solving complex problems in most sciences. The same methods will open up vast new possibilities in medicine……..

As patients' conditions and medical technologies become more complex, the role of machine learning will grow, and clinical medicine will be challenged to grow with it.

As in other industries, this challenge will create winners and losers in medicine. But we are **optimistic that patients**, whose lives and medical histories shape the algorithms, **will emerge as the biggest winners** as machine learning transforms clinical medicine."

Fundamental patient-driven goals for integrated diagnostics



1) What disease does the patient have? (diagnosis)

2) How much of the disease is there? (residual disease)

3) Who needs treatment? (prognosis)

4) What is the best treatment for this patient? (therapy)

5) What dose? (pharmacogenomics, dynamics)

6) Precision diagnostics scaled at population level for impact at individual level

Acknowledgements

MSKCC

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