Plcc Alliance

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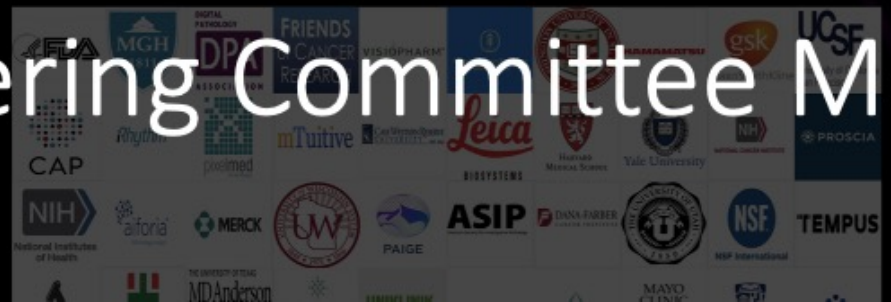
Join

Pathology Innovation Collaborative Community

Plcc

The Alliance for Digital Pathology

A collaborative community with FDA participation



Steering Committee Meeting

October 2022

Aubrey Walker
PIcc Project Manager

- B.S. in Hospitality and Business Management
- Previous experience from the Hospitality and Tourism Industry, I changed career paths during the COVID-19 Pandemic
- You can reach me at digipathalliance@gmail.com
- Fun Fact: I love to travel; I have been to 43 of the 50 States! (And 7 Countries!)

Looking forward to positively contributing to the Alliance as it works towards its aim of coming together to transform the field of digital pathology.

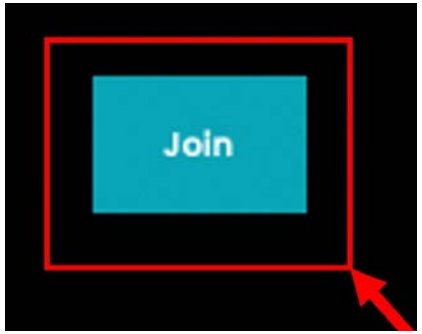
Project Management PIcc

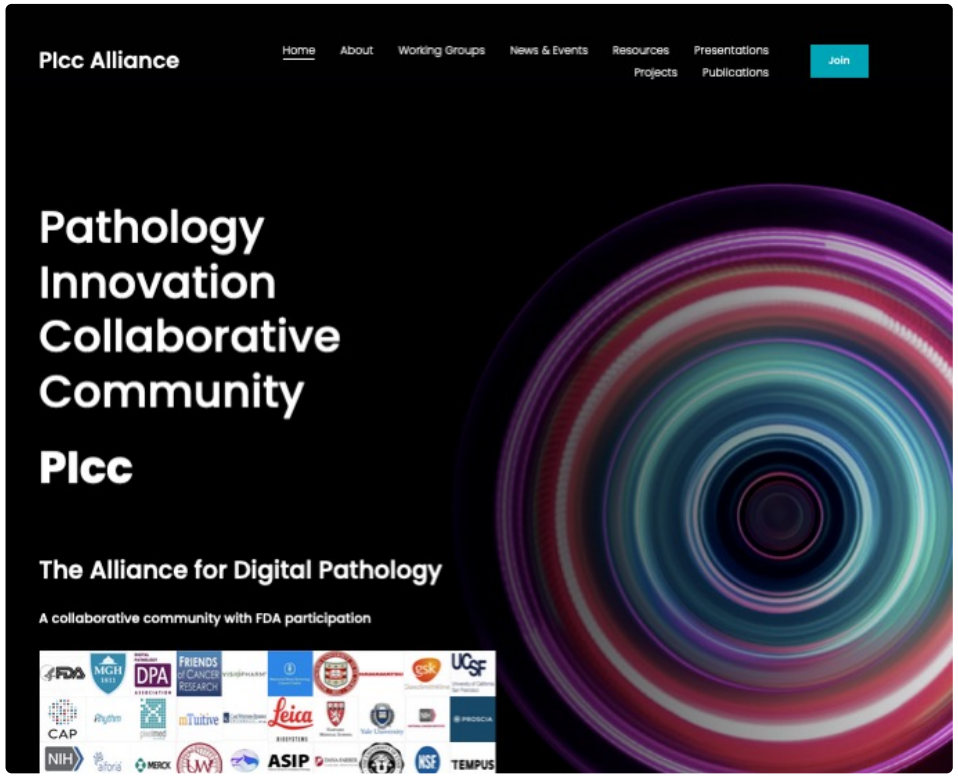
Ula Green, BS
PIcc Project manager

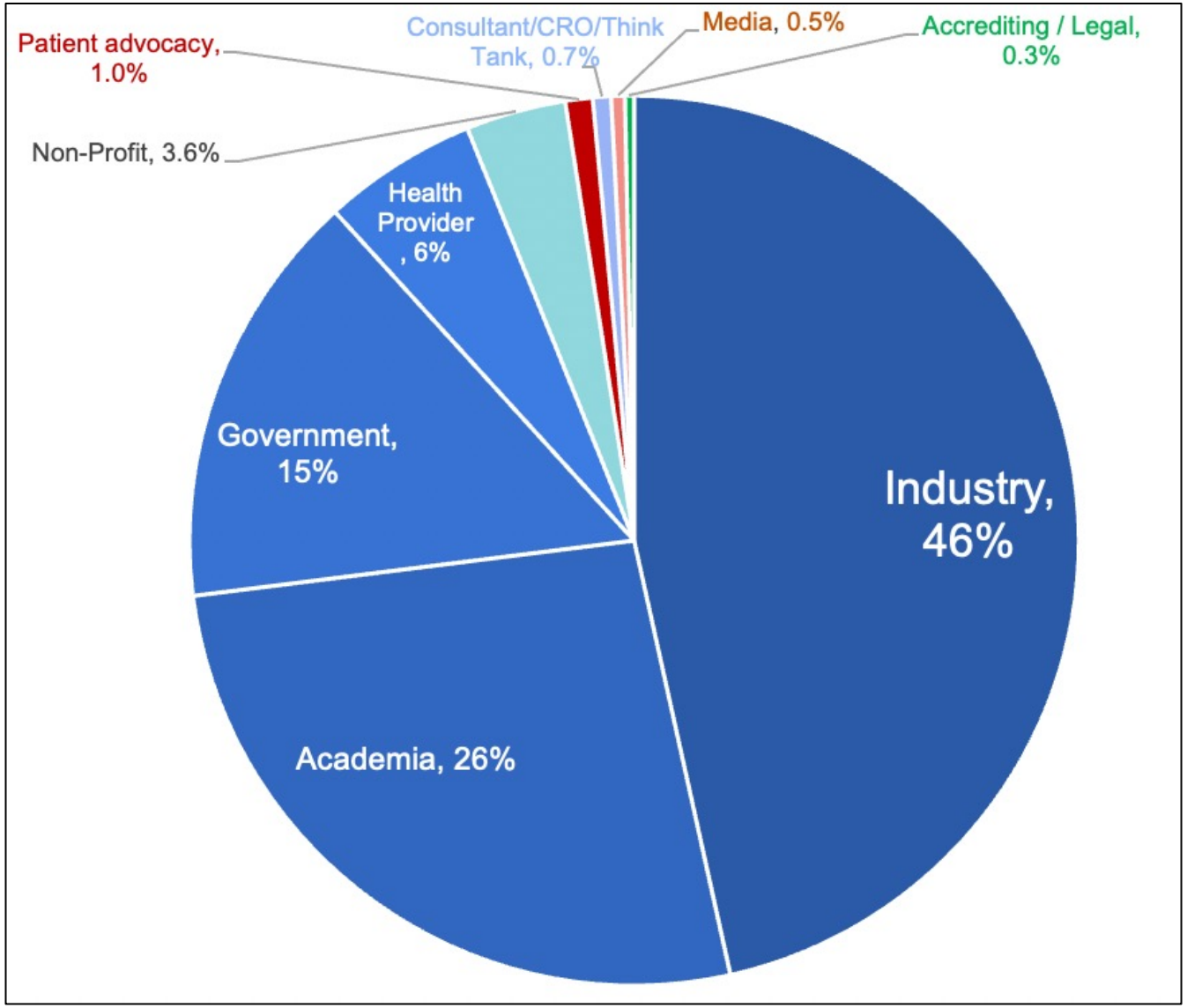
Noor Falah, MS
MDIC, PIcc Project manager

Aubrey Walker, BS
PIcc Project manager

October 25th, 2022
N=647 members







FDA

FDA Superoffice: Office of Therapeutic Products (OTP)

Statement of Organization, Functions, and Delegations of Authority

A Notice by the Food and Drug Administration on 09/28/2022

PUBLISHED DOCUMENT

AGENCY:

Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION:

Notice.

SUMMARY:

The Food and Drug Administration's (FDA), Center for Biologics Evaluation and Research (CBER), Office of Tissues and Advanced Therapies (OTAT) has modified its organizational structures.

DOCUMENT DETAILS

Printed version: PDF

Publication Date: 09/28/2022

Agencies: Food and Drug Administration

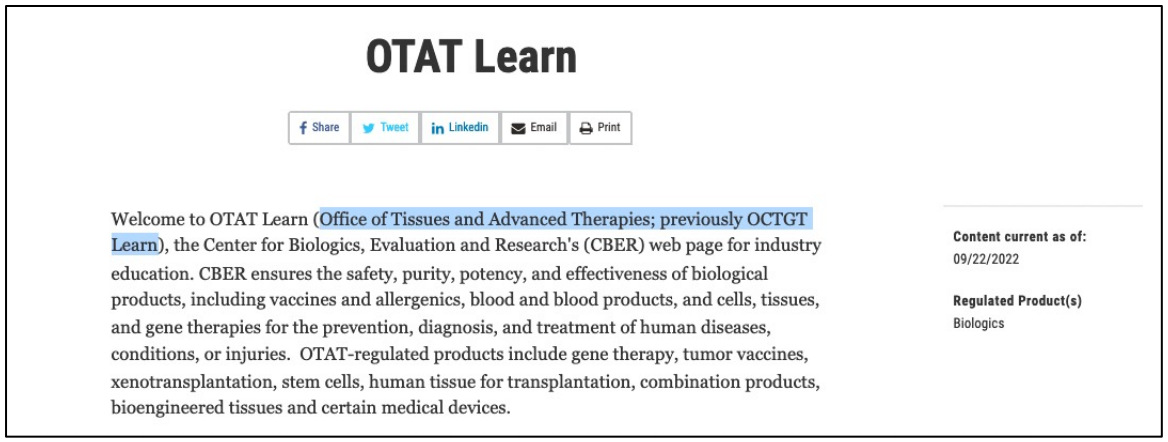
Dates: These new organizational structures were approved by the Secretary of Health and Human Services on August 8, 2022, and effective on September 16, 2022.

Effective Date: 09/16/2022

CBER's OTAT has been renamed the Office of Therapeutic Products (OTP) and is part of the FDA's commitments negotiated with industry under the Prescription Drug User Fee Act (PDUFA) VII agreement for fiscal years 2023-2027.

A report published last week by the Alliance for Regenerative Medicine (ARM) on the state of the cell and gene therapy industry noted that the upcoming reauthorization of PDUFA by the U.S. Congress "will provide vital funding for new personnel and programs to support FDA review of the coming wave of new therapies."

CTP/OTP => not center for tobacco products
OTP (CMS) => also not Opioid Treatment Program



OTAT Learn

Share Tweet Linkedin Email Print

Welcome to OTAT Learn (Office of Tissues and Advanced Therapies; previously OCTGT Learn), the Center for Biologics, Evaluation and Research's (CBER) web page for industry education. CBER ensures the safety, purity, potency, and effectiveness of biological products, including vaccines and allergenics, blood and blood products, and cells, tissues, and gene therapies for the prevention, diagnosis, and treatment of human diseases, conditions, or injuries. OTAT-regulated products include gene therapy, tumor vaccines, xenotransplantation, stem cells, human tissue for transplantation, combination products, bioengineered tissues and certain medical devices.

Content current as of: 09/22/2022

Regulated Product(s) Biologics

Interactions with Office of Tissues and Advanced Therapies

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The Office of Tissues and Advanced Therapies, known as OTAT, is one of three product offices within CBER responsible for regulatory oversight of biological products. OTAT's mission is to promote public health through a data-driven process to provide regulatory oversight that helps ensure medical products are safe and effective. In doing so, OTAT strives to lead all regulatory decisions with data, impartiality, and compassion.

OTAT oversees development for a wide variety of products including purified and recombinant proteins for hematology, antivenins, gene therapies, cell therapies, therapeutic tissue engineered products, human tissue products, therapeutic vaccines and other antigen-specific active immunotherapies, certain devices, and xenotransplantation products. Xenotransplantation is any procedure that involves the transplantation, implantation, or infusion of cells, tissues, or organs from a nonhuman animal source into a human recipient.

Content current as of: 06/23/2022

Regulated Product(s) Biologics

TPLC Advisory Program (PILOT)

CDRH Launches the Total Product Life Cycle Advisory Program Pilot

Program Intended to Speed Access to High Quality, Safe, Effective, and Innovative Medical Devices

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Content current as of: 10/11/2022

Regulated Product(s) Medical Devices

The following is attributed to Jeff Shuren, M.D., J.D., director of the FDA's Center for Devices and Radiological Health

Today, the FDA's Center for Devices and Radiological Health (CDRH) announced it is launching the Total Product Life Cycle (TPLC) Advisory Program (TAP) Pilot. TAP is a voluntary program intended to de-risk the medical device valley of death by providing industry with earlier and more frequent interactions with CDRH, more strategic input from stakeholders, and proactive, strategic advice from CDRH to spur more rapid development of high-quality, safe, effective, and innovative medical devices first in the world that are critical to public health.

The TAP Pilot is a new component of the Medical Device User Fee Amendment (MDUFA) V Agreement, which was signed into law on September 30, 2022, and reauthorized for five years. A key goal of the TAP Pilot is to improve various aspects of medical device

Medical Devices; Voluntary Total Product Life Cycle Advisory Program Pilot

A Notice by the Food and Drug Administration on 10/12/2022

This document has a comment period that ends in 76 days. (01/10/2023) SUBMIT A FORMAL COMMENT

PUBLISHED DOCUMENT

AGENCY:

Food and Drug Administration, HHS.

ACTION:

Notice; request for comments.

SUMMARY:

The Food and Drug Administration's (FDA, Agency, or we) Center for Devices and Radiological Health (CDRH or Center) is announcing its voluntary Total Product Life Cycle (TPLC) Advisory Program (TAP) Pilot that will begin in fiscal year (FY) 2023 with the initial phase, hereafter referred to as the TAP Pilot Soft Launch. The TAP Pilot is one of the commitments agreed to between FDA and industry as part of the reauthorization of the Medical Device User Fee Amendments for FY 2023 through FY 2027 (MDUFA V). The long-term vision for TAP is to help spur more rapid development and more rapid and widespread patient access to safe, effective, high-quality medical devices of public health importance. Over the course of MDUFA V, the voluntary TAP Pilot is intended to

DOCUMENT DETAILS

Printed version: PDF

Publication Date: 10/12/2022

Agencies: Food and Drug Administration

Dates: Beginning January 1, 2023, FDA is seeking requests for enrollment in the TAP Pilot Soft Launch for FY 2023. Either electronic or written comments on this notice must be submitted by January 10, 2023 to ensure that the Agency considers your comment on this notice before it begins work on the next phase of the TAP Pilot.

Comments Close: 01/10/2023

Document Type:

First-Ever FDA 510(k) Clearance of an AP control

Boston Cell Standards Wins First-Ever FDA 510(k) Clearance for Anatomic Pathology Controls

FDA clearance introduces first immunohistochemistry IHControls panel for evaluating breast cancers

October 06, 2022 07:00 AM Eastern Daylight Time

BOSTON--(BUSINESS WIRE)--Boston Cell Standards, a company standardizing cancer diagnostic tissue testing with the first immunohistochemistry (IHC) laboratory reference standards, today announced it received 510(k) clearance from the U.S. Food & Drug Administration for its IHControls® panel (HER2/ER/PR) for evaluating breast cancers. This clearance represents a first-in-category regulatory approval.

"IHControls represent a giant step forward in standardization in the anatomic pathology lab, especially in detecting low estrogen receptor-expressing tumors"

Tweet this

IHControls are the first truly quantitative linear range controls for IHC labs. This panel provides anatomic pathologists a reproducible, cost-effective solution for on-slide quality control, to safeguard against the potential for incorrect results and increase physician confidence in making diagnoses and selecting treatments.

"IHControls represent a giant step forward in standardization in the anatomic pathology lab, especially in detecting low estrogen receptor-expressing tumors," said Dr. Matthias Szabolcs, Director, Immunohistochemistry Laboratory, at Columbia University Medical Center/New York-Presbyterian Hospital. "Today, we can establish which patients will not benefit from an immunotherapy, but not how well they will respond to another treatment. IHControls may give anatomic pathologists the ability to increase positive predictive value, allowing us to determine which patients will benefit, and by how much."

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K220163

Device Name
Her2/ER/PR IHControls® - Level H
Her2/ER/PR IHControls® - Level M
Her2/ER/PR IHControls® - Level L

Indications for Use *(Describe)*

HER2/ER/PR IHControls® -Level H
HER2/ER/PR IHControls® -Level H are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples.

HER2/ER/PR IHControls® -Level H are not intended to be used for scoring HER2, ER, and PR IHC stained slides.

HER2/ER/PR IHControls® -Level H are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.

HER2/ER/PR IHControls® -Level M
HER2/ER/PR IHControls® -Level M are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples.

HER2/ER/PR IHControls® -Level M are not intended to be used for scoring HER2, ER, and PR IHC stained slides.

HER2/ER/PR IHControls® -Level M are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.

HER2/ER/PR IHControls® -Level L
HER2/ER/PR IHControls® -Level L are peptide based qualitative on-slide controls to monitor the performance of the analytic components (antigen retrieval and immunostaining) of the immunohistochemical (IHC) staining process for certain human epidermal growth factor receptor type II (HER2), estrogen receptor (ER) and progesterone receptor (PR) IHC stains. It is indicated for use with formalin-fixed paraffin-embedded (FFPE) breast tumor samples.

HER2/ER/PR IHControls® -Level L are not intended to be used for scoring HER2, ER, and PR IHC stained slides.

HER2/ER/PR IHControls® -Level L are an additional control to the run controls specified in the HER2, ER, or PR IHC device labeling and are not intended to replace the controls approved or cleared as part of an IHC device.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

[1] Bogen S. A root cause analysis into the high error rate for clinical immunohistochemistry. Appl Immunohistochem Mol Morphol 27, 329-338 (2019)
[2] SR Sompuram, et. al. Quantitative assessment of immunohistochemistry laboratory performance by measuring analytic response curves and limits of detection. Arch. Pathol. Lab. Med. 2018 142(7):851-862.
[3] K Vani, et. al. The importance of epitope density in selecting a sensitive positive IHC control. .J. Histochem. Cytochem. 2017 65(8):463-477.
[4] SR Sompuram, et. al. Selecting an optimal positive IHC control for verifying antigen retrieval. J. Histochem. Cytochem. 2019 67(4):275-289.

First-Ever FDA 510(k) Clearance of an AP control

Table 1. HER2/ER/PR IHControls® Immunoreactivity: Levels H, M, and L

Level H (BRLS11)	Level M (BRL2U04)	Level L (BRL2W08)
HER2 CB11	HER2 CB11	HER2 CB11
HER2 4B5	HER2 4B5	HER2 4B5
HercepTest	HercepTest	HercepTest
PR 636	PR 636	PR 636
PR 16	PR 16	PR 16
ER EP1	ER EP1	ER EP1
	ER 1D5/2.123	ER 1D5/2.123
	ER 6F11	ER 6F11
	PR 1294	PR 1294
	PR 1E2	PR 1E2
	ER SP1	ER SP1

Table 3. Specificity Testing - List of Primary Antibodies, Targets, and Test Results

	Marker	Organ	Antibody	Tissue Control	IHControls®
1.	Bcl-6	Tonsil	GI191E/A8	Positive	Negative
2.	C4d	Tonsil	SP91	Positive	Negative
3.	CD10	Tonsil	SP67	Positive	Negative
4.	CD138	Tonsil	B-A38	Positive	Negative
5.	CD20	Tonsil	L26	Positive	Negative
6.	CD34	Tonsil	QBEnd/10	Positive	Negative
7.	CD5	Tonsil	SP19	Positive	Negative
8.	CD56	Tonsil	MRQ-42	Positive	Negative
9.	CMV	Placenta	CMV	Positive	Negative
10.	Cyclin D1	Lymphoma	SP4-R	Positive	Negative
11.	Cytokeratin 20	Colon	SP33	Positive	Negative
12.	Cytokeratin 7	Lung	SP52	Positive	Negative
13.	EFGR	Normal Skin	5B7	Positive	Negative
14.	Keratin	Skin	34BE12	Positive	Negative
15.	Ki-67	Tonsil	30-9	Positive	Negative
16.	Mart-1	Melanoma	A103	Positive	Negative
17.	MITF	Melanoma	C5/D5	Positive	Negative
18.	p53	p53	BP53-11	Positive	Negative
19.	p63	Prostate	4A4	Positive	Negative
20.	Pan Keratin	Appendix	AE1/AE3/PCK26	Positive	Negative
21.	Podoplanin	Tonsil	D2-40	Positive	Negative
22.	PSA	Prostate	PSA	Positive	Negative
23.	S100	S100	4C4.9	Positive	Negative
24.	Somatostatin	Pancreas	Somatostatin	Positive	Negative
25.	TAG 72	Colon	B72.3	Positive	Negative
26.	TTF-1	Thyroid	8G7G3/1	Positive	Negative
27.	Breast	Breast ca	ER SP1	Positive	Positive
28.	Breast	Breast ca	HER2 4B5	Positive	Positive
29.	Breast	Breast ca	PR 1E2	Positive	Positive

5.8.2 Shelf Life

The shelf life for each HER2/ER/PR IHControl® level, when stored at 2 – 8° C, was tested in real time over approximately 2 years. **Table 4** summarizes product shelf life.

Table 4. Product Shelf-Life

Product	Shelf Life (days)
Level H (BRLS11)	392
Level M (BRL2U04)	392
Level L (BRL2W08)	392

Tissue Agnostic Drug Dev.

GUIDANCE DOCUMENT

Tissue Agnostic Drug Development in Oncology

Draft Guidance for Industry

OCTOBER 2022

Download the Draft Guidance Document | Read the Federal Register Notice

Draft | Level 1 Guidance

Not for implementation. Contains non-binding recommendations.

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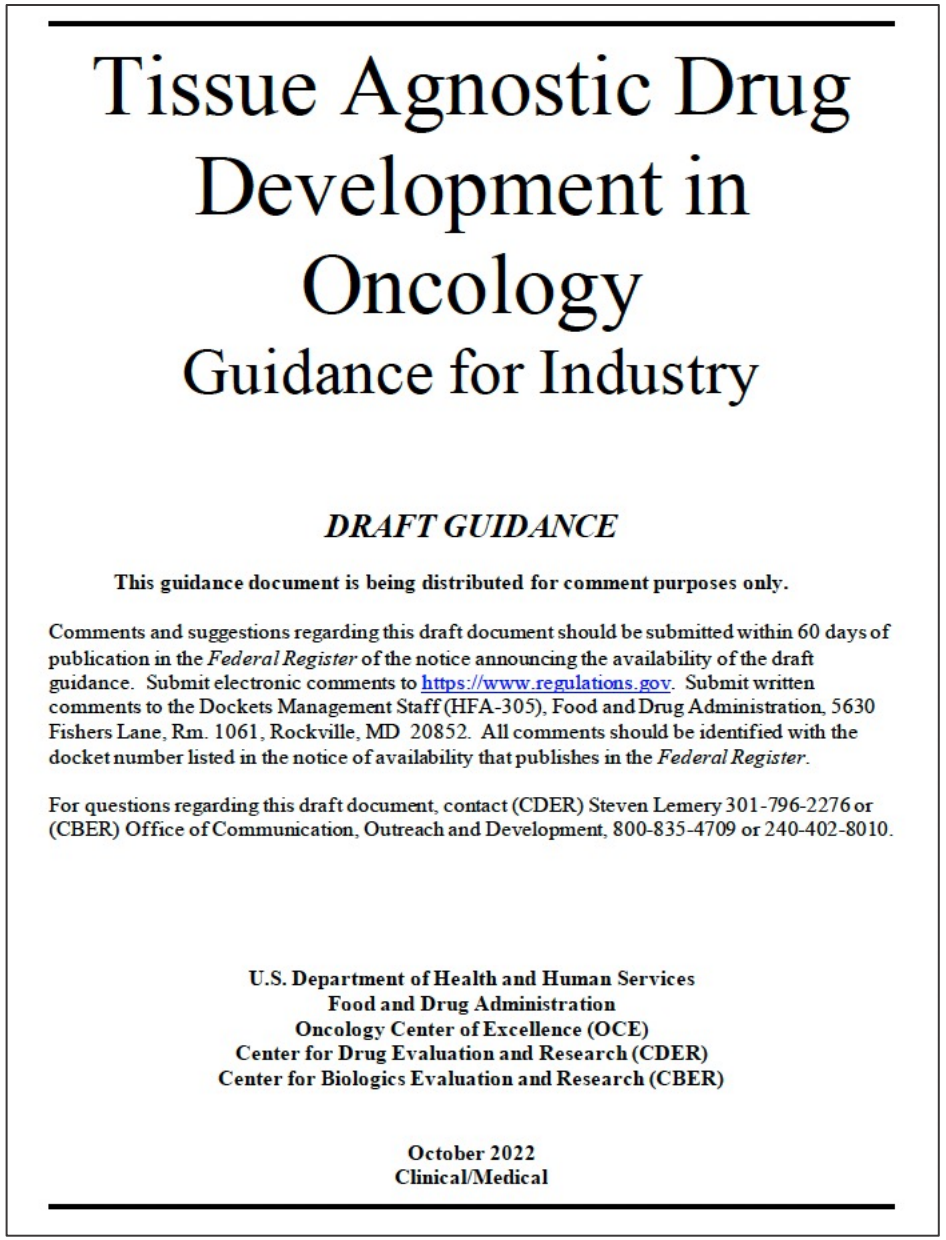
Docket Number: FDA-2022-D-0286

Issued by: Oncology Center of Excellence
Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research

Content current as of: 10/17/2022

Regulated Product(s)
Biologics
Drugs

This guidance provides recommendations to sponsors regarding considerations for tissue agnostic drug development in oncology. For the purpose of this guidance, the term tissue agnostic oncology drug refers to a drug that targets a specific molecular alteration(s) (a kind of biomarker) across multiple cancer types as defined, for example by organ, tissue, or tumor type. A tissue agnostic oncology drug can therefore be used to treat multiple types of cancer (e.g., colorectal, thyroid, and breast cancers) with the targeted molecular alteration (e.g., either the same targeted molecular alteration or targeted molecular alterations affecting a single pathway). Although applications for a tissue agnostic oncology drug are reviewed for safety and effectiveness under the same legal and regulatory standard as drugs indicated for a tissue specific cancer, the development of a tissue agnostic oncology drug raises issues that generally do not arise in more traditional development approaches. This guidance describes the development of tissue agnostic drugs, scientific considerations in determining when tissue agnostic oncology drug development may be appropriate, and, if appropriate, issues to be addressed during such development.



Tissue Agnostic Drug Development in Oncology

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Steven Lemery 301-796-2276 or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2022
Clinical/Medical

A. Biology

A robust understanding of the biology (e.g., molecular pathophysiology of the cancer, molecular alteration(s), drug's mechanism of action, and response to the drug) across cancer types is essential, because it will form the basis for the scientific rationale for tissue agnostic development of a specific drug and may provide support for a conclusion that the drug's effect across cancer types would be expected to be similar. Nonclinical models and existing scientific data may provide support for a drug's mechanism of action in different cancer types.[10] See section IV.A, Nonclinical Assessment, for additional information.

Sponsors should have an appropriate understanding of the molecular alteration(s), such as an understanding of the pathophysiology of the molecular alteration across cancers, including how the molecular alteration influences the natural history of the underlying cancers. In some cases,

G. Diagnostic Considerations

Tissue agnostic indications are identified by a molecular alteration that can range from simple genetic alterations such as single nucleotide changes, amplifications or fusions, or complex phenotypic alterations such as microsatellite instability or tumor mutation burden that occur broadly across cancers but infrequently in many cancer types. The identification of molecular alteration-defined populations is dependent on the availability of accurate and reliable diagnostic tests that can identify patients irrespective of cancer type. When accurate testing for molecular alterations is essential for the safe and effective use of the drug, an FDA-cleared or -approved companion diagnostic for this intended use should be commercially available at the time of drug approval to identify patients in the health care setting.

There are unique challenges regarding the development of a companion diagnostic in the tissue agnostic oncology drug setting, for example, variability in specimen collection and handling

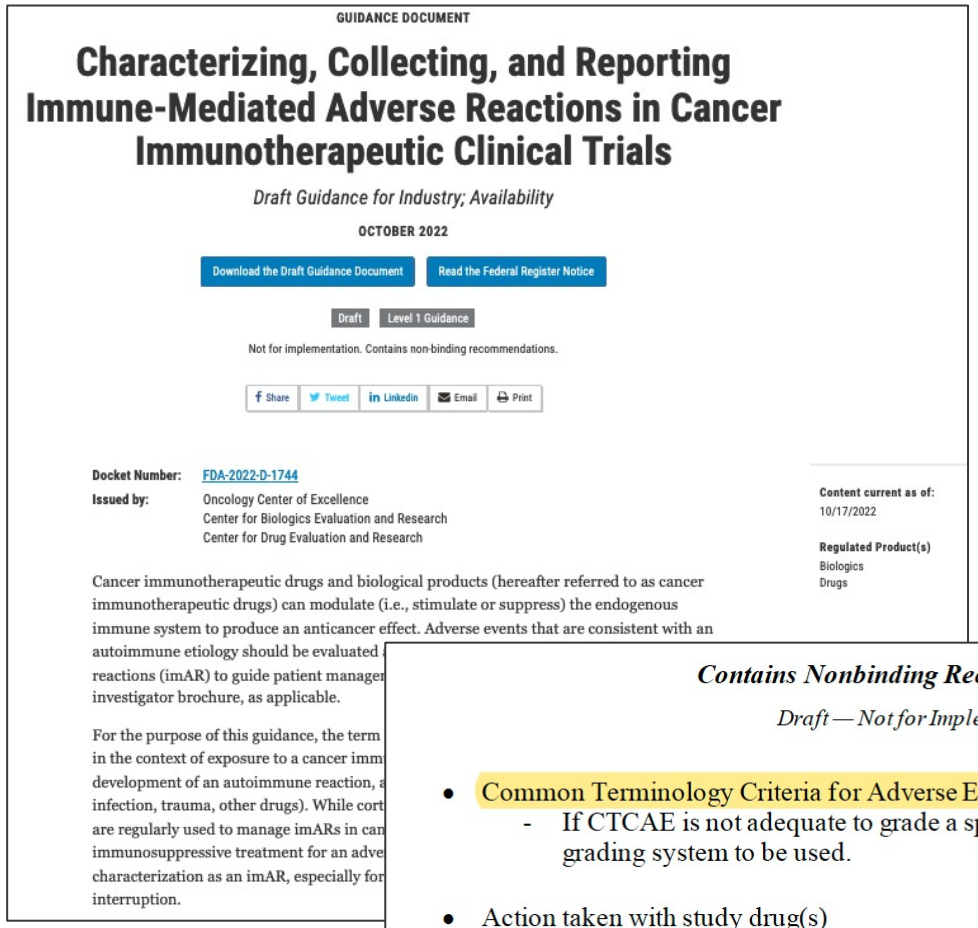
[29] FD&C Act § 505B(a)(1).
[30] See the draft guidance for industry *Bioavailability Studies Submitted in NDAs or INDs – General Considerations* (February 2019). When final, this guidance will represent the FDA's current thinking on this topic.
[31] See footnote 7.
[32] For additional information regarding these regulations, see section III.A.1 of the guidance for industry *Cancer Clinical Trial Eligibility Criteria: Minimum Age Considerations for Inclusion of Pediatric Patients*.

Cancer diagnostics

"is ***not*** mentioned"

Diagnostic considerations simply assume that
The "diagnosis of cancer" has been rendered

Immune-Mediated Adverse Events



GUIDANCE DOCUMENT

Characterizing, Collecting, and Reporting Immune-Mediated Adverse Reactions in Cancer Immunotherapeutic Clinical Trials

Draft Guidance for Industry; Availability

OCTOBER 2022

Download the Draft Guidance Document | Read the Federal Register Notice

Draft | Level 1 Guidance

Not for implementation. Contains non-binding recommendations.

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Docket Number: FDA-2022-D-1744

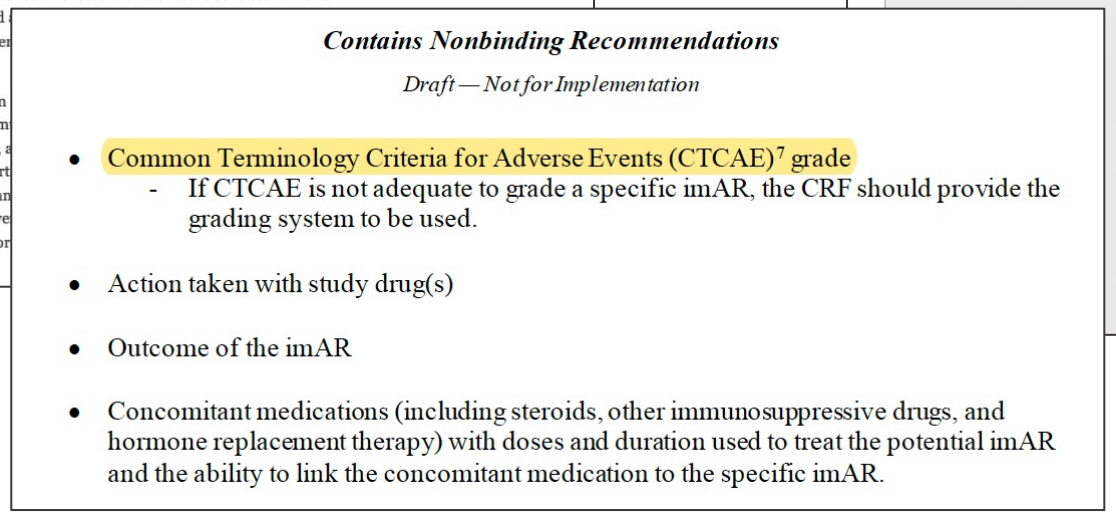
Issued by: Oncology Center of Excellence
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research

Content current as of: 10/17/2022

Regulated Product(s)
Biologics
Drugs

Cancer immunotherapeutic drugs and biological products (hereafter referred to as cancer immunotherapeutic drugs) can modulate (i.e., stimulate or suppress) the endogenous immune system to produce an anticancer effect. Adverse events that are consistent with an autoimmune etiology should be evaluated
reactions (imAR) to guide patient manage
investigator brochure, as applicable.

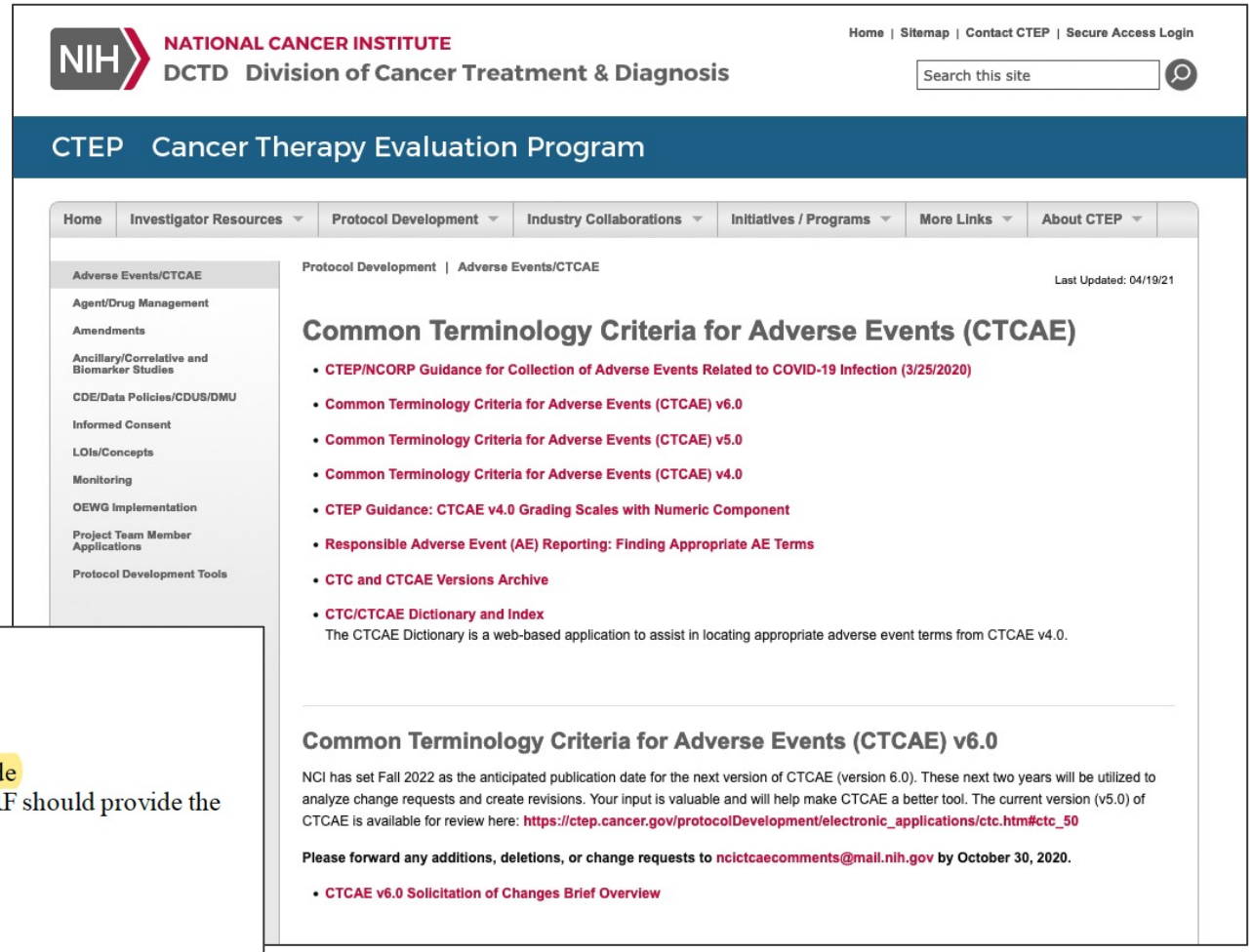
For the purpose of this guidance, the term
in the context of exposure to a cancer imm
development of an autoimmune reaction, a
infection, trauma, other drugs). While cort
are regularly used to manage imARs in can
immunosuppressive treatment for an adve
characterization as an imAR, especially for
interruption.



Contains Nonbinding Recommendations

Draft — Not for Implementation

- Common Terminology Criteria for Adverse Events (CTCAE)[7] grade
  - If CTCAE is not adequate to grade a specific imAR, the CRF should provide the grading system to be used.
- Action taken with study drug(s)
- Outcome of the imAR
- Concomitant medications (including steroids, other immunosuppressive drugs, and hormone replacement therapy) with doses and duration used to treat the potential imAR and the ability to link the concomitant medication to the specific imAR.



NIH NATIONAL CANCER INSTITUTE
DCTD Division of Cancer Treatment & Diagnosis

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- Adverse Events/CTCAE
- Agent/Drug Management
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- Ancillary/Correlative and Biomarker Studies
- CDE/Data Policies/CDUS/DMU
- Informed Consent
- LOIs/Concepts
- Monitoring
- OEWG Implementation
- Project Team Member Applications
- Protocol Development Tools

Protocol Development | Adverse Events/CTCAE

Last Updated: 04/19/21

Common Terminology Criteria for Adverse Events (CTCAE)

- CTEP/NCORP Guidance for Collection of Adverse Events Related to COVID-19 Infection (3/25/2020)
- Common Terminology Criteria for Adverse Events (CTCAE) v6.0
- Common Terminology Criteria for Adverse Events (CTCAE) v5.0
- Common Terminology Criteria for Adverse Events (CTCAE) v4.0
- CTEP Guidance: CTCAE v4.0 Grading Scales with Numeric Component
- Responsible Adverse Event (AE) Reporting: Finding Appropriate AE Terms
- CTC and CTCAE Versions Archive
- CTC/CTCAE Dictionary and Index
  The CTCAE Dictionary is a web-based application to assist in locating appropriate adverse event terms from CTCAE v4.0.

Common Terminology Criteria for Adverse Events (CTCAE) v6.0

NCI has set Fall 2022 as the anticipated publication date for the next version of CTCAE (version 6.0). These next two years will be utilized to analyze change requests and create revisions. Your input is valuable and will help make CTCAE a better tool. The current version (v5.0) of CTCAE is available for review here: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50

Please forward any additions, deletions, or change requests to ncictcaecomments@mail.nih.gov by October 30, 2020.

- CTCAE v6.0 Solicitation of Changes Brief Overview

Presentation to: Oncology Center of Excellence (“across center”)

U.S. FOOD & DRUG ADMINISTRATION

DEVELOPING A DATASET TO VALIDATE COMPUTATIONAL MODELS THAT ANALYZE DIGITAL PATHOLOGY IMAGES TO ASSESS TUMOR-INFILTRATING LYMPHOCYTES (TILS) IN BREAST CANCER

Brandon D. Gallas

Division of Imaging, Diagnostics, Software Reliability

Office of Science and Engineering Laboratories

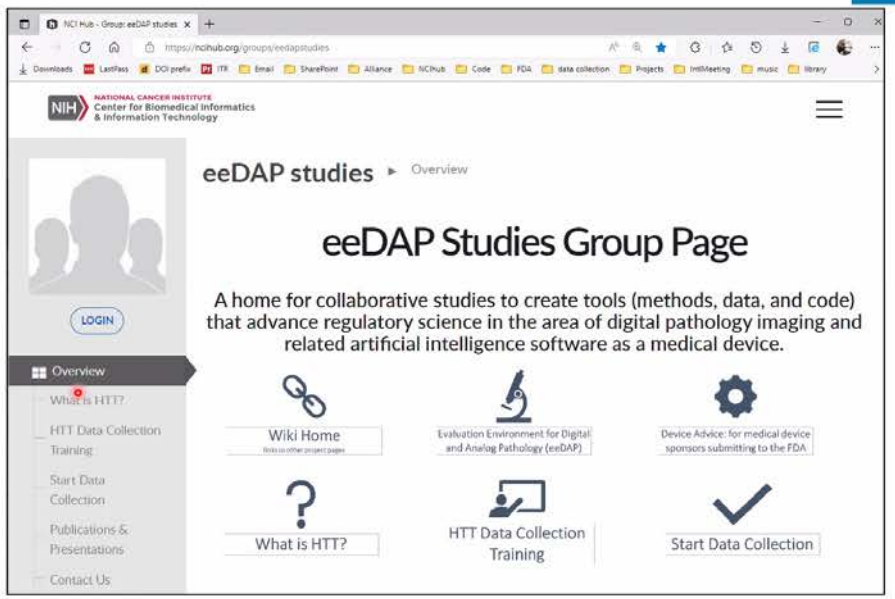
Center for Devices and Radiological Health

U.S. Food and Drug Administration

GOV Original Sound: Off Recording View

High-Throughput Truthing (HTT) Project

- In Transition … Preparing Pivotal Study
- Project presentations and publications
- Pathologist training materials
- Access to data-collection Platforms



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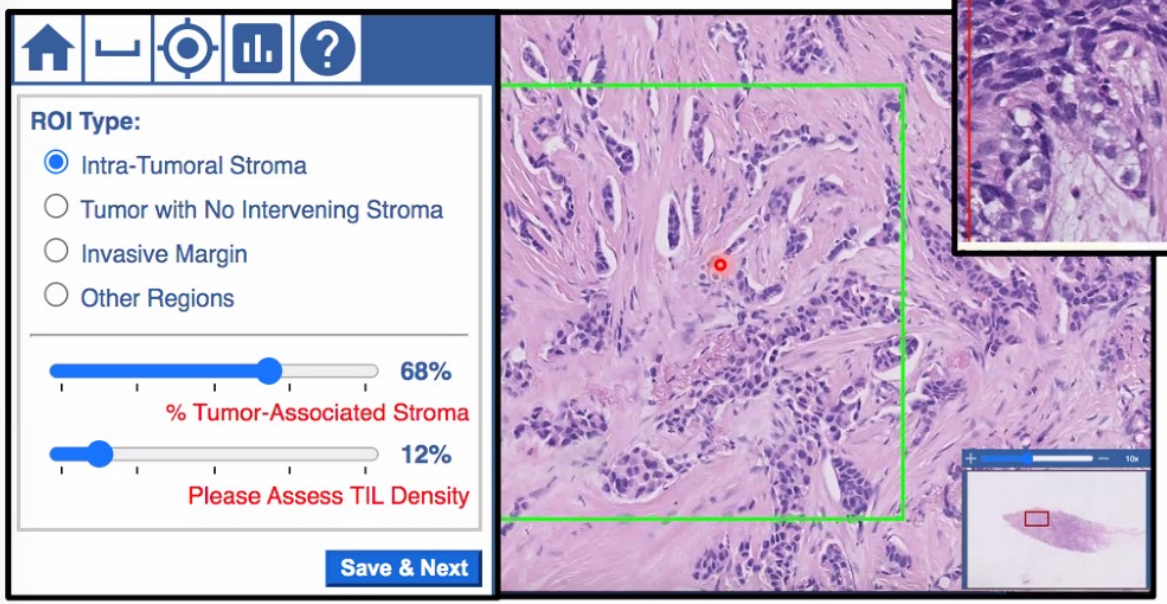
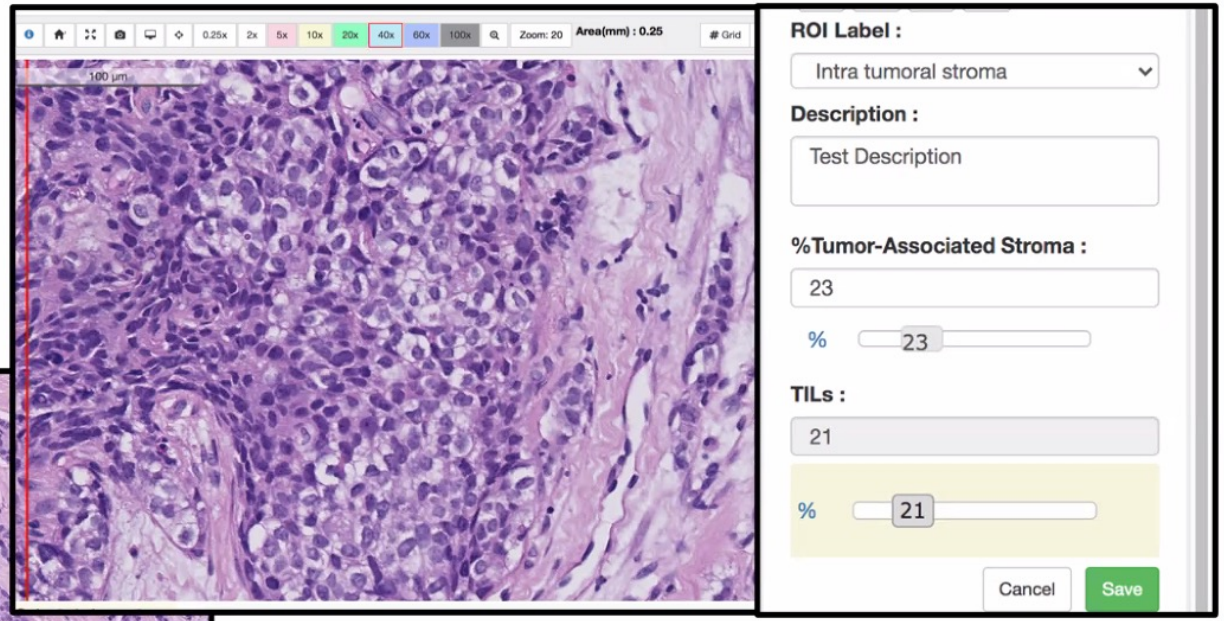
Kristin.Wessel...
Kristin.Wessel@fda.hhs....
York.Tomita@f...
York.Tomita@fda.hhs.gov

Unmute Stop Video Participants 61 Chat Share Screen Live Transcript Reactions Leave

Data-Collection Platforms: Digital

caMicroscope: Open Source
https://github.com/camicroscope/caMicroscope





PathPresenter:
https://pathpresenter.net/about

LEGISLATIVE UPDATES

OCTOBER 04, 2022

FACT SHEET: Biden-Harris Administration Announces Key Actions to Advance Tech Accountability and Protect the Rights of the American Public

OSTP › BRIEFING ROOM › PRESS RELEASES

Today, the Biden-Harris Administration's Office of Science and Technology Policy released a Blueprint for a "Bill of Rights" to help guide the design, development, and deployment of artificial intelligence (AI) and other automated systems so that they protect the rights of the American public. President Biden is standing up to special interests and has long said it is time to hold big technology companies accountable for the harms they cause and to

Administration Priorities COVID Plan

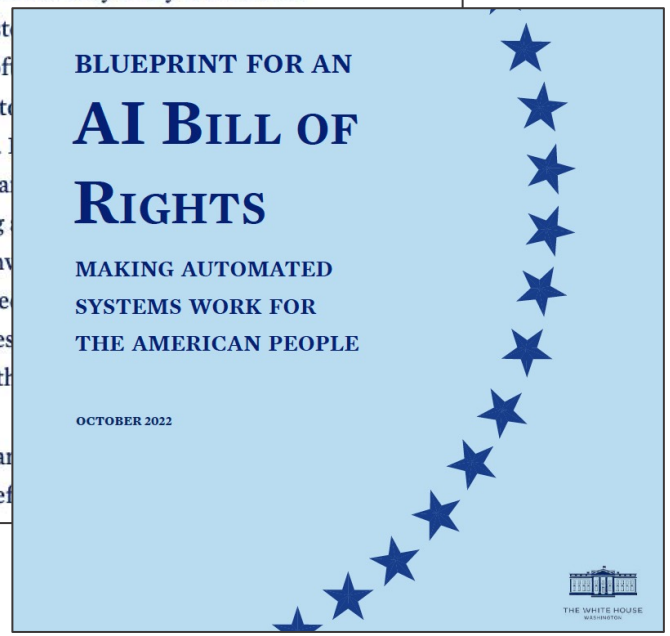
BLUEPRINT FOR AN AI BILL OF RIGHTS

MAKING AUTOMATED SYSTEMS WORK FOR THE AMERICAN PEOPLE

OSTP

Among the great challenges posed to democracy today is the use of technology, data, and automated syst
rights of the American public. Too of
limit our opportunities and prevent our access t
services. These problems are well documented.
world, systems supposed to help with patient ca
ineffective, or biased. Algorithms used in hiring
been found to reflect and reproduce existing unv
new harmful bias and discrimination. Unchecke
has been used to threaten people's opportunities
pervasively track their activity—often without th

These outcomes are deeply harmful—but they ar
systems have brought about extraordinary benef



BLUEPRINT FOR AN

AI BILL OF RIGHTS

MAKING AUTOMATED SYSTEMS WORK FOR THE AMERICAN PEOPLE

OCTOBER 2022

THE WHITE HOUSE
WASHINGTON

Safe and Effective Systems

Algorithmic Discrimination Protections

Data Privacy

Notice and Explanation

Human Alternatives, Consideration, and Fallback

- **Access to critical resources and services, including but not limited to:**
  - **Health and health insurance technologies** such as medical AI systems and devices, AI-assisted diagnostic tools, algorithms or predictive models used to support clinical decision making, medical or insurance health risk assessments, drug addiction risk assessments and associated access alg -orithms, wearable technologies, wellness apps, insurance care allocation algorithms, and health insurance cost and underwriting algorithms;
  - **Financial system algorithms** such as loan allocation algorithms, financial system access determi- nation algorithms, credit scoring systems, insurance algorithms including risk assessments, auto -mated interest rate determinations, and financial algorithms that apply penalties (e.g., that can garnish wages or withhold tax returns);

JAMA Health Forum™

JAMA Forum

Reforms Needed to Modernize the US Food and Drug Administration's Oversight of Dietary Supplements, Cosmetics, and Diagnostic Tests

Scott Gottlieb, MD; Mark B. McClellan, MD, PhD

Author affiliations and article information are listed at the end of this article.

Congress is in the process of reauthorizing the user fee programs that help fund operations of the US Food and Drug Administration (FDA), but legislators could not reach final agreement on 3 major provisions intended to modernize the agency's regulatory framework, advance innovation, and strengthen its ability to protect consumers. These provisions address the FDA's oversight of dietary supplements, cosmetics, and diagnostic tests for patients—and represent once-in-a-generation reforms developed through a largely bipartisan process.

All 3 industries are benefiting from technological advances that offer new opportunities to improve people's health, but also create new uncertainties and risks. For each of these industries, evidence indicates that products that slipped through a porous regulatory framework have put some individuals at risk. Industry participants have also expressed concerns about difficulties in advancing potentially beneficial new kinds of innovations under the FDA's existing regulatory authorities, which have not kept up with the market's current state.

The 3 provisions were years in the making. Aspects of each took shape while we individually served as FDA commissioner at 2 points over the last 20 years,[1] reflecting how long the FDA and many of its stakeholders have sought these new measures. Their absence from the final bill

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MDIC Updates

https://mdic.org/

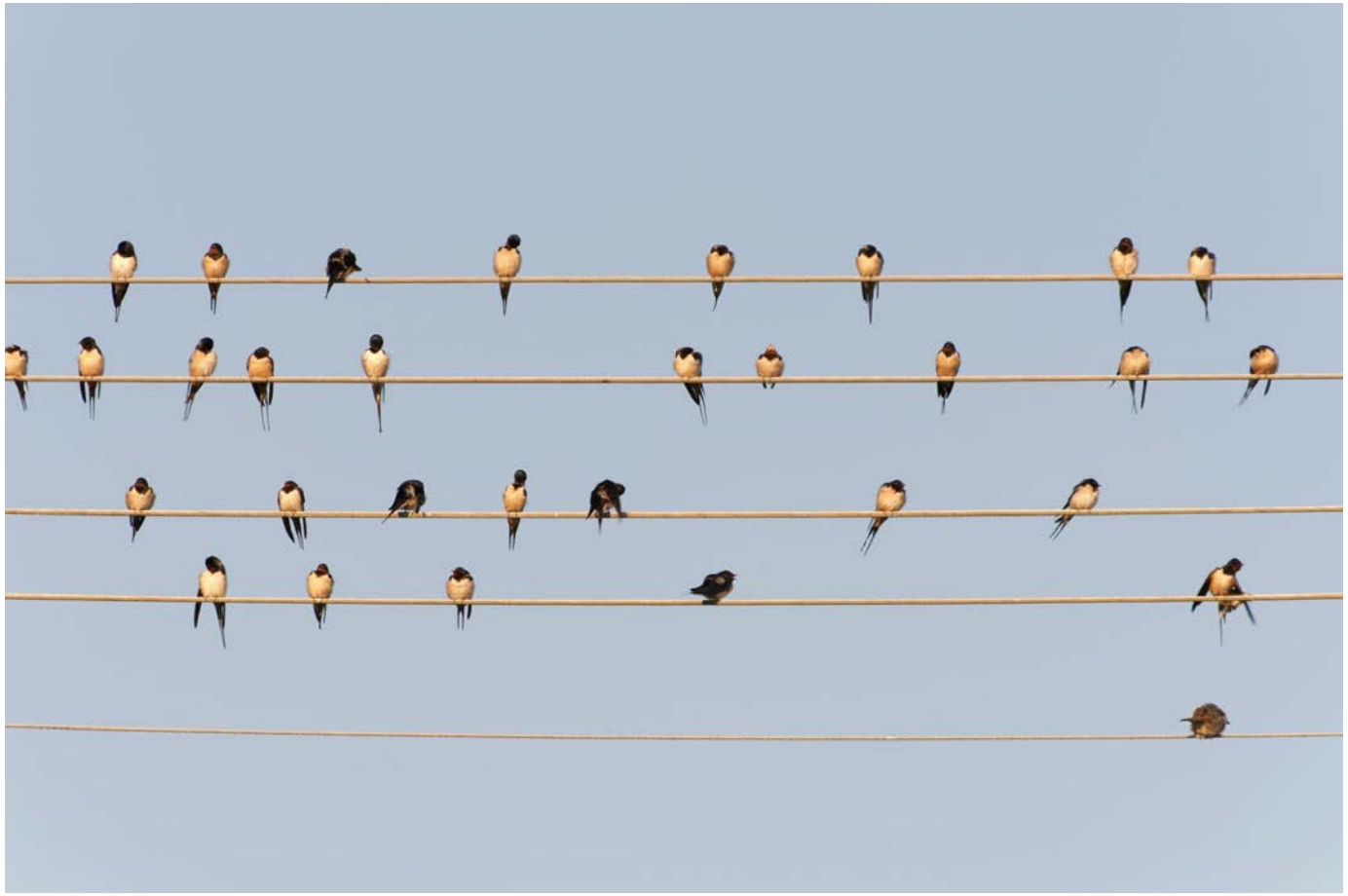
Noor Falah, MS

- Project Manager for Cybersecurity at MDIC and PIcc
- Bench research- Effect of Neuropeptide Y on development of Ewing sarcoma
- Clinical research- Early Identification of Maternal CV Risk
- Georgetown University- MS, 2021
- George Mason University-BS, 2020
- Fun fact- avid baker

MDIC Updates

- Cybersecurity Threat-modeling Virtual Bootcamps: 12/12-12/16, 2022 and 3/13-3/17, 2023
  - https://mdic.org/project/2022-threat-modeling-bootcamps/
- Medical Device Cybersecurity Maturity: MDIC Industry Benchmarking Report 2022 has been released
  - https://mdic.org/resource/cybersecurity-benchmarking-report/
- MDIC Partners with PerkinElmer's Horizon Discovery to Improve Accuracy of Next Generation Sequencing-Based Cancer Diagnostics (SRS Project)
  - https://mdic.org/news/medical-device-innovation-consortium-mdic-partners-with-perkinelmers-horizon-discovery-to-improve-accuracy-of-next-generation-sequencing-based-cancer-diagnostics/
- MDIC Live Online Series: On Medical Extended Reality (MXR) November 10, 2022 @ 1:30pm
  - LinkedIn Live
- Coming Soon:
  - AI/ML in IVDs: A framework for a predetermined change control plan for AI/ML-enabled IVDs, including both software as a medical device (SaMD) and in a medical device (SiMD)
  - 5G enabled healthcare technologies: MDIC landscape Report (Coming November 2022)
  - Computational modeling & simulation (CM&S) in medical device & diagnostics: case studies and landscape analysis (Coming November 2022)
- Please contact Noor Falah nfalah@mdic.org or Jithesh Veetil jveetil@mdic.org with any questions about MDIC initiatives

Professional Societies



Council on Informatics and Pathology Innovation

Charge

To identify and recommend strategic direction on current and emerging medical information science, data science, and computational technologies that could impact the practice of pathology; provide informatics domain information and expertise to the CAP in furtherance of its programs and mission; and support appropriate engagement with external stakeholders.

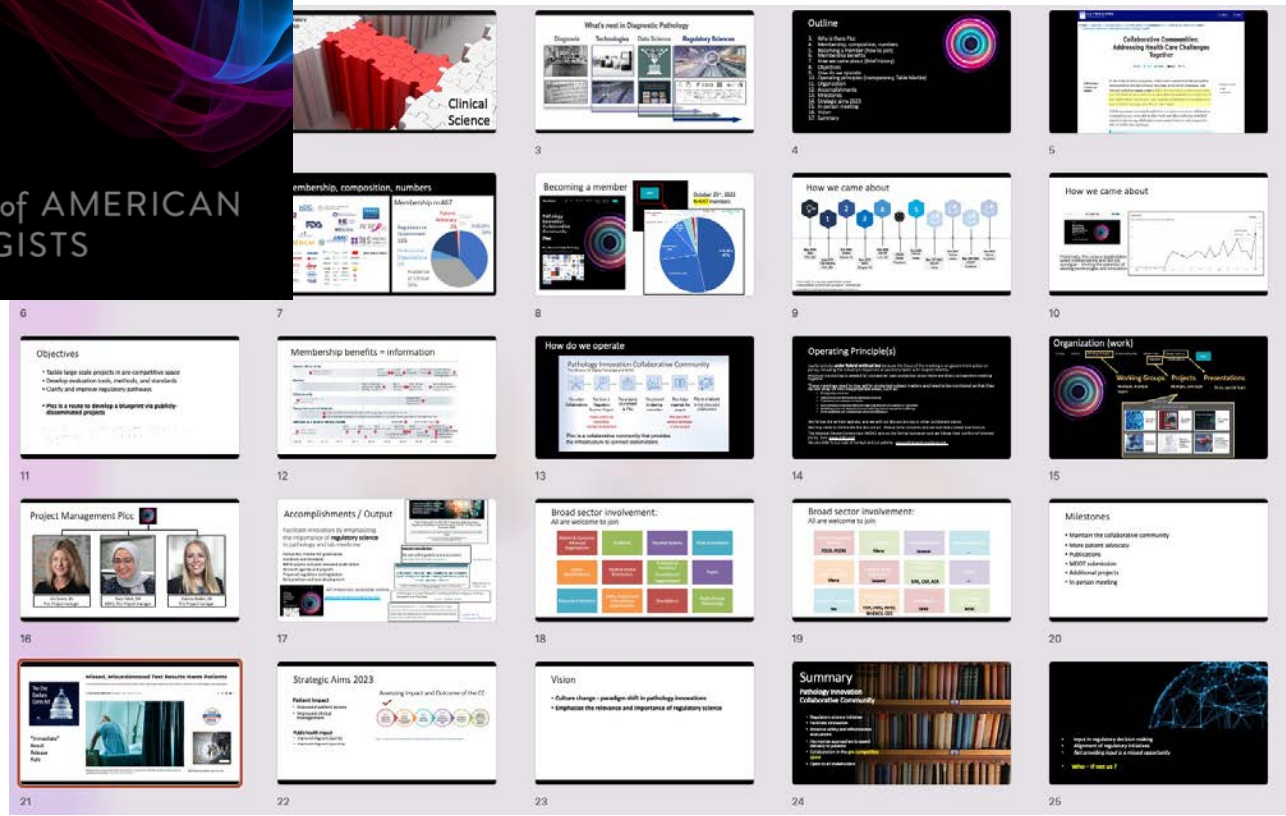
This council reports directly to the **Board of Governors**. View a list of the **Current Council Members**.

Membership

The council comprises the Chair and Vice-Chair (VC), chairs of the constituent committees (listed below); 11 members-2 junior members; and 2 advisors.

- **Artificial Intelligence (AI) Committee**
- **Cancer Committee**
- **Digital and Computational Pathology Committee (DCPC)**
- **Informatics Committee (IC)**
- **Pathology Electronic Reporting (PERT) Committee**

November 4-5th 2022



Mismatch Repair and Microsatellite Instability Testing for Immune Checkpoint Inhibitor Therapy

Guideline From the College of American Pathologists in Collaboration With the Association for Molecular Pathology and Fight Colorectal Cancer

Angela N. Bartley, MD; Anne M. Mills, MD; Eric Konnick, MD, MS; Michael Overman, MD; Christina B. Ventura, MPH, MT(ASCP); Lesley Souter, PhD; Carol Colasacco, MLIS, SCT(ASCP); Zsofia K. Stadler, MD; Sarah Kerr, MD; Brooke E. Howitt, MD; Heather Hampel, MS, LGC; Sarah F. Adams, MD; Wenora Johnson, BS; Cristina Magi-Galluzzi, MD, PhD; Antonia R. Sepulveda, MD, PhD; Russell R. Broaddus, MD, PhD

• *Context.*—The US Food and Drug Administration (FDA) approved immune checkpoint inhibitor therapy for patients with advanced solid tumors that have DNA mismatch repair defects or high levels of microsatellite instability; however, the FDA provided no guidance on which specific clinical assays should be used to determine mismatch repair status.

Objective.—To develop an evidence-based guideline to identify the optimal clinical laboratory test to identify defects in DNA mismatch repair in patients with solid tumor malignancies who are being considered for immune

Design.—The College of American Pathologists convened an expert panel to perform a systematic review of the literature and develop recommendations. Using the National Academy of Medicine–endorsed Grading of Recommendations Assessment, Development and Evaluation approach, the recommendations were derived from available evidence, strength of that evidence, open comment feedback, and expert panel consensus. Mismatch repair immunohistochemistry, microsatellite instability derived from both polymerase chain reaction and next-generation sequencing, and tumor mutation burden

DIGITAL PATHOLOGY
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ABOUT MEMBERSHIP COLLABORATE PATHOLOGY VISIONS

PODCAST PUBLICATIONS EVENTS

WHY ATTEND PV?

CME & CE

TRAVEL AWARD RECIP

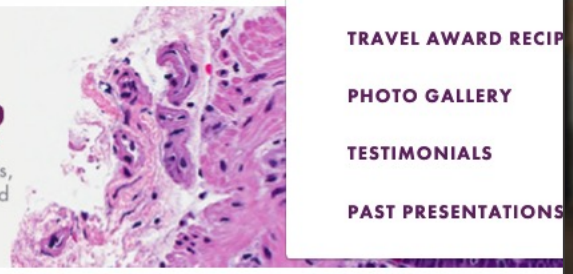
PHOTO GALLERY

TESTIMONIALS

PAST PRESENTATIONS

WHAT IS THE DIGITAL PATHOLOGY ASSOCIATION?

The DPA is a nonprofit organization comprised of pathologists, scientists, technologists and industry representatives dedicated to advancing the field of digital pathology.



PATHOLOGY VISIONS

SAVE THE DATE OCTOBER 29-31

HYATT REGENCY ORLANDO | ORLANDO, FL

#PathVisions23

NEWS

AMA Announces Codes

AMA Addition of Digital Pathology

Webinar: Can AI Regulatory Scien

Digital Pathology Association
6,506 followers
1w •

We're getting all checked in and kicking off #PathVisions22. It's so good to see everyone again!

The American Society for Clinical Pathology's 2021 Wage Survey of Medical Laboratories in the United States

Edna Garcia, MPH,[1] Iman Kundu, MPH,[1] and Karen Fong[2]

From the [1]American Society for Clinical Pathology (ASCP) Institute of Science, Technology, and Policy, Washington, DC, USA; and [2]ASCP Board of Certification, Chicago, IL, USA.

KEY POINTS

- The COVID-19 pandemic had a significant effect on staffing, workload, and work-life balance of many laboratory professionals.
- Even with the salary increases reported from the results of this survey, it is evident that the increases have not kept up with the current inflation.
- Focus on visibility, recruitment and retention, and diversity are essential to develop long- and short-term solutions.

ABSTRACT

Objectives: To inform the pathology and laboratory field of the most recent national wage data. Historically, the results of this biennial survey have served as a basis for additional research on laboratory recruitment, retention, education, marketing, certification, and advocacy.

Methods: The 2021 Wage Survey was conducted through collaboration between the American Society for Clinical Pathology (ASCP) Institute of Science, Technology, and Policy in Washington, DC, and the ASCP Board of Certification in Chicago, IL.

Results: Compared with 2019, results show that mean hourly wage for staff-level personnel increased for only two occupations—cytologist and medical laboratory sci-

KEY WORDS

Wage survey; CME; Laboratory workforce; Certification; Technologists; Taskforce on workforce; Recruitment; Retention; Urban; Rural; COVID-19 pandemic; Workforce steering committee

WHO/IARC

International Agency for Research on Cancer

World Health Organization

- https://www.iarc.who.int/vacancy/it-database-and-web-developer-req-2207536/
- https://www.iarc.who.int/vacancy/scientist-exposure-req-2207524/
- https://www.iarc.who.int/vacancy/scientist-epidemiology-req-2207525/
- https://www.iarc.who.int/vacancy/scientist-toxicology-req-2207533/
- https://www.iarc.who.int/vacancy/scientist-toxicology-req-2207526/
- https://careers.who.int/careersection/ex/jobdetail.ftl?job=2207525

IT Database and Web Developer

Branch/Service: Evidence Synthesis and Classification Branch (ESC)

Requisition Number: REQ-2207536

Grade: LY5

Contractual Arrangement: Fixed-term appointment

First Published: 10 August 2022

Closing Date: 31 August 2022

MORE INFORMATION (access for IARC/WHO staff members)

MORE INFORMATION (access for external candidates)

ctDNA

Results from two studies suggest that this approach is essential to refining liquid biopsy use in early cancer detection and to check tumour progression

Presentations at the Molecular Analysis for Precision Oncology (MAP) Congress 2022 suggest that combining different liquid biopsy methodologies with other technologies may improve the limit of detection (LOD) and the reference range of liquid biopsies, with some implications for early cancer detection and monitoring of tumour progression. In a study from France, the use of a new highly sensitive methodology confirmed that hypomethylation of circulating retrotransposons will be valuable in the development of more efficient, non-invasive diagnostic tests across cancer types (Abstract 5MO). Hypomethylation of LINE-1 elements (L1PA), a shared feature of many cancers, were detectable in cell-free DNA (cfDNA) and discriminated well between plasma from 123 healthy individuals and 394 patients with a number of different cancers including metastatic colorectal, breast, lung and uveal cancers and non-metastatic tumours (area under the curve [AUC] 0.95). The results showed 67–98% sensitivity at 99% specificity across cancers. The robustness of LP1A hypomethylation as a marker was confirmed on an independent validation cohort of plasma from 30 healthy patients and 160 patients with cancers including metastatic breast, colorectal, gastric and lung cancers and non-metastatic ovarian cancers (AUC 0.99).

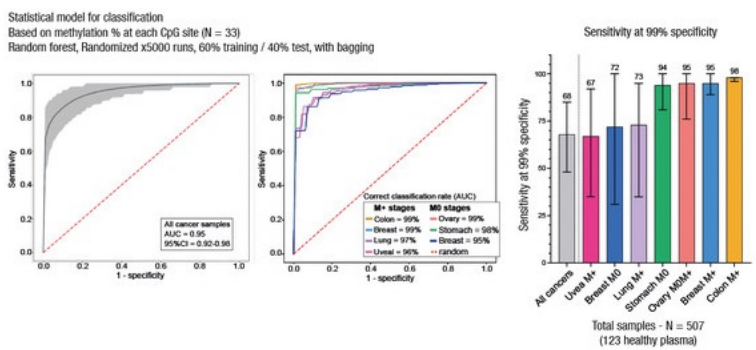


Figure. LP1A hypomethylation discriminates cancer patients (MAP 2022, Abstract 5MO)

Poster area at the Molecular Analysis for Precision Oncology Congress 2022 in Amsterdam (14-16 October 2022)

Diversity & Inclusion

Human Rights Campaign

Human Rights Foundation

https://www.hrc.org/resources/workplace

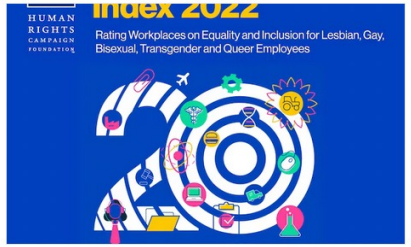
HRC works to provide employers the resources they need to improve and promote fairness in the workplace.

HUMAN RIGHTS CAMPAIGN FOUNDATION™

Talking About Pronouns in the Workplace

Community

Poverty generally refers to a lack of basic necessities, resources and income, though its exact definition is often widely debated and measured in a variety of ways. A common way...



WORKPLACE

2023 CEI Criteria Evolution: Toolkit and FAQ

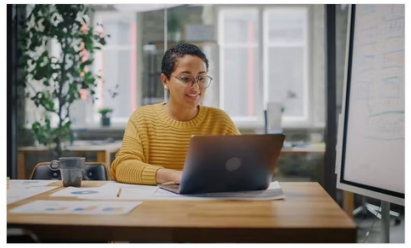
The Human Rights Campaign Foundation is excited to share the upcoming changes to the CEI, and, moreover, grateful for the opportunity to raise the bar for LGBTQ+ inclusive workplaces.

This...

WORKPLACE

The Wage Gap Among LGBTQ+ Workers in the United States

In an HRC Foundation analysis of nearly 7,000 full-time LGBTQ+ workers, median earnings were about $900 weekly, about 90% of the $1,001 median weekly wage a typical worker earns in...



WORKPLACE

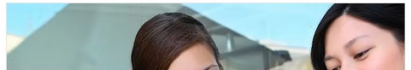
The LGBTQ+ Women's Wage Gap in the United States

Last Updated 6/12/22

PUBLICATIONS, STATE & LOCAL POLICY, WORKPLACE

MEI 2021: See Your Cities' Scores

HRC's Municipal Equality Index (MEI) demonstrates the ways that many cities can — and do — support the LGBTQ+ people who live and work there, even where states and the...



WORKPLACE, GLOBAL

HRC Equidad AR and BR: Global Workplace

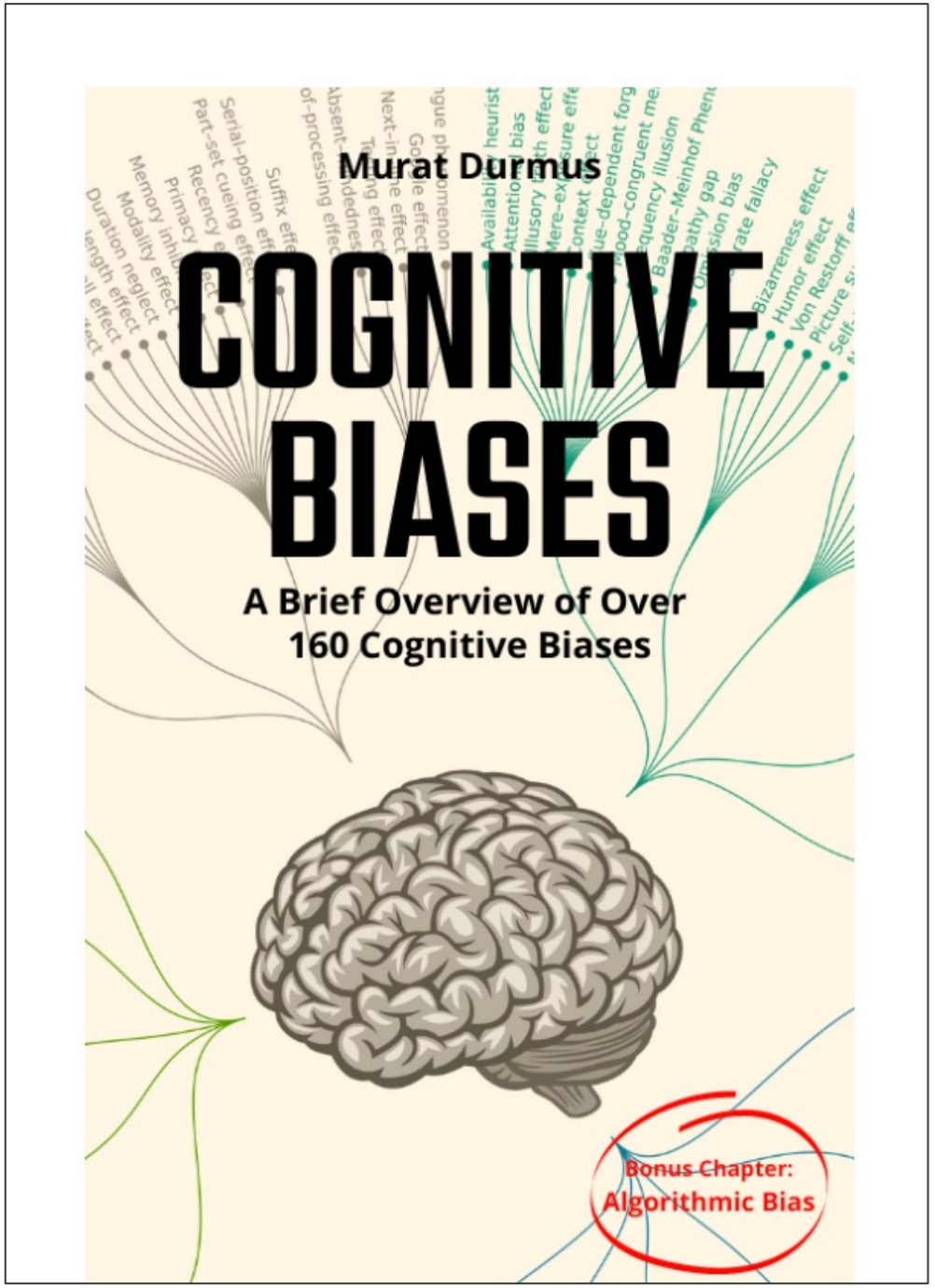
Article: 5 Specifications That The FDA's Diversity Plan Needs To Include

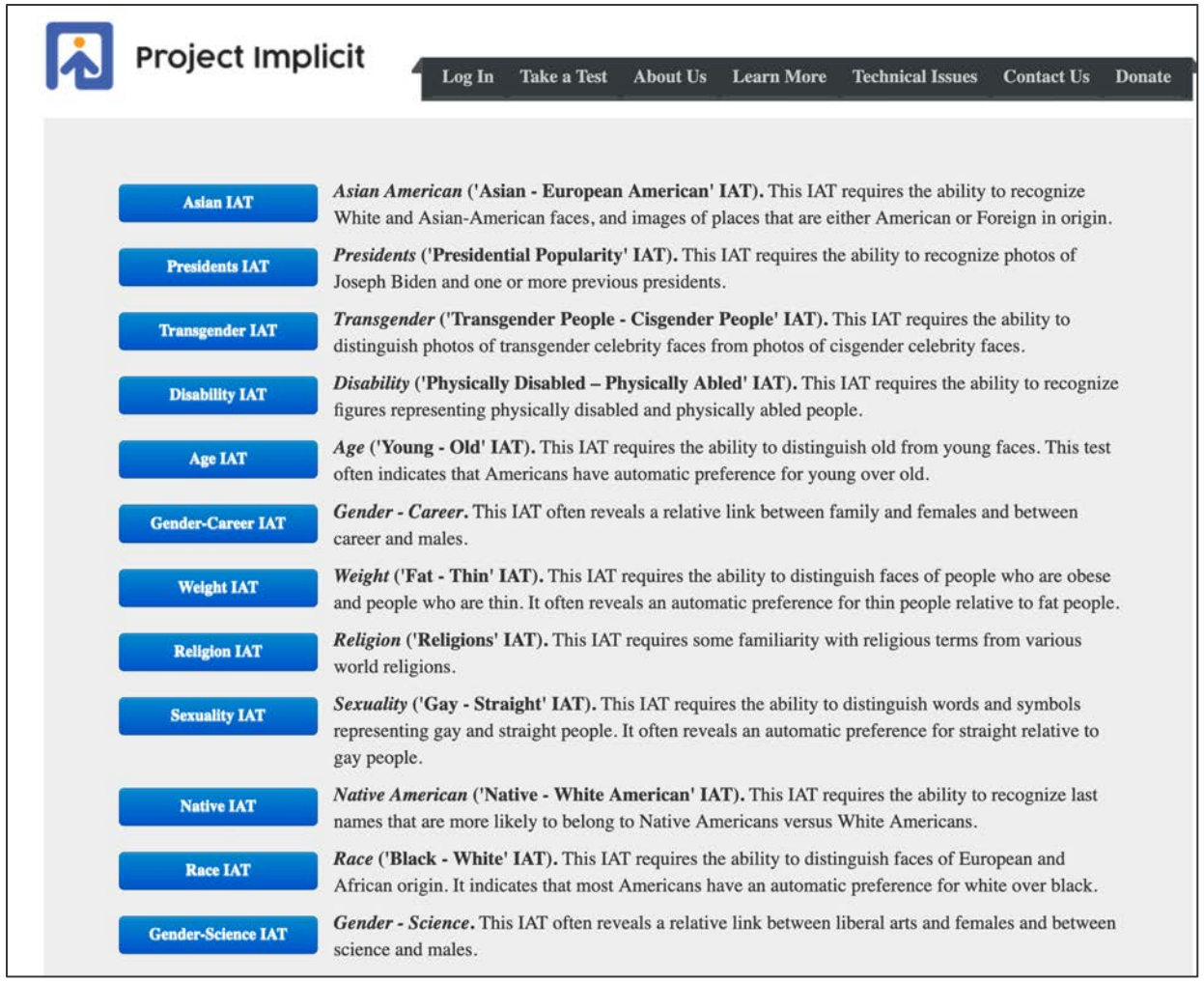
- In April 2022, the FDA made available for public comment its *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials*
- https://www.regulations.gov/docket/FDA-2021-D-0789

1. **Implement A Community Engagement Plan**
2. **Be More Inclusive With Your Eligibility Criteria**
3. **Provide Resources For Patients To Address/Overcome Barriers To Trial Adherence**
4. **Include Sites In Diverse Areas**
5. **Take On Accountability For Diversity Plan Adherence**

Maimah Karmo is the founder and CEO of the Tigerlily Foundation and is also a 16-year survivor of breast cancer.

Link to article: https://www.clinicalleader.com/doc/specifications-that-the-fda-s-diversity-plan-needs-to-include-0001





https://implicit.harvard.edu/implicit/takeatest.html

Patient advocacy

Pre-analytics: http://appiagroup.org/tops/

APPIA

Anatomical Pathology Patient Interest Association

THE APPIA MISSION

Cooperative industry partners dedicated to advancing anatomic pathology to benefit patient care by advocating an practices.

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Tissue Optimization and Pre-analytic Standardization (TOPS) Program

What Is TOPS?

TOPS (Tissue Optimization and Pre-analytic Standardization) is APPIA's first education program for your entire health care delivery team on the criticality of tissue pre-analytics. The TOPS program serves the interests of the patient's diagnostic sample by providing best practice suggestions and guidelines on tissue handling and pre-analytics for surgeons, nurses, pathologists, laboratory technologists, educators and patient advocacy groups.

TOPS Program Training Materials

Available Materials:

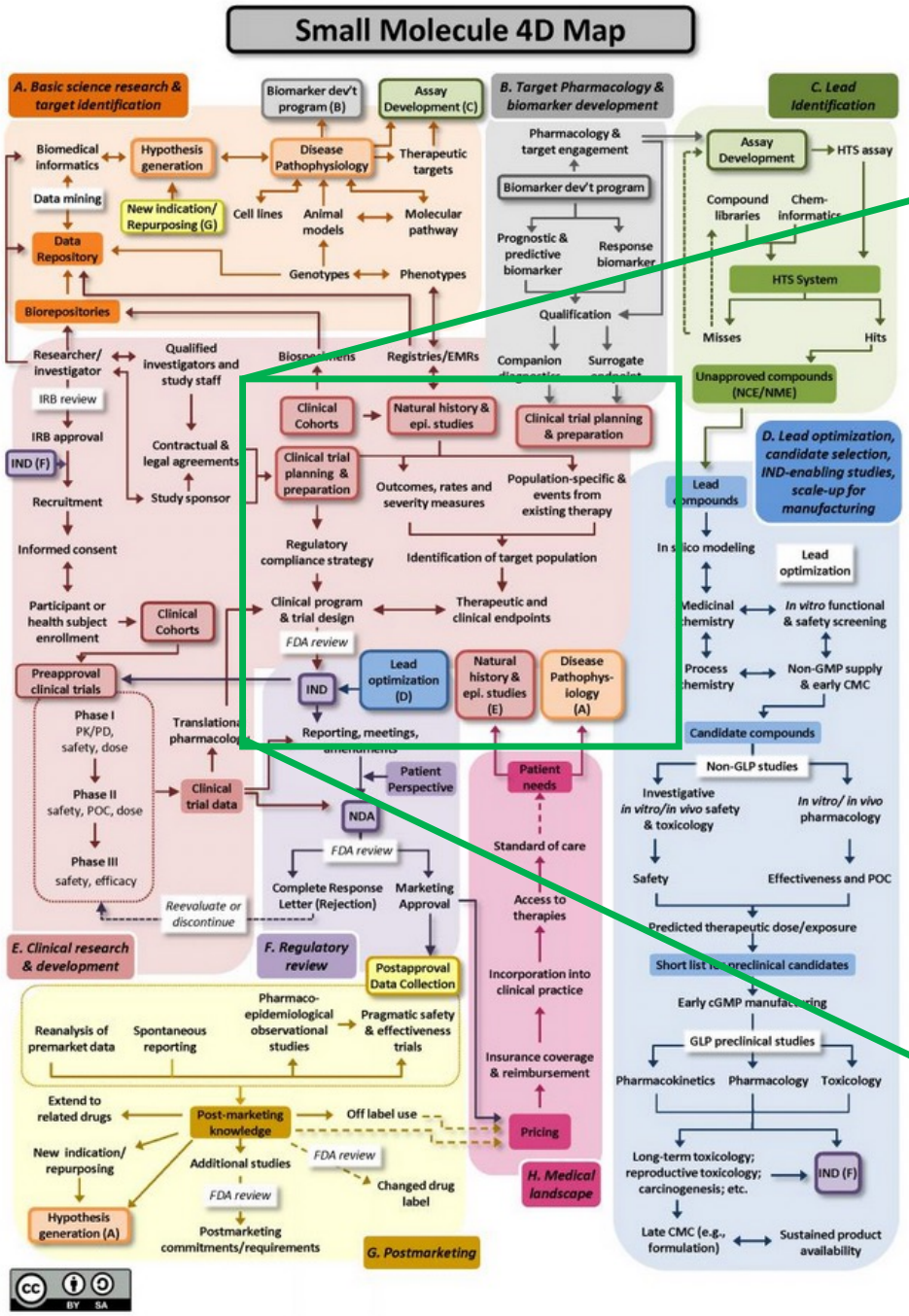
- APPIA TOPS Program – for Advocacy Groups (.pptx)
- APPIA TOPS Program – for Laboratory Personnel (.pptx)
- APPIA TOPS Program – for Oncology & OR Nurses (.pptx)
- APPIA TOPS Program – for Surgeons (.pptx)
- APPIA TOPS Program – Full Presentation for Pathologists

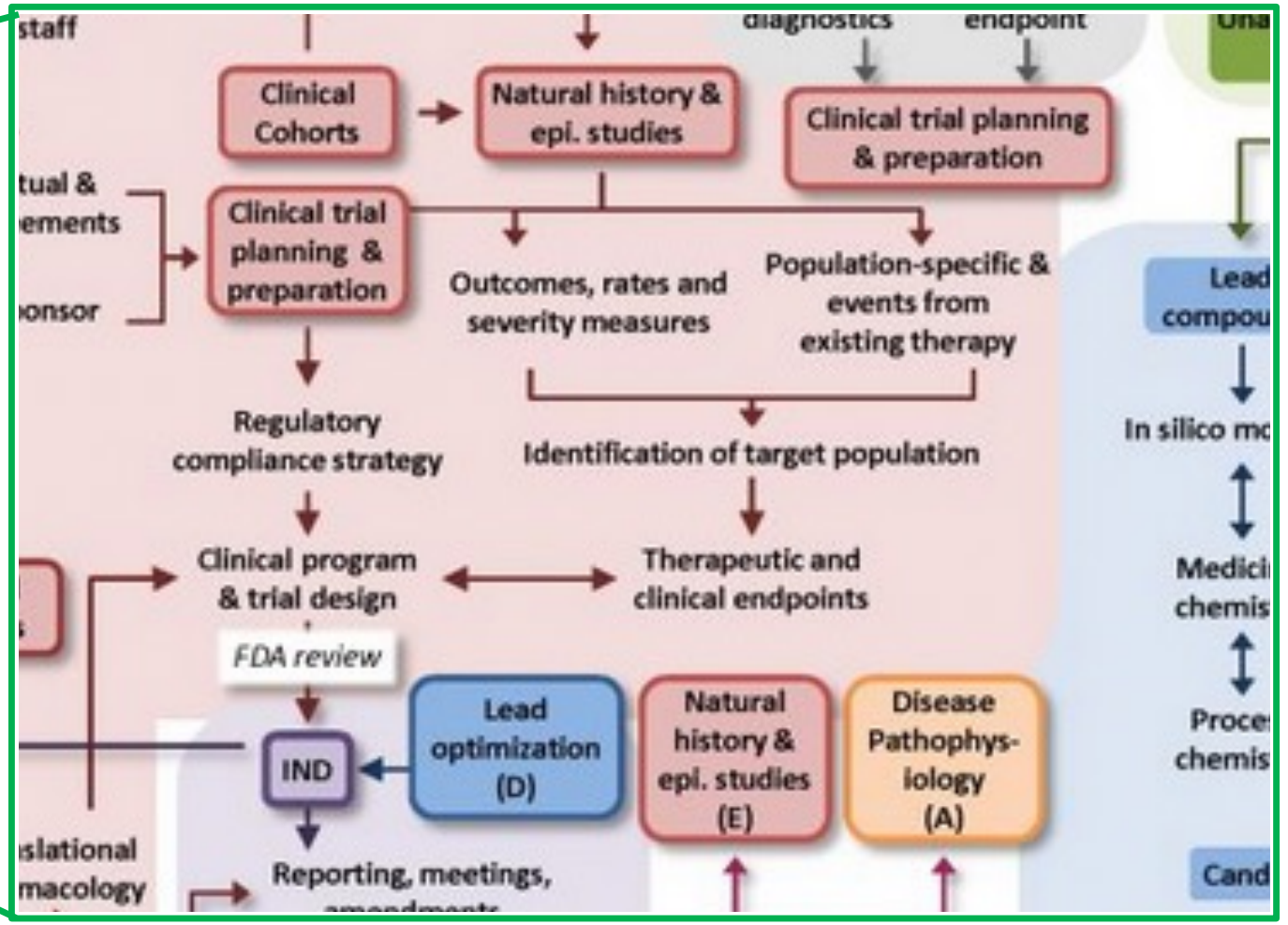
TOPS: General Tissue Handling Guidelines

Best practices for handling specimens from tissue procurement t

Resources

NIH-National Center for Advancing Translational Sciences: **4D MAPS**





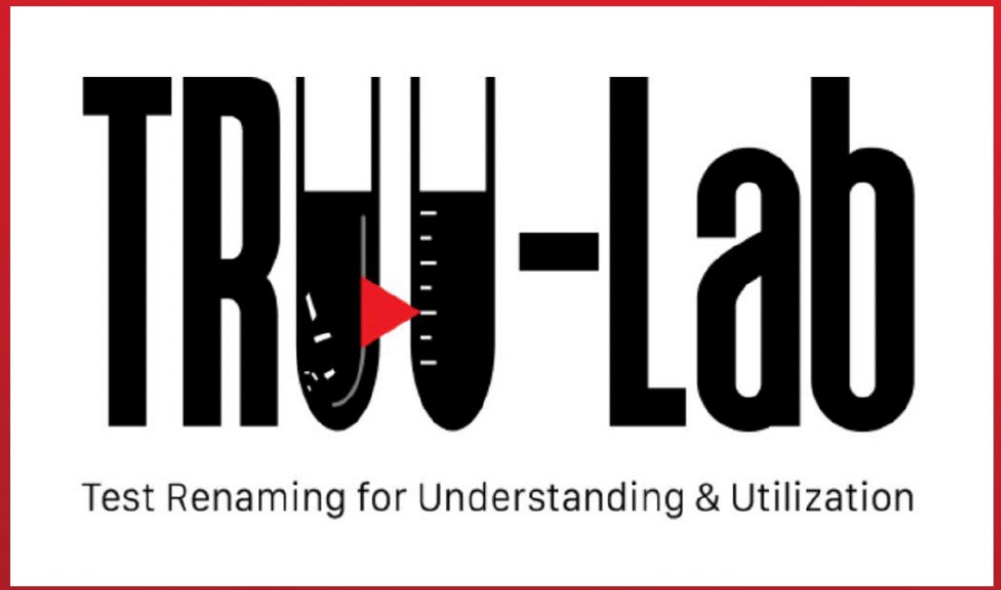
https://ncats.nih.gov/translation/maps

Standardizing Lab Test Names: the TRUU-Lab Initiative

Ila Singh, MD, PhD

Chief of Laboratory Medicine, Texas Chil
Professor, Baylor College of Medicine

TRUU-Lab



DEPARTMENT OF PATHOLOGY

Texas Children's Hospital

Baylor College of Medicine

Publications

nature biomedical engineering

ARTICLES

https://doi.org/10.1038/s41551-022-00929-8

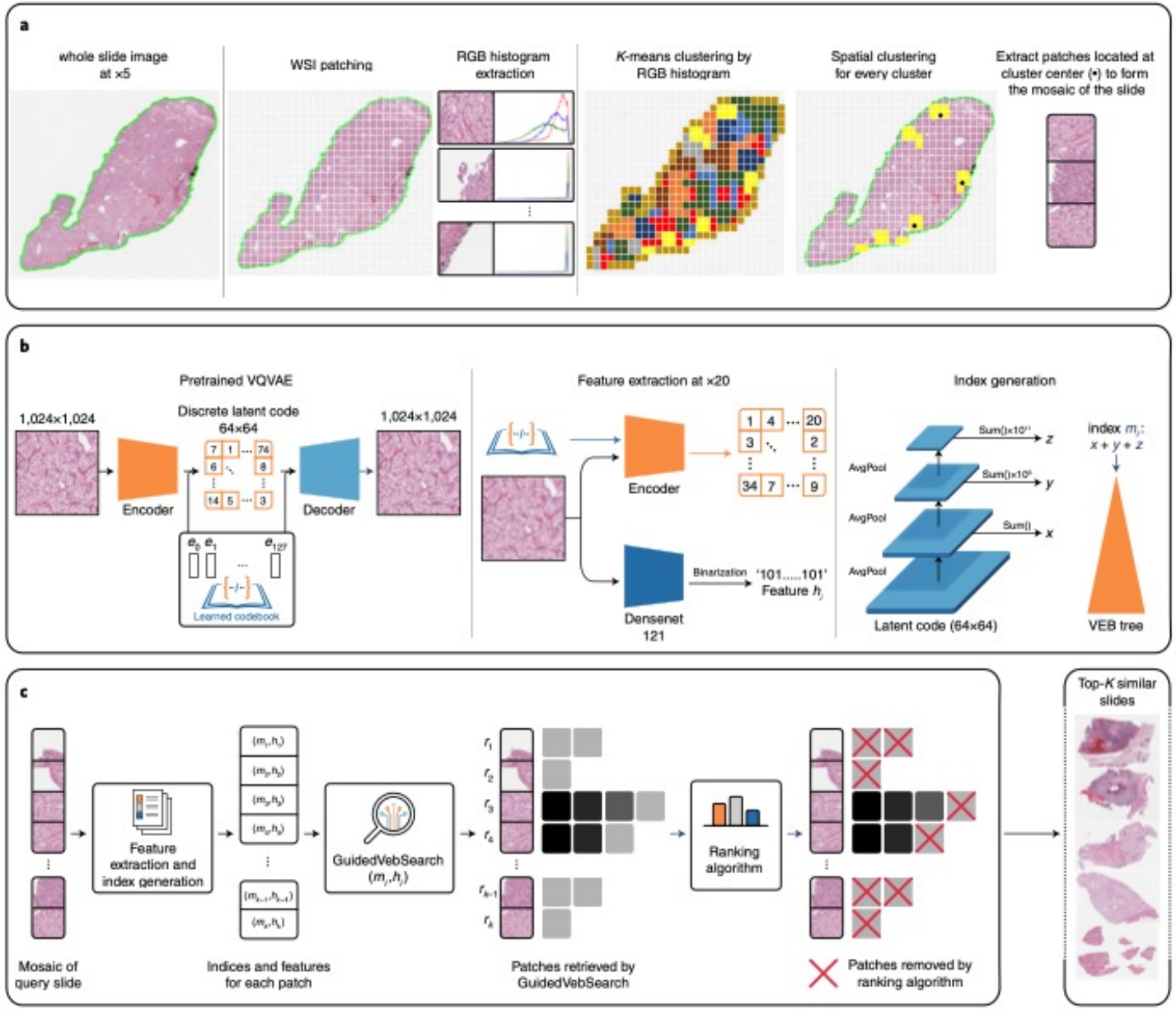
OPEN

Fast and scalable search of whole-slide images via self-supervised deep learning

Chengkuan Chen[1,2,3,4], Ming Y. Lu[1,2,3,4,5,7], Drew F. K. Williamson[1,2,3,7], Tiffany Y. Chen[1,3,4], Andrew J. Schaumberg[1] and Faisal Mahmood[1,2,3,4,6] ✉

The adoption of digital pathology has enabled the curation of large repositories of gigapixel whole-slide images (WSIs). Computationally identifying WSIs with similar morphologic features within large repositories without requiring supervised training can have significant applications. However, the retrieval speeds of algorithms for searching similar WSIs often scale with the repository size, which limits their clinical and research potential. Here we show that self-supervised deep learning can be leveraged to search for and retrieve WSIs at speeds that are independent of repository size. The algorithm, which we named SISH (for self-supervised image search for histology) and provide as an open-source package, requires only slide-level annotations for training, encodes WSIs into meaningful discrete latent representations and leverages a tree data structure for fast searching followed by an uncertainty-based ranking algorithm for WSI retrieval. We evaluated SISH on multiple tasks (including retrieval tasks based on tissue-patch queries) and on datasets spanning over 22,000 patient cases and 56 disease subtypes. SISH can also be used to aid the diagnosis of rare cancer types for which the number of available WSIs is often insufficient to train supervised deep-learning models.

The increasing availability of technologies allowing for the routine creation of high-resolution whole-slide images (WSIs) has triggered tremendous excitement for the field of digital pathology. Whereas the rich morphologic content analysed by pathologists was once locked in glass slides, whole-slide imaging historical repositories in the absence of electronic pathology reports. A critical challenge that hinders large scale, efficient adoption of histology whole-slide image search and retrieval systems is scalability. This is a unique challenge for WSI retrieval systems[18] as compared with other image databases since they need to efficiently


a
whole slide image at ×5
WSI patching
RGB histogram extraction
K-means clustering by RGB histogram
Spatial clustering for every cluster
Extract patches located at cluster center (•) to form the mosaic of the slide
b
Pretrained VQVAE
1,024×1,024
Discrete latent code 64×64
Encoder
Decoder
1,024×1,024
Learned codebook
Feature extraction at ×20
Encoder
Densenet 121
Binarization
'101.....101'
Feature h_i
Index generation
AvgPool
Sum()×10^12
Sum()×10^6
Sum()
z
y
x
Latent code (64×64)
index m_i: x + y + z
VEB tree
c
Mosaic of query slide
Feature extraction and index generation
Indices and features for each patch
GuidedVebSearch (m_i,h_i)
Patches retrieved by GuidedVebSearch
Ranking algorithm
Patches removed by ranking algorithm
Top-K similar slides

USCAP

www.nature.com/modpathol

REVIEW ARTICLE OPEN

Check for updates

Digital pathology and artificial intelligence in translational medicine and clinical practice

Vipul Baxi[1]✉, Robin Edwards[1], Michael Montalto[2] and Saurabh Saha[1]

Traditional pathology approaches have played an integral role in the delivery of diagnosis, semi-quantit
assessment of protein expression, and classification of disease. Technological advances and the increase
medicine have recently paved the way for the development of digital pathology-based approaches for
assessments, namely whole slide imaging and artificial intelligence (AI)–based solutions, allowing us to
information beyond human visual perception. Within the field of immuno-oncology, the application of suc
development and translational research have created invaluable opportunities for deciphering complex
discovery of novel biomarkers and drug targets. With an increasing number of treatment options availab
practitioners face the growing challenge of selecting the most appropriate treatment for each patient. T
utilization of AI-based approaches substantially expands our understanding of the tumor microenvironm
approaches to patient stratification and selection for diagnostic assays supporting the identification of t
regimen based on patient profiles. This review provides an overview of the opportunities and limitations
based methods in biomarker discovery and patient selection and discusses how advances in digital pat
considered in the current landscape of translational medicine, touching on challenges this technology m
clinical settings. The traditional role of pathologists in delivering accurate diagnoses or assessing bioma
diagnostics may be enhanced in precision, reproducibility, and scale by AI-powered analysis tools.

Modern Pathology (2022) 35:23–32; https://doi.org/10.1038/s41379-021-00919-2

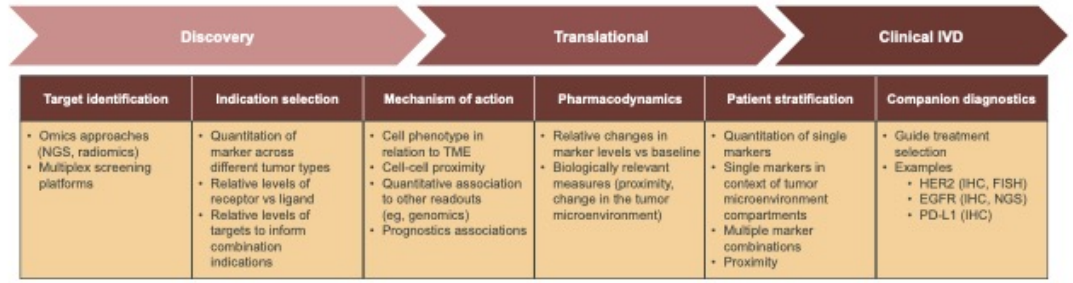


Fig. 1 Digital pathology: from drug discovery to clinical diagnostics. Dx diagnostic, EGFR epidermal growth factor receptor, FISH fluorescence in situ hybridization, HER2 human epidermal receptor 2, IHC immunohistochemistry, IVD in vitro diagnostic, MOA mechanism of action, NGS next-generation sequencing, PD pharmacodynamics, PD-L1 programmed death-ligand 1, TME tumor microenvironment.

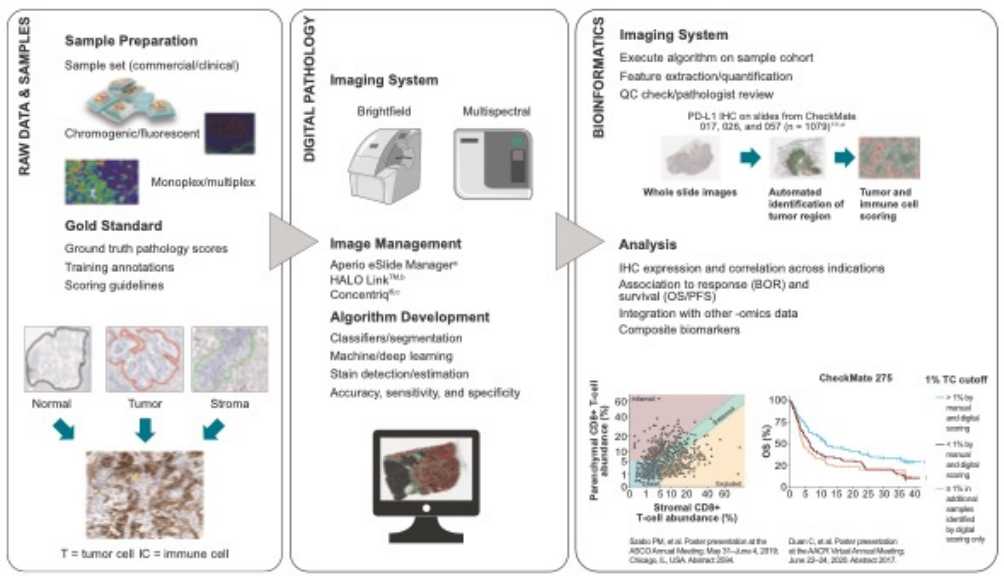


Fig. 2 Digital prognostic pathology workflow. BOR best overall response, IHC immunohistochemistry, OS overall survival, PFS progression-free survival, QC quality control. [a]Leica Biosystems; [b]Indica Labs; [c]Proscia; [d]PD-L1 IHC 28-8 pharmDx. Dako/Agilent Technologies.

nature communications

Article

https://doi.org/10.1038/s41467-022-33718-7

Integrative analysis of *KRAS* wildtype metastatic pancreatic ductal adenocarcinoma reveals mutation and expression-based similarities to cholangiocarcinoma

Received: 10 December 2021

Accepted: 29 September 2022

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Oncogenic *KRAS* mutations are absent in approximately 10% of patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) and may represent a subgroup of mPDAC with therapeutic options beyond standard-of-care cytotoxic chemotherapy. While distinct gene fusions have been implicated in *KRAS* wildtype mPDAC, information regarding other types of mutations remain limited, and gene expression patterns associated with *KRAS* wildtype mPDAC have not been reported. Here, we leverage sequencing data from the PanGen trial to perform comprehensive characterization of the molecular landscape of *KRAS* wildtype mPDAC and reveal increased frequency of chr1q amplification encompassing transcription factors *PROX1* and *NR5A2*. By leveraging data from colorectal adenocarcinoma and cholangiocarcinoma samples, we highlight similarities between cholangiocarcinoma and *KRAS* wildtype mPDAC involving both mutation and expression-based signatures and validate these findings using an independent dataset. These data further establish *KRAS* wildtype mPDAC as a unique molecular entity, with therapeutic opportunities extending beyond gene fusion events.

Comparison of FDA Table of Pharmacogenetic Associations and Clinical Pharmacogenetics Implementation Consortium guidelines

Supplementary material is available with the full text of this article at *AJHP* online.

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Purpose. Healthcare professionals need a clear understanding of information about gene-drug interactions in order to make optimal use of pharmacogenetic (PGx) testing. In this report, we compare PGx information in the US Food and Drug Administration (FDA) Table of Pharmacogenetic Associations with information presented in Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines.

Summary. Information from CPIC guidelines and the FDA Table of Pharmacogenetic Associations do not have a high level of concordance. Many drugs mentioned in CPIC guidelines are not listed in the FDA table and vice versa, and the same gene-drug association and dosing recommendation was reported for only 5 of the 126 drugs included in either source. Furthermore, classification of drugs in specific sections of the FDA table does not correlate well with CPIC-assigned or provisionally assigned clinical actionability levels. The Pharmacogenomics Knowledge Base (PharmGKB) clinical annotation levels are generally high for drugs mentioned in CPIC guidelines. PharmGKB clinical annotation levels are often unassigned or are lower level for drugs listed on the FDA table but not in CPIC guidelines. These differences may be due in part to FDA having access to PGx information that is unavailable in published literature and/or because PGx classifications are based on criteria other than clinical actionability.

Conclusion. There are important differences between the PGx infor-

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Development and technical validation of an artificial intelligence model for quantitative analysis of histopathologic features of eosinophilic esophagitis

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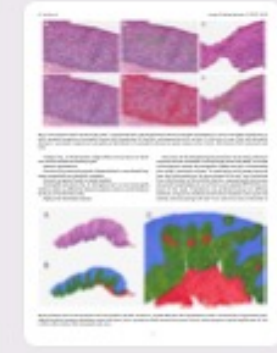
ABSTRACT

Background: In an attempt to provide quantitative, reproducible, and standardized analyses in cases of eosinophilic esophagitis (EoE), we have developed an artificial intelligence (AI) digital pathology model for the evaluation of histologic features in the EoE/esophageal eosinophilia spectrum. Here, we describe the development and technical validation of this novel AI tool.

Methods: A total of 10 726 objects and 56.2 mm^2 of semantic segmentation areas were annotated on whole-slide images, utilizing a cloud-based, deep learning artificial intelligence platform (Aiforia Technologies, Helsinki, Finland). Our training set consisted of 40 carefully selected digitized esophageal biopsy slides which contained the full spectrum of changes typically seen in the setting of esophageal eosinophilia, ranging from normal mucosa to severe abnormal-






Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x-y of this issue

Emergence of BRCA Reversion Mutations in Patients with Metastatic Castration-resistant Prostate Cancer After Treatment with Rucaparib

Andrea Loehr [a], Arif Hussain [b], Akash Patnaik [c], Alan H. Bryce [d], Daniel Castellano [e], Albert Font [f], Jeremy Shapiro [g], Jingsong Zhang [h], Brieuc Sautois [i], Nicholas J. Vogelzang [j], Gurkamal Chatta [k], Kevin Courtney [l], Andrea Harzstark [m], Francesco Ricci [n], Darrin Despain [o], Simon Watkins [p], Charmin King [q], Minh Nguyen [a], Andrew D. Simmons [a], Simon Chowdhury [r, s], Wassim Abida [t]

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original BRCA mutations. The incidence of BRCA reversion mutations increased with the duration of rucaparib treatment. The frequency of reversion mutations was higher in patients with an objective (58%) or a prostate-specific antigen (69%) response compared with those without either (39% and 29%, respectively).

Conclusions

These findings suggest that BRCA reversion mutations are a significant mechanism of acquired resistance to rucaparib in patients with BRCA+ mCRPC, with evidence of subclonal convergence promoting systemic resistance.

Patient summary

Men with BRCA mutated metastatic castration-resistant prostate cancer enrolled in TRITON2 were treated with rucaparib after progressing on one to two lines of androgen receptor–directed and one taxane-based therapy. Cell-free DNA from the plasma of 100 patients, collected after radiographic or prostate-specific antigen progression before May 5, 2020, was analyzed by next-generation

REVIEW

Rise of the Machines: Artificial Intelligence and the Clinical Laboratory

Shannon Haymond[a,b] **and Christopher McCudden**[c,*]

Background: Artificial intelligence (AI) is rapidly being developed and implemented to augment and automate decision-making across healthcare systems. Being an essential part of these systems, laboratories will see significant growth in AI applications for the foreseeable future.

Content: In laboratory medicine, AI can be used for operational decision-making and automating or augmenting human-based workflows. Specific applications include instrument automation, error detection, forecasting, result interpretation, test utilization, genomics, and image analysis. If not doing so today, clinical laboratories will be using AI routinely in the future, therefore, laboratory experts should understand their potential role in this new area and the opportunities for AI technologies. The roles of laboratorians range from passive provision of data to fuel algorithms to developing entirely new algorithms, with subject matter expertise as a perfect fit in the middle. The technical development of algorithms is only a part of the overall picture, where the type, availability, and quality of data are at least as important. Implementation of AI algorithms also offers technical and usability challenges that need to be understood to be successful. Finally, as AI algorithms continue to become available, it is important to understand how to evaluate their validity and utility in the real world.

Summary: This review provides an overview of what AI is, examples of how it is currently being used in laboratory medicine, different ways for laboratorians to get involved in algorithm development, and key considerations for AI algorithm implementation and critical evaluation.

INTRODUCTION

Artificial intelligence (AI) is a decades-old concept that is becoming a new practical reality in medicine. AI algorithms are being developed at a rapid pace and now becoming available for diagnosis, treatment, and prognosis. AI is broadly defined as computers imitating human thinking but can be further subdivided as shown in Fig. 1 into Artificial General Intelligence (AGI), Artificial Narrow Intelligence (ANI), and Artificial Superintelligence (ASI). AGI, also called "strong AI," refers to full mimicry of human reasoning, learning, and decision-making. For example, AGI would describe the ability to solving any real-world problem that humans encounter daily. AGI is variably estimated to be either decades away or never to occur because of the extent of progress needed (1).

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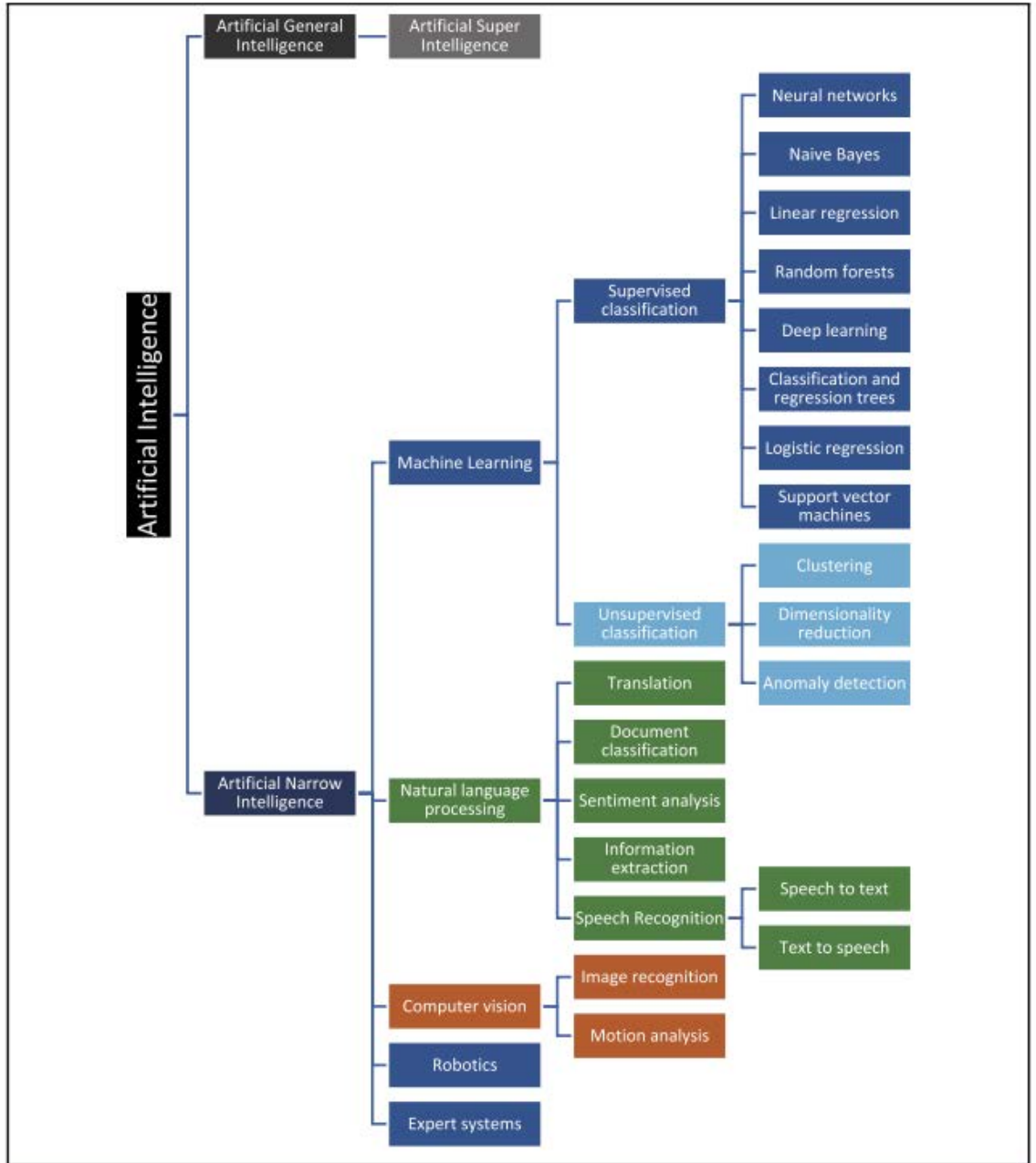

Fig. 1. Hierarchy of artificial intelligence concepts and tools.

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Claudia Bellini*, Andrea Padoan, Anna Carobene and Roberto Guerranti, on behalf of the Italian Society of Clinical Biochemistry and Clinical Molecular Biology Big Data and Artificial Intelligence Working Group

A survey on Artificial Intelligence and Big Data utilisation in Italian clinical laboratories

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published online September 6, 2022

Abstract

undertaken BAI projects, f
ships. The majority consid
fessional judgements, indi
Conclusions: The questio
back from SIBioC particip

Table 1: Characteristics of the survey.

Section	Question	Additional note when provided
Section 1: General characteristics (questions 1–6)	(1) Professional profiles of respondents	
	(2) Sex	
	(3) Age	
	(4) Type of workplace organisation	
	(5) Region of Italy where the laboratory/facility is situated	
	(6) Average number of test/year performed in the lab	
Section 2: Adequacy of digital equipment (questions 7–15)	(7) How many laboratory workstations with Internet connection are there in relation to the number of operators?	Indicate the operator/workstation ratio
	(8) Is a corporate Wi-Fi network available?	
	(9) Is the laboratory equipped with workstations for working and/or holding online meetings?	Webcam equipment, microphone, possibility to install appropriate software
	(10) How would you rate the quality of connections in terms of speed and stability?	1: totally inadequate; 4: completely adequate
	(11) How would you rate the software equipment of the workstations?	1: totally inadequate; 4: completely adequate
	(12) How would you rate the hardware equipment of the workstations?	1: totally inadequate; 4: completely adequate
	(13) How often do you use the cloud in your lab?	1: never; 4: always
	(14) Which cloud platform(s) do you use in your laboratory?	Multiple items can be selected
	(15) To what purposes do you use the cloud?	Multiple items can be selected

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Article

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The spatial transcriptomic landscape of non-small cell lung cancer brain metastasis

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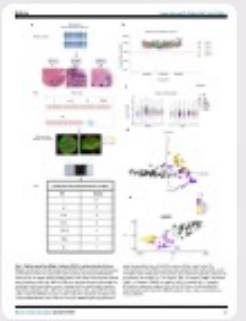
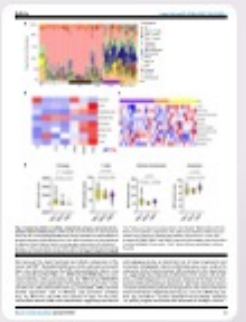
Qi Zhang[1,4] ✉, Rober Abdo[1,2,4], Cristiana Iosef[2,3], Tomonori Kaneko[2], Matthew Cecchini[1], Victor K. Han[3] & Shawn Shun-Cheng Li[2,3] ✉

Brain metastases (BrMs) are a common occurrence in lung cancer with a dismal outcome. To understand the mechanism of metastasis to inform prognosis and treatment, here we analyze primary and metastasized tumor specimens from 44 non-small cell lung cancer patients by spatial RNA sequencing, affording a whole transcriptome map of metastasis resolved with morphological markers for the tumor core, tumor immune microenvironment (TIME), and tumor brain microenvironment (TBME). Our data indicate that the tumor microenvironment (TME) in the brain, including the TIME and TBME, undergoes extensive remodeling to create an immunosuppressive and fibrogenic niche for the BrMs. Specifically, the brain TME is characterized with reduced antigen presentation and B/T cell function, increased neutrophils and M2-type macrophages, immature microglia, and reactive astrocytes. Differential gene expression and network analysis identify fibrosis and immune regulation as the major functional modules disrupted in both the lung and





Big data in basic and translational cancer research

Peng Jiang[1]✉, *Sanju Sinha*[1], *Kenneth Aldape*[2], *Sridhar Hannenhalli*[1], *Cenk Sahinalp*[1] *and Eytan Ruppin*[1]✉

Abstract | Historically, the primary focus of cancer research has been molecular and clinical studies of a few essential pathways and genes. Recent years have seen the rapid accumulation of large-scale cancer omics data catalysed by breakthroughs in high-throughput technologies. This fast data growth has given rise to an evolving concept of 'big data' in cancer, whose analysis demands large computational resources and can potentially bring novel insights into essential questions. Indeed, the combination of big data, bioinformatics and artificial intelligence has led to notable advances in our basic understanding of cancer biology and to translational advancements. Further advances will require a concerted effort among data scientists, clinicians, biologists and policymakers. Here, we review the current state of the art and future challenges for harnessing big data to advance cancer research and treatment.

Cancer is a complex process, and its progression involves diverse processes in the patient's body[1]. Consequently, the cancer research community generates massive amounts of molecular and phenotypic data to study cancer hallmarks as comprehensively as possible. The rapid accumulation of omics data catalysed by breakthroughs

database[3] — the largest genomics data repository to our knowledge — contained approximately 1.1 million samples with 'cancer' as a keyword. However, ImageNet, the largest public repository for computer vision, contains 15 million images[4]. Second, cancer research data are typically heterogeneous and may contain many dimensions

Events

Next steering committee meeting

11/30/2022

Digital Pathology AI Workshop

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Other events

- https://epredia.com/events/unlock-the-power-of-digital-pathology-cambridge/

- https://web.cvent.com/event/c495b5a4-ab5c-4ec4-a5b9-df63bba5eae6/websitePage:6eb3a7c7-6dc4-467c-b55f-4f7652b1f6cd