NCT NATIONAL CENTER FOR TUMOR DISEASES HEIDELBERG

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Colon cancer - using digital tools to search for old and new biomarkers

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www.kather.ai

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Potential conflicts of interest

Employed by

RWTH Aachen University Hospital, Germany
Heidelberg University Hospital, Germany
Leeds University, UK (honorary)

Consulting / Advisory Board / Collaboration

Owkin, France
Panakeia, UK
MSD
Eisai

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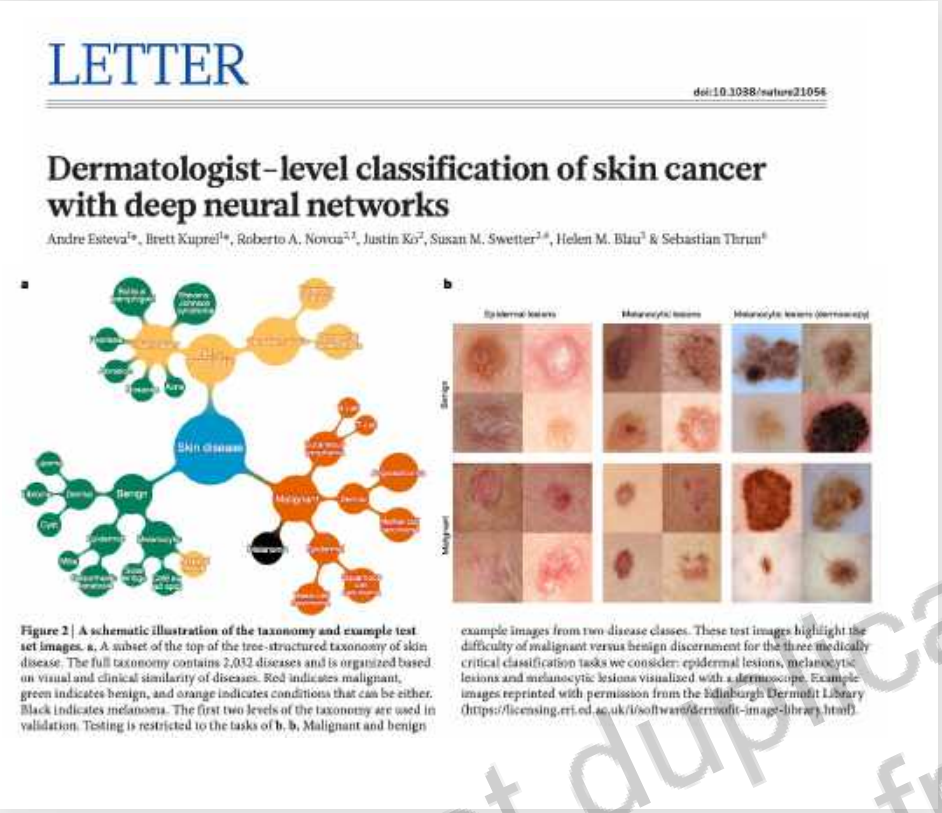
Image classification



LETTER

doi:10.1038/nature21056

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva[1]*, Brett Kuprel[1]*, Roberto A. Novoa[2,3], Justin Ko[2], Susan M. Swetter[2,4], Helen M. Blau[5] & Sebastian Thrun[6]

Figure 2 | A schematic illustration of the taxonomy and example test set images. a, A subset of the top of the tree-structured taxonomy of skin disease. The full taxonomy contains 2,032 diseases and is organized based on visual and clinical similarity of diseases. Red indicates malignant, green indicates benign, and orange indicates conditions that can be either. Black indicates melanoma. The first two levels of the taxonomy are used in validation. Testing is restricted to the tasks of **b**, Malignant and benign example images from two disease classes. These test images highlight the difficulty of malignant versus benign discernment for the three medically critical classification tasks we consider: epidermal lesions, melanocytic lesions and melanocytic lesions visualized with a dermoscope. Example images reprinted with permission from the Edinburgh Dermofit Library (https://licensing.eri.ed.ac.uk/i/software/dermofit-image-library.html).

1 mm
Histology
3966 px

Chest CT
4096 px

Colonoscopy
1024 px

Dermoscopy
299 px

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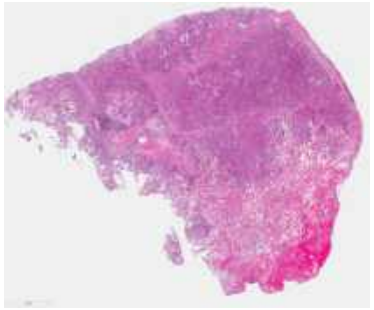
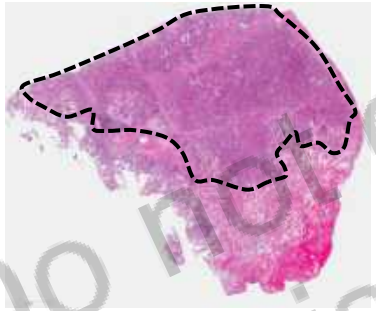
Esteva et al., Nature 2017; Echle et al., British Journal of Cancer 2020

How does it work?

a **tumor detection**

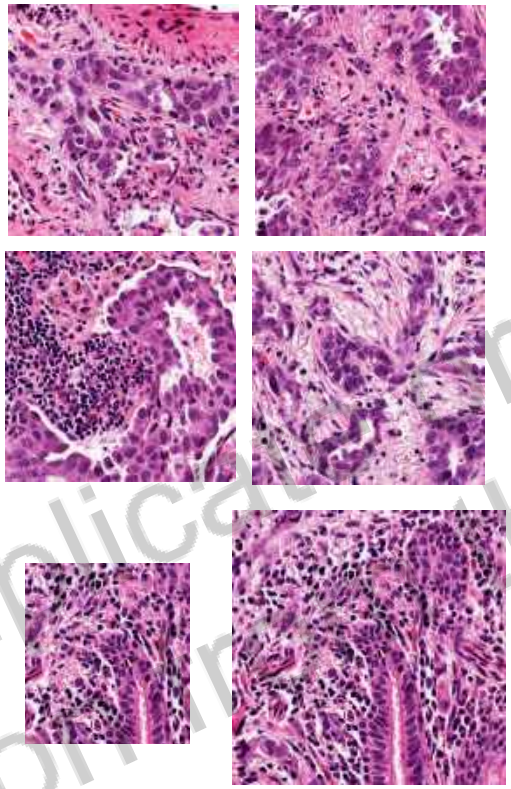


Option 1: weakly supervised learning



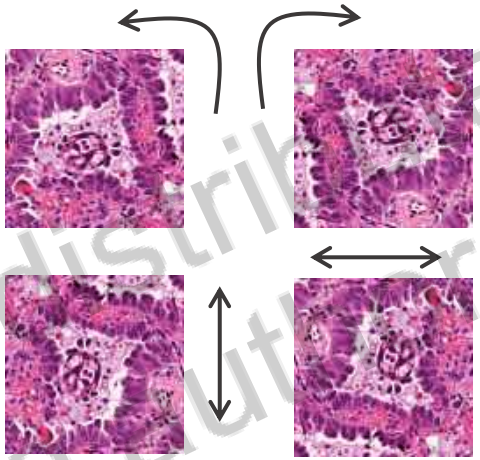
Option 2: restrict to tumor tissue

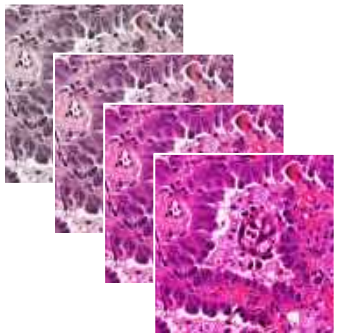
b **library preparation**



size and magnification may vary

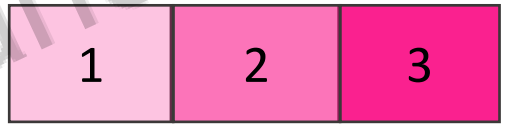
c **preprocessing**



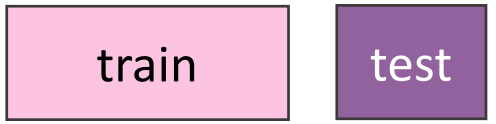


d **training and testing**

Option 1: train-test split

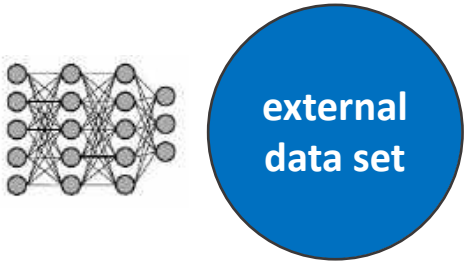


Option 2: cross-validation



Option 3: external testing

e **external validation**



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Echle et al., British Journal of Cancer 2020

The principle of supervised deep learning

supervised, unsupervised,
reinforcement learning

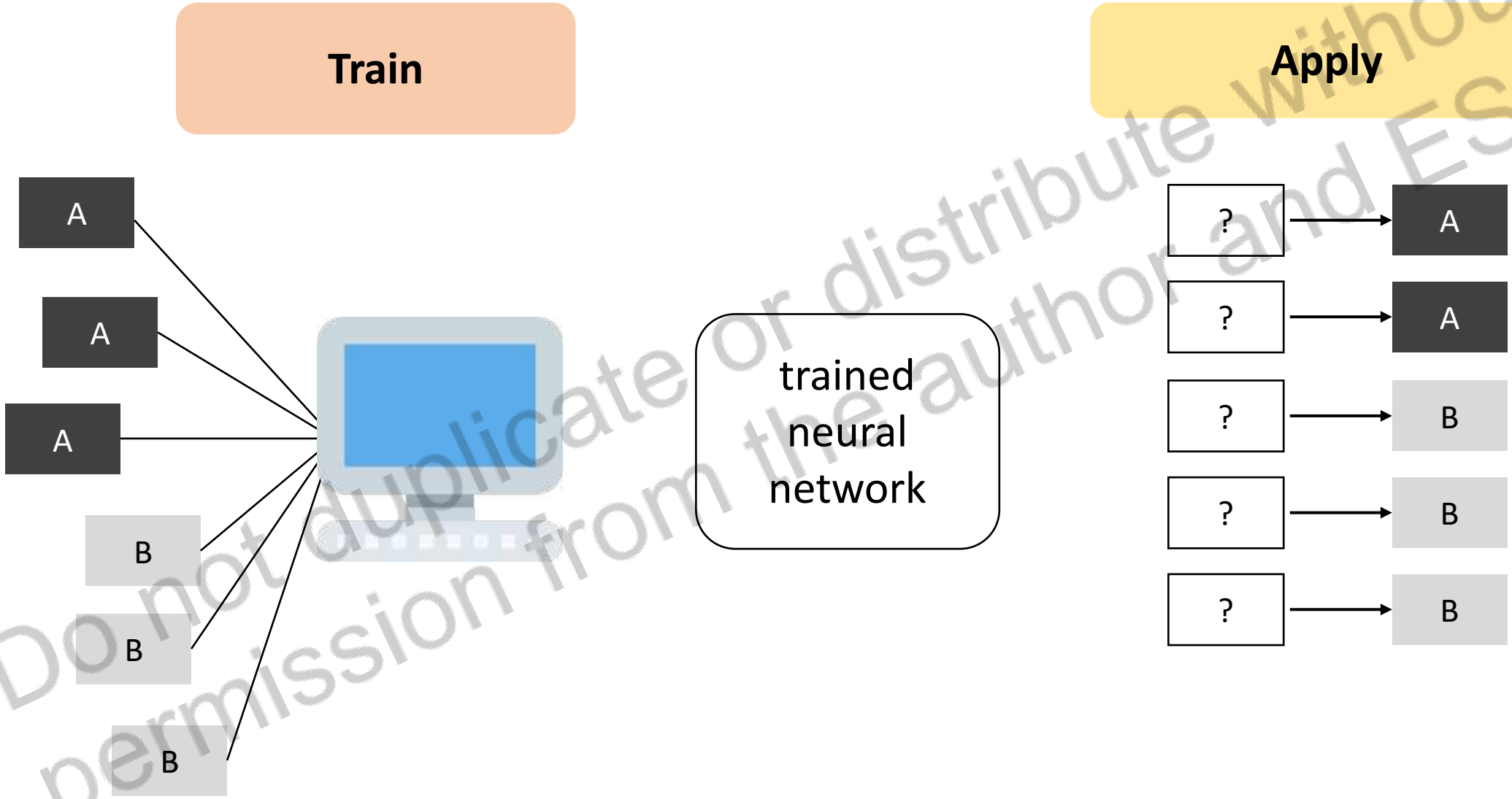

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Image classification is easy

PLOS ONE

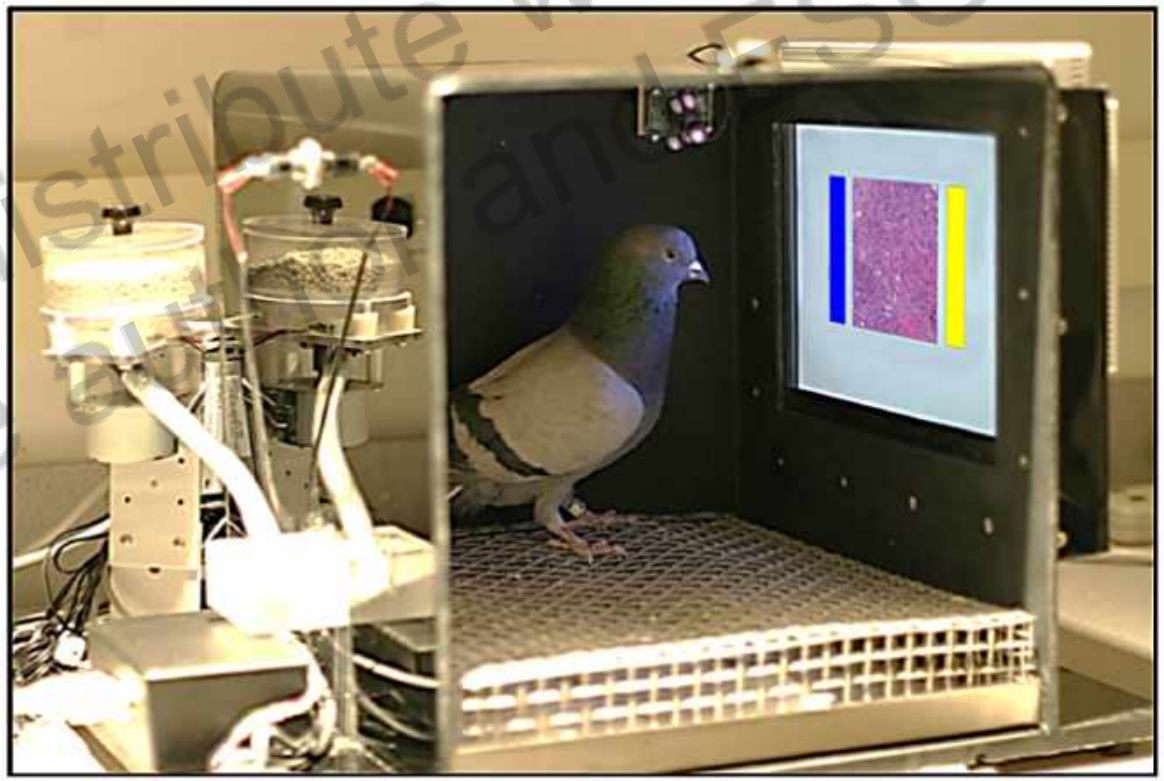
RESEARCH ARTICLE

Pigeons (*Columba livia*) as Trainable Observers of Pathology and Radiology Breast Cancer Images

Richard M. Levenson[1]*, Elizabeth A. Krupinski[3], Victor M. Navarro[2], Edward A. Wasserman[2]*

1 Department of Pathology and Laboratory Medicine, University of California Davis Medical Center, Sacramento, California, United States of America, **2** Department of Psychological and Brain Sciences, The University of Iowa, Iowa City, Iowa, United States of America, **3** Department of Radiology & Imaging Sciences, College of Medicine, Emory University, Atlanta, Georgia, United States of America

* levenson@ucdavis.edu (RML); ed-wasserman@uiowa.edu (EAW)



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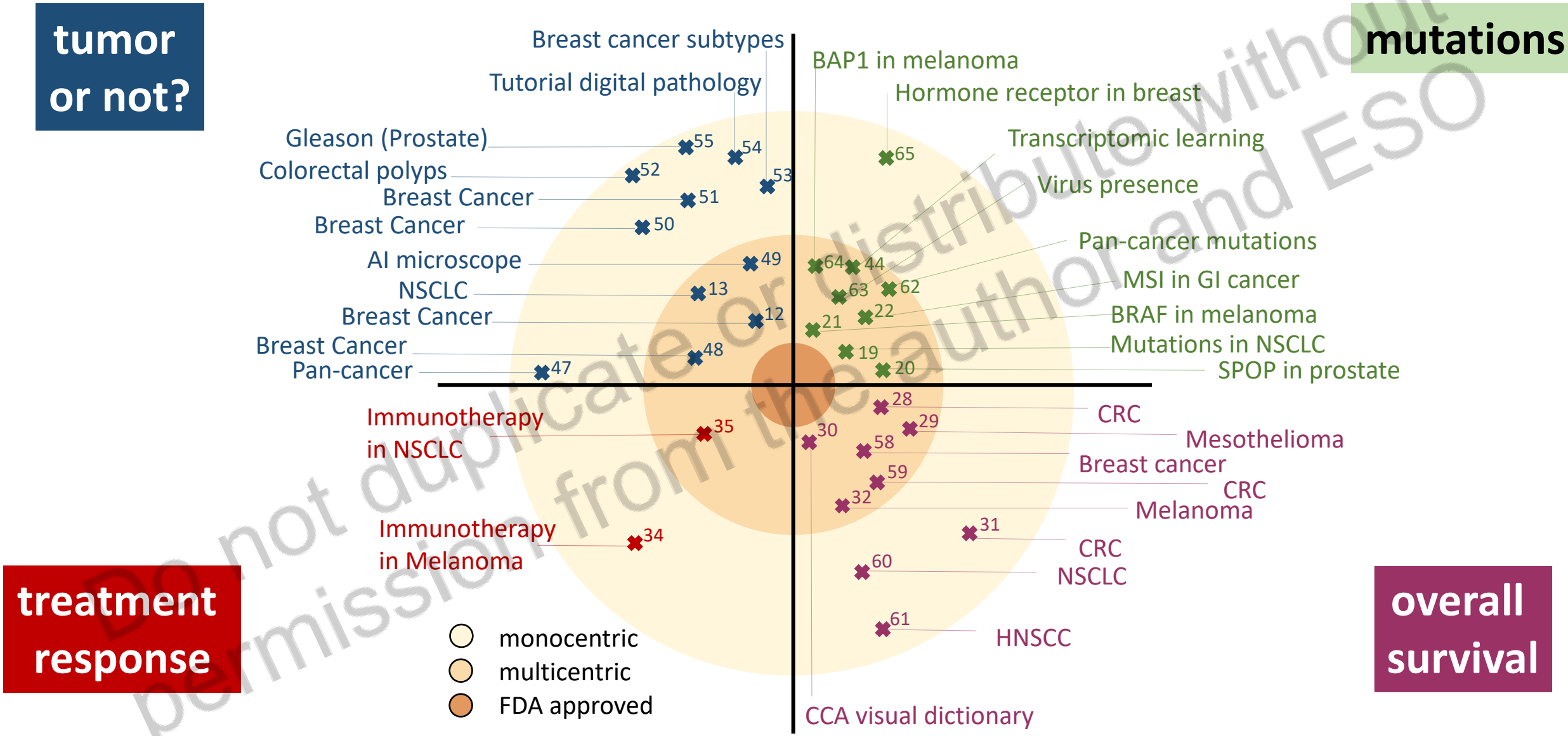
Levenson et al., 2015; https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0141357

What is the context?



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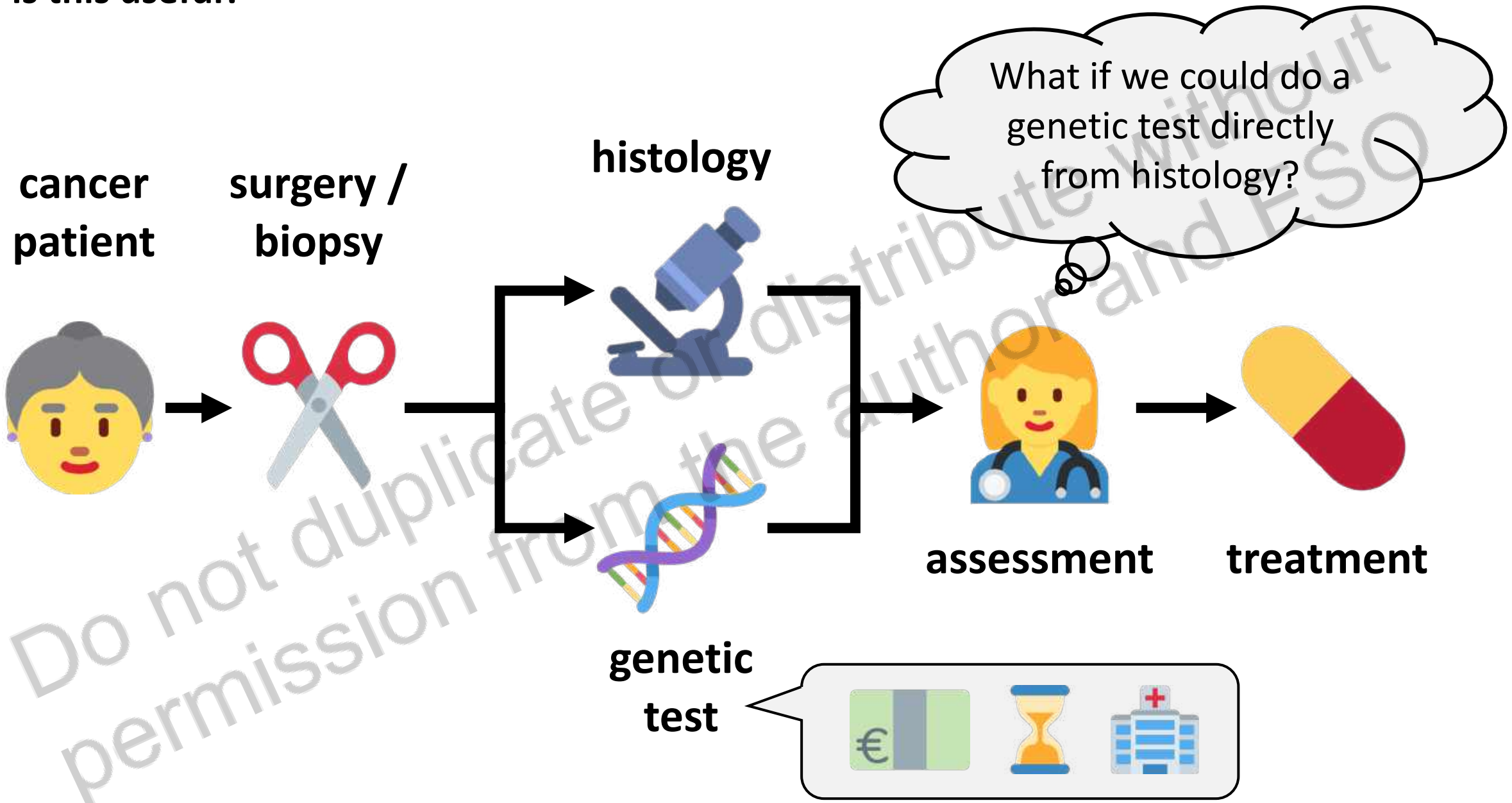
Echle et al., British Journal of Cancer, 2020

Why is this useful?



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Kather et al., Nature Medicine 2019

Icons: Twitter Twemoji

Hypothesis

Specific genetic alterations in cancer …

… elicit changes in the phenotype of …

- tumor cells (1st order)
- TME (2nd order)

Deep learning can infer genotype from histology images

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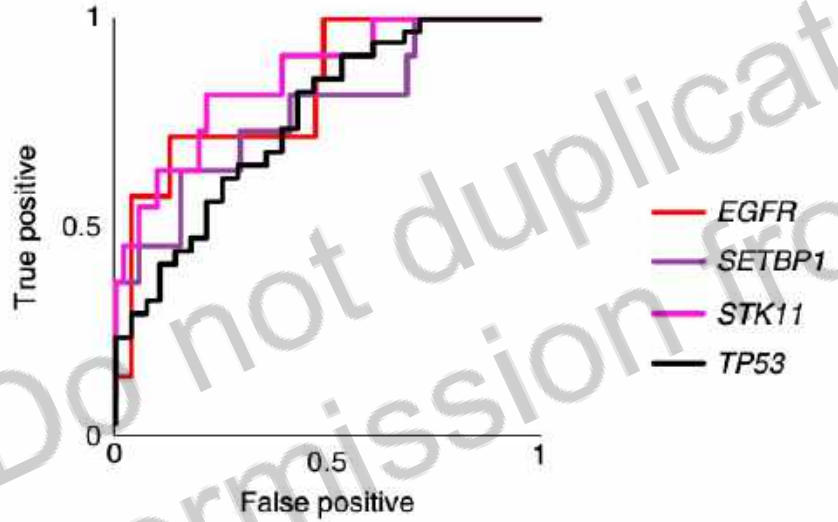
Kather et al., Nature Cancer, 2020

Histology-based genotyping

nature medicine
ARTICLES
https://doi.org/10.1038/s41591-018-0177-5

Classification and mutation prediction from non–small cell lung cancer histopathology images using deep learning

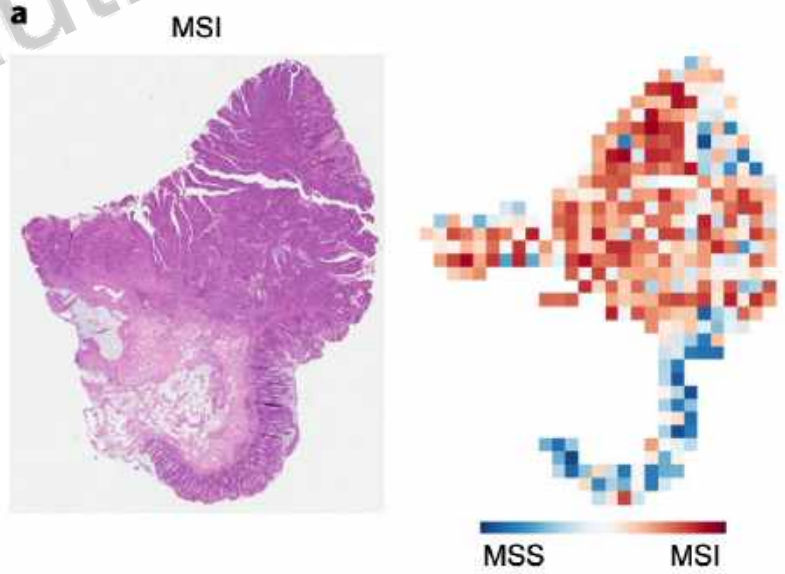
Nicolas Coudray[1,2,9], Paolo Santiago Ocampo[3,9], Theodore Sakellaropoulos[4], Navneet Narula[3], Matija Snuderl[3], David Fenyö[5,6], Andre L. Moreira[3,7], Narges Razavian[8*] and Aristotelis Tsirigos[1,3*]



nature medicine
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-019-0462-y

Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer

Jakob Nikolas Kather[1,2,3,4,5*], Alexander T. Pearson[4], Niels Halama[2,5,6], Dirk Jäger[2,3,5], Jeremias Krause[1], Sven H. Loosen[1], Alexander Marx[7], Peter Boor[8], Frank Tacke[9], Ulf Peter Neumann[10], Heike I. Grabsch[11,12], Takaki Yoshikawa[13,14], Hermann Brenner[2,15,16], Jenny Chang-Claude[17,18], Michael Hoffmeister[15], Christian Trautwein[1] and Tom Luedde[1*]



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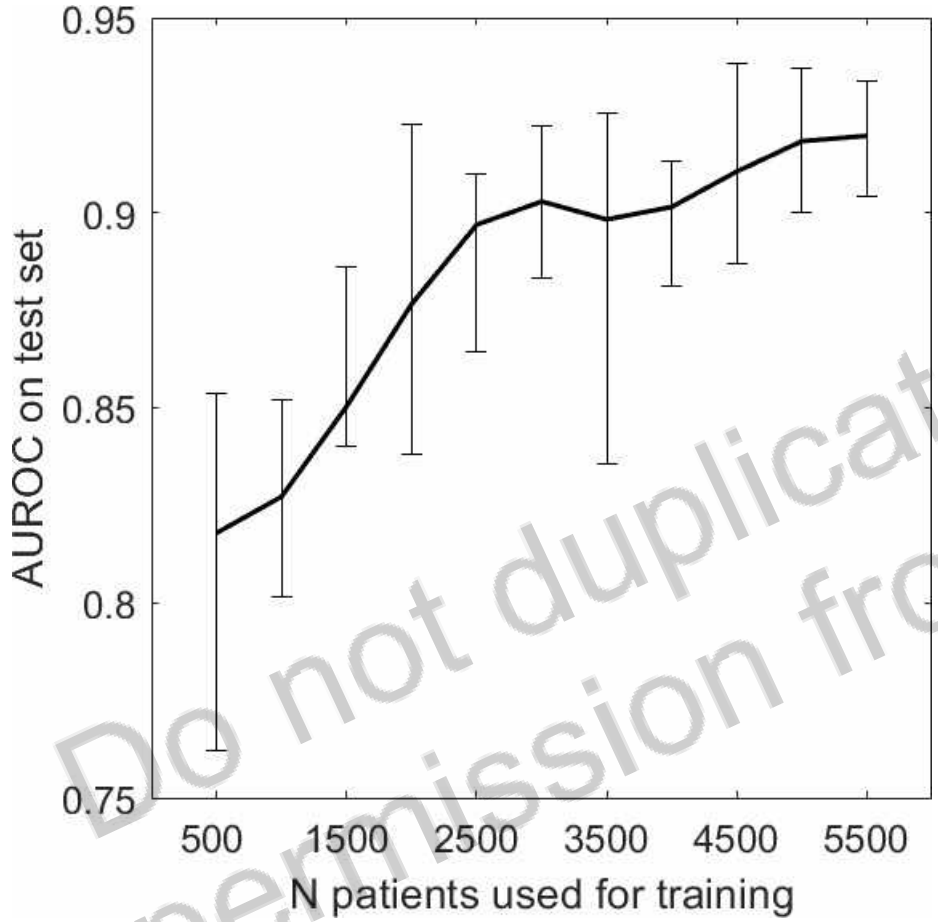
Coudray et al., Nature Medicine 2018

Kather et al., Nature Medicine 2019

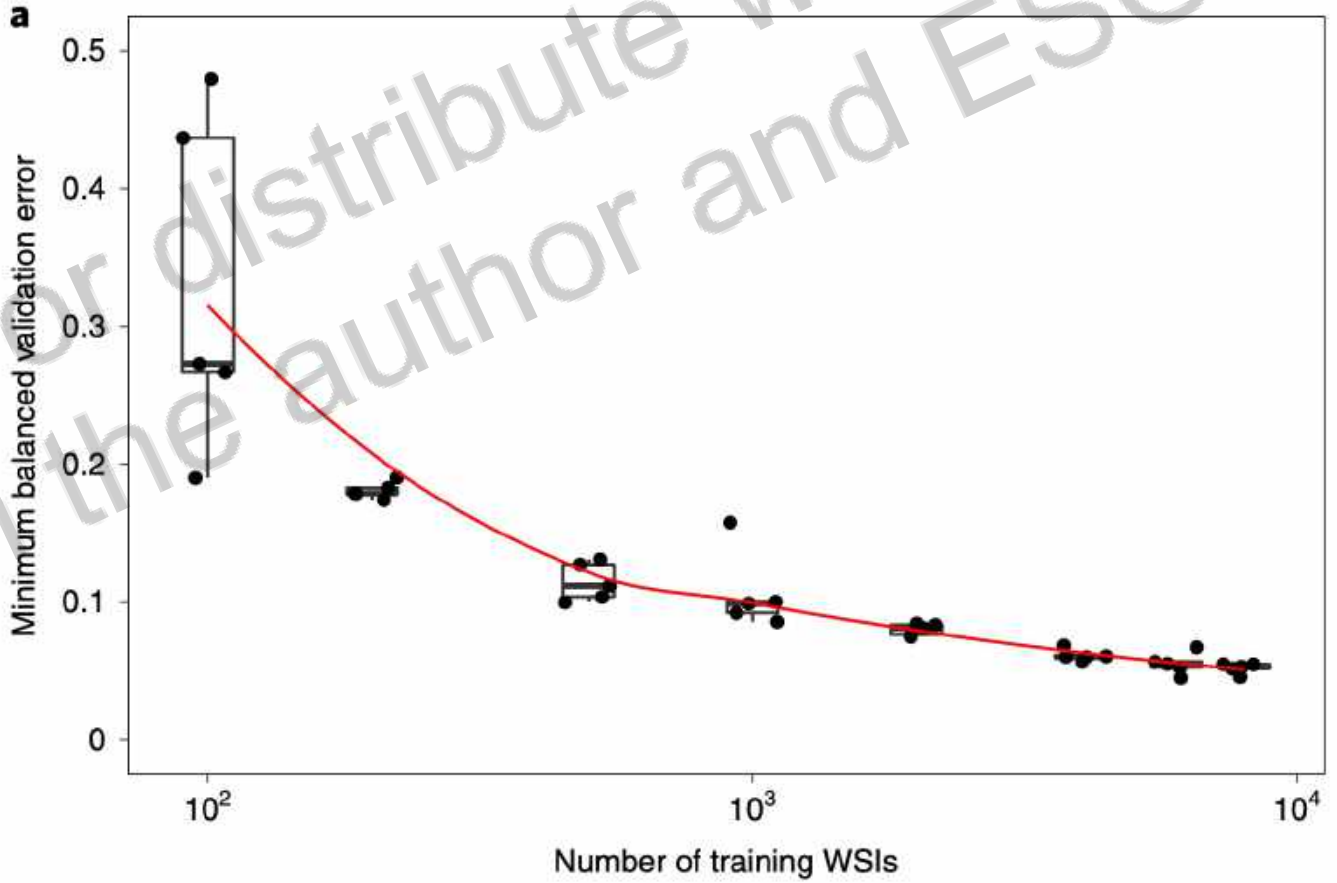
How many patients should we train on?

learning curve for MSI detection
(test on n=906)



Echle et al., Gastroenterology 2020

learning curve for weakly supervised
prostate cancer detection



Campanella et al., Nature Medicine 2019

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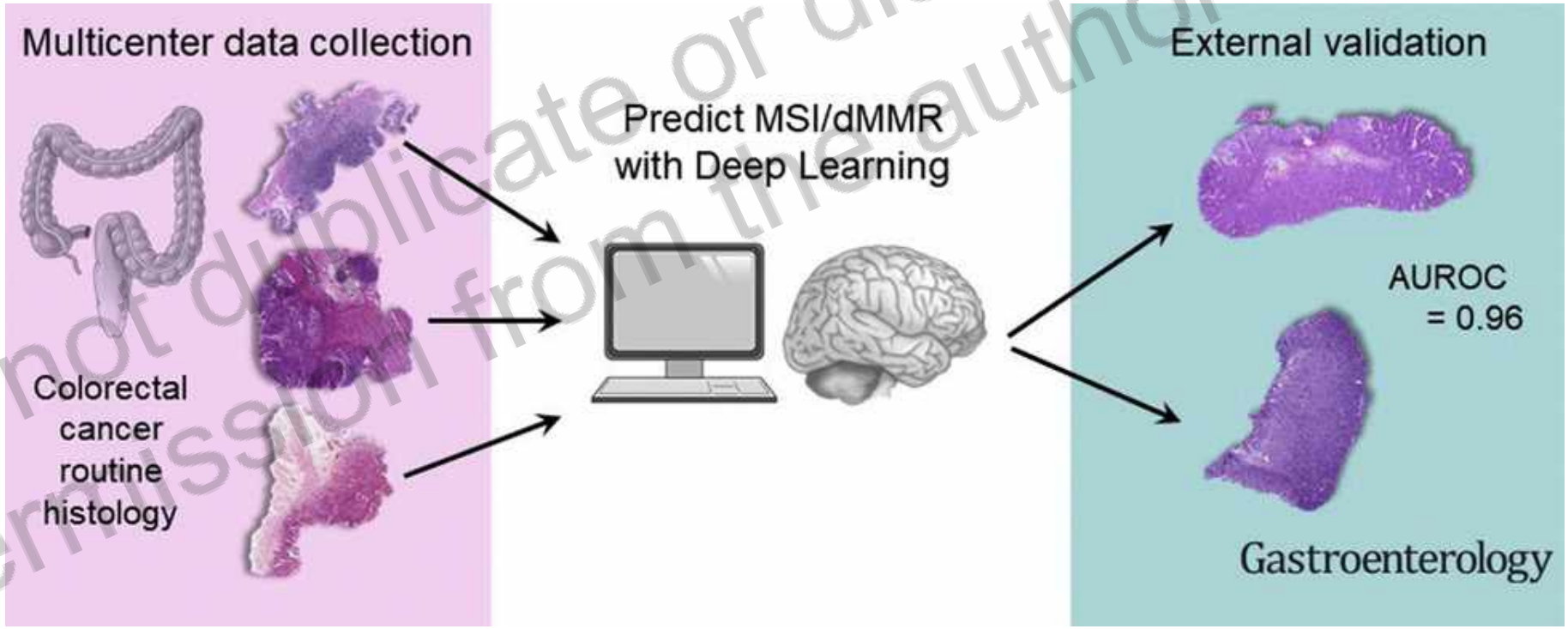
Multicentric, retrospective validation

Clinical-Grade Detection of Microsatellite Instability in Colorectal Tumors by Deep Learning

Gastroenterology aga American Gastroenterological Association

Amelie Echle,[1] Heike Irmgard Grabsch,[2,3] Philip Quirke,[3] Piet A. van den Brandt,[4] Nicholas P. West,[3] Gordon G. A. Hutchins,[3] Lara R. Heij,[5,6,7] Xiuxiang Tan,[5,6,7] Susan D. Richman,[3] Jeremias Krause,[1] Elizabeth Alwers,[8] Josien Jenniskens,[4] Kelly Offermans,[4] Richard Gray,[9] Hermann Brenner,[8,10,11] Jenny Chang-Claude,[12,13] Christian Trautwein,[1] Alexander T. Pearson,[14] Peter Boor,[7] Tom Luedde,[1,15] Nadine Therese Gaisa,[7] Michael Hoffmeister,[8] and Jakob Nikolas Kather[1,3,11,16]



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Echle et al., Gastroenterology 2020

Pan-cancer application

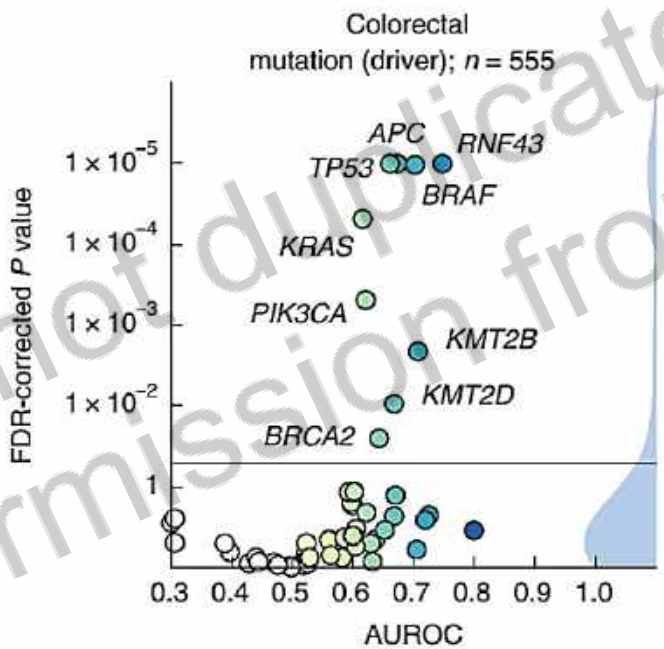
nature cancer

ARTICLES

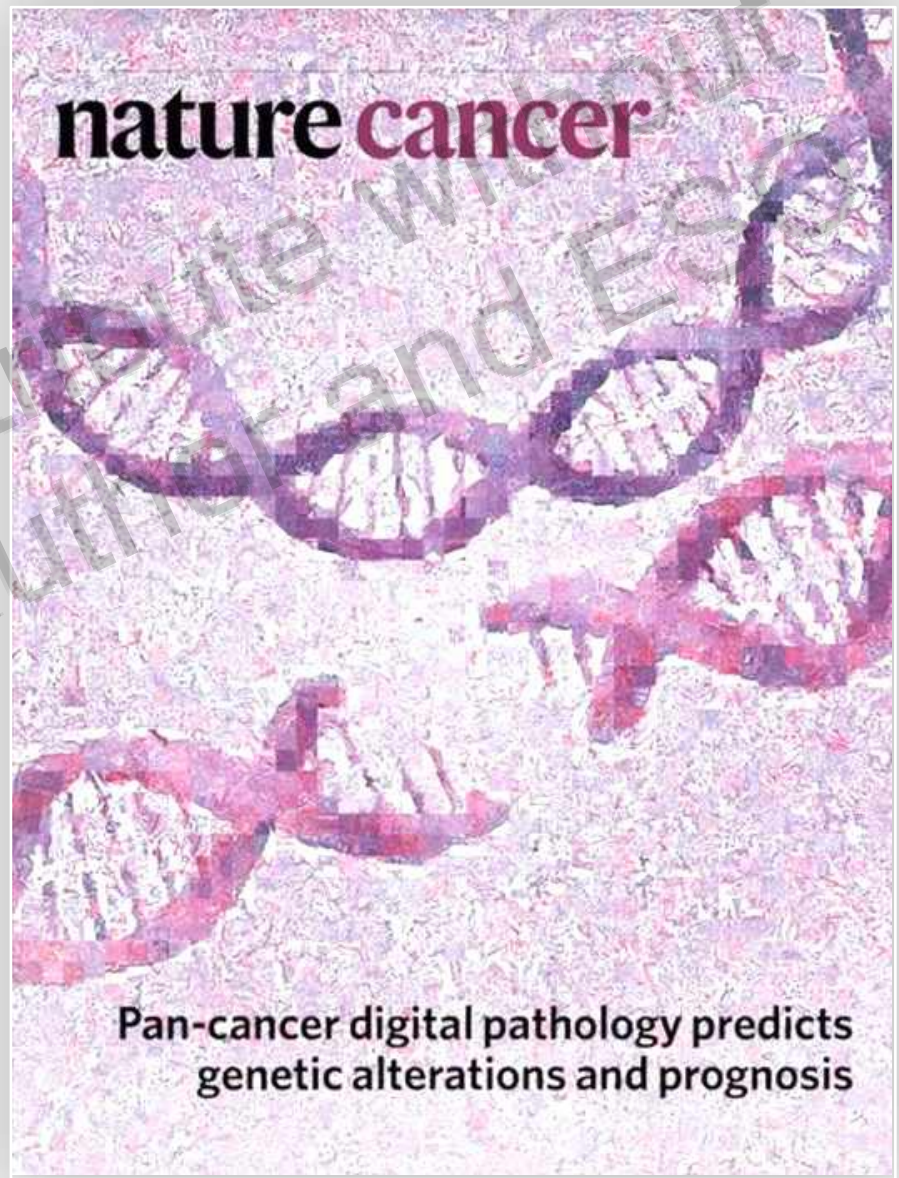
https://doi.org/10.1038/s43018-020-0087-6

Pan-cancer image-based detection of clinically actionable genetic alterations

Jakob Nikolas Kather[1,2,3], Lara R. Heij[4,5,6], Heike I. Grabsch[7,8], Chiara Loeffler[1], Amelie Echle[1], Hannah Sophie Muti[1], Jeremias Krause[1], Jan M. Niehues[1], Kai A. J. Sommer[1], Peter Bankhead[9], Loes F. S. Kooreman[7], Jefree J. Schulte[10], Nicole A. Cipriani[10], Roman D. Buelow[6], Peter Boor[6], Nadina Ortiz-Brüchle[6], Andrew M. Hanby[8], Valerie Speirs[11], Sara Kochanny[12], Akash Patnaik[12], Andrew Srisuwananukorn[13], Hermann Brenner[2,14,15], Michael Hoffmeister[14], Piet A. van den Brandt[16], Dirk Jäger[2,3], Christian Trautwein[1], Alexander T. Pearson[12,19] and Tom Luedde[17,18,19]



BRAF is directly targetable (2nd line)



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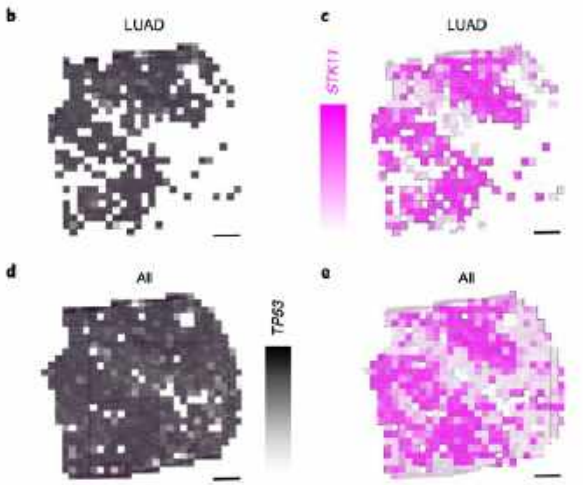
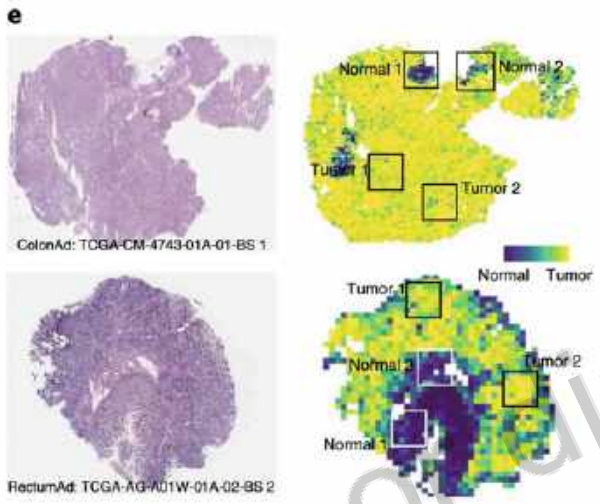
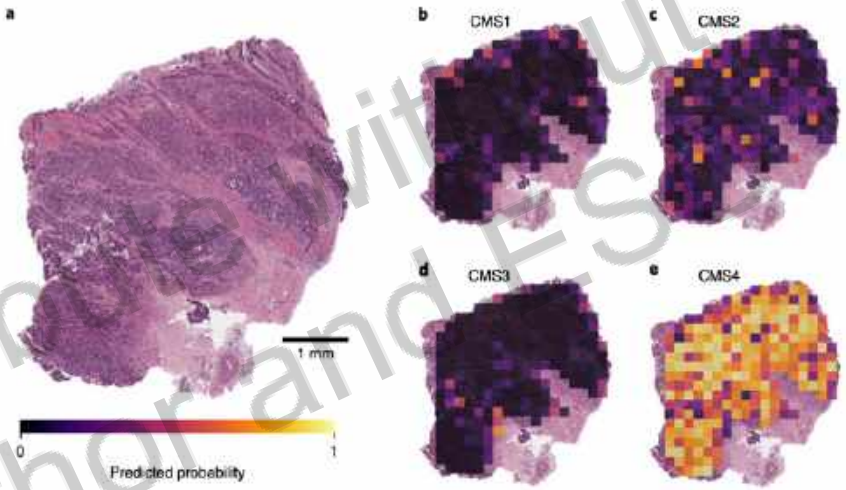
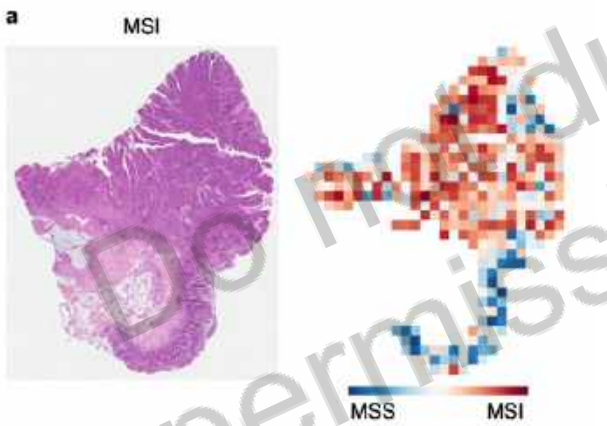
Kather et al., Nature Cancer 2020

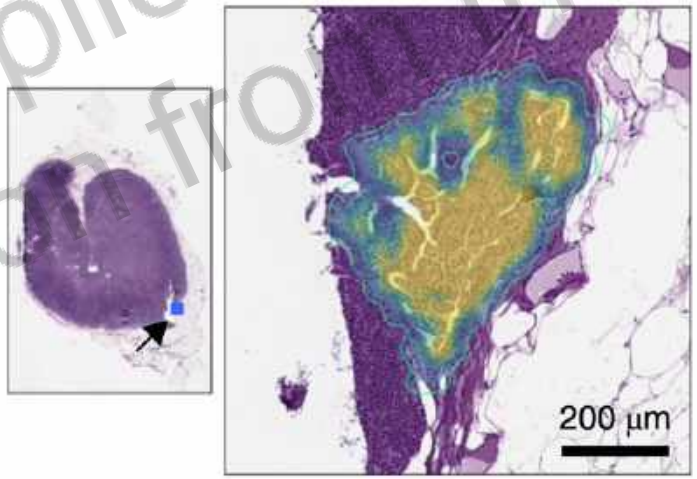
Training with only slide labels yields spatially resolved predictions

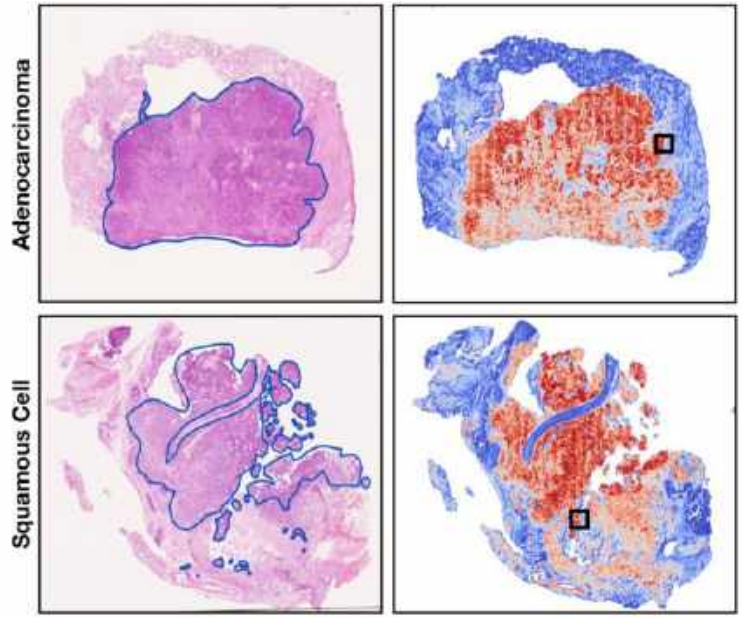












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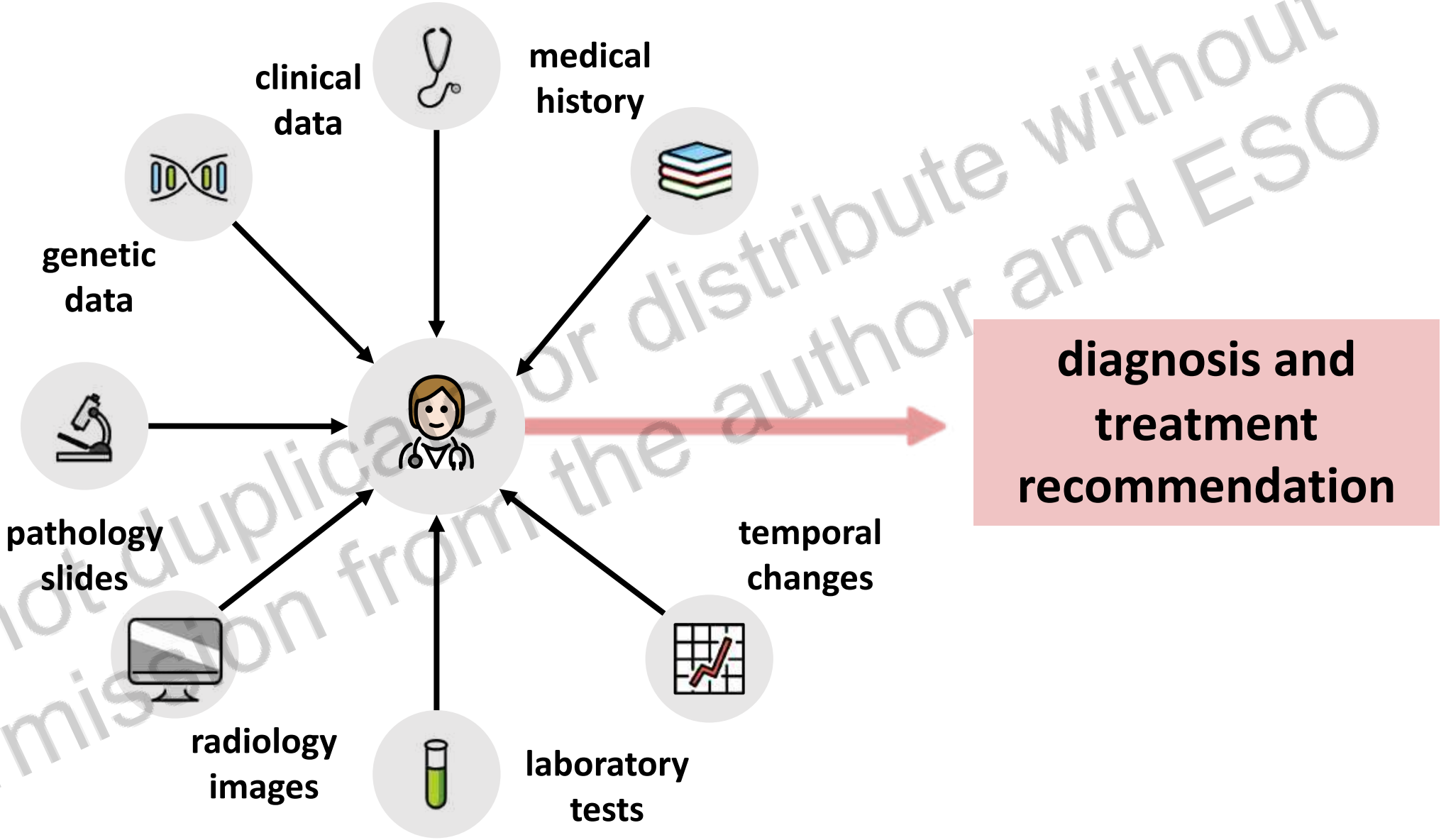
Coudray, Nat Med 2018 / Kather, Nat Med 2019 / Fu, Nat Cancer 2020 / Kather, Nat Cancer 2020 / Campanella, Nat Med 2019 / Lu, Nat Biomed Eng 2021

Real-world decision-making



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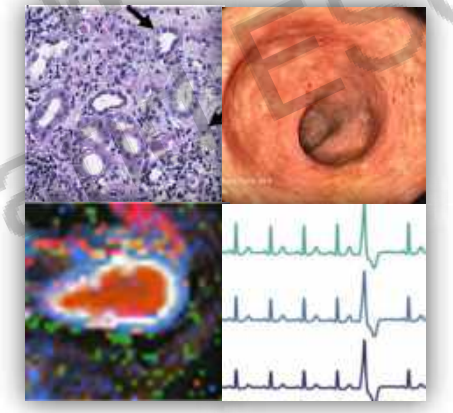
own data, unpublished, image credit: OpenMoji

Human plus AI

Hardware

Algorithms

Data



Ask the right questions and implement in the real world

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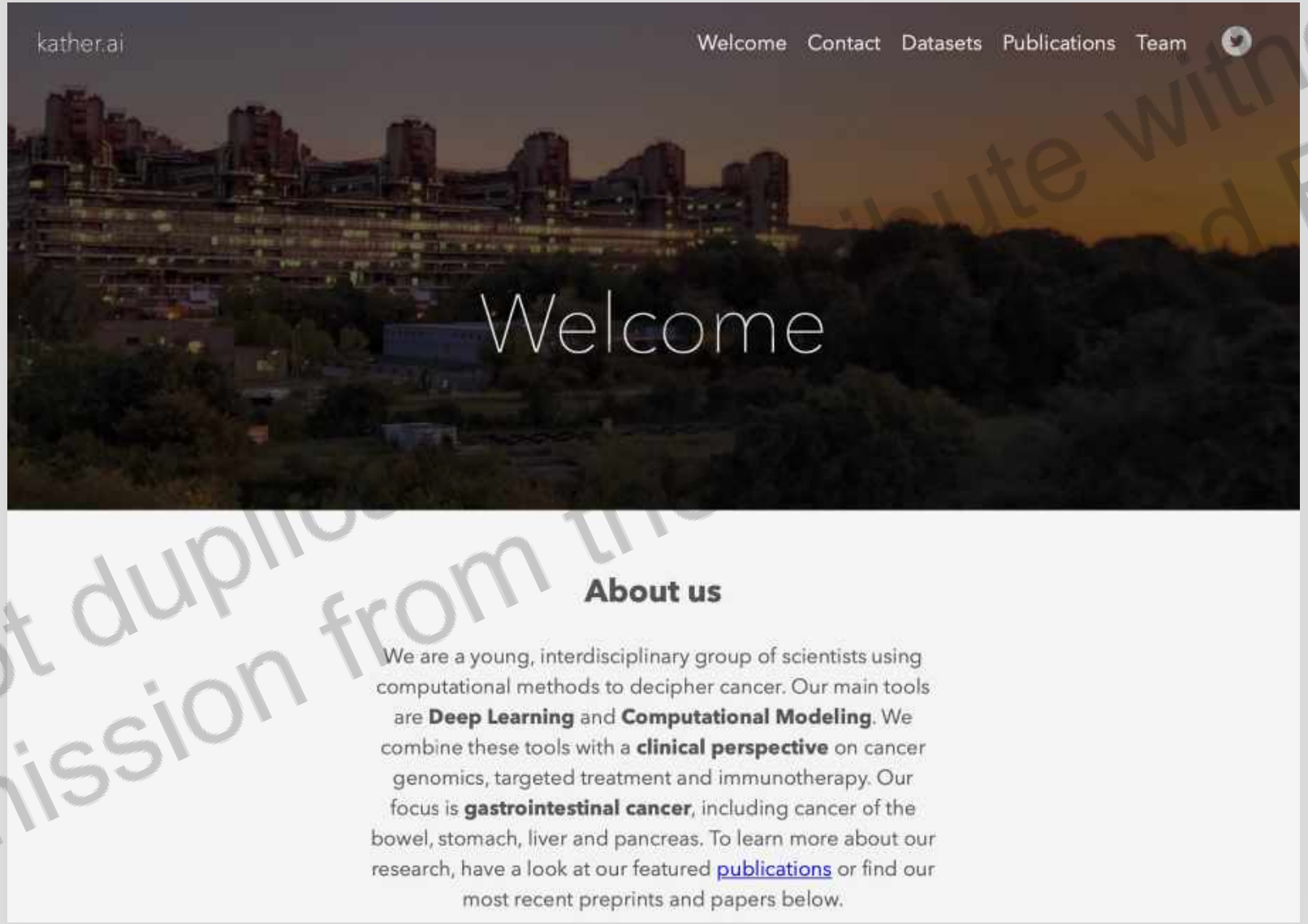

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Support and awards

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DKTK

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