



**AI-ON-Lab** 

# Intelligenza Artificiale e NSCLC

### Arsela Prelaj, MD, PhD

Al-ON-Lab leader (Artificial Intelligence for Oncology lab), and Medical Oncologist, at Istituto Nazionale Tumori di Milano PhD in Bioengineering and Al, Politecnico di Milano, Italy ESMO Real-World Data and Digital Healt working group member





### Congresso Nazionale

CARCINOMA DEL POLMONE: QUALI NOVITÀ NEL 2024? V EDIZIONE

28 OTTOBRE 2024

## **Physics Nobel scooped by machine**learning pioneers

John Hopfield and Geoffrey Hinton pioneered computational methods that enabled the development of neural networks.



# **Chemistry Nobel goes to developers** of AlphaFold AI that predicts protein structures

This year's prize celebrates computational tools that have transformed biology and have the potential to revolutionize drug discovery.







University of Washington USA

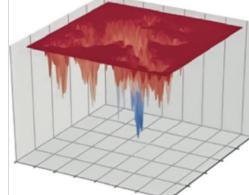
"för datorbaserad proteindesign

"for computational protein design

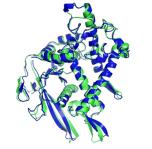
Google DeepMind Google DeepMind United Kingdom United Kingdom

"för proteinstrukturprediktion"

for protein structure prediction



"I hope when we look back on AlphaFold, it will be the first proof point of Al's incredible potential."



T1037 / 6vr4 90.7 GDT (RNA polymerase domain) T1049 / 6v4f 93.3 GDT (adhesin tip)

Experimental result Computational prediction

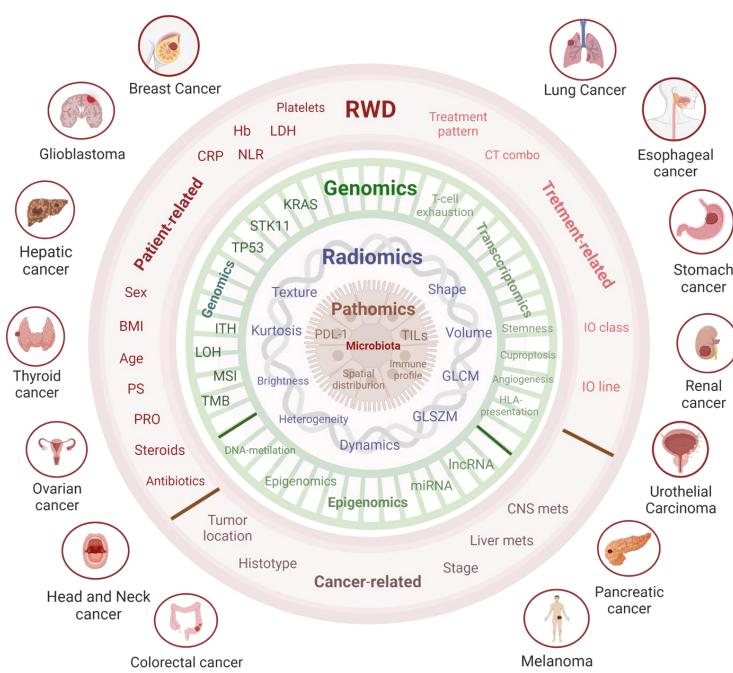
### Machine memory

In 1982, Hopfield, a theoretical biologist with a background in physics, came up with a network that described connections between virtual neurons as physical forces<sup>1</sup>...

Optimizing the synergy between physics and machine learning. Nat Mach Intell 3, 925 (2021). https://doi.org/10.1038/s42256-021-00416-w; Jumper, J. et al. Nature 596, 583-589 (2021).

# What Al Can Do?Image: Second state of the second sta

- 2. discover new patterns and biomarkers
- 3. drive new wet experiments



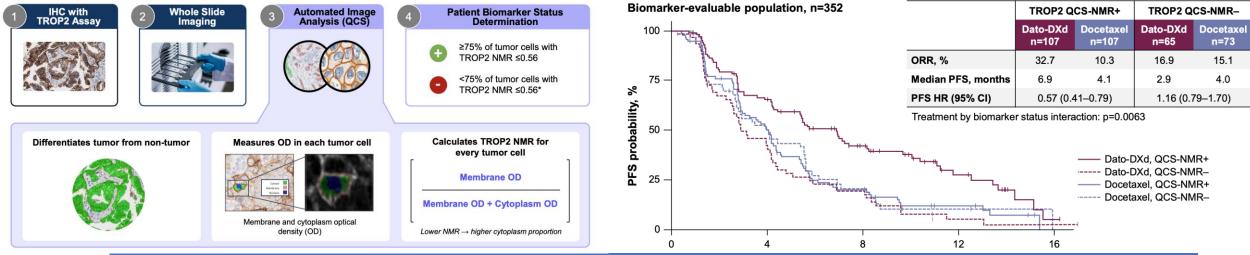
# IMMUNE BIOMARKER DISCOVERY WITH AI: Example

### Normalized Membrane Ratio of TROP2 by Quantitative Continuous Scoring is Predictive of Clinical Outcomes in TROPION-Lung01

<u>Marina Chiara Garassino</u>,<sup>1</sup> Jacob Sands,<sup>2</sup> Luis Paz-Ares,<sup>3</sup> Aaron Lisberg,<sup>4</sup> Melissa Johnson,<sup>5</sup> Maurice Pérol,<sup>6</sup> Danielle Carroll,<sup>7</sup> Ansh Kapil,<sup>8</sup> Vincent Haddad,<sup>7</sup> Deise Uema,<sup>9</sup> Hadassah Sade,<sup>8</sup> Myung-Ju Ahn,<sup>10</sup>

Patients receiving Dato-DXd who were TROP2 QCS-NMR+ had a higher ORR and longer PFS compared with those who were TROP2 QCS-NMR–

QCS is a novel, fully-supervised computational pathology approach that precisely quantifies and locates targets like TROP2 TROP2 QCS-NMR positivity is predictive for longer PFS with Dato-DXd in the biomarker-evaluable population



TROP2 QCS-NMR has the potential to be the first TROP2 biomarker and the first computational pathology biomarker for predicting clinical response to Dato-DXd in NSCLC



### Arsela Prelaj

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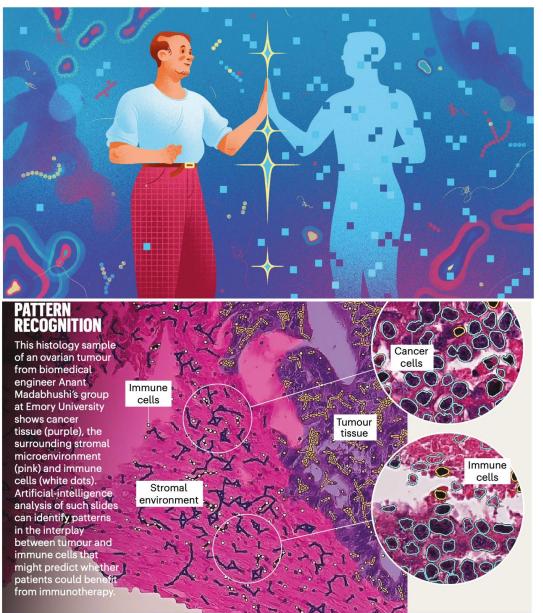
WCLC 2024, Garassino et al.

# Al-based **DECISION SUPPORT SYSTEM**

# FROM RESEARCH TO CLINIC

# nature

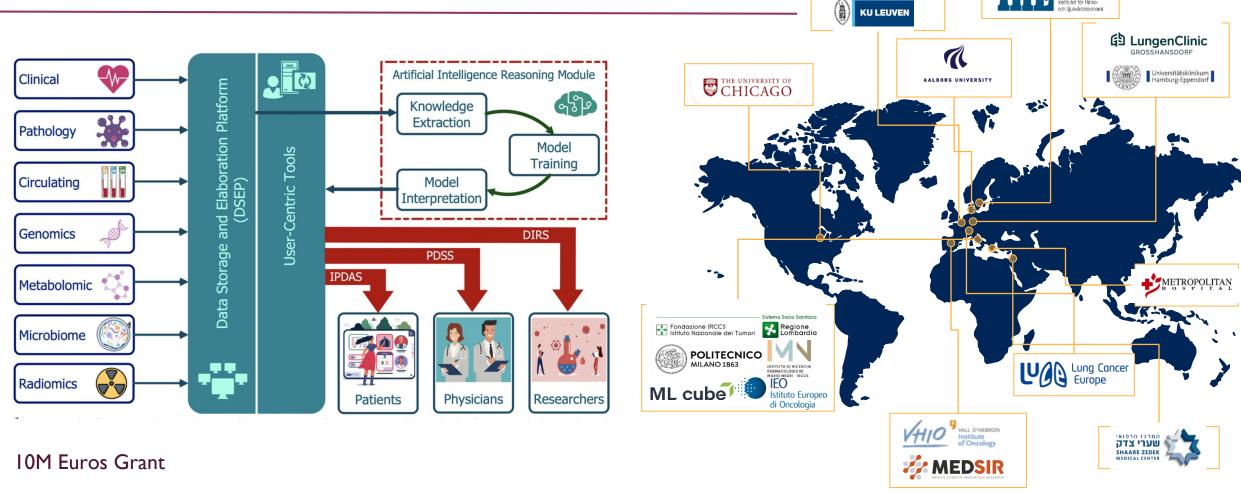
### **By Michael Eisenstein**



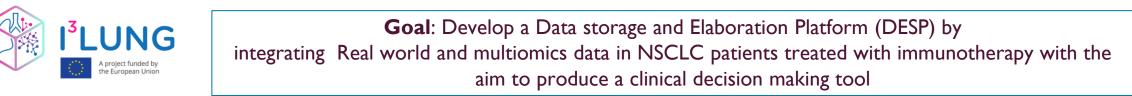
# Clinical Decision Making With Ai For Treatment Selection

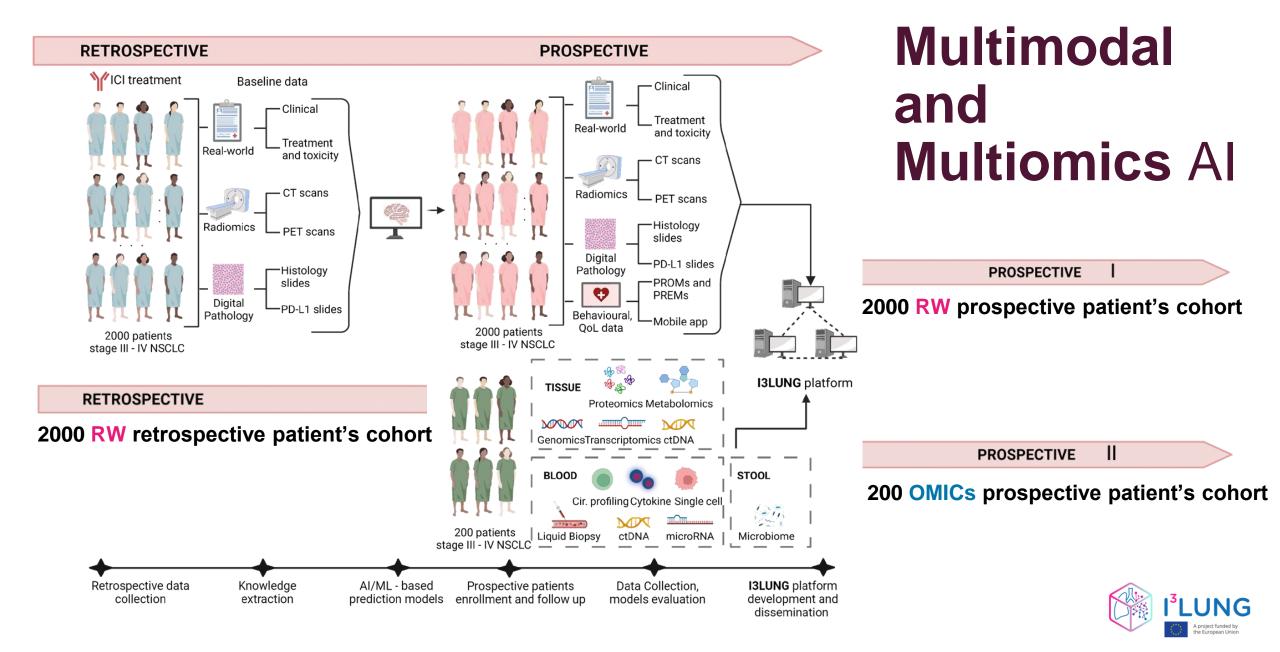
Prelaj's group has also evaluated AI-guided prediction of immunotherapy response in people with NSCLC, and has generally been impressed with its ability to deliver useful predictions. "These tools are trustworthy, and are working," she says. In 2022, her group spearheaded the I<sup>3</sup>LUNG Project, a five-year initiative that has recruited 2,200 people with NSCLC in Europe, the United States and Israel. I<sup>3</sup>LUNG aims to develop a deep-learning model for predicting the response to checkpoint inhibitors - either alone, or in combination with other therapies – on the basis of imaging, histology and data from clinical records. The researchers will then validate the model's ability to identify effective treatment strategies in a prospective cohort of people with cancer<sup>3</sup>.

## THE I3LUNG PROJECT - OVERVIEW



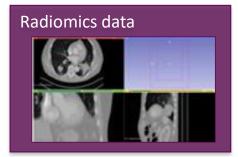
ne Swedish Institute ir Health Economics istitutet för Hälso-





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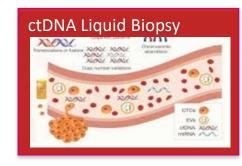




NGRWD: RWD IMAGES QoL









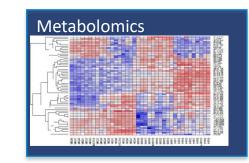


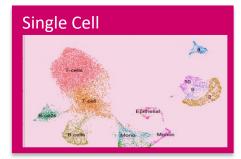
**BLOOD** level



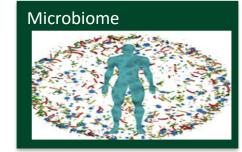


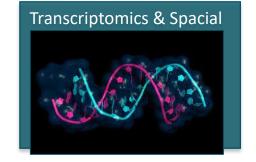
SINGLE CELL Blood level











**STOOL** 

level

TISSUE level

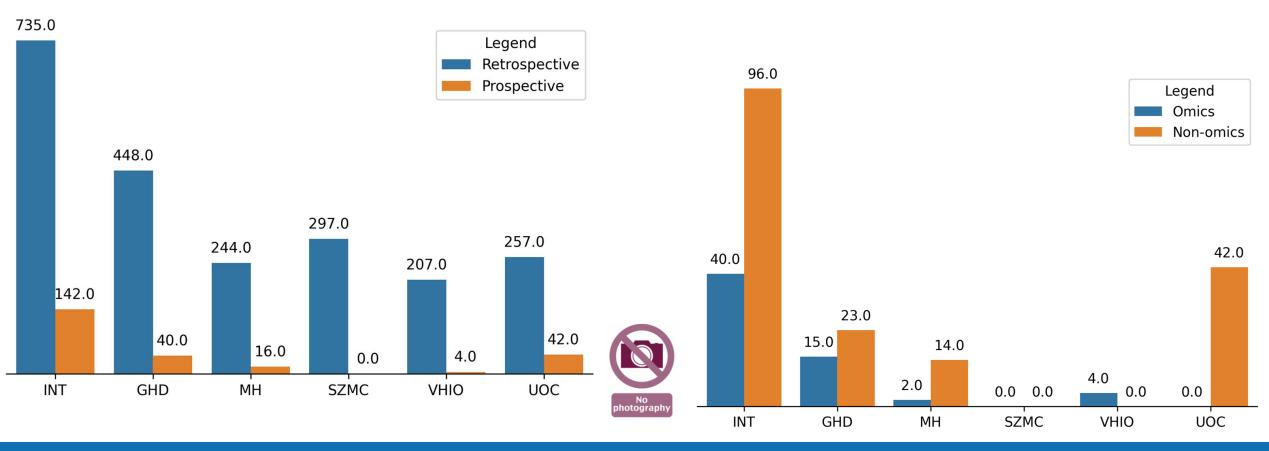


### www.i3lung.eu

**I<sup>3</sup>LUNG** 

# **I3LUNG: PATIENTS ENROLLMENT, MAY 2024**

Retrospective and Prospective N=2188 patients



### #1320P

### I3LUNG: Digital pathology predicts PD-L1 expression in metastatic NSCLC patients treated with immunotherapy





Arsela Prelaj<sup>1,3</sup>, Matteo Sacco<sup>2</sup>, Vanja Miskovic<sup>1,3</sup>, Daniele Lorenzini<sup>1</sup>, Francesco Trovò<sup>3</sup>, Aleksandra Zec<sup>3</sup>, Laila Roisman<sup>4</sup>, Leonardo Provenzano<sup>1</sup>, Claudia Proto<sup>1</sup>, Andrea Spagnoletti<sup>1</sup>, Cecilia Silvestri<sup>1</sup>, Alba Meya<sup>6</sup>, Alessandra Pedrocchi<sup>3</sup>, Evangelos Sarris<sup>7</sup>, Enriqueta Felip<sup>8</sup>, Filippo G.M. De Braud<sup>1</sup>, Martin Reck<sup>9</sup>, Giuseppe Lo Russo<sup>1</sup>, Alexander T. Pearson<sup>2</sup>, Marina Chiara Garassino<sup>2</sup>



 Fondazione IRCCS – Istituto Nazionale dei Tumori, Milan, Italy;
 University of Chicago Department of Medicine - Section of Hematology/Oncology, Chicago, United States of America, 3. Politecnico di Milano, Milan, Italy 4. Shaare Zedek Medical Center, Jerusalem, Israel, 5. UNIMI - Università degli Studi di Milano Statale, Milan, Italy, 6. MEDSIR - Medica Scientia Innovation Research, Barcelona, Spain, 7. Metropolitan Hospital, Athens, Greece, 8. Vall d'Hebron University Hospital, Barcelona, Spain,
 Airway Research Center North, German Center for Luna Research, Lungenclinic, Grosshansdorf, Germany

### **I**3LUNG

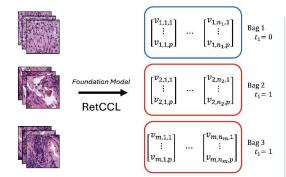


I3LUNG is a project funded by the European Union through the Horizon 2020 program that aims to develop Artificial Intelligence (AI)-based tools to predict the response of advanced non-small cell lung cancer (NSCLC) patients to immune checkpoint inhibitors (ICIs). The project brings together a consortium of 16 partners from 10 countries (Belgium, Denmark, Italy, Germany, Greece, Spain, Sweden, Switzerland, the United States, and Israel). Utilizing patient data, which includes digital pathology slides (DPS), genomics, radiomics, along with other patient characteristics, the overall goal is to develop a platform to guide therapeutic decisions in immuno-oncology for both healthcare professionals and patients.

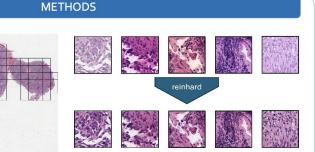
### INTRODUCTION

- Immunotherapy (IO) is the new standard of care for patients with advanced NSCLC, yet only 30-50% of patients benefit from it long-term.
- A better understanding of tumor features could help guide treatment decisions.
- To date, Programmed Death-Ligand 1 (PD-L1) remains the only biomarker used to predict IO efficacy, demonstrating its unique predictive ability, even if not perfect.
- A specific morphology has been found to be associated with PD-L1 expression, introducing new scenarios for the biological interpretation of the immune response.
- Utilizing AI and machine learning processes to analyze DPS could help create decision making tools for more individualized prediction of response.

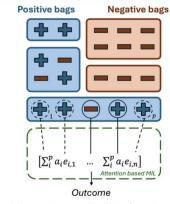
Digital Pathology whole slide images are very large images, and to feed them into Artificial Neural Network-based models we extracted square tiles [299x299x2] at 10x magnification from the whole slide images.



Large-scale AI models, known as foundation models, are developed using vast datasets and a training approach called self-supervised learning. This method does not rely on manually labeled data. Instead, it presents the model with a complex task inherent to the data itself. By solving this task, the model learns to identify and extract important features from the input information on its own. For this task, we used RetCCL, a model trained on TCGA and PAIP datasets. Once processed through RetCCL, tiles are converted into vectors of biologically relevant features.



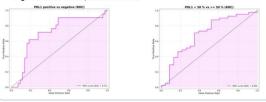
Reinhard normalization was employed to reduce batch effect.



Slides are now converted into bags of vectors. Assuming that not all tiles are equally relevant for our task, we need a model able to learn not only the patterns associated with a certain outcome, but also which tiles to focus on to find those patterns. For this goal, we used an Attention-Based Multiple Instance Learning model, which employs the attention mechanism to infer the importance of each tile vector.

### RESULTS

- Among the 2188 pt enrolled in the I3LUNG retrospective cohort, 474 patients had available DPS and PD-L1 status to be considered for the present analysis.
- PD-L1 expression was high (>50%), low (1-49%) and negative in 145 (37%), 129 (32%) and 127 (33%) patients within the training cohort, respectively, and 24 (33%), 23 (32%) and 26 (35%) among the validation cohort, respectively.
- PD-L1 high vs low/negative status through DPS were able to be predicted with an area under the curve (AUC) of 0.69; while for PD-L1 positive vs negative an AUC of 0.71 was achieved.



### CONCLUSIONS

- To our knowledge, this is the largest series to date demonstrating a correlation between morphological features and PD-L1 expression in lung cancer.
- Data suggests that PD-L1 high and negative have different morphological phenotype.
- This rapid and generalizable model underscores the potential for morphological features to serve as valuable biomarkers in elucidating the mechanisms of immune responses.
- Within I3LUNG integration of genomic and radiomic data will probably allow to improve the ability to assess patient prognosis at diagnosis.

### ACKNOWLEDGEMENTS

We sincerely thank the patients and their families for their invaluable participation in this study. This project has received funding from the European Union's Horizon Europe research and innovation programme. We are grateful for the collaborative efforts of our consortium partners. Their expertise has been crucial to the success of the IgLUNG project.





### ESMO > Meeting Calendar > Past Meetings ESMO Congress 2024

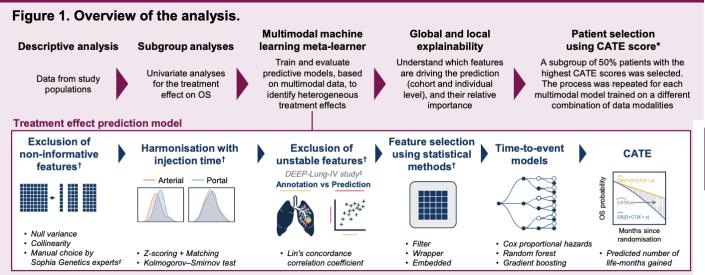
POSTER



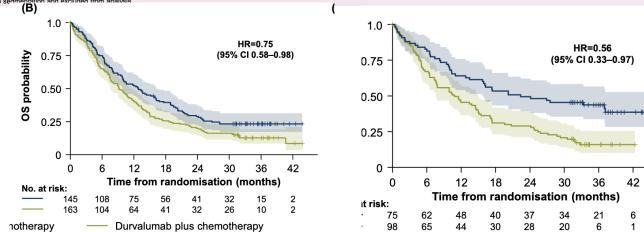
Corresponding Author email: Arsela. Prelaj@istitutotumori.mi.it Arsela Prelaj DOIs: AstraZeneca, Training of personnel, Advisory Board, coordinating PI; BMS, Advisory Board, Local PI; Italfarma, Training of personnel; Janssen, travel grant, Advisory Board, Lilly, Invited Speaker, Local PI; MEDSIR, Invited Speaker, Novartis, Invited Speaker, Roche, Invited Speaker, Icoal PI; Bare, Icoal PI; Bare,

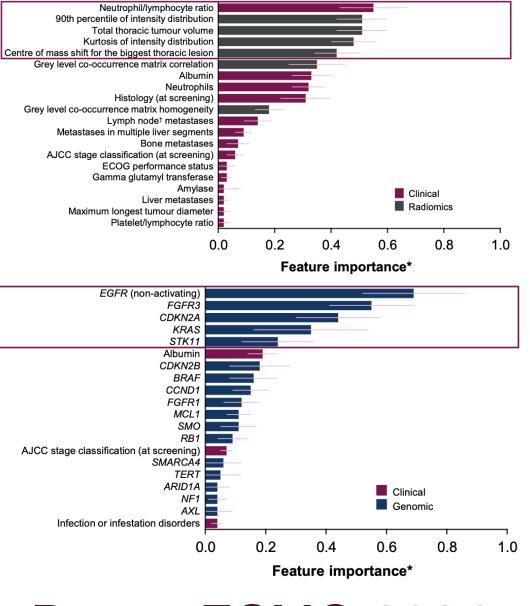
### Poster 1325P

TRIDENT: Machine learning multimodal signatures to identify patients that would benefit most from tremelimumab addition to durvalumab plus chemotherapy with data from the POSEIDON trial



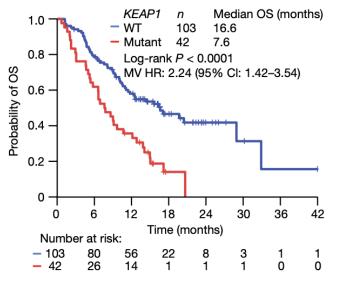
\*CATE score (defined as the difference of RMSTs at 24 months after randomisation) is calculated per-patient. The higher the score for the patient, the higher the expected benefit of tremelimumab plus durvalumab and chemotherapy vs durvalumab plus chemotherapy. Tonly relevant for derivation of the radiomics modality. \*Non-relevant features in the context of metastatic NSCLC tumours and non-interpretable features were removed \*DEEP-Lung-IV (NCT04994795) was used to identify unstable features by comparing the feature value when extracted from annotation to deep learning prediction. Features with low correlation were considered sensitive to sementation and excluded from analysis

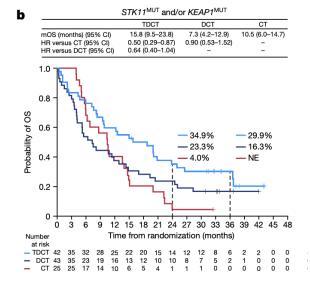


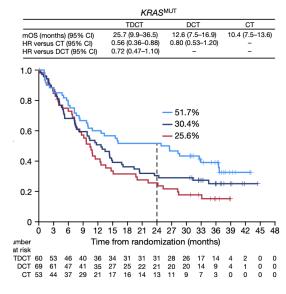


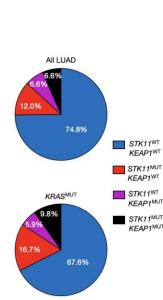
Poster ESMO 2024

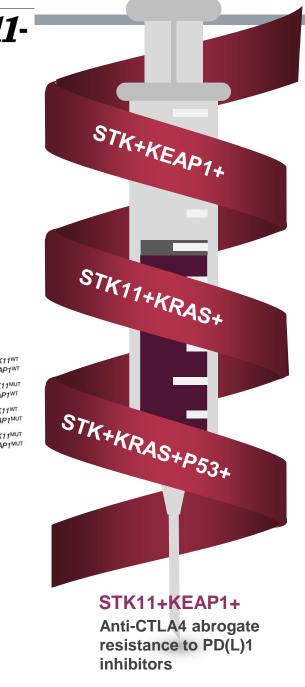
### **nature** Article CTLA4 blockade abrogates *KEAP1/STK11*related resistance to PD-(L)1 inhibitors





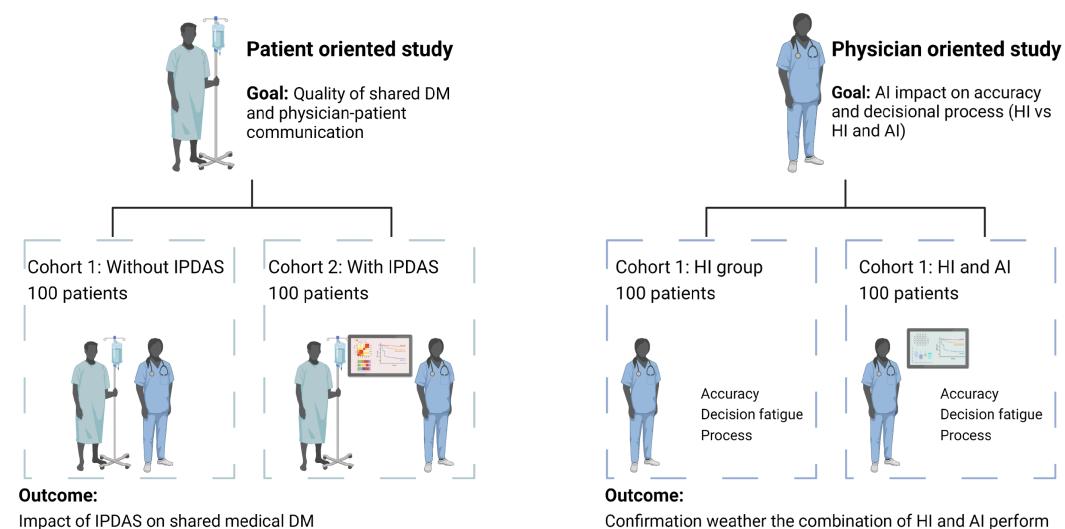






# Papers under submission: PDSS and IPDAS tools





better respect to HI alone (target +15%)

# MOVING FROM PREDICTIVE AI TO GENERATIVE AI

Predictive based MODELS Using task specific – AI
Using FM to extract meaningful information
Predict the outcome

Generative based MODELS

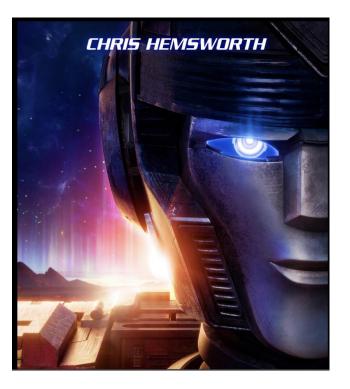
- Using LLMs and FMs to generate decisions
- Create synthetic data and images

# LARGE LANGUAGE MODELS

# **FOUNDATION MODELS**

# Generative AI exists because of the Transformer

### Google Brain 2017



**Attention Is All You Need** 

Ashish Vaswani\* Google Brain avaswani@google.com Noam Shazeer\*<br/>Google BrainNiki Parmar\*<br/>Google Research<br/>nikip@google.com

Jakob Uszkoreit\* Google Research usz@google.com

Llion Jones\* Google Research llion@google.com Aidan N. Gomez<sup>\* †</sup> University of Toronto aidan@cs.toronto.edu Łukasz Kaiser\* Google Brain lukaszkaiser@google.com

Illia Polosukhin\* <sup>‡</sup> illia.polosukhin@gmail.com

### Abstract

The dominant sequence transduction models are based on complex recurrent or convolutional neural networks that include an encoder and a decoder. The best performing models also connect the encoder and decoder through an attention mechanism. We propose a new simple network architecture, the Transformer, based solely on attention mechanisms, dispensing with recurrence and convolutions entirely. Experiments on two machine translation tasks show these models to be superior in quality while being more parallelizable and requiring significantly less time to train. Our model achieves 28.4 BLEU on the WMT 2014 English-to-German translation task, improving over the existing best results, including ensembles, by over 2 BLEU. On the WMT 2014 English-to-French translation task, our model establishes a new single-model state-of-the-art BLEU score of 41.0 after training for 3.5 days on eight GPUs, a small fraction of the training costs of the best models from the literature.



### Computer Science > Artificial Intelligence

[Submitted on 6 Apr 2024]

### Autonomous Artificial Intelligence Agents for Clinical Decision Making in Oncology

Dyke Ferber, Omar S. M. El Nahhas, Georg Wölflein, Isabella C. Wiest, Jan Clusmann, Marie-Elisabeth Leßman, Sebastian Foersch, Jacqueline Lammert, Maximilian Tschochohei, Dirk Jäger, Manuel Salto-Tellez, Nikolaus Schultz, Daniel Truhn, Jakob Nikolas Kather

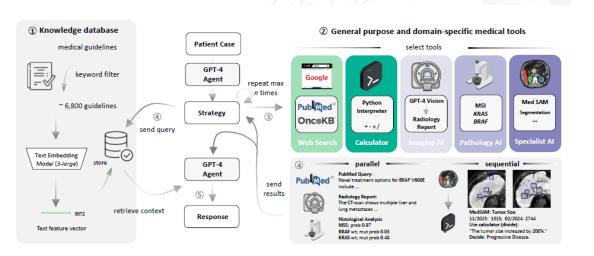


Figure 1: High-level overview of the RAG-Agents framework.



Fondazione IRCCS Istituto Nazionale dei Tumori



# Autonomous AI x CDM

Ms. Xing, a 33-year-old patient, was diagnosed with cholangiocellular carcinoma in early 2023. Following her diagnosis, she underwent a complete surgical resection (RO) and was treated with adjuvant chemotherapy using capecitabine for six months. Subsequent imaging showed no evidence of disease recurrence until September of the same year, when MRI imaging "September2023.png") revealed a new, solitary metastasis.

In response, a treatment regimen of gencitable and cisplatin was initiated. Considering Ms. Xing's young age, a liver biopsy was performed for comprehensive panel diagnostics. Both imaging results and panel findings are made available for review:



Radiology Report (\* ...) Liver: There is one single hypointense lesion in the left lobe of the liver, measuring approximately 0.4 cm in its greatest dimension (Location: [475, 250, 490, 275]). Highly suggestive for recurrence of the known cholangiocellular carcinoma.

lymph Nodes: There is no enlargement of the abdominal or pelvic lymph nodes. Peritoneum: No evidence of peritoneal implants or significant fluid accumulation is present. Storng supplicion of a recurrence of the homon CCC due to a solitary metertaris in the left liver.

Clinical Context

### Molecular Report Summary:

Microsatellite-Instability High, Mutation in BRAF V600E and CD74-ROS1 variant fusion. No alterations in NTRK or FGFR2.

Help

Currently, the patient experiences recurrent arctites with notable abdominal tension. Also, a new MRI-scan was performed yesterday ('February2024,png') by our in house radiologists. According to the later radiology report, the MRI scan performed on the patient with the system ID X-09.22 and documented as "February2024,png" revealed a single metastatic lesion in the left lobe of the liver, delineated by the coordinates 455, 270, 505, 320. The report emphasizes the importance of a comprehensive review by comparing these findings with the images from a previous examination in Systember 2022 during the forthcoming tumor board meeting for a detailed analysis. Also, the imaging findings suggest the prevence of prevences of previous examination in prevences of prevences of previous examination in previous examination in prevences of prevences of previous examination in previous examination in prevences of previous examination in the suggest the previous examination in the suggest the previous examination in the suggest the prevences of previous examination in the suggest the previous examination in the suggest the prevence of prevences of previous examination in the suggest the prevence of previous examination in the previous examination in the suggest the previous examination in the integration of the suggest the prevence of previous examination in the suggest the prevence of previous examination in the previous examin carcinomatosis. Her system ID is X-09.22.

Please investigate the current state of the disease. What does the new MRI scan show

Did the metastail grow? In case of progress, what (targeted) treatment options could exponent of the molecular tumor board tomorrow? Be sware that the patient is extremely young and we need all options we could find. Also check say options you can find on good er pubmed. Question

Progressive

Disease

+ tool results

patient context

+ question

RAG

<u>=0</u>

patient context

+ auestion

MSS

BRAF mut

KRAS wt

+ tool results

+ medical context

Stage 1: Strategy + Tools extract location from text 09/2023 divide GPT-4 Assistant 518 / 133 = 3.89 SAM solution 02/2024 segmented area strategy define target: **BRAF**, mutation Onc<sub>@KB</sub> 600E1 collect [CD74-ROS1, Onc<sub>@KB</sub> variant fusion clinical select tools and genomic define queries: **\*\*\*** \*\*\*\* \* information targeted treatment Google options for cholangiocellular cancer with BRAF V600E mutation and and targets Pub Med CD74-ROS1 fusion? nt ID define targets: [MSI, KRAS, BRAF]

### Stage 2: Generate response

The latest MRI scan from February 2024 reveals that the metastatic lesion in Ms. Xing's left liver lobe has notably enlarged, growing from an area of 133 in September 2023 to 518, signifying a progression in her condition. This significant increase highlights the critical need to consider further treatment avanues for Ms. Xing, Given Ms. Xing's medical history and the molecular characteristics of her tumor, including the BRAF V600E mutation and CD74-ROS1 variant fusion,

several targeted therapy options emergé: 1. Dabrafenib and Trametinib: This combination is recommended for BRAF

V600E-mutated tumors, including cholangiocellular carcinoma, based on their effectiveness in other cancers with similar genetic alterations [Tool]. The combination has FDA approval for BRAF V600E mutant unresectable or metastatic melanoma and other solid tumors excluding colorectal cancer, with noted effectiveness in biliary tract cancer [Tool]. 2. Crizotinib, Entrectinib, and Repotrectinib: These drugs are identified treatments for ROSI-

positive tumors, primerily in NSCLC. Given the CD74-ROS1 fusion in Ms. Xing's tumor, these options could be explored for their potential applicability, despite the primary association with NSCLC

1001.3. Encorsfemile and Binimetinib: This combination, highlighted through a Google search, could be considered based on their effectiveness in cancers with BRAF V500E mutations [Tool]. Although not specifically indicated for chalengiocelluler carcinome, their use in similar genetic contexts suggests potential applicability. Regarding chemotherapy options, the current guidelines for cholangicellular carcinome recommend systemic chemotherapy as the primary treatment for advanced disease. Given Ms. Xing's prior treatment with gencitabine and cisplatin, alternative regimens could

include - FOLFOX (fluorouracil, leucovorin, and oxaliplatin) as a second-line treatment option, especially for patients who have progressed on a gencitabine-based regimen [55].

For Ms. Xing, considering her young age and the urgent need for effective management strategies, participation in clinical trials exploring novel agents or combinations should be strangly considered. This includes trials for targeted therepize based on her tunor's molecular profile or emerging immunotherapy options for cholangiocellular carcinoma.

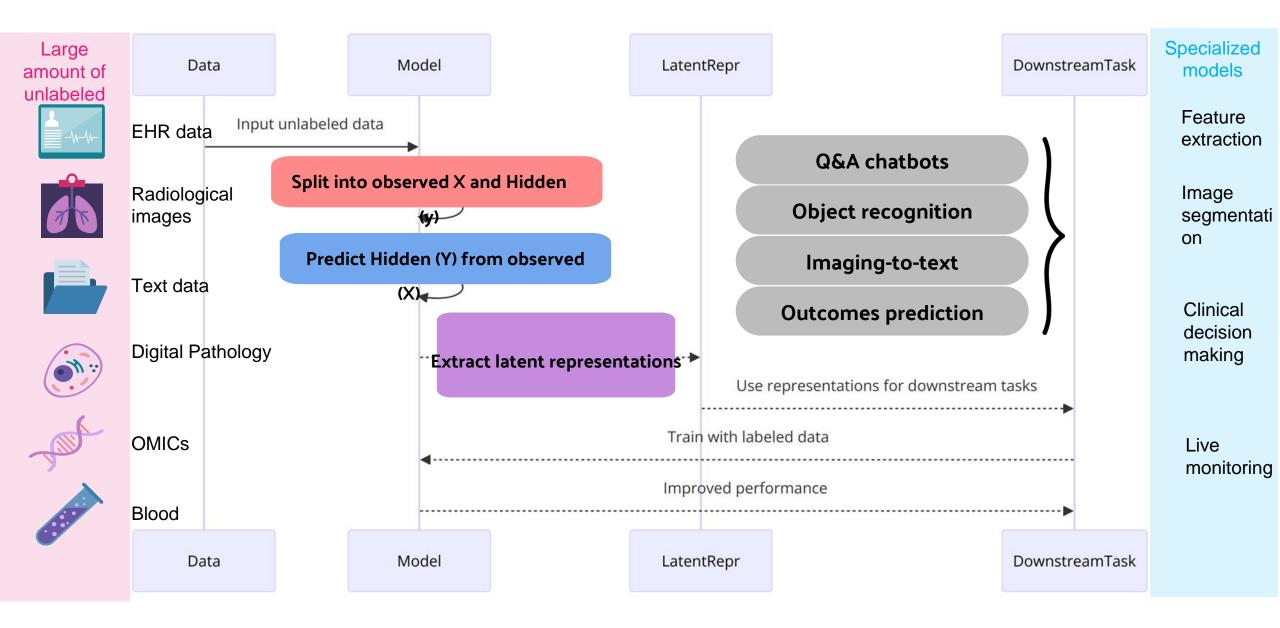
Given the conflicting information on microsatellite status, further clarification is needed The 'check mutations' tool indicated Microsatellite Stability (MSS), however, the perients materials cost provided histophetic is identify (h3), induces, its perients materials confirmed, immunotherapy with pendralizames could be considered, as it has shown effectively ends in the first constrained [37]. In summary, for the tumor board discussion, the recommended approach includes exploring targeted therapy options such as Dabrafenib and Trametinib for the BRAF V600E mutation and potentially Crizotinib or Entrectinib for the CD74-ROS1 fusion Additionally, considering second-line chemotherapy options and the possibility of clinical trial participation are crucial steps. The significant progression of Ms. Xing's disease necessitates a prompt and comprehensive evaluation of these treatment strategies to

optimize her care. To refine our approach and ensure the most accurate and personalized treatment recommendations for Ms. Xing, could you please provide the latest comprehensive genomic profiling of her tumor? This includes any recent sequencing data that anglet reveal additional actionable mutations or variants not previously identified. Additionally, detailed information regarding her response to past treatments, including any side effects experienced and the duration of response, would greatly enhance our ability to tailo future therapy options. This data is crucial for leveraging our resources to their fullest potential in guiding Ms. Xing's treatment plan.

# MAXIMIZING DATA usage improving technology

# **FOUNDATION MODELS**

# What the F. Models doeas with self-supervized learning





ESMO > Meeting Calendar > Past Meetings ESMO Congress 2024

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BARCELONA ESVO

# FM for digital pathology: At WS level

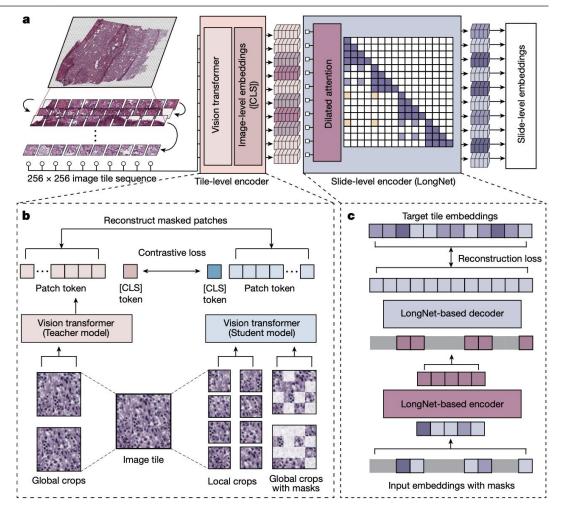
Article Open access | Published: 22 May 2024

# A whole-slide foundation model for digital pathology from real-world data

**Whole-Slide Modelling**: Prov-GigaPath overcomes subsampling limitations by training on 1.3 billion image tiles from 171,000 slides, preserving full slide context.

**State-of-the-Art Performance**: Achieves top results in 25 of 26 tasks, with significant improvements in 18 tasks, through large-scale pretraining.

**Al-Powered Innovation**: Uses real-world data from 30,000 patients and 31 tissue types, setting a new standard in digital pathology with vision–language models.



Xu, H., Usuyama, N., Bagga, J. et al. A whole-slide foundation model for digital pathology from real-world data. Nature 630, 181–188 (2024). https://doi.org/10.1038/s41586-024-07441-w

# FM for single-cell multi-omics

### nature methods

Article

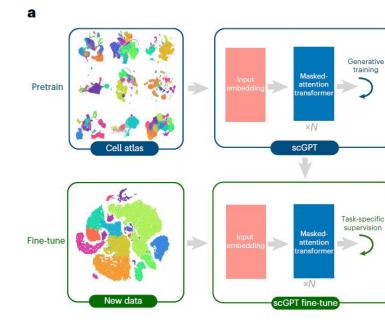
https://doi.org/10.1038/s41592-024-02201-0

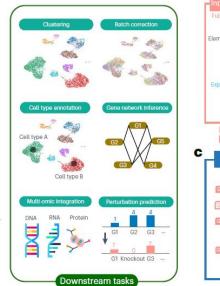
### scGPT: toward building a foundation model for single-cell multi-omics using generative AI

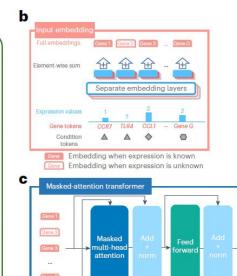
Received: 12 July 2023

Accepted: 30 January 2024

Haotian Cui  $^{12,3,8}$ , Chloe Wang $^{12,3,8}$ , Hassaan Maan  $^{01,3,4}$ , Kuan Pang  $^{02,3}$ , Fengning Luo $^{2,3}$ , Nan Duan  $^{05}$  & Bo Wang  $^{01,23,4,67}$ 







The model scGPT is generatively pretrained on large-scale scRNAseq data from cell atlases.

For downstream applications, the pretrained model parameters can be fine-tuned on new data.

They applied scGPT in a variety of tasks including cell type annotation, batch correction, multi-omic integration, genetic perturbation prediction and gene network inference.

Cui, Haotian, et al. Nature Methods 2024

# Foundation Model for cancer imaging biomarkers

- a. Foundation model pre-training
- **b.** Clinical application of the Foundation model (3 use cases)
- c. Foundation model **implementation** (2 approaches)
- d. Performance evaluation

Google DeepMind and Google Research

2024-5-7

# Advancing Multimodal Medical Capabilities of Gemini

Google Research and Google DeepMind  $^\dagger$ 

Pai, Suraj, et al. Nature machine intelligence, 2024; https://github.com/Google-Health/imaging-research/tree/master/ct-foundation%0A

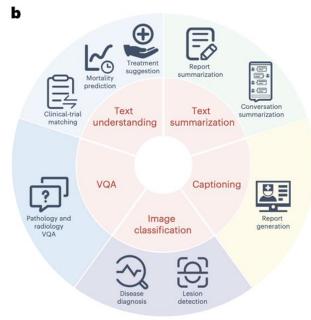
### nature machine intelligence



# A generalist vision language foundation model

# nature medicine





**BiomedGPT** handles multimodal inputs and performs diverse downstream tasks.

The expected form of output for each task is determined by feeding the specific instruction to the model.

### Pathology and radiology VQA



Q: What is seen at this stage, associated with regeneration and repair?

A: Numerous reactive type II pneumocytes.

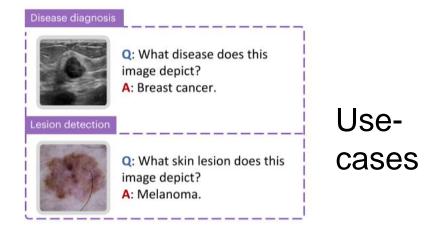
Q: Are bite cells like this one in the smear associated with regeneration and repair at this stage? A: No.

### Report generatio



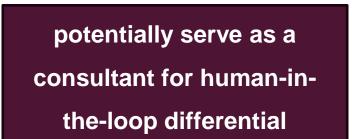
Q: What are the findings based on the image?

**A**: The nasogastric tube is in adequate position, and there is a resolution of the gastric distention. There is still mild bibasilar atelectasis. There are no pneumothorax no pleural effusion.



# Multimodal generative AI pathchat – Copilot pathchat PathChat flexibility:

- Multi-choice questions (accuracy image only 78.1%, when provided with clinical context 89.5%)
- answering open ended questions (accuracy 78.7%)
- interactive multi-turn conversation





What morphological features are present in this image?

The image shows a tumour composed of spindle cells, which are elongated and have a fusiform shape. These cells are arranged in fascicles, which are bundles or groups of cells aligned in a parallel or whorled pattern. Additionally, there are scattered melanincontaining cells within the tumour.

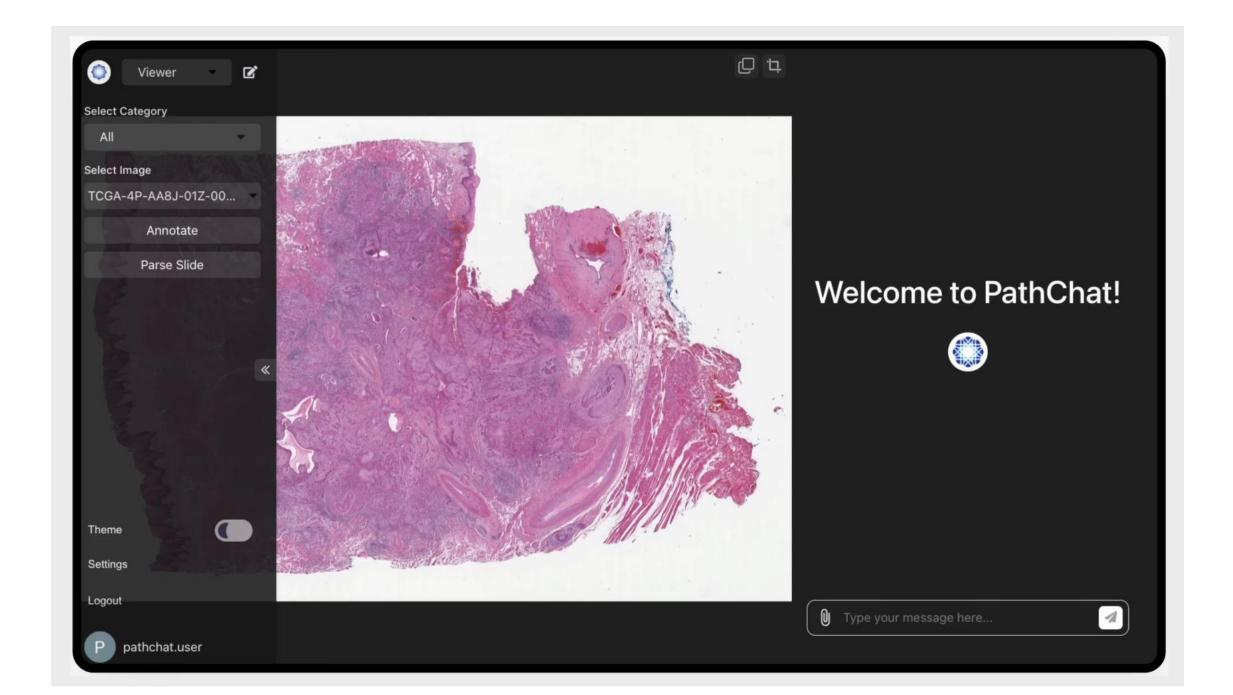
> This tumour was found in the liver of a patient. Is it a primary tumour or a metastasis?

PathChat

PathChat

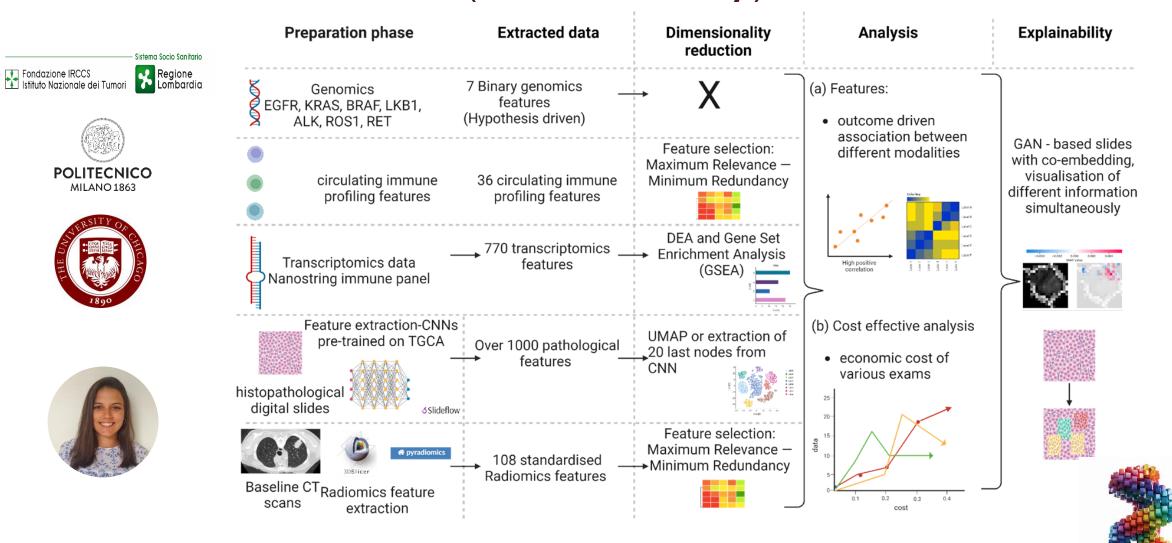
Based on the information provided, this tumour is most likely a metastasis rather than a primary tumour. The presence of spindle cells and melanin-containing cells further supports the possibility of a metastatic melanoma. The liver is a common site for metastasis of melanoma, especially when it has spread from the skin. Human

Human



# HOW we CAN BETTER EXPLAIN WITH FOUNDATION MODELS

# MULTIOMIC- FM-based Explainability in NSCLC patients treated with IO first line (PEOPLE study)



otograph

# WE NEED TO BUILD DATA FOR AI

f in 🗙

🗘 Apollo 11

to 🗸 La Rete News Rassegna stampa Domande frequenti Contatti

### Unity is Strength

Centri di ricerca italiani per strategie terapeutiche avanzate per il tumore al polmone

# 2016 → APOLLO 2020→ APOLLO II FEDERATED NETWORK



# 48 Centri di ricerca avanzata sul tumore al polmone

Creazione di una rete di centri italiani che si occupano di pazienti affetti da tumore del polmone NSCLC avanzati già trattati o candidati a ricevere una terapia a base di ICI



### Real world data da tutti i centri attivi

Sviluppo di un database nazionale Real World per i pazienti affetti da tumore del polmone trattati con TERAPIE INNOVATIVE (ad es. immunoterapia, terapie target, anticorpi coniugati)



https://apolloll.network/



Sviluppo di una biobanca multilivello nazionale registrata con impostazione e armonizzazione delle procedure operative per la raccolta, la conservazione e la spedizione dei campioni biologici.

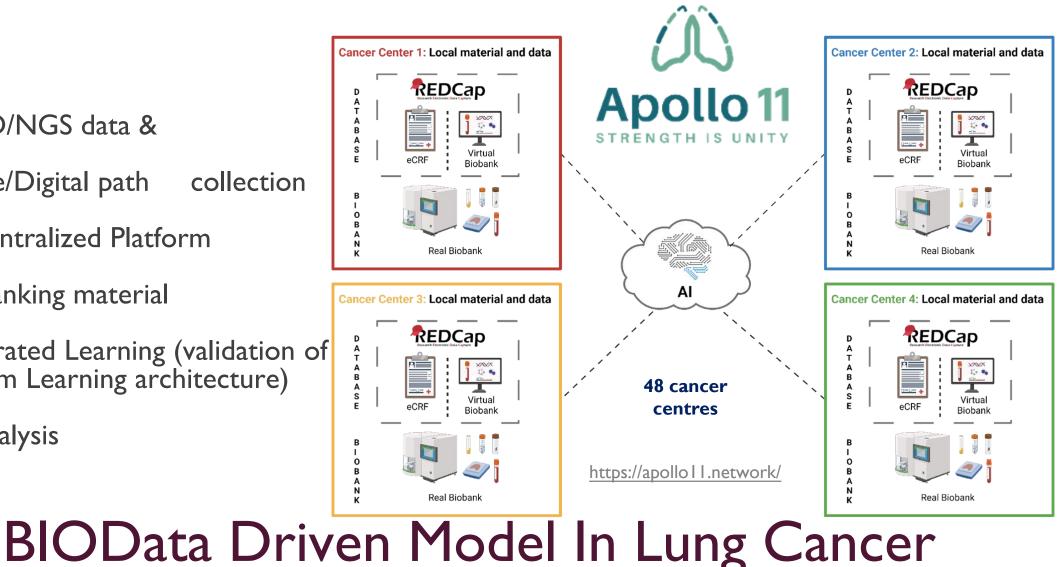


### Intelligenza Artificiale

Creazione di un modello predittivo di intelligenza artificiale (AI) per migliorare la previsione della risposta, portando in ultima analisi a una migliore sopravvivenza e qualità di vita dei pazienti oncologici

# How we can build BIG DATA: Apollo 11 use case

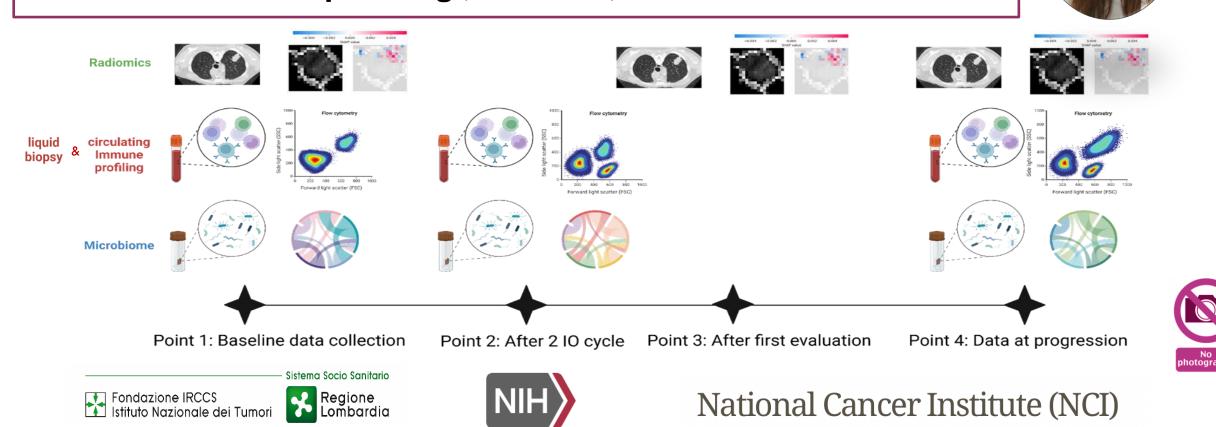
- RWD/NGS data &
- Image/Digital path collection
- **Decentralized Platform**
- **Biobanking material**
- Federated Learning (validation of Swarm Learning architecture)
- Al analysis



Prelaj A, et al. APOLLO 11. Consortium in Advanced Lung Cancer Patients Treated With Innovative Therapies: Integration of Real-World Data and Translational Research. Clin Lung Cancer. 2024 Mar;

PEOPLE interventional prospective trial: 2 host vs 2 tumor time-series biomarkers to explore secondary resistance in IO first-line NSCLC patients treated with immunotherapy

Evaluation of the influence of longitudinal interventional therapies: e.g., Steroids, antibiotics



# TRAINING AND EDUCTION

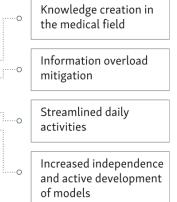
### Al is FOUNDAMENTAL ESMO BETTER MEDICINE



### PERSPECTIVES

### **Oncology education in the age of artificial intelligence**

A. Prelaj<sup>1,2\*</sup>, G. Scoazec<sup>3</sup>, D. Ferber<sup>4,5</sup> & J. N. Kather<sup>6,7,8</sup>

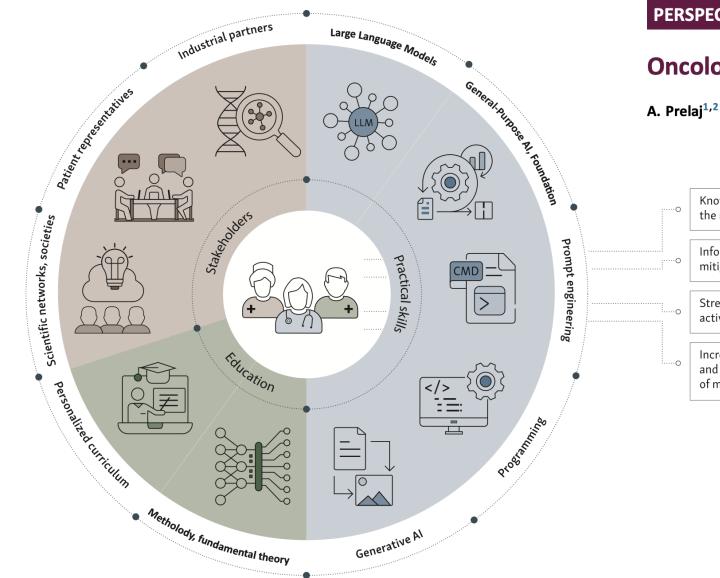


1. Al Principles: Understanding methodology, feature selection, model validation, and bias management. Interpreting

2. Al Data: Oncologists need to critically assess AI outputs to avoid over-reliance.

3. Al-Driven Research: Oncologists require advanced skills to collaborate with data scientists on AI models.

4. Patient-Centric AI: Oncologists should guide patients using AI tools for selfassessment and health information.



# AI CONGRESS

SAVE THE DATE

# 3rd edition ARTIFICIAL INTELLIGENCE FOR ONCOLOGY

PRESIDENT OF THE CONFERENCE

MILAN, ITALY 8-9MAY 2025 & ONLINE

### Hibrid Event organized by:

Sistema Socio Sanitario
Fondazione IRCCS
Istituto Nazionale dei Tumori
Regione
Lombardia



### Invited speakers from:



Memorial Sloan Kettering Cancer Center

VALL D'HEBRON Institute of Oncology

TECHNISCHE UNIVERSITÄT DRESDEN





AALBORG UNIVERSITY

ALCON!

Sass



UC School of Medicine



Endorsed by:



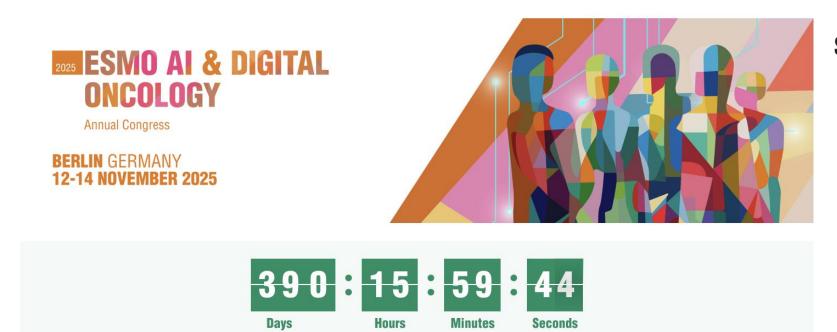
ASC

American Society of Clinical Oncology Making a world of difference in cancer care

D¢L

# FIRST ESMO AI CONFERENCE

ESMO > Meeting Calendar ESMO AI & Digital Oncology Congress 2025



### Scientific Co-Chairs

- Mireia Crispin Ortuzar, Cambridge, UK
- Rudolf Fehrmann, Groningen, Netherlands
- Jakob Kather, Dresden, Germany



### Arsela Prelaj

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## ACKNOWLEDGEMENTS

AI-ON Lab



Spetses, Greece June 2024

Sistema Socio Sanitario Fondazione IRCCS Istituto Nazionale dei Tumori





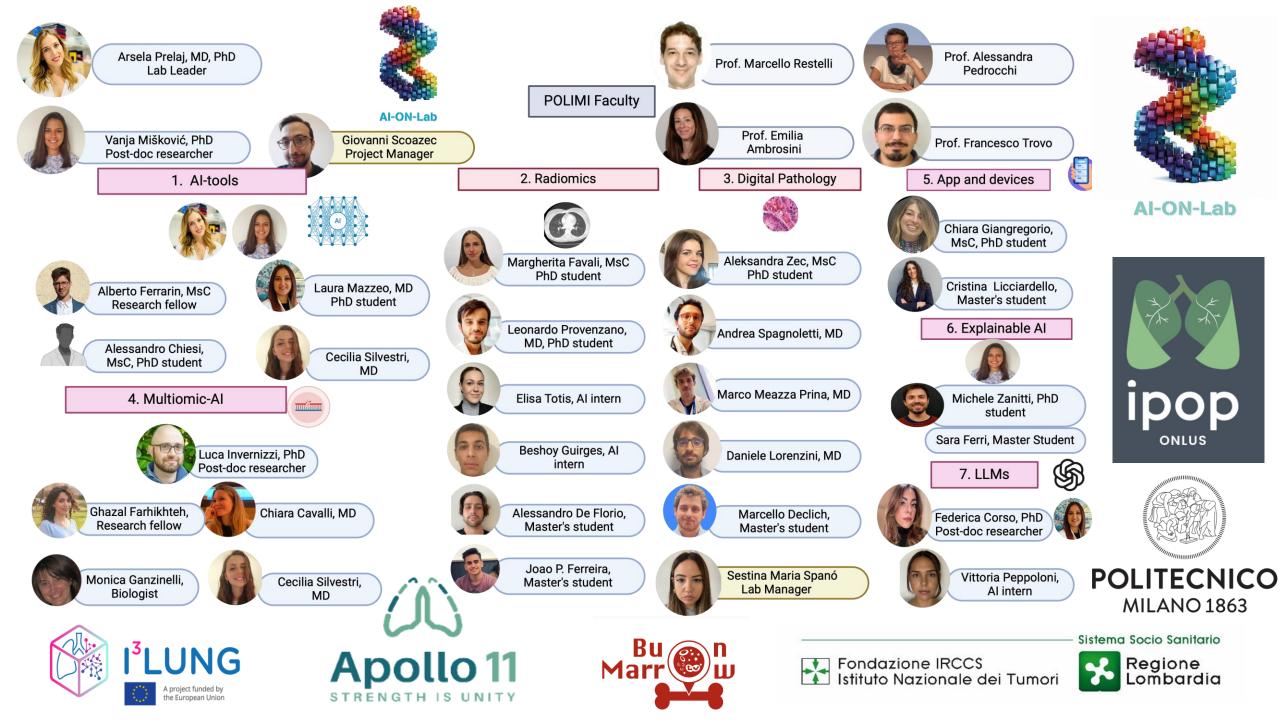


**AI-ON-Lab** 

Medical Oncologist:

Giuseppe Lo Russo, Claudia Proto Marta Brambilla, Mario Occhipinti Laura Mazzeo, Teresa Beninato Rita Leporai, Marco Meazza And all the Resident Doctors Biologist: Monica Ganzinelli

Miriam Fink, **Case Manager** Diana Andra Dumitrascu, Teresa Serra, **Study Nurses** Rosa Maria Di Mauro, **Study Coordinator** Alice Abate and Other, **Data Manager** Sestina Spanò, Fabrizio Baggio, **Project Managers** 



# **RWD:** AUTOMATIC QUALITY CHECK BUILDING

- Data cleaning and automatic quality check coding
- I. Free-text inputs: all misspellings corrected
- 2. Correct date inconsistencies
- 3. Remove inconsistencies from laboratory values and physical parameters
- (...waiting for automated data curation development...)

Hot-encoding, new features, e.g.: 1) patient's age at different time points; 2) DFI, Time between treatments; 3) number of concomitant diseases, 4) patient therapies, and 5) allergies, 6) body mass index (BMI); 7) composite blood cell counts (NLR); 8) genomic pathways

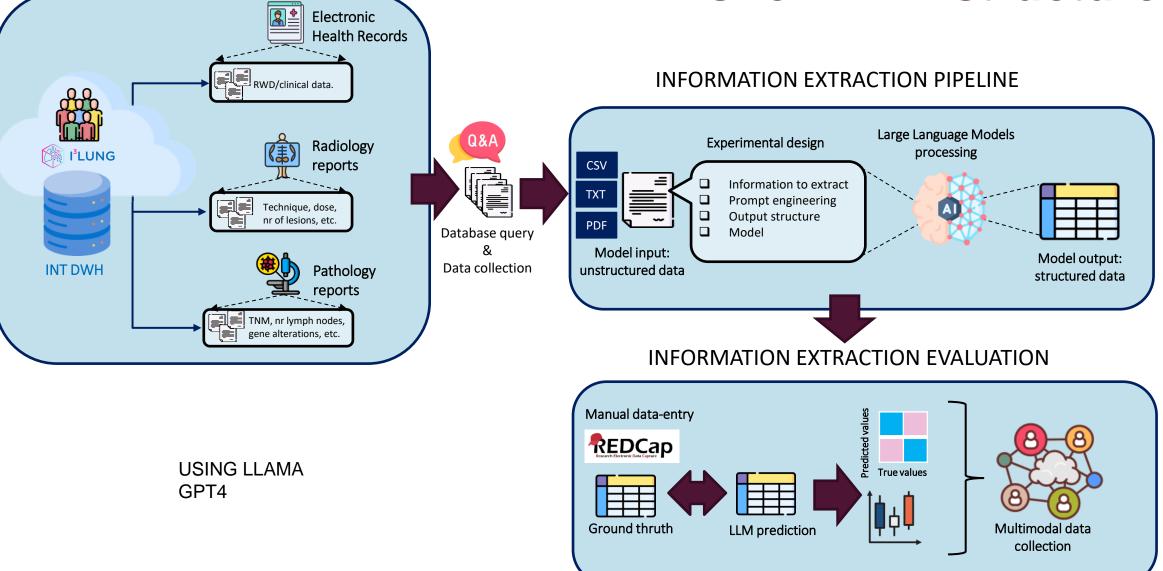
0.000 feature

I. Descriptive features

2. Features for model training

### **REAL-WORLD SCENARIO**

# LLMs for RWD structure



# GENERALIZABILITY OF THE MODEL

# **FAIRNESS AUDITING**

# nature biomedical engineering

Perspective

https://doi.org/10.1038/s41551-023-01056-8

# Algorithmic fairness in artificial intelligence for medicine and healthcare

Received: 1 October 2021

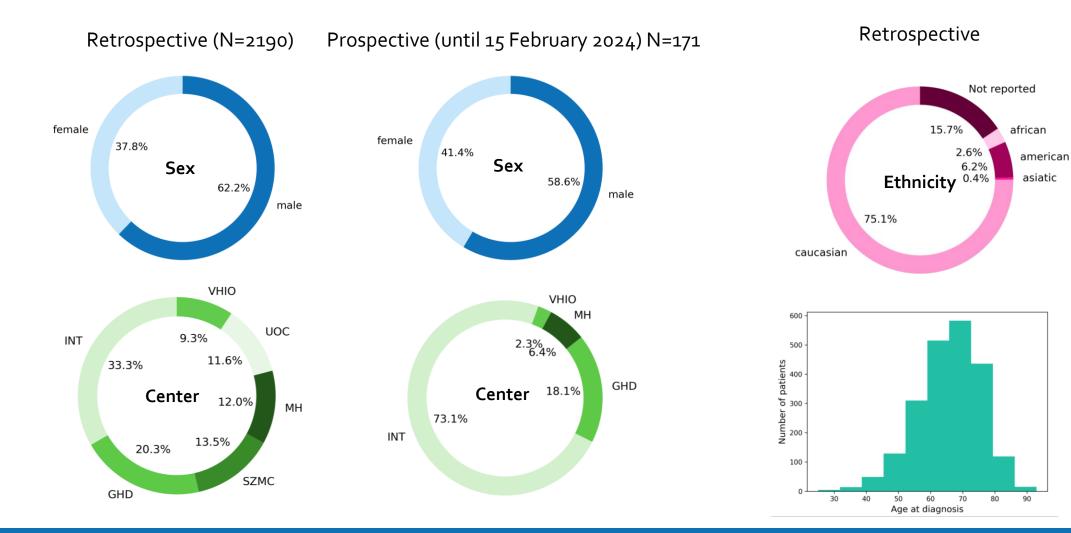
Accepted: 13 April 2023

Published online: 28 June 2023

Richard J. Chen ©<sup>1,2,3,4</sup>, Judy J. Wang ©<sup>1,5</sup>, Drew F. K. Williamson ©<sup>1,3</sup>, Tiffany Y. Chen ©<sup>1,3</sup>, Jana Lipkova ©<sup>1,2,3</sup>, Ming Y. Lu ©<sup>1,3,4,6</sup>, Sharifa Sahai<sup>1,2,3,7</sup> & Faisal Mahmood ©<sup>1,3,4,8,9</sup>

# Preliminary bias analysis





# Comparison of multimodal AI for image analysis

Participants Pool

Model name

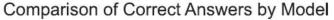
945 NEJM Image Challenge cases.

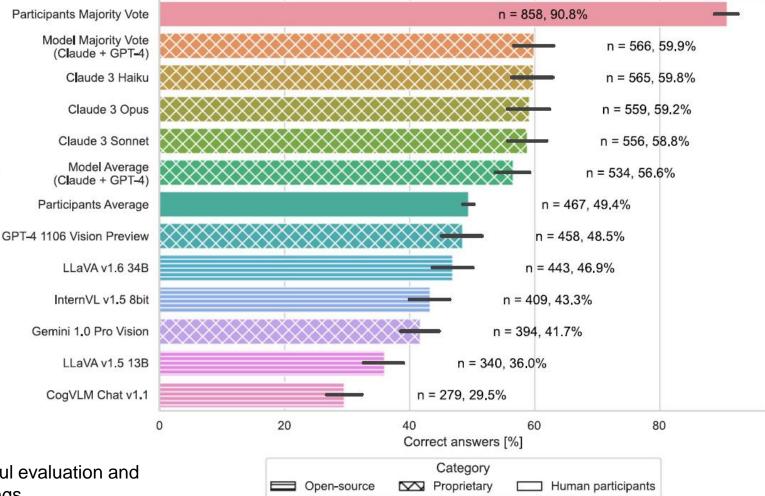
Nine multimodal AI models, were evaluated using a standardized prompt to answer the medical image challenges.

Anthropic's Claude 3 models achieved the highest accuracy (58.8% to 59.8%).

The study highlights issues such as AI models' selectivity in answering questions, the need for regulatory oversight, and the importance of transparency in AI decision-making.

Al has potential in medical diagnostics but requires careful evaluation and ethical considerations before deployment in clinical settings.





Kaczmarczyk, Robert, et al. npj Digital Medicine 2024.

