La ricerca clinica e traslazionale nel carcinoma polmonare

Ricerca nazionale e internazionale

Paolo Marchetti

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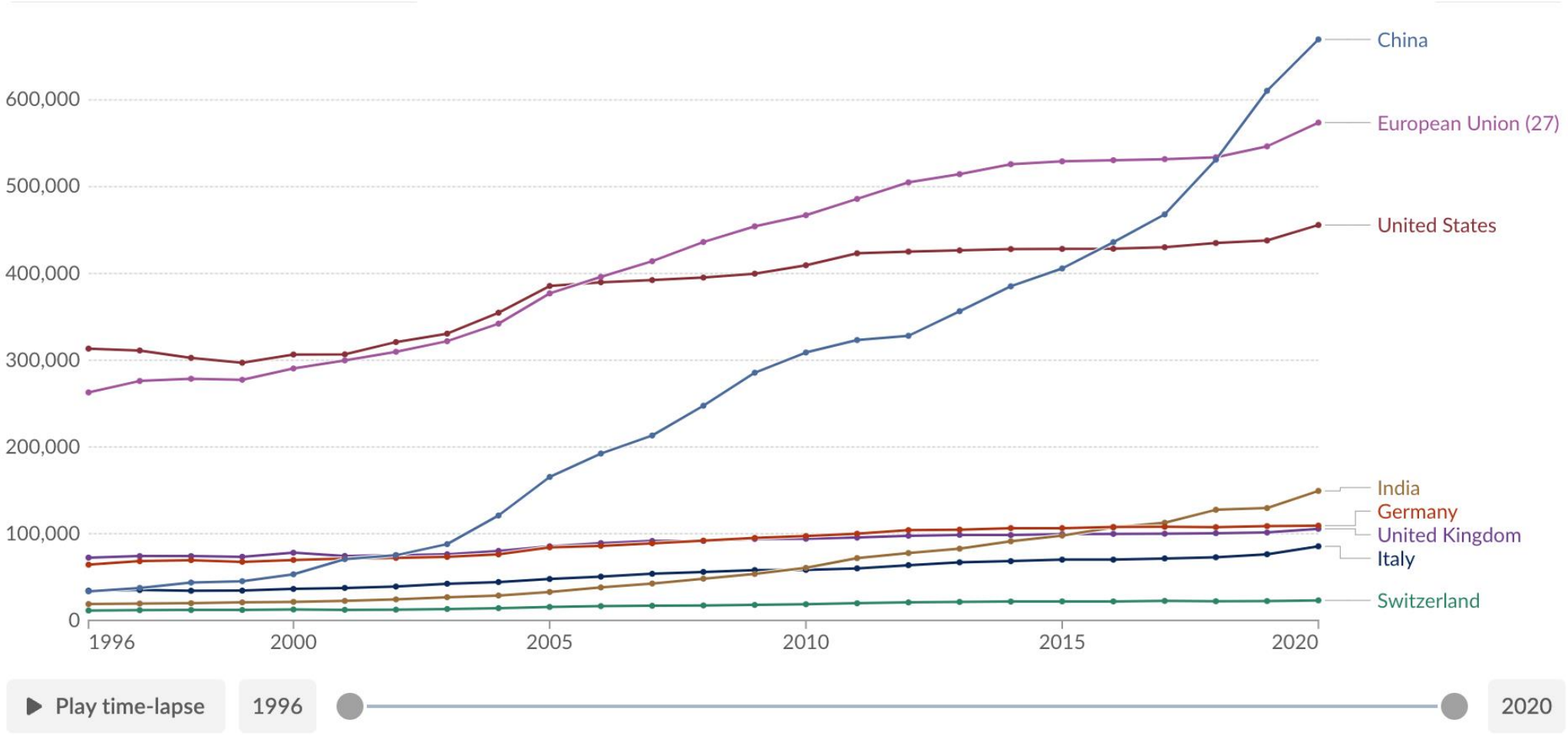
Annual articles published in scientific and technical journals

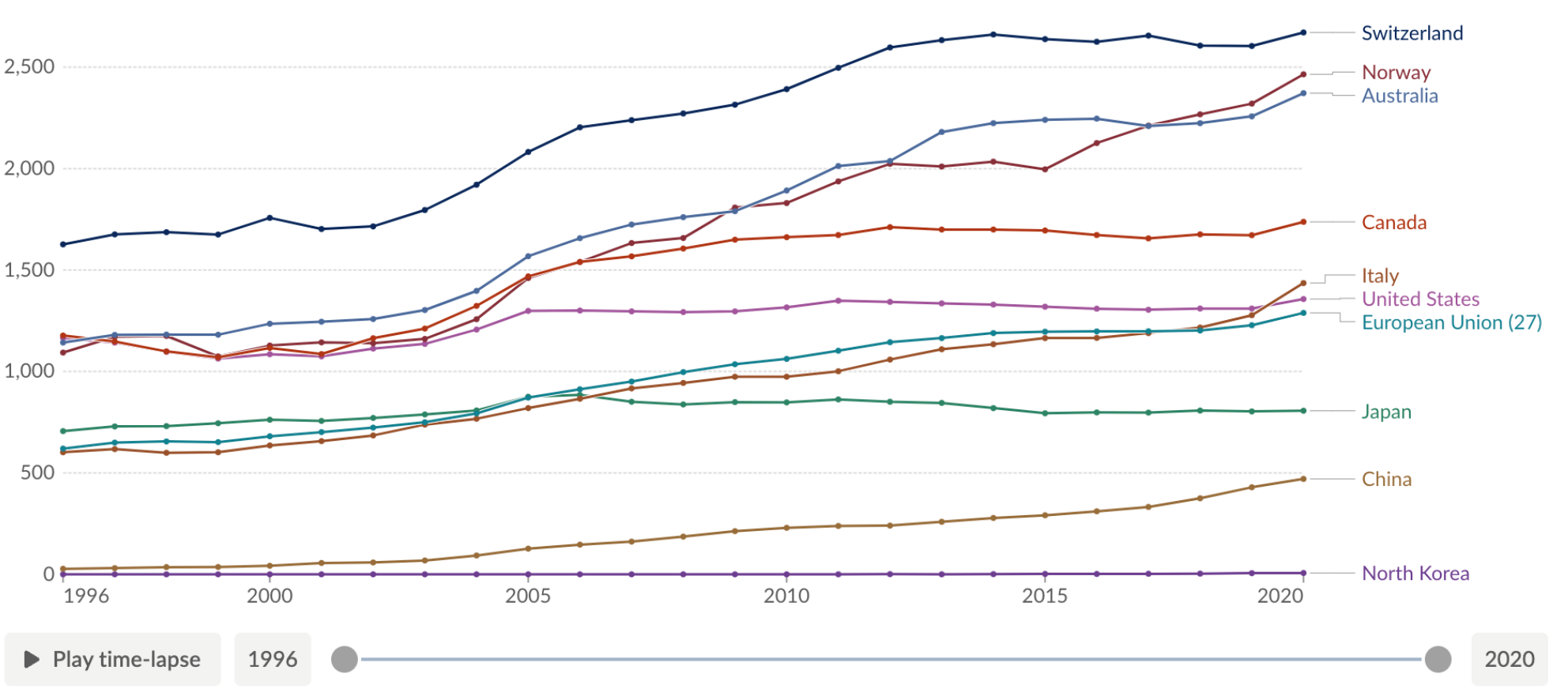
Includes physics, biology, chemistry, mathematics, clinical medicine, biomedical research, engineering and technology, and earth and space sciences



OurWorldinData.org/research-and-development, 2023

Annual articles published in scientific and technical journals per million people, 1996 to 2020

Includes physics, biology, chemistry, mathematics, clinical medicine, biomedical research, engineering and technology, and earth and space sciences

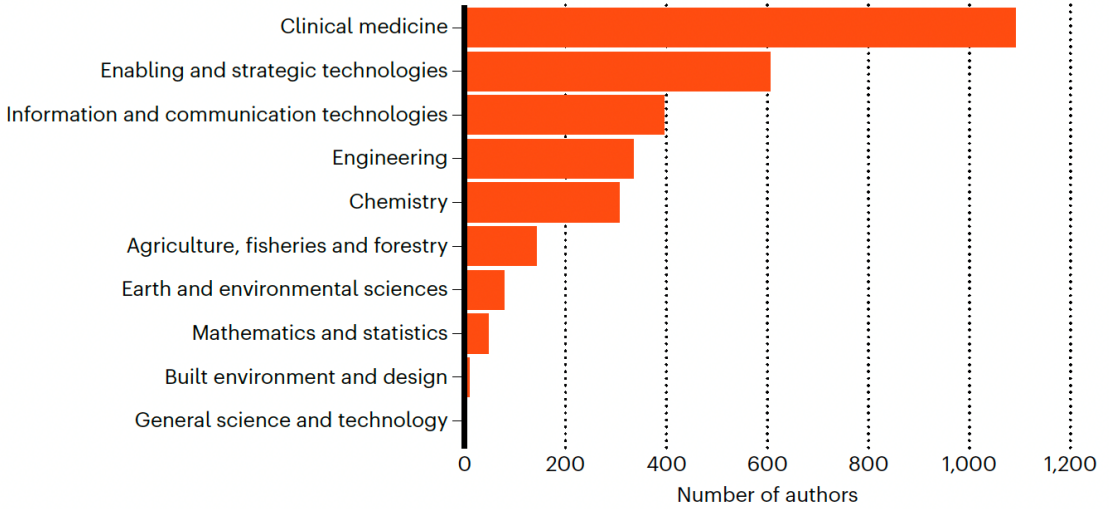


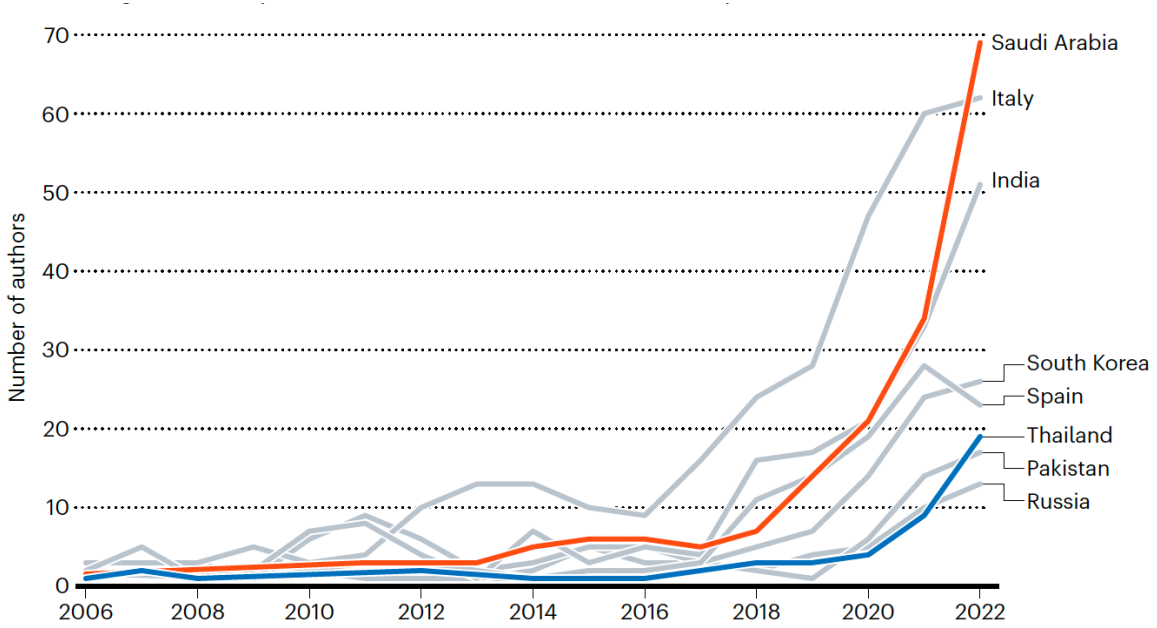
OurWorldinData.org/research-and-development, 2023

NUMBER OF ‘EXTREMELY PRODUCTIVE’ AUTHORS CONCERNS SCIENTISTS

HYPER PRODUCTIVE FIELDS

Between 2000 and 2022, most extremely productive authors outside physics worked in subjects such as clinical medicine, technology and engineering.





SOURCE: J. P. A. IOANNIDIS *ET AL.* PREPRINT AT BIORXIV HTTPS://DOI.ORG/K9B3 (2023)

G. Conroy, Nature | Vol 625 | 4 January 2024

Scientists are publishing too many papers — and that's bad for science!

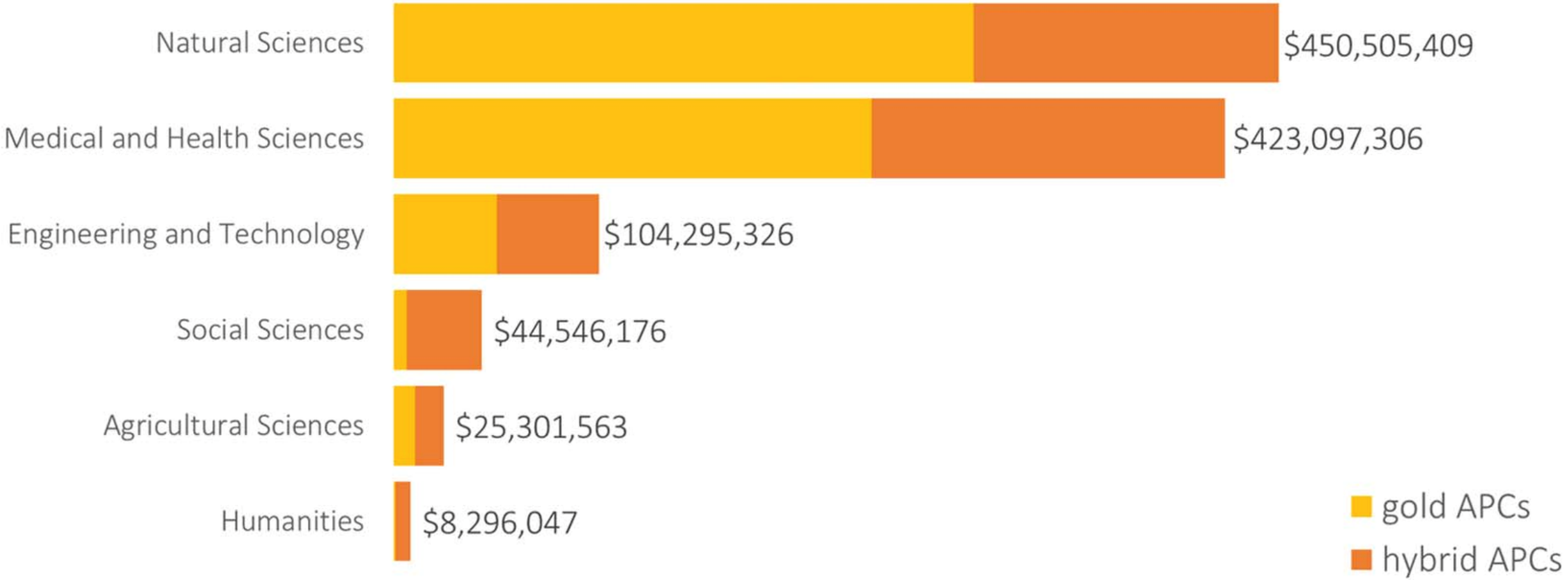
Difference between lower and upper estimate of total APC revenue (in USD) per publisher based on differing APC information for 933 journal-year combinations for gold OA.

Publisher	Lower estimate	Upper estimate	Difference	Difference %
Elsevier	$221,441,616	$230,750,669	$9,309,054	4.2
Sage	$31,576,202	$32,660,019	$1,083817	3.4
Springer Nature	$589,674,3808	$648,463,842	$58,789,463	10.0
Taylor & Francis	$76,765,557	$85,135,828	$8,370,271	10.9
Wiley	$141,316,332	$141,460,621	$144,289	0.1
All publishers	**$1,060,774,086**	**$1,138,470,980**	**$77,696,894**	**7.3**

Leigh-Ann Butler et al., The oligopoly's shift to open access: How the big five academic publishers profit from article processing charges. Quantitative Science Studies 2023; 4 (4): 778–799.

Scientists are publishing too many papers — and that's bad for science!

Total amount of APCs for gold and hybrid publications (n = 505,555) per OECD Field of Science.



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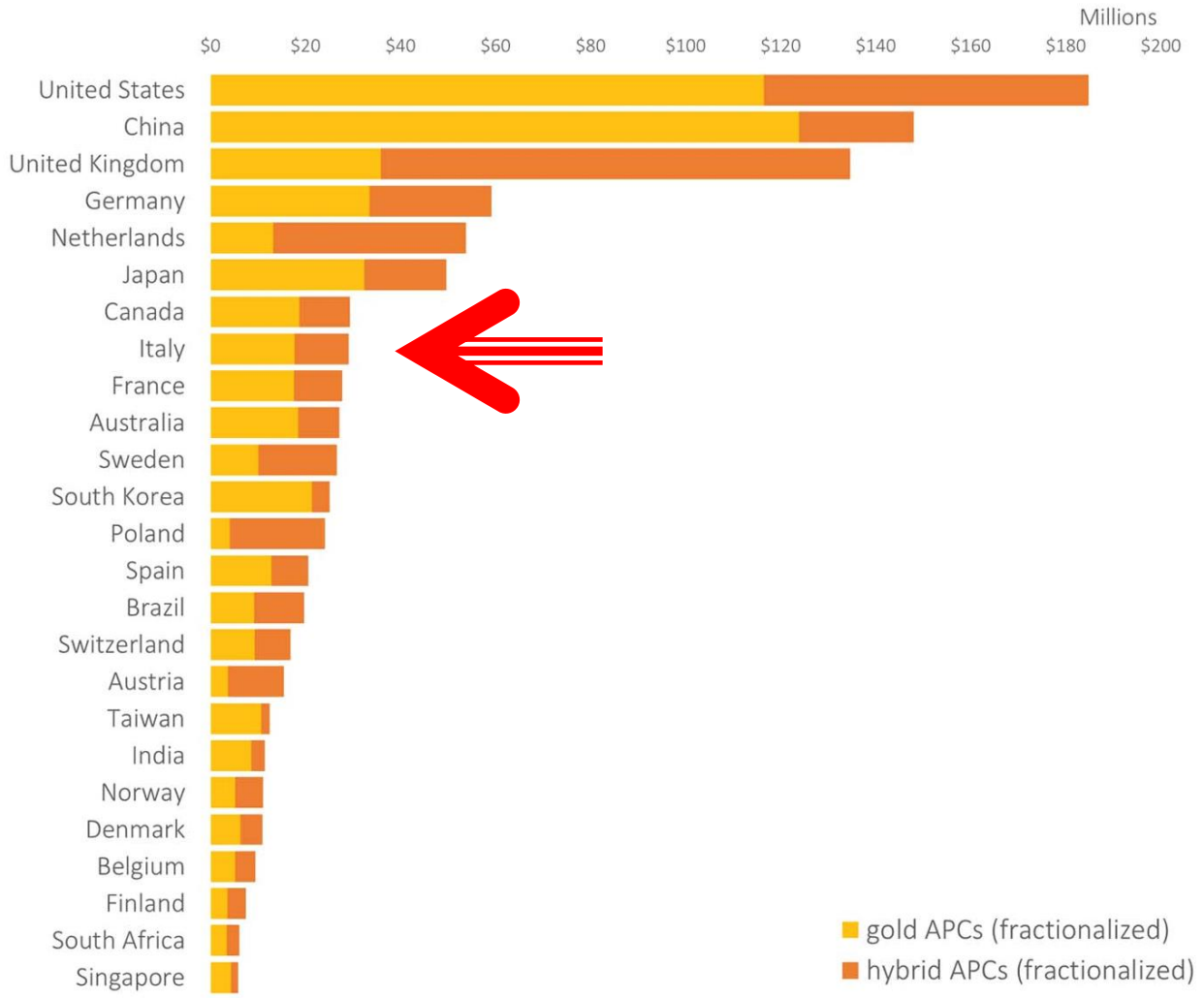
Top 25 countries by total amount of APCs expenditures 2015–2018 based on fractionalized publications.



Leigh-Ann Butler et al., The oligopoly's shift to open access: How the big five academic publishers profit from article processing charges. Quantitative Science Studies 2023; 4 (4): 778–799.

Researchers built an ‘AI Scientist’ — what can it do?

AI Scientist conducts its own ‘experiments’ by running the algorithms and measuring how well they perform.

At the end, it produces a paper, and evaluates it in a sort of automated peer review.

After ‘*augmenting the literature*’ this way, the algorithm can then start the cycle again, building on its own results.

Davide Castelvecchi *Nature* **633**, 266 (2024)

The Landscape of Lung Cancer Research

Recent Successes in Lung Cancer Research

- Targeted therapies and immunotherapies
- Antibody-Drug Conjugates (ADCs)
- Innovative clinical trial designs
- Multiomics and AI integration

Limitations of Current Approaches

- Therapy resistance
- Limited applicability of some targeted treatments
- Complexities in patient diagnostic-therapeutic trajectories

Integrative Approaches

- Combines genomics, transcriptomics, and radiomics
- Utilizes AI for R-Model development (APOLLO 11 Trial)
- Creates a virtual biobank and research consortium

The Clouds of Cancer Complexity

- Microbiota interference
- Drug-drug interactions
- Patient diagnostic-therapeutic trajectory optimization
- Cancer data workflow improvements

Personalized Medicine and Biomarkers

- Comprehensive tumor profiling
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Regulatory and Care Model Innovations

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- Multidisciplinary team expansion
- Focus on health equity

Future Directions

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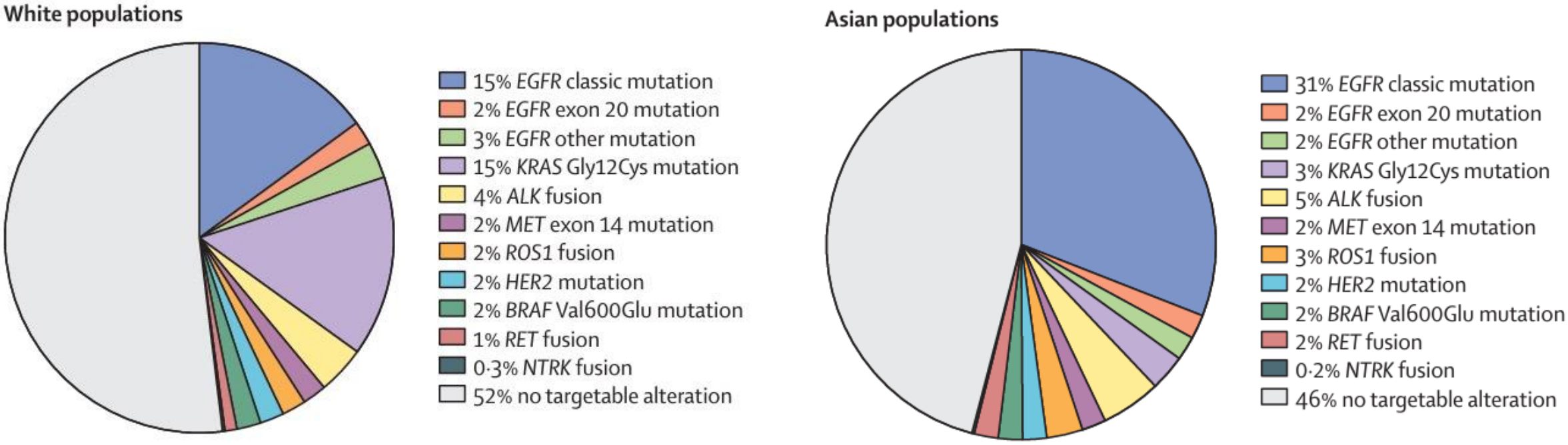
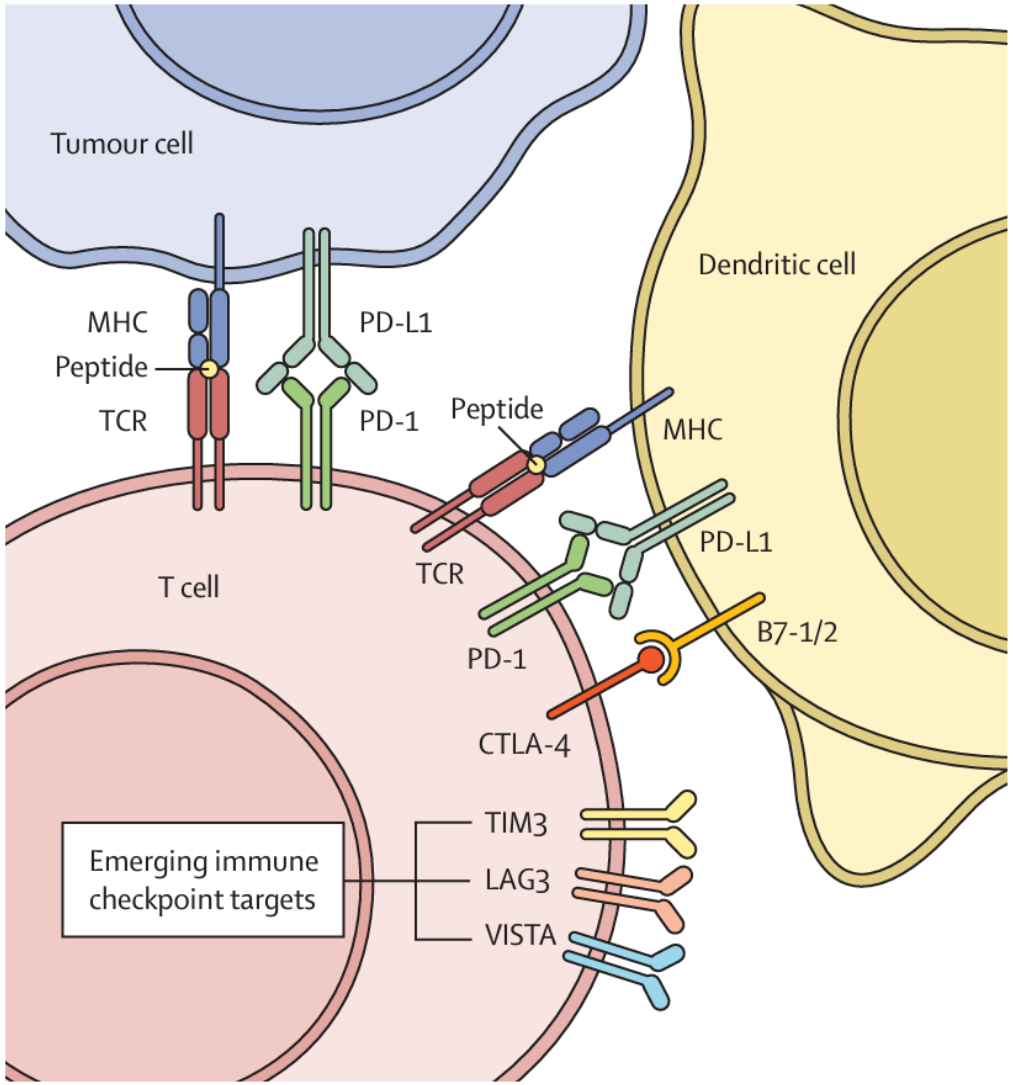
Molecular alterations in NSCLC in White and Asian populations



May-Lucie Meyer et al., Lancet Vol 404 August 24, 2024

May-Lucie Meyer, Bailey G Fitzgerald, Luis Paz-Ares, Federico Cappuzzo, Pasi A Jänne, Solange Peters, Fred R Hirsch New promises and challenges in the treatment of advanced non-small-cell lung cancer. Lancet Vol 404 August 24, 2024

Targets of immune checkpoint inhibitors



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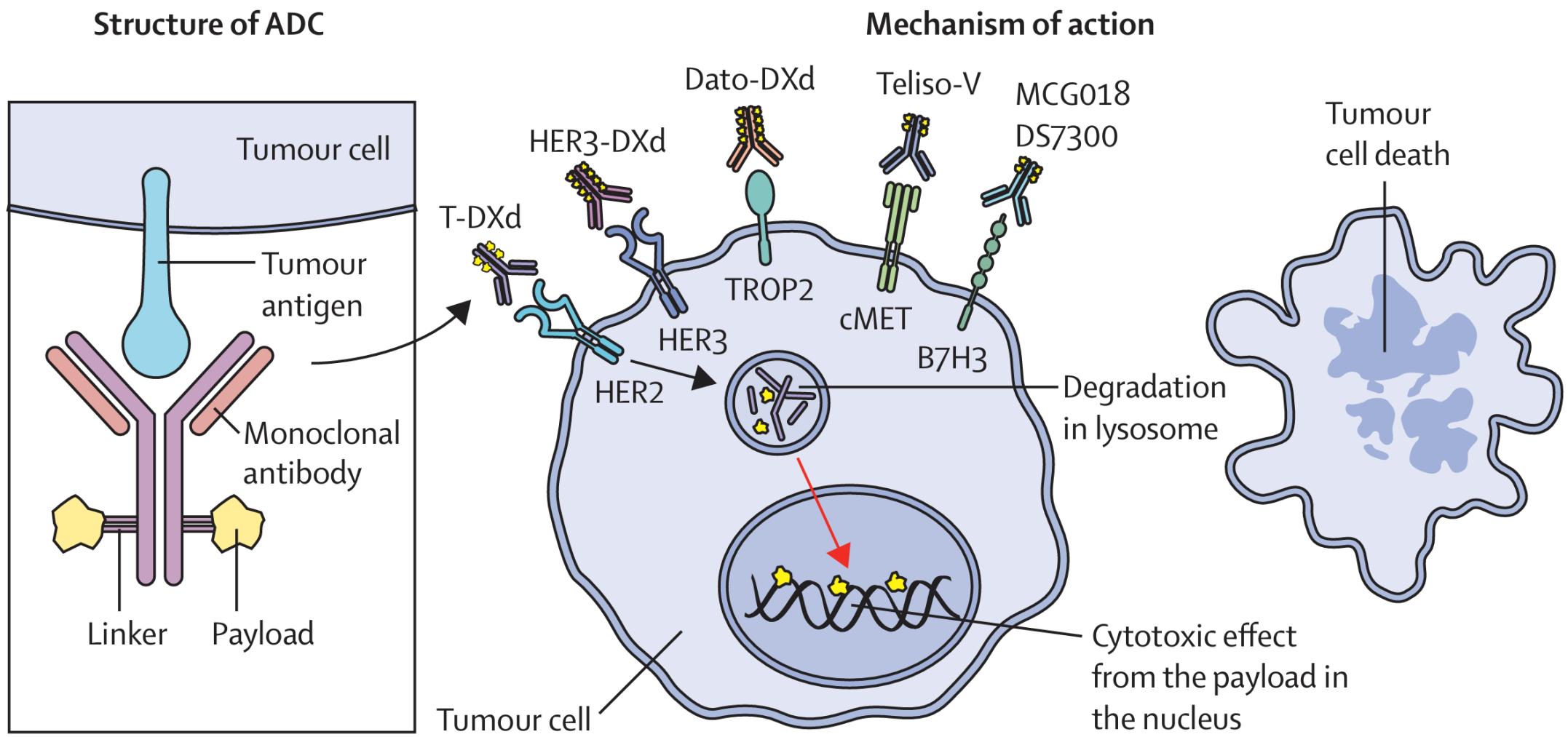
Structure, mechanism of action, and main studied ADCs in NSCLC



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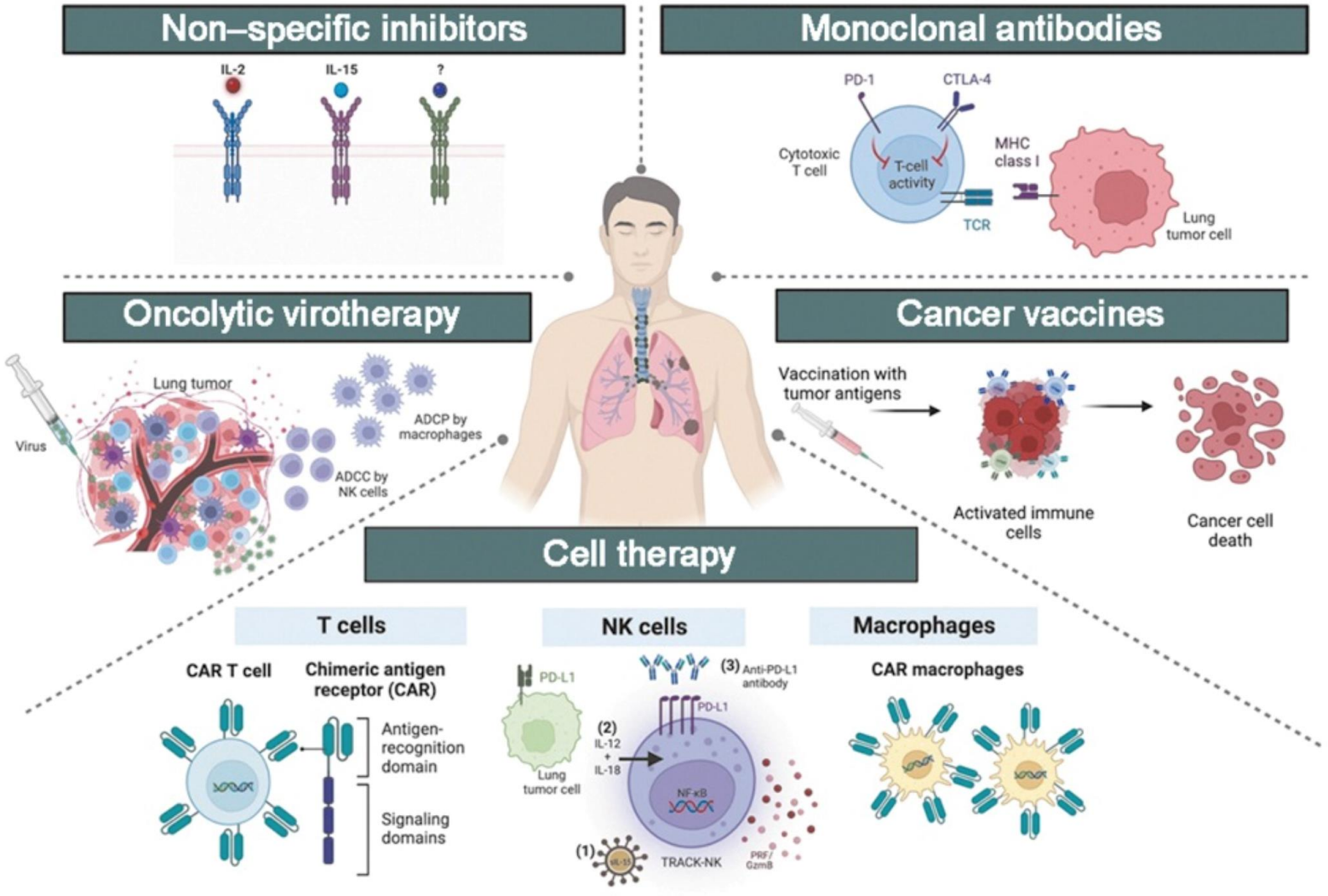
Recent advances and remaining challenges in lung cancer therapy



Barr Tasha et al., Chinese Medical Journal 137(5):p 533-546, March 05, 2024

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The future of clinical trials—goals, ideas, and discussion

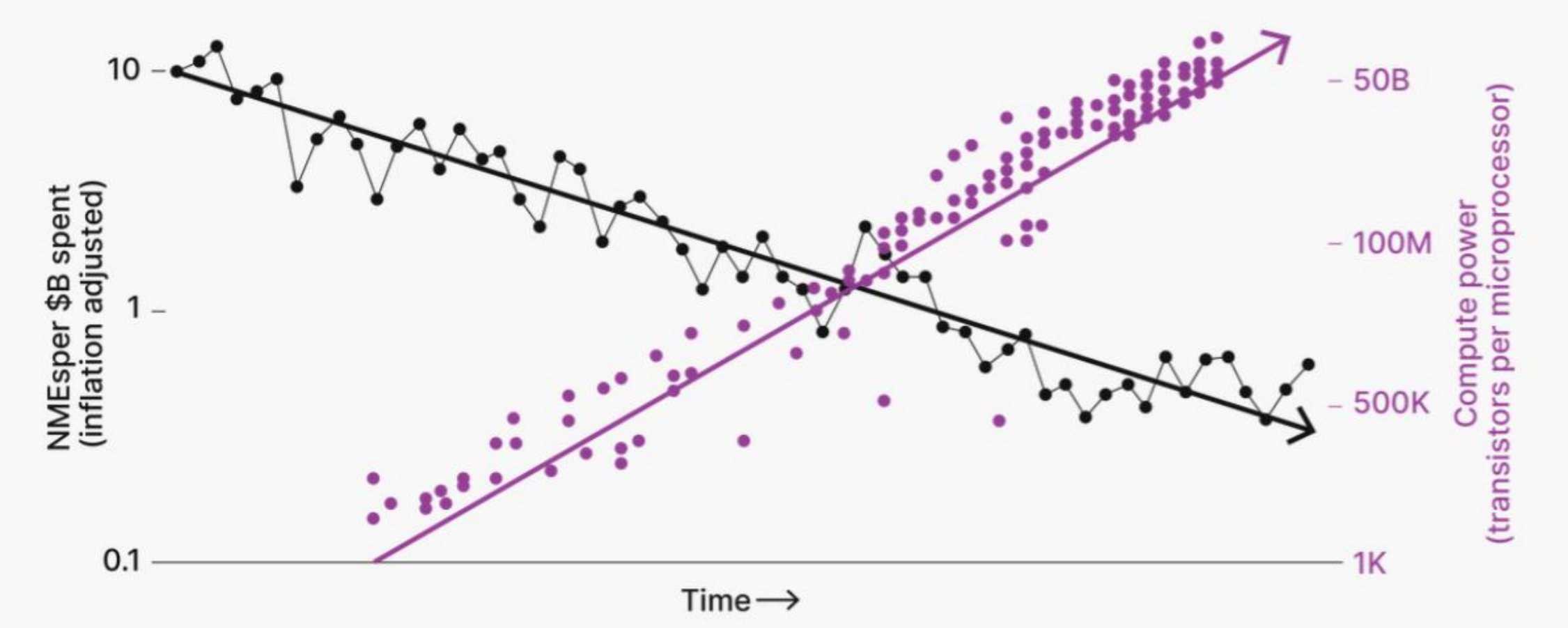
Clinical trials remain the mainstay of knowledge generation in medicine. Despite challenges such as increasing (regulatory) requirements in clinical trials for all involved stakeholders, new technologies, integrative approaches as well as forward-thinking trial designs can positively contribute to the evolution of clinical research for the benefit of patients.

- Patient-centric approach and less restrictive trial designs
- Decentralization and regional/institutional diversity for better patient engagement
- Involvement and education of diverse healthcare teams
- Digitalization and artificial intelligence
- Translational research and biomarker-guided therapy
- Trends in clinical statistics and trial designs
- Regulations and funding of academic research
- Building professional operational structures

Michael Gnant et al., memo (2024) 17:77–86 https://doi.org/10.1007/s12254-024-00969-7

Biology is enormously complex and highly networked

Drug discovery is becoming slower and more expensive over time, meanwhile computing power is becoming faster and less expensive over time



Drug discovery should be about alleviating patient suffering, not testing their patience.

Patients and their families often endure significant hardship, particularly when enrolled in control groups of new drug trials or participating in Phase I or II studies—often out of desperation, with no other therapeutic options.

The lengthy regulatory requirements can force them to sacrifice months, even years, of precious time.

Biology is enormously complex and highly networked

Pipeline Strategy

Build internal pipeline in indications with potential for accelerated path to approval. Learn more >

- Precision Oncology
- Rare Disease

Partnership Strategy

Partner in complex therapeutic areas requiring large financial commitment and competitive market dynamics.

Leverage partner knowledge and clinical development capabilities. Learn more >

- Neuroscience
- Other large, intractable areas of biology

Data Strategy

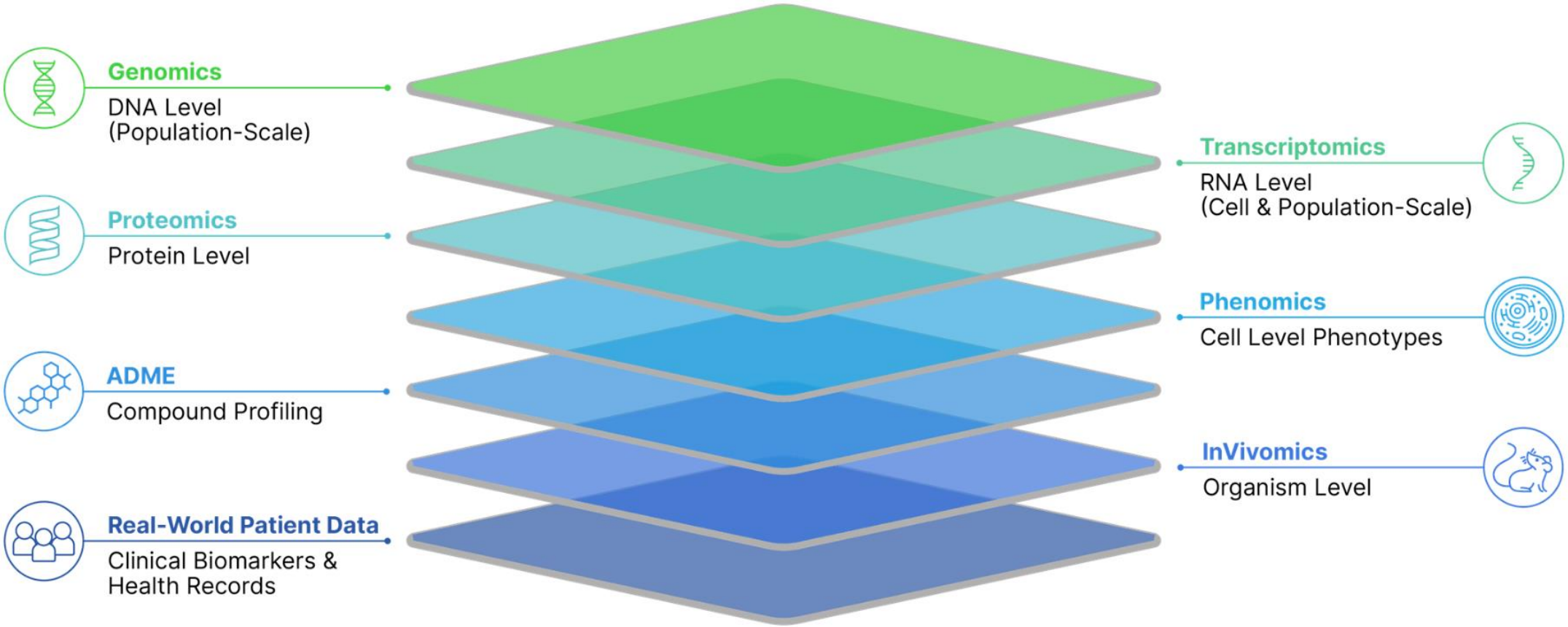
License subsets of data and key tools.

Direct generations of new data to maximize pipeline and partnership value-drivers. Learn more >

- Licensing
- Augment Recursion OS

Biology is enormously complex and highly networked

>50 petabytes	Up to 2.2M /week	Top 500	>50 cell types	>6 trillion
of proprietary biological, chemical, & patient-centric data	wet lab experiment profiling genes and compounds	supercomputer BioHive-1 across any industry	produced at scale, including >1T hiPSC-derived neuronal cells	gene and compound relationships profiled in our Maps



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Evidence generation
Innovative precision oncology trials

- Platform trials, also known as multiple arm, multiple stage studies, are randomized controlled clinical trials which simultaneously investigate several treatments in different study arms against a single control arm, all embedded in one trial.

- The trial design is adaptive, meaning that treatment arms may be discontinued, and new study arms investigating a specific drug-target match may be added.

- Patients may also be reassigned to a new treatment arm based on their response to previous treatment and/or change in biomarker status.

- This trial approach dissolves the classic stepwise trial design and aims at accelerating drug development.

Stenzinger A, Moltzen EK, Winkler E, et al. Implementation of precision medicine in healthcare—A European perspective. J Intern Med. 2023;294:437–454

ARGO Trial Platform
Navigating genomic landscape to unveil a precision approach in oncology

PROMOTER AND SCIENTIFIC COORDINATION	FMP - FONDAZIONE PER LA MEDICINA PERSONALIZZATA (PROF. PAOLO MARCHETTI, PRESIDENT ACC - ALLIANCE AGAINST CANCER (PROF. RUGGERO DE MARIA MARCHIANO, PRESIDENT
NO-PROFIT PROMOTER	RES - FONDAZIONE RICERCA E SALUTE
NO-PROFIT SPONSOR (PATRONAGE):	SAPIENZA UNIVERSITY OF ROME, FONDAZIONE ROMA SAPIENZA, REGIONE LAZIO, ISTITUTO SUPERIORE DI SANITÀ – ISS, ISTITUTO NAZIONALE DI FISICA NUCLEARE – INFN, CINECA, FONDAZIONE RICERCA E SALUTE – RES, ASSOCIAZIONE ITALIANA DI ONCOLOGIA MEDICA – AIOM, FEDERATION OF ITALIAN COOPERATIVE ONCOLOGY GROUPS - FICOG, FONDAZIONE PERIPLO, FAVO, FONDAZIONE INCONTRADONNA, ANDOS, ROPI
PROTOCOL STEERING COMMITTEE:	DOMENICO ALVARO, MAURO BIFFONI, ETTORE CAPOLUONGO, ARTURO CAVALIERE, SAVERIO CINIERI, PIERFRANCO CONTE, CHIARA CREMOLINI, GIUSEPPE CURIGLIANO, LUCIA DEL MASTRO, CARLO DELLA ROCCA, RUGGERO DE MARIA, MASSIMO DI MAIO, VALENTINA GUARNERI, IMMA ESPOSITO, STEFANIA GORI, LISA LICITRA, SARA LONARDI, FEDERICA MAZZUCA, NELLO MARTINI, NICOLA NORMANNO, PIER GIUSEPPE PELICCI, FRANCO PERRONE, CARMINE PINTO, GIANCARLO PRUNERI, ANNA SAPINO, PAOLO BRUZZI. CANCER PATIENT ASSOCIATIONS: FRANCESCO DE LORENZO, ADRIANA BONIFACINO, FLORI DEGRASSI, FABRIZIO NICOLIS
PRINCIPAL INVESTIGATOR OF THE COORDINATING SITE:	ANDREA BOTTICELLI, SAPIENZA UNIVERSITY OF ROME, POLICLINICO UMBERTO I, ROME, ITALY

ARGO Trial Platform
Navigating genomic landscape to unveil a precision approach in oncology

Primary Objective

Evaluate the efficacy (meant as PFS – *Progression Free Survival*) and the benefit in QoL (*Quality of Life*) (meant as PROs - *Patient-Reported Outcomes*) of TT (*Tailored Treatment*) vs TCP (*Therapy at choice of physician*) in homogeneous groups of patients by the same molecular alterations in homogeneous groups of neoplasia

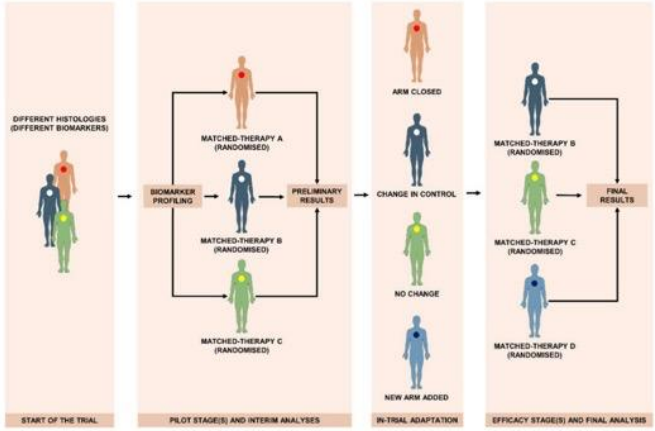
Hierarchical Approach :

PFS

↓

PROs

Platform Trial adaptative design



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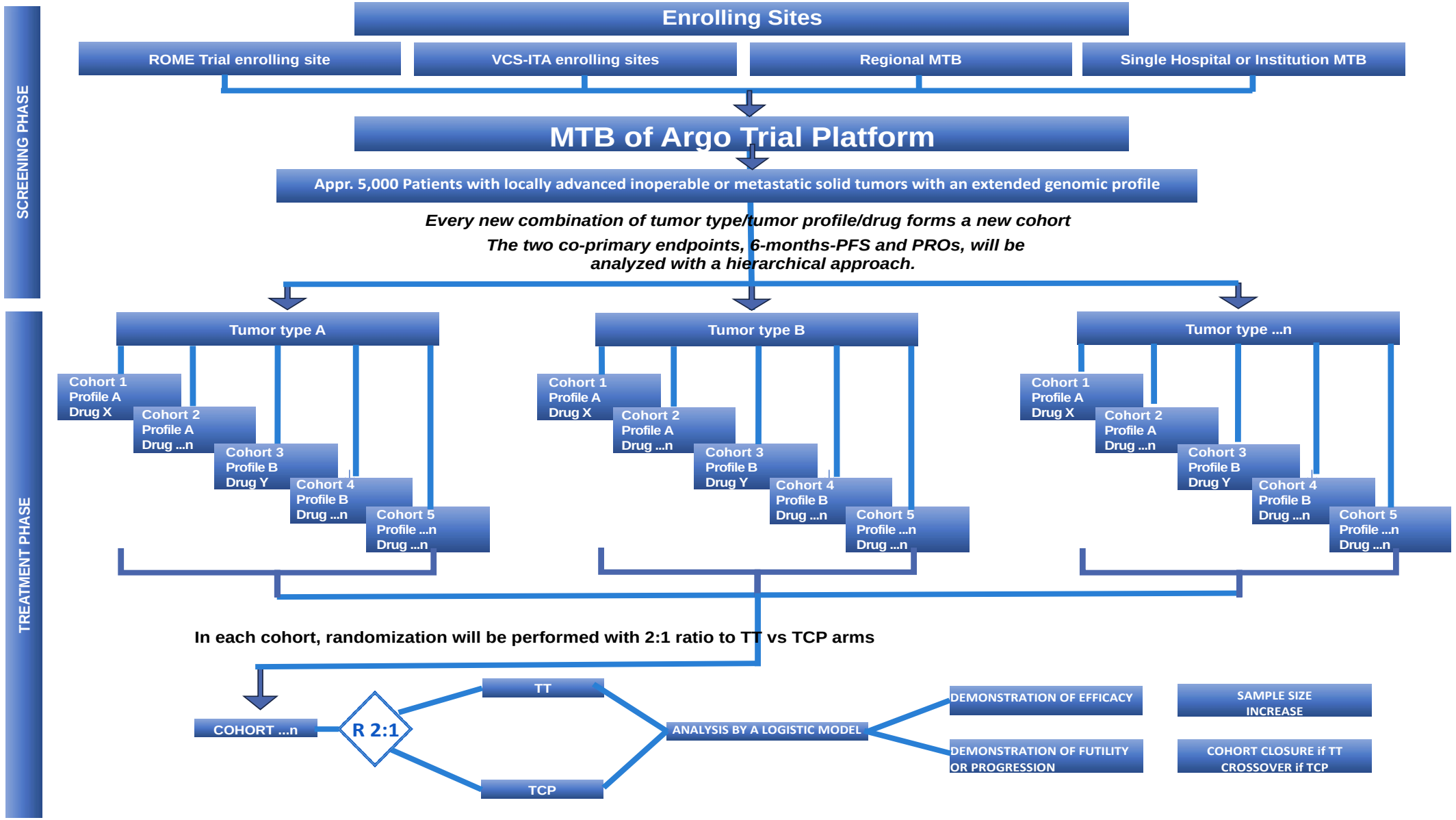

From *Precision* Oncology to *Interplayed* Oncology

Systemic Interactions in Cancer Treatment

- **Interconnected Systems**: Cancer cells interact not only with immune, endocrine, and metabolic systems but also with the entire exposome
- **Evaluating Influences**:
  - How drugs affect these systems individually and collectively
  - Importance of systemic approaches in treatment planning
- **Research Directions**: Focus on holistic approaches to understand multidimensional influences

Fmp Fondazione per la Medicina Personalizzata

FONDAZIONE RICERCA E SALUTE

CINECA

INFN Istituto Nazionale di Fisica Nucleare