The Pezcoller Foundation

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Table of Contents

Picture on front page:
Prof. William G. Kaelin, 2019 Nobel Laureate and Chairman of the Pezcoller Symposium, at the Poster Session

February 2025 marked the 45th anniversary of the Pezcoller Foundation, which was established in 1980 to promote cancer research and support young researchers.
Throughout the years, the Foundation has awarded numerous prestigious prizes to cancer researchers, in partnership with the AACR and EACR. It has also provided talented young researchers with scholarships and opportunities to connect with world-class scientists at Pezcoller Symposia, Seminars, and Lectures. All this has contributed to the Foundation's growing reputation within the international, national and local scientific community.
Since 1989, the Pezcoller Foundation has gained credibility and scientific prestige, particularly through the Pezcoller Symposia. Under the leadership of Dr. Enrico Mihich first, then Dr. David Livingston, and most recently, the 2019 Nobel laureate Dr. William Kaelin, the Foundation has flourished.
Thanks to the passionate work of these leaders and the support of the Scientific Standing Committee, the Pezcoller Symposia have become widely appreciated as one of the "not-to-be-missed" annual meetings on cancer research.
This year's Symposium, "Studying and Treating Cancer in the Digital Era," is the 36th in an uninterrupted series. As always, it features topics at the forefront of cancer research and top international scientists in the field.
«Advances in digital technologies, including artificial intelligence, are transforming basic cancer research and clinical cancer medicine – says Chairman Dr. Kaelin – These advances create immense opportunities and significant challenges». This Symposium includes the use of large ("big") data and AI in basic cancer biology, cancer target selection, drug development, pathology, and radiology.
While the topic this year is very innovative, the experience gained in this area is still limited as a result. This may explain the smaller number of abstracts submitted for poster presentations. However, almost all of them are of high quality, according to the eight-member selection committee chaired by Dr. Massimo Loda. We sincerely thank Dr. Loda and the committee for their hard work.
Attendance is also somewhat lower in this context, but this aligns with the new, selective topic. In addition to the informal atmosphere and extensive discussion time, the symposia always aim to promote qualified participation and support talented young researchers.
In any case, we have 171 participants this year, mostly Italian as always, but also from other European and non-European countries.
Once again, this year's Symposium offers two important opportunities for young scientists. First, you can meet editors from five leading scientific journals: Nature Cancer, Cancer Discovery, Cancer Cell, BMC Springer Nature, and Molecular Systems Biology (EMBO). Second, you can attend a career development panel discussion chaired by William Kaelin.
Both have now become well-established traditions that emphasize the Pezcoller Symposia's special focus on young researchers, as have the Symposium Highlights. Thanks to our collaboration with the CIBIO Department at the University of Trento and the European School of Oncology in Milan, the Highlights will be presented at an ESO international online event in September 2025.
Finally, I would like to thank the AACR, the EACR, and the Mark Foundation, which are once again supporting the participation of young people in the Symposium, proving its scientific value and the close cooperation with the Foundation.
Thus, in addition to the four Begnudelli Awards provided by the Pezcoller Foundation and the EMBO Award, which is voted by all participants, two more awards and seven Travel Grants have been given, to researchers from Spain, Brazil, the United States, Switzerland and Italy.
Furthermore, I would like to express my deepest gratitude to everyone who contributed to the organization and management of this Symposium: first the chairman, Dr. William Kaelin and the members of the Scientific Standing Committee and the Poster Evaluation Committee. Then, the Pezcoller Foundation staff; the Orikata agency; Jam Session technical services and, last but not least, the Humanities Department of the University of Trento for hosting the Symposium in this prestigious and comfortable venue.

President
Enzo Galligioni

The Pezcoller Foundation

36th PEZCOLLER SYMPOSIUM

PROGRAM

June 23-24, 2025
Trento, Italy
Humanities Department, University of Trento (via Tommaso Gar 14)

Studying and Treating Cancer in the Digital Era

Chairman: Kaelin William G. (2019 Nobel Laureate)
Moderators:

Alberto Bardelli
Chiara Bonini
Giannino Del Sal
Francesca Demichelis
Massimo Loda
Stefano Piccolo
Brenda A. Schulman

Day 1 - Monday, June 23, 2025

7.45 ***Registration***

8.30 ***Welcome:*** *Enzo Galligioni*

8.40 ***Focus and Goals:*** *William G. Kaelin*

8.50 ***Moderator:*** *Alberto Bardelli* SESSION 1

David Livingstone Keynote Lecture

"Therapeutic discovery in the Digital Era"

William R. Sellers, MD

Broad Institute of MIT and Harvard

9.30 Discussion

9.45 ***"Modeling malignancy across scales: from virtual tumors to predictive oncology"***

Christina Curtis, PhD

Stanford University

10.10 Discussion

10.25 Coffee break and poster exhibition

10.55 ***Moderator:*** *Brenda A. Schulman* SESSION 2

"Data science approaches to uncovering cancer mechanisms and computational discovery of ligands to target them"

M. Madan Babu, PhD

St. Jude Children Research Hospital

11.20 Discussion

11.35 ***"Insights from images: applying microscopy and AI to drug discovery in oncology and beyond"***

Anne Carpenter, PhD

Broad Institute of MIT and Harvard

12.00 Discussion

12.15 ***"Leveraging Single-Cell Technologies to Engineer the Immune System"***

Ido Amit, PhD

Weizmann Institute of Science (Israel)

12.40 Discussion

12.55 Lunch and poster exhibition

14.25 ***EACR-AACR-Mark Foundation Travel Grants***

14.30 ***Moderator:*** *Giannino Del Sal* SESSION 3

"Hypothesis-driven data-heavy computations exploit germline-somatic liaisons for the understanding of cancer evolution"

Francesca Demichelis, PhD

CIBIO, University of Trento

14.50 Discussion

15.05 ***"Origins of somatic de novo chromosome rearrangements unveiled by systematically coupling imaging and genomics"***
Jan O. Korbel, PhD
European Molecular Biology Laboratory, Heidelberg
15.30 Discussion

15.45 Cookie break and poster exhibition

16.05 ***Moderator:*** *Chiara Bonini* SESSION 4
"AI and Data Science in Cancer Imaging"
Maryellen L. Giger, PhD
University of Chicago
16.30 Discussion

16.45 ***Moderator:*** *William G. Kaelin*
Career Development Panel Discussion
17.30 END OF DAY 1

19.30 ***SOCIAL DINNER***

Day 2 - Tuesday, June 24, 2025

8.30 ***Moderator:*** *Stefano Piccolo* SESSION 1
Enrico Mihich Keynote Lecture
"Where Form Meets Function: Decoding Tissue Architecture"
Dana Pe'er, PhD
Memorial Sloan Kettering Cancer Center
9.10 Discussion

9.25 ***"Beyond RWE and clinical applications: large foundation models in cancer biology research"***
Carlo B. Bifulco, MD
Providence Genomics, Oregon
9.50 Discussion

10.05 ***"AI for Precision Medicine: development and discovery of computational biomarkers for oncology and beyond"***
Francesco Ciompi, PhD
Radboud University, Nijmegen
10.30 Discussion

10.45 Coffee break and poster exhibition

11.15 ***Moderator:*** *Massimo Loda* SESSION 2
"Multimodal, generative and agentic AI for oncology"
Faisal Mahmood, PhD
Massachusetts General Hospital, Brigham and Women's Hospital
11.40 Discussion

11.55 ***"AI-Powered Pathology: scaling precision cancer diagnostics in the Digital Age"***
Andrew H. Beck, MD, PhD
PathAI, Boston
12.20 Discussion

12.35 Lunch and poster exhibition

14.05 ***Moderator:*** *Massimo Loda*
Pezcoller Awards and EACR, AACR, The Mark Foundation Awards 4 Best Poster Lectures

15.15 ***Moderator:*** *Francesca Demichelis* SESSION 3
"Accelerating safe and effective AI use at the point of care"
Suchi Saria, PhD
Johns Hopkins University
15.40 Discussion

15.55 ***"Enhancing precision cancer medicine with biologically guided artificial intelligence"***
Eliezer M. Van Allen, MD
Harvard Medical School
16.20 Discussion

16.35 ***"Automating scientific discovery and hypothesis generation with language model agents"***
Andrew D. White, PhD
University of Rochester
17.00 Discussion

17.15 ***EMBO Poster Prize***

17.20 ***Closing Remarks:*** *William G. Kaelin*

17.30 END OF DAY 2

Standing Committee

- **William G. Kaelin, MD** – *Chairman of the Symposia*
  Dana-Farber Cancer Institute, Boston, MA
- **Chiara Ambrogio, PhD**
  University of Torino, Italy
- **Alberto Bardelli, PhD**
  IFOM, Milano, Italy
- **Chiara Bonini, MD, PhD**
  San Raffaele Institute, Milano, Italy
- **Giannino Del Sal, PhD**
  IGCEB, Trieste, Italy
- **Francesca Demichelis, PhD**
  University of Trento, Italy
- **Giulio Draetta, MD**
  MD Anderson Cancer Center, Houston, TX
- **Margaret Foti, MD**
  CEO of the AACR
- **Dr. Enzo Galligioni, MD**
  The Pezcoller Foundation, Trento, Italy
- **Massimo Loda, MD, PhD**
  Weill Cornell Medicine, New York, NY
- **Stefano Piccolo, PhD**
  University of Padova, Italy
- **Brenda A. Schulman, PhD**
  Max Planck Institute, Martinsried, Germany
- **Charles Swanton, PhD**
  The Francis Crick Institute
  CR-UK London Research Institute

Faculty

- **Ido Amit**
  Weizmann Institute,
  Rehovot, Israel
- **Mohan Madan Babu**
  St. Jude Children Hospital,
  Memphis, TE
- **Andrew Beck**
  PathAI,
  Boston, MA
- **Carlo Bifulco**
  Oregon Regional Laboratory,
  Providence, RI
- **Anne Carpenter**
  Broad Institute of MIT,
  Cambridge, MA
- **Francesco Ciompi**
  Radboud University Medical Center,
  Nijmegen, Netherlands
- **Christina Curtis**
  Stanford University,
  CA
- **Francesca Demichelis**
  University of Trento,
  Italy
- **Maryellen Giger**
  University of Chicago,
  Chicago, IL
- **Jan Korbel**
  European Molecular Biology Laboratory,
  Heidelberg, Germany
- **Faisal Mahmood**
  MGH and Brigham and Women's Hospital,
  Boston, MA
- **Dana Pe'er**
  Memorial Sloan Kettering Cancer Center,
  New York, NY
- **Suchi Saria**
  Johns Hopkins University,
  Baltimore, MD
- **William Sellers**
  Broad Institute of MIT
  Cambridge, MA
- **Eliezer VanAllen**
  Harvard Medical School,
  Boston, MA
- **Andrew White**
  Future House,
  San Francisco, CA
  University of Rochester,
  New York, NY

Discussants

- **William G. Kaelin, MD** – *Chairman of the Symposia*
  Dana-Farber Cancer Institute, Boston, MA
- **Alberto Bardelli, PhD**
  IFOM, Milano, Italy
- **Chiara Bonini, MD, PhD**
  San Raffaele Institute, Milano, Italy
- **Giannino Del Sal, PhD**
  IGCEB, Trieste, Italy
- **Francesca Demichelis, PhD**
  University of Trento, Italy
- **Massimo Loda, MD, PhD**
  Weill Cornell Medicine, New York, NY
- **Stefano Piccolo, PhD**
  University of Padova, Italy
- **Brenda A. Schulman, PhD**
  Max Planck Institute, Martinsried, DE

36th Pezcoller Symposium

Studying and treating cancer in the Digital Era

Trento, Italy, June 23-24, 2025

ABSTRACTS OF LECTURES

William SELLERS
Broad Institute of MIT, Cambridge, MA
Monday, June 23
8:50

Therapeutic Discovery in the Digital Era

Discovery and development of highly effective cancer therapeutics remains a complex, failure-prone endeavor that relies heavily on trial and error. Assays often fall short of capturing mechanisms relevant to the cellular context; novel target classes remain underexplored due to limitations in assay development; chemical libraries, though extensive, cover only a narrow and biased portion of potential chemical space; and empirical tuning of pharmacologic properties frequently derails promising leads. While biologic discovery has advanced significantly, especially in identifying binders to target antigens, the full coverage of epitope space is rarely achieved, and the combinatorial landscape of binder formats, orientations, and linkers creates a search space far too large to exhaust experimentally. Failures in biotherapeutics also stem from issues of developability and, occasionally, immunogenicity. In our current digital era, machine learning can address challenges in drug development by extending our reach into discovery spaces that remain inaccessible to direct experimentation. Yet, many biological problems lack datasets that are appropriately tailored for machine learning, highlighting an urgent need not only to collect the right data but also to design large-scale experimental approaches with specific machine learning algorithms in mind. For example, structure prediction tools have significantly advanced our ability to probe protein function, but their impact is often limited by data quality and scale. Bridging these gaps will require a convergence of scalable experimental systems with *in silico* screening and AI-driven tools. Systematic discovery efforts will play a central role in generating datasets bespoke to the application of machine learning tools. This integration of experimental and computation science has the potential to reframe how we identify vulnerabilities in cancer and develop the therapies to address them.

Christina CURTIS
Stanford University, CA
Monday, June 23
9:45

Modeling malignancy across scales: from virtual tumors to predictive oncology

In this talk I will outline how computational and machine learning techniques can yield quantitative and mechanistic insights into tumor progression and treatment response to advance predictive oncology. I will provide several vignettes illustrating the power of these approaches to forecast disease progression, to define novel targets, to inform patient stratification, and to predict therapeutic benefit. Given the absence of ground truth data on human tumor progression, I will begin by outlining the utility of 'virtual tumors' and inference of evolutionary dynamics from somatic sequencing data to infer the timing and patterns of metastatic seeding. Subsequently, I will show how machine learning can be deployed to define robust molecular classifications of disease and underlying vulnerabilities- as exemplified by the integrative subgroups of breast cancer, which predict late distant relapse over two decades. Further, I will describe the unexpected role of hereditary and immune interplay in sculpting somatic evolution, tumor subtypes, and patient outcomes. I will go on to show how this phenomenon of germline-mediated immunoediting generalizes across tumor types with implications for risk stratification and cancer interception. Lastly, I will describe how tumor-immune interactions can be quantified *in situ* via spatial profiling to define relapse-associated features, dynamic changes in response to targeted and immunotherapy, and predictive biomarkers. I will end by outlining how these multi-modal measurements can be harnessed to enable digital (molecular) twins throughout a patient's journey.

Mohan Madan BABU
St. Jude Children Hospital, Memphis, TE
Monday, June 23
10:55

Data science approaches to uncovering cancer mechanisms and computational discovery of ligands to target them

The advent of large-scale multi-omics datasets has increased the power of computational approaches to study cancer biology. The combination of this era of big data with advances in machine-learning and computational power opens new possibilities to study cancer and identify new therapeutic avenues. In this talk, I will present our ongoing efforts on applying data-science approaches to understand mechanisms driving cancer and design new therapeutics. I will present a family of deep-learning models to predict cancer vulnerabilities at the patient, and cancer sub-type level. For this, we build upon the efforts to characterize cell-line vulnerabilities led by the DepMap initiative and integrate prior biophysical knowledge into the model by including genetic and physical interactions into the model architecture. Building upon the base model, which shows predictive power, we present a family of cancer-specific fine-tuned models, further improving performance on specific cancer lineages. We deployed this approach onto a cohort of patient-derived acute myeloid leukaemia samples, which allowed us to identify new vulnerability genes specifically enriched in AML. Complementing this target identification strategy, I will also present a computational strategy that we have developed to search for novel drug-like molecules that could act on the identified targets. Our approach combines structure-based virtual screening with machine learning to identify potential new compounds for different therapeutic modalities, including inhibition, allosteric modulation and targeted protein degradation.

Anne CARPENTER
Broad Institute of MIT, Cambridge, MA
Monday, June 23
11:35

Insights from images: applying microscopy and AI to drug discovery in oncology and beyond

Cell images contain a vast amount of quantifiable information about the status of the cell: for example, whether it is diseased, whether it is responding to a drug treatment, or whether a pathway has been disrupted by a genetic mutation. We aim to go beyond measuring individual cell phenotypes that biologists already know are relevant to a particular disease. Instead, in a strategy called image-based profiling, often using the Cell Painting assay, we extract hundreds of features of cells from microscopy images. Just like transcriptional profiling, the similarities and differences in the patterns of extracted features reveal connections among diseases, drugs, and genes, with many applications in cancer research. In fact, these strategies underpin drug discovery platform companies such as Recursion and SyzOnc.

Because images are inexpensive and high-throughput, we can carry out experiments at very large scale, yielding single-cell profiles for hundreds of thousands of samples through public-private consortia (JUMP, OASIS, VISTA, NIH IGVF) and pooled barcode-based optical screens. Cell morphology is therefore a powerful data source for cancer systems biology alongside molecular omics.

Ido AMIT
Weizmann Institute, Rehovot, Israel
Monday, June 23
12:15

Leveraging single-cell technologies to engineer the immune system

Immunotherapy - the science of engineering the immune system to combat the most common human diseases – such as cancer, neurodegeneration, and autoimmune disease has been pursued for more than a century. Yet only recently has this powerful strategy finally taken center stage in medicine. The past few years have seen unprecedented clinical responses and rapid drug development. Several scientific revolutions from genomics to functional genomics, synthetic biology and machine learning are converging to open new opportunities for developing powerful and disruptive therapies for major diseases. Single cell genomics hold the potential to revolutionize basic and translational research of the immune system. I will discuss how recent single cell genomic studies are changing our perspective of various immune related pathologies from cancer to autoimmune disease and neurodegeneration. Finally, I will consider recent and forthcoming technological and analytical advances and their huge potential impact on the future of immunology research and immunotherapy.

Francesca DEMICHELIS
University of Trento, Italy
Monday, June 23
14:30

Hypothesis-driven data-heavy computations exploit germline-somatic liaisons for the understanding of cancer evolution

Significant heritability is observed for common cancer types worldwide. We hypothesized that

the molecular mechanisms by which inherited genetics facilitate cancer initiation might transit through the cooperation with specific somatic genomic events. This cooperation, in turn, dictates the tumor features. Hypothesis-driven interrogation of curated datasets crossing genotyping, molecular characterization, and cell-type-specific chromatin status can nominate germline-somatic tandems that lead to cancer initiation. Specifically, we observed cell-autonomous inherited-genotype-specific production of steroids in prostate cancer cells in the presence of the early somatic SPOP mutation. We suggest opportunities to jointly model germline-somatic tandems to help untangle the complexity of human cancer.

Jan KORBEL
European Molecular Biology Laboratory, Heidelberg, Germany
Monday, June 23
15:05

Origins of somatic de novo chromosome rearrangements unveiled by systematically coupling imaging and genomics

I will introduce Machine Learning-Assisted Genomics and Imaging Convergence (MAGIC), an autonomous platform that combines live-cell imaging, real-time machine learning, and single-cell genomics to investigate patterns of somatic chromosomal aberrations. When applied to non-transformed human cell lines, MAGIC uncovers baseline rates and mechanistic origins of chromosomal instability. The targeted induction of DNA double-strand breaks along chromosomes triggers distinct chromosomal alteration (CA) processes, revealing stable isochromosomes, coordinated segregation and amplification of isoacentric segments in multiples of two, and complex CA outcomes, influenced by the chromosomal break location. The large-scale experimentation enabled by MAGIC provides insights into de novo CA formation, paving the way to unravel fundamental determinants of chromosome instability.

Maryellen L. GIGER
University of Chicago, Chicago, IL
Monday, June 23
16:05

AI and Data Science in Cancer Imaging

Artificial Intelligence in medical imaging involves research in task-based discovery, predictive modeling, and robust clinical translation. Quantitative radiomic analyses, an extension of computer-aided detection (CADe) and computer-aided diagnosis (CADx) methods, are yielding novel image-based tumor characteristics, i.e., signatures that may ultimately contribute to the design of patient-specific cancer diagnostics and treatments. Beyond human-engineered features, deep networks are also being investigated in the diagnosis of disease on radiography, ultrasound, MRI, molecular imaging, and others. The method of extracting characteristic radiomic features of a region can be referred to as “virtual biopsies”. In addition, there is a critical need for curated, diverse, and re-usable data to enable development of trustworthy AI. The crucial role of data in AI is exemplified through the creation and benefits of MIDRC (midrc.org; data.midrc.org) with specific focus on curated data, representative data, validation methods and sequestered data, understanding of potential biases, and sustainability.

Dana PE’ER
Memorial Sloan Kettering Cancer Center, New York, NY
Tuesday, June 24
8:30

Where Form Meets Function: Decoding Tissue Architecture

There is considerable hype around the potential for AI in cancer, yet most patient cohorts are small, cancer is complex, and AI is data hungry. One area where AI has enormous potential is tissue biology. Spatial profiling technologies can now measure tens of millions of cells and their spatial neighborhoods in tissue, representing the ideal input for powerful new AI techniques. While many approaches are specifically designed for this type of data, major challenges pervade all levels of analysis, from segmenting cells in imaging-based spatial transcriptomics data, to representing and interpreting cellular neighborhoods, predicting responses to perturbation, inferring cell-cell communication or cell-state relationships, and modeling tissue dynamics. I will discuss some of our AI approaches for representing, comparing and embedding tissue neighborhoods and how these can be used to interpret tissue biology, resolve relevant biological variation and capture the progression of dynamic spatial processes. To demonstrate the potential for these approaches to extract biological insight, I will bring examples from pancreatic and prostate cancers.

Carlo BIFULCO
Oregon Regional Laboratory, Providence, RI
Tuesday, June 24
9:25

Beyond RWE and Clinical Applications: Large Foundation Models in Cancer Biology Research

The coming of age of pathology foundation models in 2024 has significantly advanced computa-

tional pathology, demonstrating superior performance across multiple pathology tasks.
We discuss the opportunities presented by H&E-based analysis to gain both predictive and mechanistic insights into tumor biology, leveraged through generative AI approaches, including virtual staining techniques and multimodal architectures. Examples include the generation of virtual multiplex immunofluorescence from standard H&E slides and spatial biology datasets leading to the creation of a population-scale virtual tumor immune microenvironment atlas. This enables the identification of distinct immune phenotypes and the discovery of novel biomarker associations, as well as confirming established tumor response immune patterns. The presentation also introduces a multimodal patient representation integrating pathology, radiology, and clinical data. This comprehensive embedding enables predicting therapy responses in oncology and facilitating patient matching for clinical trials.

Collectively, these developments illustrate the potential of pathology foundation models in cancer research to extend beyond pathology applications towards broader clinical predictive capabilities and as a tool for hypothesis generation for a novel mechanistic understanding of tumor biology.

Francesco CIOMPI Tuesday, June 24
Radboud University Medical Center, Nijmegen, Netherlands 10:05

AI for precision medicine: development and discovery of computational biomarkers for oncology and beyond

One of the promises of precision medicine is to provide robust and reproducible tools to identify the right treatment for the right patient at the right time. In digital pathology, artificial intelligence (AI) has achieved human level performance at some diagnostic tasks and can provide the building blocks for development and discovery of novel histologic biomarkers. In this talk, I will introduce the field of computational pathology for precision medicine, show recent results on development of hypothesis-driven histologic biomarkers, ongoing research on hypothesis-free discovery of novel biomarkers, and sketch current and possible future directions in the field of biomarker discovery in oncology and beyond, in the era of multimodal foundation models.

Faisal MAHMOOD Tuesday, June 24
MGH and Brigham and Women's Hospital, Boston, MA 10:05

Multimodal, Generative, and Agentic AI for Pathology

Advances in digital pathology and artificial intelligence have presented the potential to build models for objective diagnosis, prognosis and therapeutic-response and resistance prediction. In this talk we will discuss our work on: (**1**) Data-efficient methods for weakly-supervised whole slide classification with examples in cancer diagnosis and subtyping (Nature BME, 2021), identifying origins for cancers of unknown primary (Nature, 2021) (**2**) Discovering integrative histology-genomic prognostic markers via interpretable multimodal deep learning (Cancer Cell, 2022; IEEE TMI, 2020; ICCV, 2021; CVPR, 2024; ICML, 2024). (**3**) Building unimodal and multimodal foundation models for pathology, contrasting with language and genomics (Nature Medicine, 2024a, Nature Medicine 2024b, CVPR 2024). (**4**) Developing a universal multimodal generative co-pilot and chatbot for pathology (Nature, 2024). (**5**) 3D Computational Pathology (Cell, 2024)

Andrew BECK Tuesday, June 24
PathAI, Boston, MA 11:55

AI-Powered Pathology: Scaling Precision Cancer Diagnostics in the Digital Age

Digital pathology, enhanced by artificial intelligence, enables high-throughput single-cell analyses of tumors and their microenvironments, driving the discovery of predictive biomarkers. This talk will highlight how these capabilities accelerate drug development and facilitate the integration of digital pathology and AI into diagnostic pathology laboratories. I will discuss key considerations for clinical deployment—including workflow optimization, algorithmic robustness, quality control, and monitoring—and illustrate how AI-powered digital pathology can deliver real-world impact, advancing the field of precision oncology.

Suchi SARIA Tuesday, June 24
Johns Hopkins University, Baltimore, MD 15:15

Accelerating safe and effective AI use at the point of care

Artificial intelligence offers a powerful lever for precision care, enabling health systems to anticipate complications, tailor treatments, and close care gaps at the individual patient

level. Yet deploying AI tools outside the lab reveals a gauntlet of real-world challenges. Model performance often deteriorates when confronted with local EHR idiosyncrasies, incomplete or delayed data feeds, and clinical workflows that differ from development settings. Shifts in patient demographics, coding practices, or treatment protocols—whether gradual or sudden—can undermine reliability over time. These drifts demand not only ongoing performance surveillance, but localized retraining and calibration to stay clinically relevant. Moreover, even technically robust tools are easily sidelined if they feel opaque, interruptive, or misaligned with frontline needs. Gaining clinician trust requires careful design that surfaces rationale, minimizes alert fatigue, and fits seamlessly into existing systems. Implementation is not a one-and-done effort, but a continuous process involving governance, feedback loops, and iterative tuning. Based on a decade of experience building and deploying AI tools, I'll describe state of the art approaches and open challenges around enabling AI at the point of care.

Eliezer VAN ALLEN
Harvard Medical School, Boston, MA

Tuesday, June 24
15:55

Enhancing precision cancer medicine with biologically guided artificial intelligence

Precision cancer medicine, which has the overarching goal of using molecular, pathologic, and clinical data to match the patients with the optimal therapies, has begun to transform cancer care in many domains. However, there remain significant challenges implementing this strategy for patients, particularly related to (i) synthesizing all prior knowledge about molecular states that are relevant to selective treatment response, (ii) relating these properties to patient-specific molecular, pathologic, and clinical patterns, and (iii) delivering these insights in a proper manner at the point-of-care. Increasingly, novel artificial intelligence (AI) strategies are making significant impact in addressing each of these challenges. In this presentation, we will share emerging AI technologies for enhancing these approaches, with concrete examples on how they are informing the present and future of precision cancer medicine.

Andrew WHITE
Future House, San Francisco, CA
University of Rochester, New York, NY

Tuesday, June 24
16:35

Automating scientific discovery and hypothesis generation with language model agents

FutureHouse is a non-profit founded in 2023 to automate the intellectual tasks of science. We have automated each stage of scientific discovery - from hypothesis generation, data analysis, and literature research. We have announced our first major results on exceeding human level performance in summarizing and synthesizing literature, building a benchmark for biology tasks, and scientific agents in closed loop discovery. We have recently released open source code and launched a platform to enable others to use these agents to accelerate protein design, literature research, disease-target interactions, and bioinformatics analysis. Our first end-to-end discovery was a proposed therapeutic for dry age related macular degeneration, where the hypothesis generation, experimental design, and data analysis was all done by scientific agents. We've recently released a reasoning model that can give intuition about small molecules to language models, enabling superhuman reasoning about molecular properties and effects on humans. I will summarize the progress on these different fronts and the progress of "AI Scientists" in changing our understanding of biology.

Studying and treating cancer in the Digital Era

Trento, Italy, June 23-24, 2025

ABSTRACTS ACCEPTED for POSTER PRESENTATION

VOTE FOR THE BEST POSTER

The poster prize recognizes the scientific quality and interest of the data, as well as the poster presentation. The winner will be announced during the closing remarks at the end of the Symposium, and will receive a 200€ prize from EMBO Press!

While voting please remember that
- it is not possible to vote for your own poster
- only one vote for person will be accepted

POSTER N. 1

Applying machine learning-based approaches for deconvoluting the biology behind MiROvaR, a miRNA-based classifier for risk of relapse in ovarian cancer patients

Marina Bagnoli[1], M. Polano[2], L. De Cecco[1], M.P. Scarfone[1], D. Califano[3], L. Arenare[3], A. Tomassetti[1], F. Perrone[3], S. Pignata[3], D. Mezzanzanica[1]

1) Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
2) Centro di Riferimento Oncologico di Aviano, (CRO)-IRCCS, Aviano, Italy
3) Istituto nazionale per lo studio e la cura dei tumori Fondazione G. Pascale, Naples, Italy

Ovarian Cancer (OC) is one of the most lethal gynaecologic malignancies, with high recurrence rates and limited long-term survival due to resistance to conventional therapies. Although the introduction of PARPi is greatly changing the therapeutic landscape, identification of subgroups of patients at high clinical/biological risk possibly benefitting from alternative therapeutic regimen is still challenging. We developed a 35 miRNA-based molecular predictor, MiROvaR, reproducibly able to classify at diagnosis OC patients for their risk of relapse independently from major clinical risk factors. Major features contributing to MiROvaR are miRNAs of ChrXq27.3 cluster associated with platinum and PARPi sensitivity. Given the proven robustness of MiROvaR in different OC clinical setting, we hypothesize that application of machine learning approaches on transcriptomic and clinical data could be useful to identify key molecular players of MiROVaR performance and their role in modulating treatment responses.
197 OC samples from MITO16A/MaNGO-OV-2 trial including Bevacizumab treatment/maintenance in front-line, have been array profiled for miRNA and gene expression and classified for risk of relapse according to MiROVaR algorithm. For data integration we applied both Similarity Network Fusion combined with Consensus Clustering methods and supervised machine learning techniques as MOGONET and DIABLO (Data Integration Analysis for Biomarker discovery using Latent cOmponents), based on Partial Least Squares approach, to capture more complex relationships discriminating MiROVaR risk status.
MiROVaR confirmed its performance also in MITO16A cohort where patients classified at high risk showed a worse prognosis (HR 1.74, 95%CI 1.131–2.67; P=0.011). DIABLO algorithm by integrating clinical and multi-omics data of MITO16A case material successfully identified cancer-related genes strongly correlated with miRNAs included into MiROvaR. Functions of these were

mainly related to stemness/cell differentiation (SIX1; AXIN2; PTCH1), chromatin remodeling (SMARCB1), PARPi sensitivity and Wnt/β-cat signaling (CDK12). Features extraction based on relative gene set enrichment identified also genes related to innervation.
Pending functional validation, we identified relevant biological processes related to OC aggressiveness that could be also potential markers for patient classification and/or therapeutic intervention strategies

POSTER N. 2 — Beyond Capture Bias: A Novel Framework for Robust HLA Class I Imputation in Admixed Brazilian Exomes for Oncological Applications

Rafaela Barbosa[1], Erick Castelli[2], Leandro Colli[3], Eduardo Donadi[8], Diogo Meyer[4], Michel Naslavsky[4,5,6], Nicolas Vince[7]

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Human Leukocyte Antigen (HLA) typing is crucial for understanding anti-tumor immune responses and developing personalized therapies. However, analyzing these genes in exome data is a challenge due to the similarity between HLA genes and their extensive allelic diversity, particularly in admixed populations. Therefore, in this study we aim to develop a robust methodology for imputing germline HLA class I alleles (HLA-A, HLA-B, and HLA-C) departing Brazilian individuals exome data.
First, we preprocessed the exome data using hla-mapper v.5 to correct alignments and filter low quality variants that could impair allele imputation. Subsequently, we applied two imputation strategies by HIBAG R package: 1) using SNPs located only in the target gene exons (designated local_SNPs) and 2) integrating all SNPs present in the MHC region (called global_SNPs). The reference panel was built including 5,196 samples from HGDP, 1000 Genomes, and the Brazilian SABE cohort, thus covering the genetic diversity of the studied population.
Our findings showed that the global_SNPs model produced greater posterior probabilities for HLA-A and HLA-C, while for HLA-B the local_SNPs model proved superior. Additionally, we identified specific exomic capture failure patterns of certain HLA alleles categorized as: homozygosity in low-coverage regions, heterozygosity with unbalanced capture, and allelic interference.
Thus, we provided a potential solution for computational HLA typing in exome data that can be applied in oncology, enhancing understanding of immune responses in this context, even considering the high allelic diversity characteristic of admixed populations

POSTER N. 3 — Leveraging machine learning approaches to characterize inter-patient heterogeneity and relapse in T-ALL

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T-cell acute lymphoblastic leukemia (T-ALL) is a highly heterogeneous subtype of ALL, affecting both children and adults, with relapse occurring in approximately 20% of pediatric cases and often resulting in poor outcomes. Up to 15 distinct molecular subtypes have been identified, driven by complex genetic, epigenetic, and transcriptional alterations. To gain deeper insights into the mechanisms underpinning relapse, we applied a multi-omic approach to a unique cohort of paired diagnosis-relapse leukemia cases to dissect inter-tumoral variability upon drug resistance.
A Random Forest classifier was developed to predict T-ALL subtypes from RNA-seq data, utilizing a big data set of 1308 patients. Following subtype prediction on our paired sample cohort, we: (a) investigated genetic drivers of each subtype to validate the association between transcriptional signatures and genomic alterations using gene fusion prediction (Star-Fusion, n=8) and structural variant analysis from HiChIP data (EagleC/NeoloopFinder, n=4); and (b) explored subtype-specific transcriptional mechanisms related to relapse to determine whether resistance mechanisms are shared or subtype-specific.
The classifier achieved robust performance, with a global accuracy range from 0.78 to 0.98, successfully predicting all major subgroups (13). Upon comparing diagnosis and relapse, we observed that the majority of cases relapsed without subtype switching. In the SPI1 class, Star-Fusion identified a TCF7-SPI1 gene fusion,

confirming the classifier's validity and reinforcing the connection between transcriptional signatures and driver genes. This was further supported by HiChIP data, identifying translocation-specific neo-loops. Differential Gene Expression analysis between diagnosis and relapse, considering subtypes, outperformed class-agnostic approaches in terms of significant hits, suggesting subtype specificity of relapse events. In the TLX3 subtype, relapse was associated with increased STAT-5 and TNF alpha signaling, while the TAL1 ab-like subtype exhibited elevated Apelin signaling and upregulation of EMT-related genes.
This study highlights the importance of considering inter-tumor heterogeneity when investigating relapse mechanisms in T-ALL. The classifier's success in predicting the 13 most common T-ALL subtypes and the discovery of subtype-specific relapse mechanisms underscores the value of integrating multi-omic data to comprehensively characterize the regulatory processes driving relapse.

POSTER N. 4 — Identifying RNA Binding Proteins regulating the expression of CD155 in melanoma

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The use of immune checkpoint inhibitors (ICI) relies on blocking suppressive immune checkpoints interactions, restoring an immune cytotoxic response against tumors. This therapy has demonstrated remarkable clinical success in many patients. However, it still faces challenges such as emerging resistance mechanisms or limited efficacy in certain patient populations. A deeper understanding of the regulatory pathways governing immune checkpoint expression is therefore crucial.
RNA Binding Proteins (RBPs) are key post-transcriptional regulators of gene expression, maintaining cellular homeostasis. Their dysregulation has been linked to the development of malignancies, yet their role in immune checkpoint expression remains largely unexplored. We have performed a CRISPR/Cas9-based screening assay to identify RBPs which play a role in regulating the expression of CD155 (PVR), an emerging immune checkpoint frequently overexpressed in malignancies such as non-small cell lung cancer (NSCLC), colorectal carcinoma, breast cancer, and melanoma.
We used an RBP CRISPR/Cas9 pooled library targeting 1078 RBPs, with 10 single-guide RNAs per gene, 628 sgRNAs targeting essential genes and 1058 non-targeting sgRNAs. A375 melanoma cells were transduced at a low multiplicity of infection (MOI = 0.15). Fluorescence Activated Cell Sorting (FACS) was performed to categorize cells into CD155(high), CD155(dim) and CD155(negative) populations, followed by deep sequencing and sgRNA enrichment analysis.
We have identified a subset of candidate RBPs that were enriched in the CD155(dim) population, which are currently undergoing validation to elucidate their role in CD155 expression in melanoma cells. Additionally, cytotoxicity assays are being conducted to assess how these RBPs influence melanoma cell susceptibility to natural killer (NK) cell-mediated cytotoxicity
Our findings will contribute to a better understanding of the post-transcriptional regulation of CD155 and may reveal novel therapeutic targets to improve immunotherapy outcomes.

POSTER N. 5 — Pin1 Inhibition Restores Immune Surveillance and Enhances Immunotherapy Response in Fibrotic Breast Tumors via Transposable Element Regulation

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Tumors are dynamic and heterogeneous ecosystems that evolve through (epi)genetic changes in cancer cells and their interactions with cellular components, such as stromal, immune, and endothelial cells, and the extracellular matrix (ECM) within the tumor microenvironment (TME). Highly aggressive tumors often exhibit aberrant ECM deposition, which potentiates oncogenic signaling pathways and promotes a

suppressive tumor immune microenvironment (TIME) with mechanisms not fully understood.
We utilize mechano-biology assays to decipher Pin1 role in the regulation of NE integrity upon mechanical challenge. We generated Pin1 KO cell lines through CRISPR/Cas9 technology and further utilized for transcriptome analyses. For our in vivo studies, we utilized syngeneic models of BC to decipher changes in the TME, especially in the immune cell population. We employed ex vivo co-cultures of immune cells to test antigenicity. We also utilized tissue sections from BC patients to verify our hypothesis.
We show that Pin1, the only phosphorylation-specific cis/trans prolyl isomerase, drives therapy resistance in fibrotic breast cancer (BC) by suppressing the anti-tumor immune response through modulation of the cGAS/STING/IFN-I pathway. Mechanistically, we demonstrate that aberrant ECM deposition stabilizes Pin1, leading to its accumulation in the nucleus of desmoplastic BCs, where it plays a pivotal role in maintaining nuclear envelope (NE) and heterochromatin (HC) integrity under mechanical stress. Notably, Pin1 inhibition induces NE alterations and reactivates transposable elements (TEs) that trigger innate immunity via cGAS/STING/IFN-I signaling and adaptive immunity by generating immunogenic neoantigens. These findings were validated in preclinical models of both primary BC and lung metastases, where genetic ablation of Pin1 induces a robust anti-tumor immune response characterized by increased infiltration of NK cells and cytotoxic CD8+ T lymphocytes. This shift transforms the TME from an immune-excluded "cold" state to an immune-infiltrated "hot" state, significantly impairing tumor growth. Consequently, these changes sensitize immunotherapy-resistant BC to immune checkpoint blockade (ICB) therapy.
Our findings underscore the critical role of Pin1 in mediating tumor immune evasion driven by a stiff ECM. Targeting Pin1 represents a promising strategy to restore immune surveillance and enhance the efficacy of immunotherapy in solid tumors.

POSTER N. 6

LOSS of multimerin-2 alters vascular efficiency and immunity in cancer

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Tumor vasculature is dysfunctional, promoting hypoxia, progression, therapy resistance, and altered immune cell infiltration. Multimerin-2, an endothelial-secreted extracellular matrix glycoprotein is deposited in close association with pericytes and plays a crucial role in vascular homeostasis. Studies in Multimerin-2-/- mice show reduced pericyte coverage in the vessels. Since Multimerin-2 expression is frequently lost in tumors, this study aims to investigate the role of Multimerin-2 in pericyte biology and its impact on the tumor microenvironment.
In vitro: Human brain vascular pericytes (HBVP), human umbilical vein endothelial cells (HUVEC) and the monocytic-like cell line THP-1 were used. HBVP cells were treated with recombinant Multimerin-2 to assess viability, proliferation and pathway activation (Western blot). Haptotaxis and transmigration assays evaluated pericyte recruitment and endothelial interactions.
In vivo: Wild type and Multimerin-2-/- C57BL/6 mice received subcutaneous injections of PTEN-/- p53-/- ID8 or MC-38 cancer cells. Tumor sections underwent immunofluorescences analyses; patient samples were imaged using MANTRA™. Statistical analyses determined significance and correlations.
Multimerin-2 mediates pericyte haptotaxis and adhesion while promoting their proliferation, via an IGF1R-dependent mechanism. Consistent with the in vitro observations, tumors from Multimerin-2-/- mice exhibited reduced pericyte coverage leading to vascular instability, increased hypoxia, impaired drug delivery, and poor therapeutic response. Notably, these mice also displayed increased macrophage infiltration, paralleled by enhanced of THP-1 cell migration across through the Multimerin-2-depleted endothelium. Finally, in clinical ovarian cancer samples, Multimerin-2 expression positively correlated with pericyte coverage, underscoring its translational relevance.
Our findings demonstrate that Multimerin-2 deficiency disrupts pericyte recruitment and proliferation resulting in severe vascular destabilization, thus exacerbating intratumoral hypoxia and compromising drug delivery. Notably, Multimerin-2 loss also modulates the immune microenvironment, implying that its deficiency in tumors may significantly influence the patient outcomes. These results position Multimerin-2 as a key regulator of vascular and immune function, with potential clinical implications.

POSTER N. 7 — Deciphering ELAVL1-Mediated Post-Transcriptional Regulation in Multiple Cancers

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ELAVL1 (HuR), an RNA-binding protein, stabilizes inflammatory and pro-tumorigenic mRNAs by binding AU-rich elements (AREs) in their 3'UTRs, amplifying chronic inflammation and oncogenic signaling. Elevated HuR expression correlates with poor survival in pancancer cohorts. This study integrates multi-omics data across four cancers (ACC, KIRC, LUAD, LGG) to delineate a regulatory network where ELAVL1 interacts with transcription factors (TFs), forming a bidirectional axis that reinforces oncogenic programs.
We integrated protein-protein interactions, differential gene expression, pathway enrichment, and TF networks to identify ELAVL1-associated genes, regulatory relationships, and impacted pathways. For differential expression analysis in TCGA vs GTEx, raw counts were normalized, and batch effects were corrected using additional datasets if no adjacent healthy tissue was present in TCGA. Differential expression was calculated with edgeR (log2FC thresholds: ACC >2, KIRC/LUAD/LGG >1; p-adj <0.05). Pathway enrichment analysis (FDR<0.05) prioritized dysregulated pathways. Transcription factors targeting ELAVL1 were identified from TFLink and intersected with co-expressed genes (R≥0.75). Kaplan-Meier survival analysis utilized TCGA Pancancer data with automatic optimal cut-off determination via maximally selected rank statistics. All analyses were implemented in R.
Immune-related pathways, including cytokine signaling and antigen binding, were upregulated, driven by ELAVL1's stabilization of immune evasion factors like PD-L1. Collagen-containing extracellular matrix pathways were downregulated, reflecting ELAVL1-mediated stromal remodeling via PDGFAA. Forty-two TFs highly correlating (R≥0.75) in all four cancers with ELAVL1 included CTCF, ADNP, TARDBP, and HCFC1. TARDBP and HCFC1 are in turn regulated by ELAVL1, thus revealing a feedback mechanism linking transcriptional control and RNA stability.
ELAVL1 bridges transcriptional regulation and post-transcriptional stabilization, driving tumor adaptability through immune suppression and microenvironment remodeling. Specifically targeting ELAVL1's 3'UTR interactions could disrupt its stabilization of inflammatory cytokines and oncogenes, while combinatorial strategies may enhance therapeutic efficacy. Future work will prioritize preclinical validation of this network and clinical translation to improve survival in HuR-high cancers, leveraging ELAVL1's role as a pan-cancer hub of tumor plasticity and therapy resistance.
FAK inhibition disrupts vital oncogenic pathways in GI-NETs by impairing cell viability, proliferation, invasion and transcriptional regulation. The distinct responses between 2D and 3D cultures emphasize the relevance of tumor architecture in therapeutic sensitivity. These findings support FAK as a promising target for GI-NET treatment and provide a foundation for future research into its mechanistic role in neuroendocrine tumor biology.

POSTER N. 8 — Improved Adoptive T Cell Therapies for Colorectal Liver Metastases by Stabilization of IFNAR1 on Tumor-Specific T-Cells

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Diagnosis for colorectal cancer (CRC) are surging, and distant metastasis, particularly to the liver, play a crucial role in determining very poor prognosis for patients. Adoptive T-cell therapies (ACT) show promise for cancer treatment but often struggle in solid tumors due to the immunosuppressive tumor microenvironment (TME) and one factor to this failure is the downregulation of the type I Interferon receptor (IFNAR1) on T cells. To overcome these limitations, we stabilize IFNAR1 on CD8+ T cells, by a single amino acid substitution of Ser526 to Ala (SA) and pharmacologic approaches, to gain tumor-specific CD8+ T (OT-I-SA) cells and Chimeric Antigen Receptor T cells (CAR T-SA) cells that efficiently counteract the growth of CRC liver metastasis.
We dissected the TME of human CRC synchronous liver metastasis (n=5) with AKOYA spatial multiplex-immunofluorescence staining for IFNAR1 and immune cells markers, and we profiled the MC38- and MTO-140-derived tumors by

RNASeq. We employed both differentiated OT-I and OT-I-SA CD8+ T cells, isolated from mouse spleen, for in vitro and in vivo assay, and CAR-T cells genetically engineered to express IFNAR1-SA and the receptor for hCEA (hCEA-CAR-T-SA), a marker widelHere, we observed that IFNAR1 is downregulated in a cohort of human CRC synchronous liver metastasis (n=250) and this correlates with a high production of type I IFNs. Type I IFNs, chronically released by tumor, contribute to reducing the anti-tumor immune response exhibited by a decreased frequency of intra-tumor effector CD8+ T cells (Teff), and sustained the internalization of IFNAR1 on CD8+ T cell that cause apoptotic cell death and exhaustion. Thus, exploiting advantage for genetics and pharmacological compounds to block receptor phosphorylation or internalization by endocytosis, we highlighted that the stabilization of IFNAR1 on OT-I CD8+ T cells and hCEA-CAR-T-SA cells confer to these cells more effective in leveraging tumor-released type I IFNs to control the growth of liver metastasis, preventing T cell death and showing great tissue persistence without toxicity, with the establishment of immunological memory.y expressed by CRC cells.
Overall, these results indicate that the stabilization of IFNAR1 on ACT cellular products not only enhances their viability and persistence within CRC metastatic lesions, but also efficiently thwart CRC liver metastasis, holding promise for future development in clinics

POSTER N. 9 — Alignment to T2T-CHM13 reference genome reduces reference mapping bias and improves read mapping at clinically relevant sites

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The reference genome assembly choice impacts the alignment of sequencing reads, affecting the quality of downstream genomic analyses. The Telomere-to-Telomere (T2T) CHM13 reference genome exhibits large-scale differences with previous human genome assemblies, corrects falsely annotated regions, and adds over 200 Mb of novel genomic sequence. We investigated whether the T2T assembly enhances allelic variation analysis and read mapping at clinically relevant variants compared to hg38.
DNA sequencing human and cell line data generated with multiple designs (whole-genome and targeted sequencing) at varying coverages (30x-1000x) were aligned to T2T-CHM13v2.0 and hg38 assemblies. Pileups at high minor allele frequency dbSNP loci were used to call heterozygous genotypes (variant allele fraction (VAF) between 0.2 and 0.8) on a sample basis to quantify the inflation of reference allele counts, the so-called reference mapping bias (RMB). UCSC repository ClinVar, CpG islands, and ENCODE TFBS tracks were lifted over to hg38 and T2T reference genomes and analyzed through pairwise sequence alignment. Methylation calling was performed on realigned RRBS cell lines' whole-genome sequencing data.
Heterozygous SNP VAF distribution from T2T-aligned data showed a significantly reduced RMB compared to hg38 data. SNPs with discordant VAF estimates among assemblies reported higher VAF values in T2T with respect to hg38 (one tailed paired t-test $p < 2.2e-16$), resulting in a shift towards a more balanced allelic representation. We detected mismatches in the genomic sequence in the proximity (±150bp) of SNPs with discordant VAFs across the two assemblies, suggesting that T2T resolves genomic inaccuracies in bases proximal to SNPs. Genomic differences within ChIP-seq peaks and CpG islands showed negligible impact on TFBS enrichment analyses and methylation calling. The ClinVar annotated sites analysis revealed that regions with a sequence variation show an increase in VAF (one tailed Wilcoxon $p = 3.6e-05$) and mapping quality metrics for T2T with respect to hg38. Notably, coverage increments were observed at pathogenic variants within actionable genes, including BRCA1 exon 17 and RB1 exon 20.
The alignment to T2T assembly reduces RMB in VAF computation and globally ameliorates read mapping regardless of sequencing design. Additionally, the increase of VAF and read coverage at disease-associated genomic sites might facilitate the detection of variants for precision medicine testing.

POSTER N. 10 — Transcriptional Reprogramming by EZH2 Loss and HOXA9 overexpression mediates oncogenic program in human early T-cell precursor (ETP) acute lymphoblastic leukemia/lymphoma (ALL)

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Early T-cell precursor (ETP) acute lymphoblastic leukemia/lymphoma (ALL) is an aggressive

hematological malignancy characterized by the uncontrolled expansion of T-cell progenitors. Loss-of-function mutations in genes encoding epigenetic regulators- including key components of the Polycomb Repressive Complex 2 (PRC2), such as the EZH2 histone methyltransferase- are frequently observed in ETP-ALL patients. Nonetheless, the genetic and signaling programs driving the malignant transformation of normal T-cell subsets in early T-ALL remain poorly understood.

We report that CRISPR/Cas9-mediated genetic inactivation of EZH2 in human cord blood-derived hematopoietic stem/progenitor cells (HSPCs), followed by lentiviral transduction of known T-ALL oncogenes, efficiently generates de novo ETP-ALLs. We also used RNA-seq and Chip-seq to evaluate the gene expression profiling, transcription factor binding sites, and histone modifications modulated by EZH2 in human HOXA9-transduced ETP-ALL-like cell line, LOUCY and PEER. Finally, we analysed scRNA-seq (25 primary human ETP-ALLs), RNA-seq and clinical data from a cohort of 1,135 diagnostic T-ALLs (COG TARGET study).

Using this human ETP-ALL model, EZH2 inactivation synergizes with LYL1 and HOXA9 overexpression, promoting in vitro expansion of human progenitor T cells, blocking T-lineage commitment, and driving the development of aggressive leukemias in NSG mice. Integrated RNA-seq/ ChIP-seq of LOUCY/PEER cells revealed that EZH2 knockout combined with HOXA9 overexpression induces upregulation of stem/immature T-cell signature. Finally, multi-omic integration analysis further demonstrated that PRC2-mutated/HOXA+ leukemias exhibit stem-like phenotypes and high levels of minimal residual disease (MRD). These PRC2-mutated/HOXA+ T-ALLs also displayed GSVA enrichment for this specific gene signature enriched in transcriptional activation and chromatin remodeling genes (e.g., RUNX2, IRX3, SATB1, ARID5B, CHD1, INO80D)

This suggests that PRC2-mutated/HOXA+ T-ALLs may be governed by a distinct chromatin regulatory landscape, potentially orchestrated by chromatin remodeling complexes and transcriptional factors in the absence of PRC2 function.Collectively, these findings uncover a critical epigenetic circuit involving EZH2 loss and HOXA9-driven transcriptional reprogramming that sustains stem-like, therapy-resistant T-ALL subsets, and point to novel vulnerabilities that could be exploited to eliminate high-risk disease at its origin.

POSTER N. 11 — Highly effective in situ vaccination using engineered bacterial Outer Membrane Vesicles

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In situ vaccination (ISV) is an intratumoral immunotherapy aiming at reverting the immunosuppressive tumour microenvironment into an immune-reactive one. Four ISV formulations have been already approved and over 160 clinical trials are currently in progress.

Bacterial Outer Membrane Vesicles (OMVs) are attractive for ISV for their potent adjuvanticity and intrinsic capacity to kill cancer cells (pyroptosis). We recently showed that the intratumoral injection of OMVs completely cured 40 to 60% of mice challenged with different tumor cell lines (Caproni et al., 2023).

With the objective to reach 100% therapeutic efficacy, we tested whether the engineering of OMVs with cytokines/chemokines (collectively, cytokines), involved in trafficking and activation of immune cells, could further potentiate the OMV anti-tumorigenic properties.

Cytokine genes were chemically synthesized and cloned into the OMV-overproducing E. coliD60 strain as FhuD2 fusions. The functional activity of OMV-associated cytokines was evaluated using specific in vitro assays. Mice (BALB/c, C57BL/6) were challenged s.c. with syngeneic tumor cells (CT26, WEHI-164, MC38). Tumor growth was followed after three OMV injections (2-day intervals). Cell analysis in tumors was carried out by flow cytometry and Immuno Fluorescence.

1. The cytokine-coding genes (Flt3L, CCL3, CXCL13, CCL20, TNFa, IL2, IL15) were cloned in E. coliD60 strain. All cytokines efficiently accumulated on the surface of OMVs purified from the culture supernatants.
2. The OMV-associated cytokines preserved their biological function: CCL3-OMVs promoted PBMC migration, IL2-OMVs activated CTLL-2 cells, Flt3L-OMVs promoted the proliferation of OCI-AML5 cells, and TNFa-OMVs killed cancer cells.
3. The intratumoral injection of OMVs engineered with selected cytokines almost completely cured 100% of mice. The therapeutic efficacy correlated with the tumor infiltration of NKs, DCs and T cells.

The expression of cytokines on the surface of OMVs strongly potentiate their anti-tumor activ-

ity in ISV. Different combinations of engineered OMVs are currently being tested with the ultimate goal to select a final formulation which protects 100% of all animals, regardless of the mouse tumor model used, the tumorigenic program and the genetic makeup of the cancer cells. With this ambitious objective achieved, cytokine-OMVs can become a revolutionizing therapeutic approach for treating many solid tumors in human patients.

POSTER N. 12

PaperParser: A Scrapy-based AI Tool Leveraging Large Language Models for Efficient Scientific Literature Retrieval and State-of-the-Art Summarization

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With an exponentially growing scientific literature, it's increasingly time-consuming to remain constantly updated and write comprehensive papers. Here we introduce PaperParser, a new bioinformatic tool that combines Scrapy's web scraping ability with SciLitLLM-14B's summarization features. It turns user queries into articles, systematically extracted from the PubMed web server. Retrieval-augmented generation (RAG) techniques, artificial intelligence (AI) agent-based REPL ('read-eval-print loop'), and 'Large Language Models' (LLMs) outline a draft from SciLitLLM-14B-generated summaries. This supplies the State of the Art in a time-saving manner and allows researchers to focus on the most debatable details in favor of productivity.
Following a user query, our Scrapy-based software gathers scientific texts from the (Euro) PMC database, thanks to rpy2-bridged Python modules and R packages. SciLitLLM-14B summarizes parsed contents with accuracy and contextual details. Results are stored in a FAISS vector store, which grants quick vector similarity calculations. A short draft is generated through GPT-4o and a vector store-derived RAG retriever, which allows fast semantic search. Then, every paragraph is extended by a Python REPL leveraging a GPT-4o-mini-fueled AI agent. The AI-generated draft is then reworked with OpenAI's o3-mini-2025-01-31, led by a 'Prompt Engineering' application. This 'humanizing' step represents the creative part of PaperParser. It aims to mimic the human ability to synthesize, still preserving a scientific tone. To inspire nuances in the writing style, publications written by the target author can be imputed as 'LangChain Runnable'.
PaperParser is a novel time-saving instrument for finding academic sources. It retrieves and turns textual data into a draft complete with references. It starts with a PubMed-like query to summarize the State of the Art. Researchers can focus on the most interesting aspects and be more productive. For now, our tool limits the web search to publicly available papers and does not evaluate publications' relevance.
Our tool leverages vector storage solutions and purpose-built and general-purpose LLMs for text refinement. The balance of accuracy (granted by SciLitLLM-14B) and text humanization efforts (guided by 'Prompt Engineering') provides a diverse way to synthesize biomedical literature. Future improvements could widen data gathering to subscription-based journals and weigh the relevance of scientific sources.

POSTER N. 13

AMetastatic peritoneal fibroblasts mobilize and respond to TGF-ß1 from the extracellular matrix of colorectal cancer

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The pathophysiology of colorectal cancer (CRC) peritoneal metastases (PM) involves the activation of TGF-ß. A finely tuned interaction among cancer, stromal cells, and the extracellular matrix (ECM) is a critical mechanism in driving metastasis. Fibroblasts actively remodel the ECM and promote metastasis. In cancer, secreted TGF-ß is stored in the ECM in a latent form and activated when released from its ECM ligands. However, the interplay between ECM and fibroblasts in vitro is still under investigation.
AIMS:

a) to investigate the ability of CAF and MAF to mobilize TGFß from a patient-derived ECM;

b) to investigate the molecular response of both CAF and MAF to ECM-derived TGFß mobilization;

CRC- and healthy colon-derived ECM (CRC-ECM and HC-ECM, respectively) samples were prepared from decellularized biopsies. CAF and MAF were isolated from primary cancer and peritoneal metastases. Secreted proteins were analyzed by mass spectrometry (MS). Gene expression was evaluated by RT-qPCR. The cellu-

lar distribution and abundance of TGFbeta and TIMP1 were investigated using scRNA sequencing and multiplex IHC in matched CRC and PM patients.
Exposing CAF and MAF to CRC-ECM resulted in an increase of TGFβ and TIMP1 only in the culture media of MAF. After exposing MAF to healthy colon- or CRC-ECM we observed a specific response of MAF to CRC-ECM resulting in the increase of TIMP-1. qRT-PCR analysis of CAF and MAF exposed to CRC-ECM demonstrated that the increased abundance of TGFβ in the culture media of MAF is not related to a cell production and secretion mechanism but suggested that ECM compartment could be the main source of the TGFβ identified in the culture media of MAF. In vitro exposure to exogenous TGFβ of CAF and MAF demonstrated that MAF increased the gene expression of TIMP1, in a dose-dependent manner, which was abolished by TGFBR-I/II blockage. The CAF showed no such ability. The incubation of TGFβ-k.d MAF with CRC-ECM demonstrated suppression of TGFβ but an increase of TIMP1. Single-cell RNA sequencing and multiplex IHC demonstrated that MAF was the stromal cells with an increased TIMP1 expression with a peri-tumoral peculiar localization in both CRC and PM.
These results show that MAF, but not CAF, mobilizes TGFβ from the ECM, which induces the release of the known pro-tumorigenic modulator TIMP-1. Therefore, metastatic-specific peritoneal fibroblasts might be a promising therapeutic target for inhibiting this effect in patients with PM.

POSTER N. 14

Mucosal associated invariant T cells infiltrating resectable non-small cell lung cancer exhibit a tissue resident memory phenotype, enhanced metabolic activation and strong pro-inflammatory properties.

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Circulating mucosal-associated invariant T (MAIT) cells are an innate-like pro-inflammatory and cytotoxic population of effector memory T cells and can represent up to 10% of peripheral CD8+ T cells. Their role in cancer remains controversial. In non-small cell lung cancer (NSCLC) patients, MAIT cells are found within tumor lesions; however, limited data are available on their cell-cell interactions and functional mechanisms within the tumor microenvironment (TME). Objectives. To characterize MAIT cells in NSCLC from both phenotypic and functional perspectives.
We enrolled 37 patients with NSCLC (I, II, IIIA, 8th TNM ed). Multiparameter flow cytometry was employed to assess the phenotype and functional profile of tumor-infiltrating and circulating MAIT cells, focusing on cytokine production (IFN-γ, TNF, IL-2, Granzyme B, and IL-17). Proteome profiling of MAIT cells was conducted using ad hoc isobaric labeling-based multiplexed quantitative proteomics. Additionally, spatial transcriptomics (6k Nanostring) was used to localize MAIT cells within the tumor microenvironment (TME) and to calculate all the cell-cell interactions.
MAIT cells, defined as CD161++, TCR7.2+ within CD8+ T cells, are much more represented in blood if compared with those infiltrating the tumor lesion (median +- SEM: 4.90 +- 0.90 vs 2.77 +- 0.87, p=0.0207). However, MAIT cells infiltrating the TME exhibit a tissue-resident memory (TRM) phenotype (60.35 ± 4.79) and a pronounced polyfunctional profile biased toward Th1 characteristics. A total of 66 proteins are differentially expressed in TME-infiltrating MAIT cells (logFC >2), primarily associated with metabolic activation, indicating their potential involvement in metabolic and immune reprogramming within the TME. Spatial transcriptomic data revealed that MAIT cells are found within tertiary lymphoid structures and they interact with macrophages and B cells.
Although less abundant in the TME compared to circulation, the profile of MAIT cells provides new insights into their functional landscape in NSCLC, highlighting their potential as key players in tumor immunity.

POSTER N. 15

Plasma microRNA Signature as Companion Diagnostic for Abiraterone Acetate Treatment in Metastatic Castration-Resistant Prostate Cancer: A Pilot Study

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Abiraterone acetate (AA) serves as a medication for managing persistent testosterone production in patients with metastatic castration-resistant prostate cancer (mCRPC). However, its efficacy varies among individuals; thus, the identification of biomarkers to predict and follow treatment response is required.

In this pilot study, we explored the potential of circulating microRNAs (c-miRNAs) to stratify patients based on their responsiveness to AA.
We conducted an analysis of plasma samples obtained from a cohort of 33 mCRPC patients before and after three, six, and nine months of AA treatment. We performed Exiqon RT-qPCR panels for candidates discovery and TaqMan RT-qPCR for validation analysis. In silico analysis has been used to identify putative target genes and transcription factors of the miRNAs candidates.
Our investigation indicated that a signature based on miR-103a-3p and miR-378a-5p effectively discriminates between non-responder and responder patients, while also following the drug's efficacy over time. Interestingly, our unsupervised clustering analysis demonstrated that the miRNA signature could have effectively assisted clinicians in making more informed decisions on whether to halt or continue AA administration. Additionally, through in silico analysis, we identified target genes and transcription factors of the two miRNAs, including PTEN and HOXB13, which are known to play roles in AA resistance in mCRPC.
In summary, while a bigger cohort is required to validate these findings, our study highlights two c-miRNAs as potential companion diagnostics of AA in mCRPC patients, offering novel insights for informed decision-making in the treatment of mCRPC.

POSTER N. 16 — Methods for measuring the translational process in RNA therapies

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Epitranscriptome represents an important part of cellular machinery. This field of study has broad potential applications, both in cancer research and in basic research. Our project is divided into 2 work packages: the first aims at developing and validating high-throughput screening (HTS) and high-content screening (HCS) assays for measuring various aspects of protein synthesis regulation in cell systems, such as general translation, translation elongation rate, ribosome stalling, IRES-mediated translation, and Kozak sequence activity. The second work package aims at validating the assays to measure protein synthesis modulation in cell models of rRNA 2'-O-methylation loss-of-function.

Here, we are cloning various double fluorescence reporter plasmids, to investigate ribosome stalling, IRES-mediated translation and Kozak sequence activity in cellular models. The plasmids are then validated at automated cell imaging for HCS. General translation and elongation are studied using SunRiSE assay and OPP. Loss of FBL is obtained via transient siRNA silencing and stable KO in cellular models. RiboSeq, RiboMethSeq and mRNA seq will be used to prepare libraries, followed by bioinformatic analysis.
The first work package is almost complete: the tools were validated in HCS and showed significant differences among positive and negative controls. We are now in the process of screening various compounds that may affect ribosome stalling or IRES-dependent translation, using these tools. Moreover, we are about to start a panel assay, where we will silence FBL, responsible for ribosomal 2'O-methylation, to perform mRNA seq, RiboSeq and RIboMethSeq and investigate the effect of the silencing at transcriptomic level. This will allow a proof-of-concept validation of the assays developed. The final goal is, through these sequencing, to identify novel stalling sequences, IRES sequences or Kozak sequences that might be regulated by FBL. Moreover, we will evaluate the general translation parameters upon transient and stable silencing of FBL.
With our tools, we are developing a set of HTS and HCS assays to measure translation regulation in cell systems. These tools will allow to study the involvement of all aspects of protein synthesis in any molecular mechanism of interest; therefore, it can be applied to a broad variety of studies, from cancer to basic research.

POSTER N. 17 — Single-nuclei multiomic approach reveals permanent reprogramming of exocrine cells after pancreatitis

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Acute pancreatitis (AP) is a common inflammation of the pancreas that typically resolves without clinical complications. However, epidemiological evidence shows that individuals who suffered AP are at elevated risk of developing pancreatic cancer, even several decades after the episode. We speculated that pancreatitis establishes a pro-oncogenic memory of

inflammation via deregulation of normal tissue homeostasis. Indeed, AP-primed epithelial cells show enhanced propensity to metaplasia in vitro and accelerated repair in vivo. We tested the hypothesis that AP events induce either permanent changes in the epigenome or skewing of sub-populations in the pancreatic ecosystem.
To this end, we performed single-nuclei multiomic (RNA+ATAC) sequencing in mouse pancreata after induction of- and recovery from experimental pancreatitis.
While histological examination did not show any alteration post AP, multiomic molecular analysis revealed extensive transcriptomic and epigenomic reprogramming in acinar cells, which are cell-of-origin for pancreatic cancer. This is not linked to expansion of progenitor-like clones but is enforced on a distinct subset of acinar cells, termed idling.
In detail, idling acini sense inflammatory cues and elevate unfolded protein response (UPR). We also observed that UPR inducers promote acinar cell plasticity, linking UPR stress to pancreatic cancer initiation. Mechanistically, AP induces an irreversible increase of chromatin accessibility in acinar cells. This leads to hypertranscription and protein dyshomeostasis and to poising of the epigenome. Together, these alterations set a phenotypic state in post-mitotic epithelial cells that makes them more susceptible to oncogenic transformation.

POSTER N. 18 — Blockade of PD-L1 endocytosis by uPAR antagonist peptides to improve cancer immunotherapy

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Immune checkpoint inhibitors (ICI), such antibodies against PD-L1 and PD-1, have shown effectiveness against a large number of cancer types. The therapeutic efficacy of PD-1/PD-L1 inhibitors is high in patients with high PD-L1 expression. Recent data showed that targeting extracellular Plasminogen Activator Inhibitor (PAI-1) by its inhibitor tiplaxtinin (TPX) synergizes with anti-PD-L1 checkpoint blockade in a model of murine melanoma, improving the efficacy of melanoma treatment. PAI-1 induced the internalization of surface-expressed PD-L1, resulting in the reduction of surface PD-L1. Binding of PAI-1 to uPA/uPAR complex results in the recruitment of low-density lipoprotein receptor protein 1 (LRP1), which also mediates PD-L1 internalization. We propose to inhibit PDL-1 endocytosis by uPAR inhibitors to maintain high-cell-surface levels of PD-L1. Moreover, we propose to set up 3D co-culture system between non-small cell lung cancer cells and T cells to assess efficacy of uPAR inhibitors on immunotherapy responses.
2D and 3D cultures from A549 (non-small cell lung cancer cells) were treated with TPX and uPAR antagonist (IPR803) to evaluate the effect of TPX and IPR803 treatment on PD-L1 modulation. Surface PD-L1 expression were evaluated by FACS, confocal microscopy and western blotting. 3D co-cultures were seeded between A549 previously treated with anti-human PD-L1 and IPR803 and T cells CD8+ CD4+ to asses cytotoxic effect of T cells on tumor cells. Cytotoxicity activity of T cells were evaluated with Live/Dead staining.
Our result evidenced that in 2D and 3D cultures of A549 TPX and uPAR antagonist peptides are able to block the PD-L1 internalization and, consequently, to increase PD-L1 membrane levels. In parallel, our data highlighted in 3D co-cultures an improvement of cytotoxic effect of T cells on A549 treated with uPAR antagonists and anti-PD-L1 antibodies.
Our results evidenced that uPAR inhibition by uPAR antagonist peptides result in a significant increase in surface PD-L1 levels, opening the way for new combined therapeutic strategies with uPAR inhibitors and anti-PD-1/PD-L1. These findings have significant implications for immunotherapeutic approaches to cancer therapy.

POSTER N. 19 — Telomere maintenance and structural variants: the impact of ALT on complex genomic rearrangements

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Cancer cells must overcome telomere erosion to achieve unlimited replicative potential. Critically short telomeres can induce chromosomal fusions, structures associated with chromatin bridges and consequent complex genomic rearrangements (CGRs). Still, the broader impact of telomere maintenance on the generation of structural variation remains to be elucidated.
Alternative lengthening of telomeres (ALT) employs error-prone DNA repair mechanisms

(break-induced replication, BIR) to elongate short telomeres via recombination and synthesis at telomeric sites. Interestingly, BIR appears to also occur on chromosomes that experienced bridge breakage, leading to their segregation into micronuclei, sites where CGRs have been proven to accumulate.
This project investigates the effect of telomere maintenance and associated factors on the formation and repertoire of structural variants. ALT, intrinsically elevating recombination rates, could promote chromosomal instability and the production of CGRs.
To maximise the capturing of ongoing rearrangements, we isolated micronucleated cells with the MAGIC (Machine learning-Assisted Genomic and Imaging Convergence) platform, established in our laboratory. MAGIC allows to identify in live imaging, with the aid of machine-learning algorithms, cells carrying phenotypes of interest, to then selectively photo-label them; once the population of interest differs from the main population in fluorescence emission spectrum for specific wavelengths, it is possible to retrieve it with cell sorting, and subject it to downstream applications.
Analyses carried out on the PCAWG dataset highlighted strong correlations between ALT(-related) phenotypes and CGRs in cancer samples. To model different subsets of the PCAWG dataset, we first described the SV repertoire in non-transformed cells, and we then assessed the contribution of combinations of mutations and telomere maintenance mechanisms in perturbing their landscape. While the ALT-characteristic truncating mutations of ATRX increased the number of SVs, the simultaneous absence of p53 was fundamental to boost the complexity of the observed rearrangements. Finally, ALT induction resulted in the accumulation of distinct classes of complex rearrangements, attributable to persistent damage at telomeric DNA.
Characterising CGRs in cells with diverse genetic backgrounds and telomere maintenance mechanisms, we disentangled the role such factors have in the emergence of de novo structural variants.

POSTER N. 20

A Mathematical Model to Predict EGFR Kinetics in Cancer-Related Conditions

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The correlation between dysfunctional Epidermal Growth Factor Receptor (EGFR) signaling and cancer has made this receptor one of the most studied tyrosine kinase receptors. To improve our understanding, we developed a mathematical model to perform in-silico experiments, focusing on receptor activation and trafficking.
The model extends the Early Activation Model (EAM), introduced in [PMID: 26264748]. At first, we improved the description of the activation dynamics by modeling all Tyr receptors and adding the receptor ubiquitination. Then, we added a trafficking component to describe endocytosis, recycling, degradation, and synthesis. The model is a system of ~12k Ordinary Differential Equations describing the evolution of the quantity of EGF, the amount of Cbl and Grb2 (two molecular players involved in receptor ubiquitination), and the number of receptors in the various configurations.
The model was calibrated to reproduce the dose-response curve of EGFR phosphorylation and ubiquitination [PMID: 26264748], the recycling and degradation rates of EGFR [PMID: 18694561], and the endocytotic rate [PMID: 6279628] in different conditions (different ligan concentrations and different mutant to knockout internalization pathways). We then used the model to predict the variation of the endocytotic rate in non-physiological conditions. For instance, we simulated situations of receptor knock-down and over-expression (a typical condition in cancer) and scenarios of increased Cbl levels. In particular, the model predicted a decrease in the endocytotic rate in EGFR-OE conditions. This effect can be mitigated by increasing the Cbl level (and, consequently, the ubiquitination signal). Experiments confirmed these predictions. These results suggest that saturation of Clathrin Mediated Endocytosis and ubiquitination kinetics due to the limited amount of Cbl are the major causes of receptor dysfunction.
Our model proved to be able to mimic experimental data and predict experimental outcomes in unseen scenarios. This last aspect shows that this model can be an essential tool in designing experiments by suggesting which experiments may be of scientific interest. Additionally, we can use the model to gain insight into the role of receptor configuration in its fate and signaling outcomes. To this aim, we are performing continuous refinements and improvements of the model to support the computation of long-term predictions to achieve biological-relevant predictions

POSTER N. 21

Multi-omic computational evaluation of FOXA1 and MYC epitranscriptional regulation of prostate cancer progression

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FOXA1 and MYC oncogenes cooperate to drive prostate cancer (PCa) progression by remodeling chromatin and rewiring alternative splicing (AS) landscape. FOXA1 promotes splicing factors' expression to modulate AS, while MYC governs RNA processing machinery. Both regulations impact patient prognosis. While MYC's role in post-transcriptional (PT) regulation is well established, FOXA1's contribution remains less understood. Their interplay and overlapping influence on RNA processing is still under investigation, but their convergence in transcriptional control unveils new therapeutic opportunities to target PCa at the RNA level.
PCa cells (PC3) were depleted of either FOXA1 or MYC using siRNA. ONT mRNA and Illumina totalRNA libraries of 14 replicates (siFOXA1:4, siMYC:3, siCTRL:7) were sequenced. PC3 transcriptome was reconstructed. Differential analyses of isoform expression, usage, m6A methylation, and polyA tail length were conducted across conditions. To validate FOXA1-mediated m6A methylation, MeRIP-seq was performed on FOXA1-depleted and control samples. To evaluate RNA stability, FOXA1-depleted and control cells were treated with actinomycin D. Total RNA was collected at five time points (0-8h) and Illumina sequenced. Differential expression analyses were performed. Finally, 10x-Visium spatial transcriptomic data from five sections of a PCa were analyzed for clustering and transcriptomic signature identification.
We found that FOXA1 and MYC orchestrate a dynamic regulatory network influencing isoform expression in AS, RNA methylation, and localization. These TFs specifically remodel m6A modifications on isoforms linked to AS and RNA localization. Transcriptional blockade experiments confirmed that FOXA1 enhances mRNA stability of isoforms implicated in RNA processing. Both TFs govern polyA tail selection favouring short tails to increase expression of isoforms. Spatial analyses corroborated FOXA1MYC-mediated RNA processing regulation in distinct tumor clones. Network analyses pinpointed candidate splicing and RNA processing factors under FOXA1/MYC control, including SRSF7.
Our data highlight a central role of FOXA1/MYC interplay in controlling co- and PT programmes of PCa. These TFs fine-tune the production of isoforms involved in AS and RNA localization enhancing their expression, reshaping their m6A methylation, shortening their polyA tails. Our comprehensive catalogue of full-length isoforms driven by these TFs offers new means to tackle PCa progression.

Colorectal Cancer Neoantigen mRNA Cocktail-Based Vaccines with a Novel TLR4-Stimulating Adjuvant

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Neoantigen-based personalized mRNA vaccines represent a promising strategy for cancer immunotherapy by inducing tumor-specific CD8+ T cell responses. Lipid nanoparticle (LNP) technology enhances mRNA vaccine delivery and immunogenicity. My previous research identified 12 novel tumor-specific neoantigens capable of eliciting potent CD8+ T cell responses, leading to colorectal cancer (CRC) growth inhibition. Additionally, polysaccharides from Astragalus membranaceus (APS), known for their immunomodulatory properties to prevent CRC progression via Toll-like receptor 4 (TLR4) signaling.
This study aimed to develop a LNP platform encapsulating mRNA neoantigens and APS (a TLR4-stimulating adjuvant) for enhancing immune activation in CRC. APS was incorporated to enhance dendritic cell activation and immune response. In vitro immune activation was assessed by flow cytometry and cytokine release assays. Vaccine efficacy was evaluated in CRC mouse models, measuring tumor inhibition and immune response via tumor volume monitoring and immune cell analysis.
Preliminary results demonstrate that APS significantly enhances dendritic cell maturation and antigen presentation via TLR4 activation. This activation led to a marked upregulation of co-stimulatory molecules, including CD80 ($p < 0.01$) and CD86 ($p < 0.01$), and the secretion of pro-inflammatory cytokines, such as IL-12 ($p < 0.05$) and TNF-α ($p < 0.05$). In vitro assays using the mRNA-APS-LNP formulation induced robust antigen-specific CD8+ T cell responses, evidenced by a 3-fold increase in T cell prolif-

eration ($p < 0.01$), a 2.5-fold increase in cytotoxicity ($p < 0.01$), and a significant elevation in IFN-γ production ($p < 0.01$). These immune responses were associated with enhanced tumor cell cytotoxicity in co-culture assays, suggesting that the mRNA-APS-LNP platform activates potent anti-tumor immunity. A neoantigen-specific T cells persist in both peripheral blood and tumor tissue at significantly higher levels in the vaccine group ($p < 0.05$) compared to control groups. Tumor growth inhibition was observed in vaccinated mice, with a 45% reduction in tumor volume ($p < 0.05$) compared to controls.
This study presents a novel mRNA-LNP-based vaccine platform for CRC incorporating APS as an immune-enhancing adjuvant. Future studies will focus on optimizing the vaccine formulation and further validating its long-term efficacy and safety in clinical trials.

POSTER N. 22 — Human herpes viruses genotyping and immunological gene expression profiling in prostate cancer with prominent inflammation

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We aim to investigate the role of Herpesviridae family (HHV) in the onset and progression of prostate cancer (PCa) and to investigate the the potential local PCa immunocompromised status.
A total of 116 "tru-cut" biopsies (58 PCa and 58 benign prostatic hyperplasia [BPH]) and 49 formalin-fixed paraffin-embedded (FFPE) PCa were analyzed through Real-Time qPCR and histological examination.
Active infection with CMV, EBV, HHV6, HHV7 was detected in 11,5% of the "tru-cut" biopsies (25% in BPH and 6,9% in the PCa group). In the FFPE samples, active infection was detected in 69.4% of the patient, with type-specific rates of EBV (47%), HHV6 (38%), HHV7 (41%), CMV (2,9%), HSV2 (2,9%) and VZV (5,8%). In HHV-infected PCa cases, the histopathological landscape included in-tratumor lymphocyte infiltration with fibrosis and necrosis, periductal chronic inflammatory reaction and granulomatous lesions with foci of abscesses and necrosis, as well as inflammatory infiltration, chronic lymphadenitis, prostatic intraepithelial atrophy (PIA) and high-grade prostatic intraepithelial neoplasia (HGPIN). The majority of HHV-infected PCa patients were predominantly determined as grade G3/G4/G5 tumors, exhibiting perineural, perivascular and lymphovascular invasion, seminal vesicle invasion, senile vesicle amyloidosis and lymph node metastasis. By analysing IL1?, IL10, IL18, TNF-?, TLR4, GATA3, and CD68 expression in 50% of PCa HHV-infected FFPE, we detected hyperexpressed levels of IL1?, IL18 and TNF-? in the tumour microenvironment.
Statistical analysis demonstrated a significant association between HHV infection and PCa ($?^2$? 20.3, df = 1, $p < 0.0001$; Fisher's exact test, $p < 0.0001$) with an odds ratio of 6.50 (95% CI: 2.80–15.12). These findings suggest that long-term HHV infection contributes to an immunocompromised PCa profile and may serve as a predictor of aggressive disease progression. IL-1?, IL-18, and TNF-? are proven to be associated with tumor invasion, progression, and metastatic potential in the current study. Notably, TNF-? has been strongly correlated with lymphatic metastasis. In the digital era nowadays the free access to all useful data and aspects of cancer via scientific sharing could improve the patient's outcome chance. This research was supported by Medical University Sofia, Bulgaria; Grants No: D-187/14.06.2022; D-327/19.12.2022; D-299/18.12.2023; D-149/03.08.2023 and by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project ? BG-RRP-2.004-0004-C01.

POSTER N. 23 — Predicting cancer vulnerabilities using transcriptomics data and deep learning

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Recent advances in genomic technologies have allowed the large-scale determination of genetic dependencies in various cancer cell lines by systematic gene knock-out and cell proliferation assays. While extremely valuable, these approaches are challenging and non-trivial to

scale, limiting their applicability to clinical settings with current technologies.
To bridge this gap, we designed an AI-based model to predict cancer vulnerabilities using easily obtainable RNA-seq profiles of cancerous cells. Our model predicts cancer dependencies at the single gene level, using genome-wide transcriptomic features, and integrates physical protein-protein interaction networks to incorporate the cellular and biological context in which the dependencies are predicted
I will present the model development and design choices, its performance, current limitations, and steps taken to address them. I will then present results on its deployment to analyze retrospective patient data of several leukemia subtypes and discuss how such tools can be used to investigate, gain possible mechanistic insights, and determine sub-type specific cancer vulnerabilities in a data-lean regime.
Our results highlight how the combination of AI/ML modelling, high-throughput transcriptomics and assay-based resources can create a powerful analysis tool, which allows to interrogate cancer vulnerabilities at the single sample (e.g., individual patient) level in a fast and efficient manner.

POSTER N. 24 — Exploring the impact of common germline variants on protein function: a computational investigation of EXO5

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Understanding the impact of common genetic variants on protein structure, function, and their role in disease progression is crucial in cancer research. This study presents a comprehensive analysis of the EXO5 gene, which encodes a DNA exonuclease involved in DNA repair and was previously associated with cancer susceptibility. We employ an integrated approach combining large-scale genomic and clinical data analysis, deep learning variant effect prediction, and molecular dynamics simulations to investigate the effects of common EXO5 haplotypes on protein structure, dynamics, and cancer outcomes.
We characterize the haplotype structure of the EXO5 gene across diverse human populations using germline data from the 1000 Genome Project, identifying five common haplotypes. The fitness of the corresponding EXO5 variants is scored using the ESM-1v Protein Language Model, along with a dataset of common haplotypes of DNA repair genes.
We then conducted extensive molecular dynamics simulations to analyze structural and dynamical differences among the identified EXO5 haplotypes. The clinical significance was evaluated using survival and genomic instability data from The Cancer Genome Atlas.
MD simulations confirmed the Protein Language Model predictions, showing a reduced stability for L151P EXO5, and increased stability for other two common haplotypes. Substantial conformational changes in a region critical for DNA binding and enzyme function were revealed, especially in L151P EXO5. This variant also altered interactions with the nuclear localization signal region, potentially explaining the reduced nuclear localization observed in previous experimental studies. Analysis of TCGA data demonstrated that cancer patients carrying the L151P variant had significantly shorter progression-free survival in prostate and pancreatic cancers and exhibited increased genomic instability.
The study provides mechanistic insights into how common EXO5 variants impact EXO5 structure and function, with clinical implications for cancer progression. The destabilizing effect of L151P correlates with experimental findings, supporting its functional relevance in increasing genomic instability and worsening cancer prognosis. The integrated computational framework combining protein language models with molecular simulations offers a powerful approach to investigate the functional consequences of genetic variants, potentially applicable to other genes involved in DNA damage response and repair.

POSTER N. 25 — Vitamins C and E as Protective Agents Against Carboplatin-Induced Oxidative Damage in Sperm Cells

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Chemotherapy drugs can cause male infertility and gonadotoxicity by affecting stem cells during spermatogenesis, leading to DNA damage, chromatin alterations, and direct testicular toxicity.[1] [2] However, the direct cytotoxic effects of these drugs on mature spermatozoa (SPZ) and the underlying molecular mecha-

nisms remain poorly understood. This study aims to evaluate the direct impact of carboplatin (CBDCA) on mature SPZ and investigate the protective role of vitamins C and E in mitigating the toxicity induced by this anticancer drug Spermatozoa were directly exposed to CBDCA and co-incubated with vitamins C and E, followed by the assessment of sperm motility parameters using computer-assisted sperm analysis (CASA). The molecular mechanism of toxicity was examined by measuring malondialdehyde (MDA), a marker of lipid peroxidation.
The results showed that CBDCA affects SPZ motility, as indicated by a decrease in VSL values (5.35 ± 0.80 µm/s) compared to the negative control (10.80 ± 0.79 µm/s). This effect was particularly significant after 60 minutes of co-incubation.Furthermore, CBDCA induced lipid peroxidation in the sperm membrane, leading to elevated MDA levels (1.63 ± 0.10) compared to the negative control (0.83 ± 0.10).However, vitamins C and E demonstrated a potential protective effect against CBDCA, increasing VSL values (8.35 ± 1.25 µm/s).
In fact, pretreatment with vitamins C and E significantly reduced the MDA levels induced by CBDCA in SPZ (1.25 ± 0.61).

POSTER N. 26

Digital Driven Diagnostics, prognostics, and therapeutics for sustainable Healthcare: an overview of the D34H multicentric-multi-institutional initiative, toward simulating patient disease trajectories with Artificial Intelligence

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The Digital Driven Diagnostics, prognostics, and therapeutics for sustainable Healthcare (D34H) project, is an Italian PNC-funded ministerial initiative aiming at fostering precision medicine by developing digital and biological twins of patients affected by either of five selected diseases: Type 1 Diabetes, Multiple Sclerosis, Liver and Bile Duct Cancer, Central Nervous System Cancer, Colorectal Cancer with Liver Metastases. The initiative includes a total of 28 partners, for an overall 4-year funding amount of 150 million euros. Methodologies contributing to the prediction of disease trajectories are a central contribution of our Institute, and are described hereafter.
Our Institute's contribution to D34H is twofold. One aspect involves collecting multicenter data to populate a centralized, Azure-based platform built on a FHIR-compliant data lake. The platform architecture is designed to support Federated Machine Learning, enabling collaboration among different partners while ensuring GDPR-compliant exchange of AI models. Multi-institutional working groups are being established to develop AI-driven models to address specific research questions, such as patient stratification and the identification of prognostic factors.
A second aspect involves the creation of a new joint lab for Digital Pathology between our Institute and the local healthcare trust, with the goals of i) creating a new pool of Whole Slide Image (WSI) data related to the five diseases investigated in the current initiative, and ii) foster the creation and validation of unimodal and multimodal AI models, both as diagnostic support systems and as prognostic tools.
Up to now, data from a total of 25 724 patients has been collected. Analytical pipelines are being designed for the modeling of multicentric data. External validation of models generated for all the investigated diseases is planned either through a centralized or a federated approach.
As part of the newly established joint laboratory for Digital Pathology, a state-of-the-art IT infrastructure for data processing and a high-resolution whole slide scanner were acquired.
The involvement of our Institute in this project will have an impact in three different fields: clinical, technological and organizational, representing a concrete innovation for the territory and empowering the achievements of higher standards in the treatment of target pathologies.

POSTER N. 27

A Predictive Model for Radiation Necrosis in Brain Metastases: Enhancing Clinical Decision-Making

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Brain metastases (BM) are the most common intracranial tumors in adults, affecting approximately 20% of cancer patients. Stereotactic radiosurgery (SRS) has emerged as an important treatment option for BM. However, SRS can lead to radiation necrosis (RN), a transient side effect that can be difficult to distinguish from tumor progression and affects 5% to 25% of treated patients. While RN may resolve spontaneously without the need for further intervention, distinguishing it from tumor progression is critical, as the latter requires additional therapeutic measures. Therefore, accurate differentiation between RN and progression is essential for effective management of BM.
We performed a multivariate analysis using patient clinical data, including primary tumor details and SRS type, and a variable capturing the growth dynamics of BMs through scaling laws. Our model was developed using data from 100 patients from five institutions, including 60 with progressive tumors and 40 with RN after radiotherapy. In addition, 22 patients (10 with progression and 11 with RN) from a sixth institution were included for model validation.
Our model successfully classified patients with progressive disease or RN, achieving statistical significance ($p < 0.001$) with a receiver operating characteristic area under the curve (ROC-AUC) of 0.823 for the discovery cohort and 0.782 for the validation cohort. To facilitate clinical decision making, we developed a web application https://radiationnecrosiscalculator.com that allows clinicians to quickly estimate the probability of tumor growth being classified as RN or progression.
The ability to accurately differentiate between radiation necrosis and tumor progression in brain metastases is critical for optimizing patient management and treatment strategies. Our model shows promising predictive capabilities that can improve clinical decision making and potentially improve patient outcomes. The availability of a user-friendly web application further empowers clinicians to efficiently assess individual cases.

POSTER N. 28 — Development of a peroxisome activity-related gene expression signature with prognostic potential in ER+ breast cancer

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Breast cancer is the most prevalent type of tumor in women, with the estrogen receptor-positive (ER+) subtype being the most frequently diagnosed. Although initially responsive to endocrine therapy, about 40% of patients eventually develop resistance. Recent studies have demonstrated that in ER+ breast cancer cell line models resistant to endocrine therapy, cells exhibit lipid metabolism reprogramming, along with an increased number of peroxisomes and enhanced peroxisomal functions.
The aim of this study is to evaluate the expression of a set of peroxisome-associated genes to identify a prognostic signature in ER+ breast cancer.
Two independent ER+ breast cancer datasets were used: TCGA was used as training set of the model and METABRIC was used for validation. From the initial peroxisomal associated gene list, only genes that showed no correlation with the expression of MKI67, a proliferative marker, were selected. A univariate Cox regression analysis was performed for each gene to identify those significantly associated with overall survival (OS) and disease-free status (DFS) in the training set. A LASSO regression analysis was applied to train two distinct prognostic signatures associating candidate genes with OS and DFS.
The models were applied to ER+ samples from METABRIC to calculate two distinct risk scores and classify each patient in the validation set into “Low Risk” or “High Risk” groups. The prognostic ability of the signatures was evaluated with Kaplan-Meier analysis. Longer survival and disease-free status were observed in the “Low Risk” patient group identified using our signatures, validating their prognostic role. Using a multivariate analysis, we further demonstrated that the classification of the validation set, based on the signatures developed, remained significantly associated with the outcomes independently of the molecular PAM50 subtype.
In conclusion, the peroxisomal activity-related gene signatures here developed are significantly associated with the clinical outcomes of patients, suggesting an important role of peroxisomal activity in ER+ breast cancer.

POSTER N. 29 — Tumor ecosystems are associated with traditional pathological features in prostate cancer

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Tumor growth and progression are shaped by the complex interactions between cancer cells and the surrounding tumor microenvironment (TME). These interactions can be captured by RNA-sequencing and by the pathological observation of tumor tissue slides (e.g., stromal response, immune infiltrate, etc.). Computational frameworks have enabled us to deconvolute the TME from bulk RNA-seq, and computationally identify the image-based determinants of distinct TME ecosystems. Here, we utilized an international database of prostate cancer (PCa) hematoxylin&eosin (H&E) images and paired bulk RNA-seq data to examine how tumor TME-level information can enhance traditional pathology findings in understanding the intricate interactions within the tumor ecosystem.

On a cohort of 221 PCa patient H&E slides with matching DNA, bulk-RNA, and methylome data, we applied a published framework called EcoTyper (Luca et al., 2021) to deconvolute bulk RNA-seq data into distinct cell types and characterize their transcriptional status ("cell state"). Moreover, we calculated an overall TME-level feature called "Ecotype" (E), which provides a summary overview of the foremost functional features of each specific PCa sample. We studied if traditional PCa pathology features (e.g., grade groups, GGs) were associated with particular cell states or ecotypes and how those transcriptome-based classifications may help patient stratification.

We identified a predominant ecotype for 181/221 (82%) PCa tumor cases. An association between GG1 and E6 was noted. A Bayesian logistic regression model suggested that GG1 patients with E6 had 79% lower recurrence odds than GG1 patients with other ecotypes (0/11 vs. 11/50 patients; odds ratio = 0.21, 95%CI: 0.025-1.21). When considering only GG2 and GG3 (n=70), we found that E10 showed a significant negative trend (p=0.02), decreasing with increasing percentage of Gleason pattern 4. Similarly, specific cell states were associated with different grade groups (e.g., GG1 was enriched in myofibroblasts and chymase-positive mast cells). Lastly, using our image-analysis pipeline PathML, we developed a graph neural network model to identify the histo-morphological determinants of the distinct ecotypes on H&E images.

Characterizing the TME using transcriptome-based, ecosystem-level tools may complement traditional pathology evaluation in PCa. The definition of H&E determinants of the distinct RNA-based ecotypes may pave the way to test them on H&E PCa slides.

POSTER N. 30

Identification of determinants of disease progression and therapeutic targets in retroperitoneal liposarcomas

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Retroperitoneal soft tissue sarcomas are a heterogeneous group of rare cancers with distinct biological characteristics. Well-differentiated liposarcoma (WDLPS) is a low-grade disease that may recur locally in about 30% of patients. Dedifferentiated liposarcoma (DDLPS) is an intermediate to high-grade malignancy that may arise from a preexisting WDLPS and is characterized by a significant risk of both local and distant relapse. Although they share amplification in chromosome 12, including CDK4 and MDM2, histology-specific treatments are lacking. Our study integrates WDLPS and DDLPS transcriptomic analyses, aiming to elucidate their functional heterogeneity and identify novel therapeutic targets.

RNA-Seq data of 68 DDLPS and 39 WDLPS were normalized using the trimmed mean of M-value algorithm, heteroscedasticity was removed and differential expression analysis was performed comparing normal with tumor components. Gene sets enrichment analysis evaluated enrichment in biological mechanisms (FDR threshold 0.05 was considered for significance) and deconvolution was employed to investigate immune infiltrate composition. We exploited in-house generated patient-derived tumor models, 3 2D cell lines and 2 patient-derived xenografts (PDX), from untreated DDLPS to functionally validate therapeutic targets identified at transcriptomic analysis.

Marked transcriptional changes characterized key regulators that could contribute to liposarcoma progression, particularly in the dedifferentiation process highlighting deregulation in cell cycle, lipid metabolism, and immune modulation. Drug-target interaction analysis using ChEMBL databases indicated that, in addition to drugs that target the WDLPS/DDLPS-specific CDK4 and MDM2 drivers, drug targeting cell-cycle and DNA repair, such as AURKA and CHEK1, are overexpressed in DDLPS compared to WDLPS.

These putative targets were functionally validated in our patient-derived models, showing different tumor response in PDXs. For instance, MDM2 inhibition with milademetan resulted in different effects in the 2 tested PDX. Analysis of tumor transcriptome profiles at the end of treatment is ongoing to investigate modifiers of tumor response
In summary, our study characterizes determinants of the molecular evolution of WDLPS and DDLPS. By uncovering distinct molecular alterations acquired in DDLPS compared to WDLPS and targetable vulnerabilities, these findings provide new information for liposarcoma-specific treatment options.

POSTER N. 31 — Improving Prognosis Prediction in Colon and Gastric Cancers through a Pathomic Biomarker Analyzing the Angiogenic and Immunological Crosstalk

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Encouraging advances in Computational Pathology enable quantitative analysis of the complex and dynamic tumor microenvironment (TME) in digitized Whole Slide Images (WSIs). The crosstalk between angiogenesis and immune regulative pathways orchestrates solid cancer growth and is involved in the length of therapy response
Our work proposes a pathomic workflow providing a high-throughput analysis of TME interactions between vascular networks and immune cell clusters in H&E-stained WSIs. We used 408 WSIs in the TCGA Colon Adenocarcinoma (COAD) cohort to train our pipeline and tested it both on the TCGA Stomach Adenocarcinoma (STAD), consisting of 354 WSIs, and in a real-life cohort of 52 patients with metastatic gastric cancer, collected in the research hospital IRCCS "Saverio De Bellis", we named DBGC.
The first step leverages two deep learning networks for robust tissue segmentation; the first recognizes normal and tumoral areas including seven different histotypes, while the second delineates vessels, microvessels, and immune cell clusters in the WSI. Then, an instance-based panel of morphometric and graph-based features was extracted from instance crops and coordinates. We examined how TME modifies the phenotype of these structures, by sorting the respective histomorphological features according to the tumor or the normal tissue areas in which instances were located. We then aggregated features at the WSI-level, and then at the patient-level to develop the prognostic model. The LASSO regression served for feature selection, then a Cox-proportional Hazard Ratio model was fitted to derive the Vascular-Immune Pathomic (VIPath) biomarker. Furthermore, we investigated whether the proposed biomarker could add prognostic information beyond c-TNM classification and ECOG Performance Status.
VIpath showed potential for clinical adoption, by significantly predicting OS in TCGA-COAD (log rank $p<0.001$), TCGA STAD ($p=0.017$), and in the real-life cohort ($p=0.014$). Moreover, in this latter cohort, VIPath showed significant predictive value ($p=0.005$) in the prediction of Progression-free Survival of a second-line therapy consisting of an anti-angiogenetic and cytotoxic agent combined therapy.
Our results highlighted an increased C-index in all prediction tasks, demonstrating that VIPath improves the performance of the existing scoring systems, and that can support decisions in oncology for both prognosis prediction and efficient therapy adjustments.

POSTER N. 32 — Beyond Checkpoint Inhibitors: The Potential of Chemotherapy and Phytotherapy for Enhanced Tumour Immunogenicity in Breast Cancer

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Despite promising advancements in cancer immunotherapy, its efficacy remains variable, particularly in immunogenically "cold" tumours. Current evidence suggests that certain chemotherapies can render tumours more immunogenic, potentially enhancing their susceptibility to immunotherapeutic interventions. Additionally, in this context, the immunomodulatory properties of phytopharmaceutical products, such as Dodonaea viscosa (D. viscosa), remain largely unexplored.
Breast cancer is among the top three cancers worldwide, and patient prognosis is impacted by

disease aggressiveness, treatment resistance, and metastatic dissemination. A personalized medicine approach to immunotherapy thus has the potential to improve patient prognosis and clinical outcomes while optimizing treatment efficacy and mitigating adverse effects.
A physiologically relevant tumour-bearing mouse model was established using C57BL/6 female mice for triple negative breast cancer. Ethical clearance was obtained from the Stellenbosch University Research Ethics committee. Mice were treated with chemotherapeutic agents, D. viscosa extract, and combinations of both. Tumours were harvested post-treatment for further molecular and histological analysis. Parallel in vitro experiments were conducted using MCF-7 and MDA-MB-231 breast cancer cell lines. Immunogenicity was assessed using western blot, RT-qPCR, histology and immunohistochemistry. Additionally, a preliminary immunogenicity model was developed based on a comprehensive literature review.
Baseline differences in immunogenic phenotypes were observed between hormone receptor-positive MCF-7 and triple-negative MDA-MB-231 cells, suggesting subtype-specific immune characteristics. In both in vitro and in vivo models, various immunogenicity parameters exhibited changes across intervention groups. Variations in DNA mismatch repair proteins, immune checkpoint antigens, inflammatory cytokines, and immune infiltration were observed following individual and combination treatments.
Our findings suggest that both conventional chemotherapy and D. viscosa influence the tumour immune microenvironment in breast cancer models. The observed differences in immunogenic phenotypes between breast cancer subtypes underscore the importance of personalized immunomodulatory approaches. These data further highlight the need for developing predictive models of tumour immunogenicity, which can assist in forecasting immunotherapy responses and guiding treatment strategies

POSTER N. 33 — Comprehensive machine learning analysis of high-dimensional radiomics datasets by PYRAMID

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POSTER N. 34 — Characterization and predictive role of human-specific genes in Pediatric Acute Lymphoblastic Leukemia

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Human-specific genes represent unique human features not observed in our closest relatives, chimpanzees. These genes have been linked to human-specific aspects, including brain development and immune functions. A compelling hypothesis is that they might be responsible for increased tumor susceptibility, specifically at the level of pediatric cancers, such as cerebral and blood tumors. Acute Lymphoid Leukemia (ALL) is one of the most common leukemias in children, with 80% of pediatric cases. ALL is a malignant transformation that causes abnormal proliferation and differentiation of lymphoid progenitor cells. It correlates with genetic aberrations and complex events on multiple chromosomes. The goal of this study is to explore the involvement of human-specific genes in ALL.
Eight databases of bone marrow and blood cells expression profiles of 794 patients, divided between ALL samples and controls, were retrieved from GEO. Batch-corrected data were normalized and differentially expressed human-specific genes were extracted. Several models classifying tumor subtypes based on differentially expressed human-specific genes, employing ensemble, gradient boosting, and deep learning methods, were created. The performance was validated via cross-validation with class-balancing algorithms, followed by hyperparameter tuning. Finally, variable importance from the models was extracted and used to rank the human-specific features.
Human-specific genes linked to cancer dysregulation were identified. These genes characterize ALL subtypes, facilitate age-based stratification of patients and are involved in immune response dysregulation. By leveraging the results from subtype and age classifiers, which were generated from differentially expressed human-specific genes, consensus classifiers were established. The “human-specific classifiers” demonstrated better performance metrics than non-human-specific ones, achieving over 80% balanced accuracy along with favorable F1 and Kappa

scores. Extracted human-specific genes associated with ALL were validated through single-cell analysis.
A consensus classifier able to accurately define the correct subtype of unknown samples was created, highlighting a set of human-specific predictors associated with ALL, which can be used to characterize patients based on subtype and linked with cancer alterations. Among these, EBF1, highlighted for all the subtypes, is connected with survival, proliferation, and signaling in ALL.

POSTER N. 35 — Targeting the m6A RNA modification players as a new therapeutic approach in neuroblastoma

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Neuroblastoma (NB) is the most frequent extracranial solid tumor in children, accounting for 15% of all childhood cancer deaths. Although the 5-year survival rate of patients with high-risk disease has increased in recent decades, NB remains a challenge in pediatric oncology, and identifying novel therapeutic targets and agents is an urgent clinical need. N6-methyladenosine (m6A), the most abundant post-transcriptional mRNA modification in mammals, is tightly regulated by 'writers' and 'erasers', which deposit and remove the modification, respectively, and by 'readers', which can detect changes in mRNA modification status and influence downstream cellular processes. m6A and related proteins have been found frequently altered in different tumors and may represent a good therapeutic target also in NB.
By modulating the expression of the writer complex component METTL14 or the demethylase ALKBH5, we evaluated the impact of m6A mRNA modification on NB tumor aggressiveness in vitro and in vivo. We also investigated the effect of inhibiting m6A recognition by knocking out YTHDF reader proteins. Next, to identify a molecule capable of interfering with YTHDF m6A mRNA recognition, we screened in silico by molecular docking a library of 1.5 million compounds against the YTHDF1 protein and subsequently evaluated the 113 best-scoring compounds by homogeneous time-resolved fluorescence. We selected compound A as a low micromolar pan-YTHDF inhibitor and evaluated its effects on NB cells also by mass spectrometry analysis. Finally, we synthesized and tested more than 30 analogs in a structure-activity relationship (SAR) study.
METTL14 overexpression promotes cell proliferation and invasion in vitro and tumor progression in vivo, leading to faster tumor growth and larger tumor masses. Conversely, ALKBH5 overexpression or METTL14 knockout leads to opposite results, with a significant decrease in cell proliferation, an increase in apoptosis, and reduced invasion ability in vitro, while dramatically slowing tumor growth in vivo. Consistent with these observations, knockout of YTHDF paralogs or YTHDF inhibition with compound A also results in decreased NB cell proliferation and reduced clonogenic potential. We are now finalizing our SAR study, also guided by docking analyses.
Our results show that high levels of m6A correlate with higher NB aggressiveness and that targeting m6A deposition or m6A recognition on mRNAs could be an effective therapeutic strategy for NB treatment

POSTER N. 36 — Targeting Focal Adhesion Kinase Impairs Tumor Progression and Gene Regulation in Gastrointestinal Neuroendocrine Tumors

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Gastrointestinal neuroendocrine tumors (GI-NETs) are rare malignancies with a rising incidence and limited therapeutic options due to persistent resistance to standard treatments. Focal Adhesion Kinase (FAK), a critical regulator of tumor progression, has not been extensively studied in the context of GI-NETs. This study investigates the effects of FAK inhibition on tumor cell viability, apoptosis, invasion and transcriptional regulation to evaluate its potential as a therapeutic target.
Human GI-NET cell lines, GOT1 and COLO320DM, were used for in vitro studies. Cell viability was assessed through crystal violet staining and CellTiter-Glo assays. Western blotting and immunofluorescence were employed to evaluate protein expression and localization. Colony formation and invasive behavior were assessed using crystal violet and Transwell Matrigel assays, respectively. Caspase-3/7 activity assays measured apoptosis. FAK inhibition was induced via pharmacological agents (Protac-FAK [BI-0319]

and Y15), and siRNA-mediated knockdown was used to validate FAK-specific effects.
FAK inhibitors Protac-FAK and Y15 significantly decreased cell viability in both GOT1 and COLO320DM lines. Apoptosis analysis revealed Y15-induced caspase-3/7 activation in 2D COLO320DM and both 2D and 3D GOT1 cultures, while Protac-FAK induced apoptotic activity in GOT1 cultures under both conditions. Colony formation was impaired by both inhibitors, although colony size remained unchanged, indicating that FAK inhibition primarily hinders proliferation. Invasion was reduced in both cell lines following treatment. Protac-FAK led to reduced total FAK protein and both inhibitors suppressed ERK1/2 phosphorylation, disrupting downstream signaling. A decrease in H3K9 acetylation suggested an epigenetic role for FAK in chromatin regulation. Gene expression analyses showed that Protac-FAK modulated RB1—key gene linked to cell cycle control. These findings were validated through siRNA-mediated FAK knockdown, confirming FAK's regulatory involvement.

POSTER N. 37 — An AI-based mechano-classifier for predicting Triple Negative Breast Cancer patients' outcome

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Triple-negative breast cancer (TNBC) remains the most aggressive breast cancer subtype, characterized by poor prognosis and limited treatment options. To uncover new biological mechanisms underlying malignant transformation, we focus on the mechanobiology of TNBC. Specifically, we posit that aberrant mechanical signals in TNBC affect tissue architecture and cell fate, driving a more aggressive behaviour and ultimately impacting on patients' prognosis.
We collected surgical samples from 119 patients with early-stage TNBC, treated with upfront surgery and adjuvant chemotherapy. Histopathological slides were obtained and stained for detecting the activity of the master regulator of mechanosensing and transduction, YAP, and hematoxylin. Secondary harmonic generation and brightfield microscopy images were acquired on pathologist-annotated regions of interest including invasive breast cancer and peritumoral stroma. Clinical data regarding eventual relapse were collected for all patients. Using multiple imaging pipelines, we extracted 195 cell-intrinsic and cell-extrinsic features to train and test an XGBoost model for relapse prediction. The model was validated using 5-fold cross-validation (CV), optimizing hyperparameters through a Bayesian approach, and SMOTE to address class imbalance. Model's performances were evaluated by accuracy, AUC-ROC, precision, recall and F1-score.
In our cohort, 26 of 119 patients relapsed within 5 years. Despite the limitations of an imbalanced dataset and a relatively small cohort, our machine learning-based model shows promising results in predicting relapse in early-stage TNBC patients. Further validation of our model on independent external cohorts is warranted to confirm our preliminary results. Cell-intrinsic features capture cancer cell morphology (nuclear, cytoplasmic) and YAP nuclear/cytoplasmic ratio as a proxy for transcriptional activity and mechanical state. Cell-extrinsic features describe collagen fiber arrangements in peritumoral regions. The dataset was split into 80% training and 20% test sets. We performed 5-fold CV on the training set, selecting the best model for testing. Our model achieved a median AUC of 85%, across 10 multiple random train/test partitions. Overall, our model provides robust performances on classifying the majority class (not relapsed patients), whereas the predictive power for classifying the minority class (relapsed patients) was instead less remarkable.
Despite the limitations of an imbalanced dataset and a relatively small cohort, our machine learning-based model shows promising results in predicting relapse in early-stage TNBC patients. Further validation of our model on independent external cohorts is warranted to confirm our preliminary results.

POSTER N. 38 — Single cell RNA sequencing identifies intratumoral bacteria enhancing metastatic dissemination in prostate cancers

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Prostate cancer (PC) is one of the main contributors to cancer-related mortality in men across the world. While androgen-deprivation therapies are effective for localized and advanced tumors, resistance frequently emerges in met-

astatic cases. Emerging evidence links both gut and intratumoral microbiota to cancer progression and treatment resistance in a variety of cancers, including PC. My group previously demonstrated that gut microbiota contributes to androgen synthesis in castration-resistant PC. However, the role of the intratumoral bacteria in PC is poorly studied. For this reason, we took advantage of published data from single cell RNA sequencing (scRNA-seq) and we have developed a bioinformatic pipeline for identifying intratumoral bacteria.
We integrated 9 available datasets of human PC. The GATK PathSeq was applied to quantify the bacteria reads. We implemented a decontamination pipeline using blacklist genus and droplet-based features of scRNA-seq. Bacterial reads present at similar proportions in cell-containing and empty droplets were filtered out as potential contaminants. Cells harboring bacterial reads are considered infected.
The integrated scRNA-seq data with the GATK pipeline allow the identification of intracellular bacteria. After the removal of contaminations and confounding factors, we investigated the occurrence of infected cells considering tumor site, treatments, disease stage and cell types. Epithelial tumor cells were the most infected population, specifically in metastatic site. Different pathways related to bacteria response and inhibition of immune response appear increased in infected cells. We focused on the bacterium enriched in primary tumors and metastasis, while mainly absent in healthy and benign adjacent tissues. We performed in vitro human PC cell lines infection, demonstrating that the bacterium can enter and modify the mobility and invasion of PC cells. Moreover, in vivo administration demonstrated the capability of the bacterium to enhance metastatic dissemination
This study highlights the presence of intratumoral bacteria in PC and their potential role in disease progression and treatment resistance. By using scRNA-seq data and in vitro/in vivo experiments, we identified specific bacterial infections predominantly in metastatic epithelial tumor cells. These findings underscore the potential of targeting the tumor microbiome as a novel therapeutic strategy for treating PC treatment resistance and metastasis.

POSTER N. 39

How computational investigations can help the development of novel anticancer drugs for targeting the epitranscriptome. The case of m6A reader YTHDF1-3 proteins

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The epitranscriptome is a growing and promising area of cancer research. In particular, N6-methyladenosine (m6A) is a key RNA modification that regulates RNA fate through a complex interplay of RNA binding proteins (RBPs). Altered levels of RBPs (e.g. YTHDF1-3 proteins) are frequently found in tumors and associated with cancer initiation, progression, or drug resistance. Therefore, small molecules that can target the transcriptome are currently being investigated for their potential use in cancer treatment. However, RBPs are often difficult to target for their flexible pockets on the protein surface used to bind large RNA molecules. Computational methods can be effectively used to study these systems and design new drugs.
We designed and synthesized YTHDF1-3 inhibitors based on ab-initio and covalent molecular docking calculations and molecular dynamics (MD) simulations. The structural behavior of the YTHDF1 binding pocket was studied by MD and X-ray crystallography. We tested the compounds in biochemical assays (HTRF, REMSA, CETSA).
We reported ebselen, a covalent drug, as the first and still the most potent inhibitor of YTHDF1-3 proteins. We then designed and synthesized a library of 50 ebselen analogs. Due to the covalent mechanism of action, we used ab-initio calculations to investigate how the reactivity of the warhead can be modulated to reduce potential off-target effects. For the non-covalent interactions inside the pocket, we used docking calculations and were able to verify our predicted pose by comparison with the X-ray complex of inhibitor-YTHDF1. Moreover, the X-ray structures showed that part of the pocket undergoes a profound conformational change. To better study this, we performed MD simulations, from which we discovered that only some conformations of the binding site are accessible to the inhibitors and we are currently investigating how to consequently improve these compounds. This structural aspect is so crucial for the design of these inhibitors (but even for other similar pockets) that e.g. AI models trained non considering similar active site variations fail to predict ebselen as an inhibitor of YTHDF1-3 proteins.
Our results show how computational methods can guide the design of novel anticancer drugs even for highly flexible pockets. We have computationally explored the structural features of the binding pocket of the YTHDF1 protein and developed a library of covalent YTHDF1-3 inhibitors as potential new anticancer drugs.

Past Symposia

35. Trento, 24 - 25 June 2024
CANCER AS A SYSTEMIC DISEASE: INTERACTIONS BETWEEN TUMOR AND HOST

34. Trento, 19 - 20 June 2023
NEW TECHNOLOGIES FOR STUDYING AND TREATING CANCER

33. Trento, 13 - 14 June 2022
WHAT ARE THE OBSTACLES TO CANCER IMMUNOTHERAPY SUCCESS?

32. Virtual, 21 - 22 June 2021
AGING AND CANCER

31. Trento, 17 - 18 June 2019
CANCER AS CORRUPTED TISSUE

30. Trento, 25 - 26 June 2018
OVERCOMING THE INNATE RESISTANCE OF CANCER TO THERAPY

29. Trento, 22 - 23 June 2017
BUILDING NEW BRIDGES BETWEEN BASIC AND CANCER SCIENCE

28. Trento, 20 - 21 June 2016
INITIAL STEPS ON THE ROUTE TO TUMORIGENESIS

27. Trento, 18 - 20 June 2015
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26. Trento, 19 - 21 June 2014
CANCERS DRIVEN BY HORMONES

25. Trento, 20 - 22 June 2013
METABOLISM AND TUMORIGENESIS

24. Trento, 14 - 16 June 2012
MOLECULAR BASIS FOR RESISTANCE TO TARGETED AGENTS

23. Trento, 16 - 18 June 2011
ENGINEERING AND NANOTECHNOLOGY IN CANCER

22. Trento, 10 - 12 June 2010
RNA BIOLOGY AND CANCER

21. Trento 11 - 13 June 2009
UNCONVENTIONAL THERAPEUTIC TARGETS IN CANCER

20. Trento 11 - 13 June 2008
MOLECULAR BIOLOGY OF CANCER: 20 YEARS OF PROGRESS PUNCTUATED BY THE PEZCOLLER SYMPOSIA

19. Trento 14 – 16 June 2007
HYPOTHESIS DRIVEN CLINICAL INVESTIGATION IN CANCER

18. Trento: 27 - 29 June 2006
TUMOR MICROENVIRONMENT: HETEROTYPIC INTERACTIONS

17. Trento: 16 – 18 June 2005
MOLECULAR UNDERSTANDING OF SOLID TUMORS

16. Trento, 10 – 12 June 2004
STEM CELLS AND EPIGENESIS IN CANCER

15. Rovereto, 12 – 14 June 2003
MOLECULAR IN VIVO VISUALISATION OF CANCER CELLS

14. Trento, 30 May – 1 June 2002
THE NOVEL DICHOTOMY OF IMMUNE INTERACTIONS WITH TUMORS

13. Rovereto, 31 May – 2 June 2001
FOCUSING ANALYTICAL TOOLS ON COMPLEXITY IN CANCER

12. Trento, 1 -3 June 2000
SIGNALING CROSS-TALKS IN CANCER CELLS

11. Rovereto, 5- 7 June 1999
MOLECULAR HORIZONS IN CANCER THERAPEUTICS

10. Trento, 29 June - 1 July 1998
THE GENETICS OF CANCER SUSCEPTIBILITY

9. Rovereto, 4 – 7 June 1997
THE BIOLOGY OF TUMORS

8. Trento, 17 – 19 June 1996
GENOMIC INSTABILITY AND IMMORTALITY IN CANCER

7. Trento, 14 – 16 June 1995
CANCER GENES. FUNCTIONAL ASPECTS

6. Rovereto, 29 June – 1 July 1994
NORMAL AND MALIGNANT HEMATOPOIESIS: NEW ADVANCES

5. Trento, 9 – 11 June 1993
APOPTOSIS

4. Rovereto, 24 – 26 June 1992
ADHESION MOLECULES: CELLULAR RECOGNITION MECHANISMS

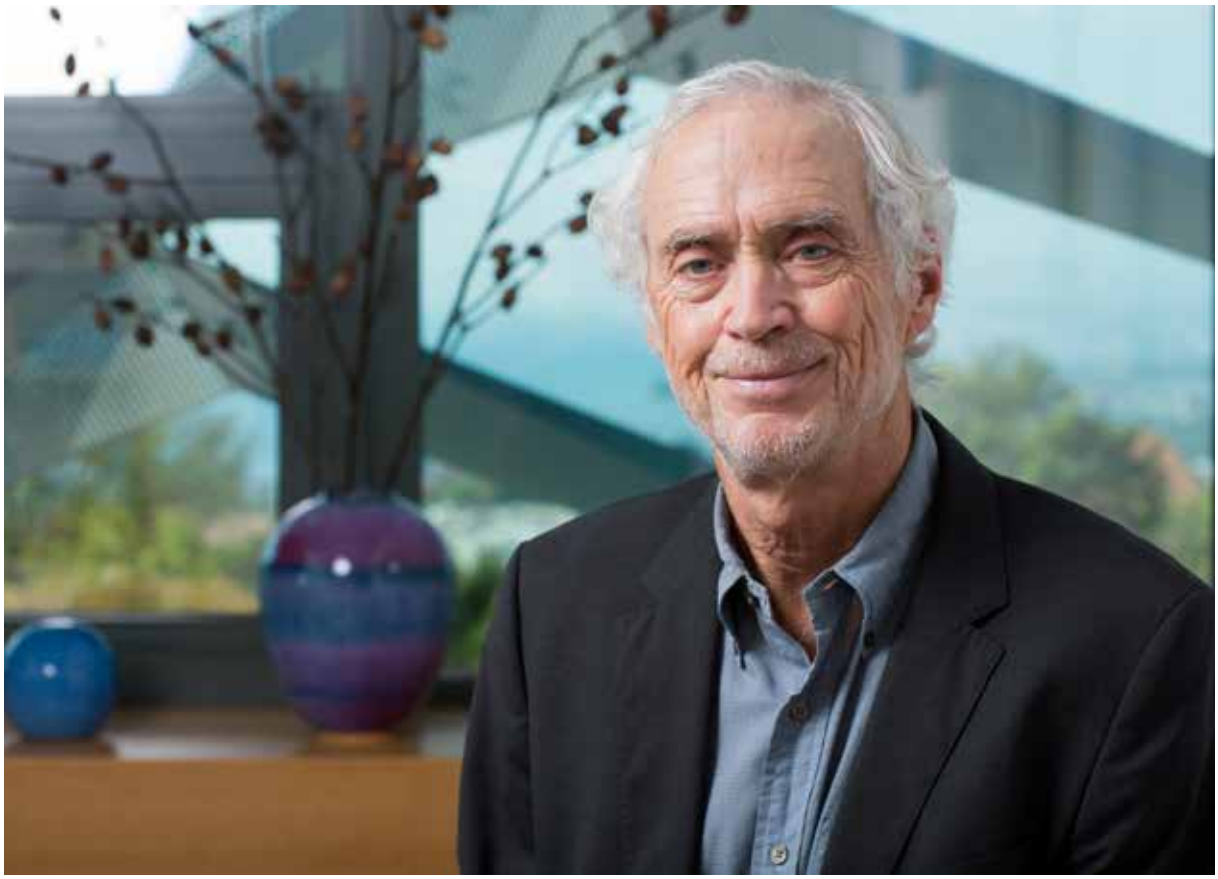
3. Trento, 5 – 7 June 1991
TUMOR SUPPRESSOR GENES

2. Rovereto, 11 – 13 June 1990
THE THERAPEUTIC IMPLICATIONS OF THE MOLECULAR BIOLOGY OF BREAST CANCER

1. Trento, 19 – 21 June 1989
DRUG RESISTANCE: MECHANISMS AND REVERSAL

Pezcoller Foundation – AACR International Award for Extraordinary Achievement in Cancer Research 2025

This International Award was established in 1997 to annually recognize a scientist who has made a major scientific discovery in basic or translational cancer research, continues to be active in cancer research, has a record of recent noteworthy publications and holds promise for substantive contributions to progress in the field of cancer. Twenty-seven top international scientists have been awarded so far and four of them have been subsequently awarded with the Nobel Prize, for the same motivations.



Dr. Douglas Hanahan is Distinguished Scholar at the Lausanne Branch of the Ludwig Institute for Cancer Research.

MOTIVATION

Hanahan is being recognized for pioneering the engineering of mouse models of tumorigenesis that uncovered mechanisms of stepwise cancer progression involving interactions among diverse cells in the tumor microenvironment; and for advancing mechanism-guided therapeutic targeting in preclinical trials, revealing treatment benefits and adaptive resistance, thereby informing innovative hallmark co-targeting strategies to prolong treatment efficacy.

Through the generation and characterization of innovative mouse models, he defined multi-step tumorigenesis by uncovering the molecular mechanisms required to drive cancer growth and helped establish the principle that malignant traits in cancer are conferred by cooperative interactions between cancer cells and co-opted host cells recruited into the tumor microenvironment.

Notably, Dr. Hanahan formulated, together with Robert Weinberg, PhD, the "Hallmarks of Cancer," a logical framework for rationalizing the vast complexity of cancer that continues to evolve and resonate broadly with the entire cancer research community.

Dr. Hanahan is revered as a quintessential scientific pioneer who has expertly helped propel and shape the emergence of functional genetics in cancer research. Early in his career, Dr. Hanahan demonstrated that oncogene expression is not sufficient to drive tumor formation, identifying that tumorigenesis requires the acquisition of secondary events, such as resistance to cell death, the induction of angiogenesis, or immune evasion.

Dr. Hanahan was also among the first to demonstrate that the tumor microenvironment is a barrier to antitumor cytotoxic T-cell activity. His studies subsequently contributed to the development of novel therapeutic strategies involving the targeting of various cell types such as immune and stromal cells present in the tumor microenvironment. Further, he helped establish the concept that inflammation can be tumorigenic and explored the tumor-promoting functions of tumor-infiltrating immune cells, cancer-associated fibroblasts, vascular cells, and extracellular proteases.

In collaboration with the late Judah Folkman, MD, Dr. Hanahan co-discovered the 'angiogenic switch', a key process in tumor growth. This fundamental work led to critical insights into therapeutic strategies for targeting tumor angiogenesis, such as the identification of unexpected adaptive resistance mechanisms, which illuminated why some monotherapies exhibit limited clinical efficacy.

More recently, he has demonstrated the potential of angiogenesis inhibitors in co-targeting treatment strategies. Additionally, Dr. Hanahan's latest research has profoundly contributed to cancer neuroscience by revealing the functional importance of co-opted neuronal signaling pathways in cancer cell invasion, metastasis, and immune evasion.

Dr. Douglas Hanahan at the AACR Annual Meeting on April 27, 2025 in Chicago, Illinois.
From the left: Dr. Giulio Draetta, Chairman of the 2024-2025 Selection Committee; Dr. Patricia LoRusso, 2024-2025 AACR President; Dr. Douglas Hanahan, 2025 Award winner; Dr. Enzo Galligioni, President of the Pezcoller Foundation; Dr. Margaret Foti, CEO of the AACR.

Dr. Hanahan's Lecture during the Award Ceremony in Trento, Italy, on May 17, 2025

Dr. Hanahan officially awarded during the Award Ceremony in Trento, Italy, on May 17, 2025.
From the left: Dr. Enzo Galligioni, President of the Pezcoller Foundation; Dr. Patricia LoRusso, 2024-2025 AACR President; Dr. Douglas Hanahan, 2025 Award winner; Dr. Margaret Foti, CEO of the AACR; Dr. Gios Bernardi, President Emeritus of the Pezcoller Foundation.

Dr. Hanahan's Scientific Lecture at CIBIO Department, University of Trento, Italy, on May 16, 2025

Call for Nominations for the 2026 Award

NOMINATION DEADLINE FOR 2026 AWARD: JUNE 30, 2025

DESCRIPTION

The prestigious Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research was established in 1997 to recognize a scientist of international renown who has made a major scientific discovery in basic cancer research or who has made significant contributions to translational cancer research.

Eligible candidates must continue to be active in cancer research; have a record of recent, noteworthy publications; and be conducting ongoing work that holds promise for continued substantive contributions to progress in the field of cancer.

The award is intended to honor an individual scientist. However, more than one scientist may be co-nominated and selected to share the award in the event that their investigations are intimately related in subject matter and have resulted in work that is worthy of the award and a joint nomination.

The award recipient will receive an unrestricted grant, a commemorative award, and present a scientific lecture in conjunction with the AACR Annual Meeting immediately following their selection. The award recipient will also present scientific lectures at the University of Padua (May 7, 2026) and at the University of Trento (May 8, 2026) in Italy, just prior to the official Award ceremony in Trento on **May 9, 2026**.

Please see the Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research book for more information on this prestigious award.

ELIGIBILITY CRITERIA

Cancer researchers affiliated with any institution involved in cancer research, cancer medicine, or cancer-related science anywhere in the world may be nominated. Such institutions include those in academia, industry, or government.

Individuals who have previously been awarded the Nobel Prize in any category are ineligible to receive this award.

Institutions and/or organizations are not eligible to receive the award.

NOMINATION CRITERIA

Nominations may be submitted by any individual, whether an AACR member or nonmember, who is currently or has previously been affiliated with any institution involved in cancer research, cancer medicine, or cancer-related sciences.

Self-nominations are prohibited.

Nominators must maintain strict confidentiality of their nominations.

Eligible nominations must include the following:

- A nomination letter written in English (Max: 1,000 words), which comprehensively describes the candidate's major scientific discovery in basic cancer research or significant contributions to translational cancer research, and the impact of these accomplishments on the field. Letter must specifically outline the candidate's current research activity and indicate how their research holds promise for continued substantive contributions to the cancer field. All publications that directly support the mentioned research accomplishments must be referenced within the provided letter.
- A brief scientific citation (Max: 50 words) highlighting the major scientific contribution(s) justifying the award candidate's nomination.

SELECTION PROCESS

- Eligible nominees will be considered by a prestigious Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research Selection Committee consisting of an international cohort of renowned cancer leaders appointed by the AACR President in consultation with the Pezcoller Foundation Council.
- The Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research Selection Committee will consider all nominations as they have been submitted and are restricted from combining submitted nominations, adding new nominees, or otherwise making alterations to any submitted nomination.
- Once chosen, the primary and alternate award recipient selections made by the Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research Selection Committee shall be sent to the AACR Executive Committee and the Pezcoller Foundation Council for final consideration and ratification.

  Selection of the award recipient shall be made on the basis of the candidate's scientific accomplishments without regard to race, gender, nationality, geographic location, or religious or political views.

For all information:

Pezcoller Foundation EACR Awards 2025

Since 2012, the Pezcoller Foundation and the European Association for Cancer Research, EACR, have collaborated to support excellence in cancer research. Presently, three Pezcoller Foundation – EACR Cancer Research Awards are made jointly by the two organizations, to celebrate academic excellence and achievements in the field of cancer research. They are:

- The Pezcoller Foundation – EACR Translational Cancer Researcher Award to **young European researchers**
- The Pezcoller – Marina Larcher Fogazzaro – EACR Women in Cancer Research Award, to European researchers who have demonstrated **academic excellence** and achievements in the field of cancer research and who have, through leadership or by example, furthered the **advancement of women** in cancer research
- The EACR – Mark Foundation – Pezcoller Foundation Rising Star Award, to very promising, **early career cancer researchers** (established in 2023 thanks to the new collaboration with the Mark Foundation, USA)

Winners of the Pezcoller Foundation – EACR Awards 2025

2025 Translational Cancer Researcher Award:
Ido Amit
Weizmann Institute of Science, Rehovot (Israel)

2025 Women in Cancer Research Award:
Karin de Visser
Netherlands Cancer Institute, Oncode Institute, Leiden University Medical Center (Netherlands)

2025 Rising Star Award:
Marta Kovatcheva
IFOM, Milan (Italy)

All information about calls for Nominations for the 2026 Awards is available on www.eacr.org.

The Pezcoller Foundation – University of Trento PhD Fellowships

The Pezcoller Foundation actively promotes and supports cancer research, with particular attention to the local community of researchers.
The Pezcoller Foundation – University of Trento PhD Fellowships are 3-year PhD fellowships for Italian researchers (€25,000/year), awarded on a competitive basis in collaboration with the University of Trento, Department of Cell, Computational and Integrated Biology (CIBIO), for cancer research projects.
The recipients of the 2023-2026 PhD Fellowships are:

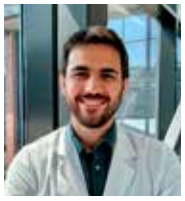
The Pezcoller Foundation - Marina Larcher Fogazzaro PhD Fellowship
Elisa Marmocchi
Project "*Development of immuno-oncology strategies for immunologically "cold" tumors*" coordinated by Prof. Andrea Lunardi

The Pezcoller Foundation - Casse Rurali Trentine PhD Fellowship
Fabio Mazza
Project "*Exploring the complex of interactions between somatic and germline coding variants in cancer*" coordinated by Prof. Alessandro Romanel (CIBIO Department) and Prof. Gianluca Lattanzi (Physics Department, UNITN)

Next call for application will open in 2026.

The Pezcoller Foundation – SIC Fellowships

The Pezcoller Foundation actively promotes and supports cancer research, with particular attention to Italian young researchers, through the Pezcoller Foundation – SIC Fellowships, assigned every 2 years.
These are two-year fellowships, € 30,000/year, for researchers working in Italian institutions, awarded on a competitive basis in collaboration with the Italian Cancer Society.
Recipients of the 2025-2026 Pezcoller Foundation – SIC Fellowships:



Gabriele Antonarelli (Istituto Europeo di Oncologia, Milano) with the research project: "*Identification of toxicity biomarkers to trastuzumab-deruxtecan (t-dxd) in patients with advanced breast cancer. Tox-dxd: an observational, non-interventional, study*"

Lucrezia Camicia (Centro di Riferimento Oncologico, Aviano) with the research project: "*Study the role of Multimerin-2 in shaping tumor vessel stability to control the chemo/immunotherapy response*"

Mattia Colucci (Casa Sollievo Sofferenza, S. Giovanni Rotondo) with the research project: "*The functional role of EZH2 inactivation in the pathogenesis of HOXA-overexpressing Tcell acute lymphoblastic leukemia*"

Andrea Costamagna (Università di Torino) with the research project: "*Exploring the role of p130Cas in early metastatic pancreatic cancer cells*"

Maria Valeria Giuli (Università Sapienza, Roma) with the research project: "*Boosting synthetic lethality in High-Grade Serous Ovarian Cancer: induction of "BRCAness" via Pin1 inhibition*"

Gaetana Porcelli (Università di Palermo) with the research project: "*Obesity Prompts a Permissive Microenvironment to Initiating-Tumor Process*"

Jessica Ruzzolini (Università di Firenze) "*Targeting YAP/TAZ signaling to overcome drug resistance in BRAF(V600E) melanoma cells*"

The Pezcoller Foundation – 2025 AACR Scholar-In-Training

The AACR-Pezcoller Foundation Scholar-in-Training Awards continue the AACR's long-standing support of the next generation of cancer researchers.
Scholar-in-Training Awards are highly competitive and recognize outstanding young investigators presenting meritorious proofreader papers at the AACR Annual Meeting.

The 2025 recipients are:

Luisa Amato
University of Campania "Luigi Vanvitelli," Napoli, Italy
"*Efficacy of DNA-PK inhibitor as maintenance strategy after cisplatin induction in SCLC*"

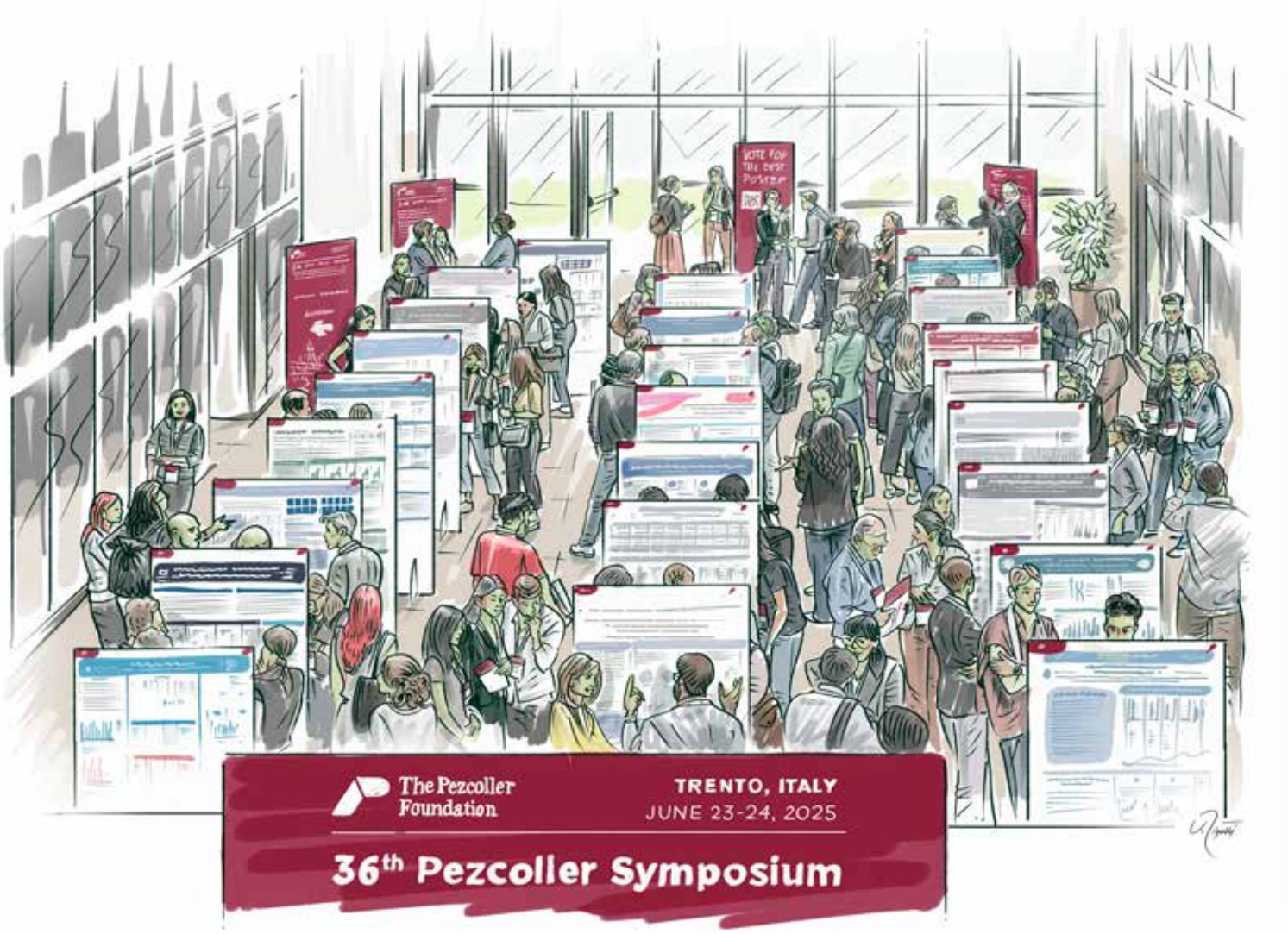
Nanna Kristjansdottir
Aarhus University, Aarhus, Denmark
"*Low T cell diversity is associated with poor outcome in bladder cancer: A comprehensive longitudinal analysis of the T cell receptor repertoire*"

Carmen Rubio Alarcon
Netherlands Cancer Institute, Amsterdam, Netherlands
"*Beyond tumor size: Biological and clinical predictors of ctDNA shedding in colon cancer*"

Bisan Abdalfatah Zohud
Universitätsklinikum Erlangen, Erlangen, Germany
"*Endothelial SPARCL1 suppresses colorectal cancer metastases through dormancy induction and EMT inhibition in colonizing tumor cells*"

Martha Zylka
St. Anna Children's Cancer Research Institute, Vienna, Austria
"*A novel organoid-based model to study pediatric tumor metastasis to the lung*"

Note



VOTE FOR THE BEST POSTER!

The author of the poster most votes will receive the
"Molecular Systems Biology Prize" (€ 200) from EMBO Press.

The poster prize recognizes the scientific quality and interest of the data,
as well as the poster presentation.

The winner will be announced during the closing remarks:
Tuesday, June 24 at 17:15.

The Pezcoller Foundation

FONDAZIONE CARITRO
CASSA DI RISPARMIO DI TRENTO E ROVERETO

Journal

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