





# Symposium on Cancer Challenges 17-19 May 2024 Frascati, Italy

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Nick Barlev Roberto Basili Giovanni Blandino Jamie Blundell Eleonora Candi Francesca Croce Giannino Del Sal Ben Greenbaum Andrei Gudkov Pierre Hainaut David Lane Arnold Levine Scott Lowe Gigi Lozano David Malkin Gerry Melino Pierluigi Nicotera Giuseppe Novelli Carol Prives Raul Rabadan

**Organizing Committee** 

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# Supporting Organizations



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# Symposium on Cancer Challenges

17-19 May 2024 Frascati, Italy

> **Chair** Arnold Levine Gerry Melino

# Organizing Committee

Dr Suzanne Christen schrist@ias.edu Dr Lucilla Bongiorno Borbone lucilla.bongiorno@uniroma2.it

# Welcome Address

Dear friends,

We would like to welcome you in Frascati, Italy, for the Symposium on Cancer Challenges from 17 to 19 May 2024.

This is a retreat-like conference, with selected public, aimed at fostering interactions and collaborations at the front edge of science. Therefore, there are indicative titles without tight schedules, leaving a free fluid programme with very large space for free discussion.

The main programme on the first day will include discussion on 6 topic on cancer challenges. Our idea is to allow discussants only 5 short presentation to open and launch a specific topics in a provocative, controversial manner and therefore allow a lively discussion for 40 minutes involving all participants. The idea is to select open topics that need future interest.

The second day includes specific scientific presentations and the third day is free for informal discussions.

We hope your stay will be enjoyable and scientifically constructive and we trust this will be a pleasant build-on of friendship and collaboration.

Yours sincerely,

The Organisational Committee The Secretariat



# Venue



Villa Mondragone Via Frascati, 51, 00040 Monte Porzio Catone RM <u>info@villamondragone.it</u> https://villamondragone.it

Villa Mondragone is a patrician villa originally in the territory of Frascati (Rome). Construction began in 1573 by Cardinal Mark Sittich von Hohenems Altemps, who commissioned the Palazzo Altemps in central Rome, on the site of the remains of a Roman villa of the consular family of the Quintilii. Pope Gregory XIII, whose heraldic dragon led to calling the villa "Mondragone", used the villa regularly and in 1582, Gregory promulgated the document (the papal bull "Inter gravissimas") which initiated the reform of the calendar now in use and known as the Gregorian calendar. Other popes who passed long periods in Villa Mondragone include Clement VIII, Paul V and Urban VIII. Property of the Jesuits, currently, the Villa belongs to the University of Rome Tor Vergata.



Villa Tuscolana Via del Tuscolo, km 1.5, 00044 Frascati RM +39 06 942900 <u>info@villatuscolana.com</u> https://www.villatuscolana.com

Built by Alessandro Ruffini, bishop of Melfi, in 1578, the villa, commissioned by the Jesuits to architect Luigi Vanvitelli, became property of the pope. In 1804 Pope Pius VII sold the Villa to prince Lucien Bonaparte during his self-imposed exile in Rome. After 1848 the Villa became the property of King Vittorio Emanuele II. Currently, the Salesians of Don Bosco have restored the building and turned it into a conference hotel.

#### RATIONALE

This is retreat-like conference, with selected public, aimed at fostering interactions and collaborations at the front edge of science. Therefore, there are indicative titles without tight schedules, leaving a free fluid programme with very large space for free discussion.

17/05/2024 We propose six main topics for the first day.18/05/2024 The second day includes specific scientific presentations19/05/2024 The third day is free for informal discussions.

### 17<sup>th</sup> May Program

<u>Panelists are allowed 10 minutes</u> each to open and launch specific topics in a provocative, controversial manner and therefore <u>allow a lively discussion for 40 minutes involving all participants</u>. The idea is to select open topics that need future interest. Examples:

Examples.

#### 1. DARK GENOME

long stretches of DNA that do not encode for traditional proteins — primarily made up of repetitive elements, or repeats, making up to 50% genome; cannot be sequenced. These repeats consist of different families, including LINEs (long interspersed elements; 21%), SINES (short interspersed elements; 15%), which include the Alu elements, and HERVs (human endogenous retroviruses, 9%). Other repeats range from small, simple sequence repeats to large arrays of tandem repeats at the center and ends of chromosomes. LINE element retrotransposons or "jumping genes," are especially powerful. These are complex mobile elements that can make copies that transpose into new locations in the genome. These activities can alter the structure of our chromosomes and are drivers of the genetic diversity important for evolution, but because these activities are very disruptive, they are tightly controlled. What is their function? Their regulation/repression? Is Viral Mimicry activating IFN responses? Is p53 repressing as its major function?

#### 2. p53 FAMILY ISOFORMS & THEYR TARGETS

Does TP53 have a functional promoter \*Delta133? to do what? What is the phenotype of the mouse KO? If not, why this second promoter is not evolutionarily conserved? What is the evolutionary meaning of having 1--> 2--> 1 promoters? Which are the transactivation domains in p53 and their regulation? What are the roles of p53 polymorphisms? The functional details of these are still not fully clarified.

Moving to the family members, are TP63/TP73 3'end splicing real? Whereas the 5' prime promoters are really functional, could the alternative splicing producing different C-terminals be laboratory artefacts?

Does the p53 family work also by epigenetic editing? Traditionally, it has been believed that inheritance is driven as phenotypic variations resulting from changes in DNA sequence. However, "epigenetic" changes in DNA methylation, histone modification, non-coding RNA biogenesis, and chromatin remodelling play crucial roles in genomic functions and regulation of gene expression. Some of these changes are inherited by the next generations as a part of epigenetic memory and play significant roles in gene expression. Recently, deadCRISPR-dCas9 enabled epigenome editing to be more specific/efficient for targeted DNA (de)methylation. Still, this may cause unintended changes/harmful effects. Moreover, epigenome editing of germline cells raise several ethical/safety issues. Is it ready for human application? Ethics?

#### 3. NEURO-IMMUNITY; INFLAMMATION

Choline acetyltransferase (ChAT), which synthesizes acetylcholine (ACh), is a critical driver of pathogenicity in autoimmune encephalomyelitis, multiple sclerosis, and cancer development by regulating both B and T cell functions. Indeed, B and T cells produce neurotransmitters such as ChaT activating cholinergic/ parasympathetic or norepinephrine functions. Conversely, neurons regulate immune B/T cell function. Accordingly, T cells can induce vasodilation in a choline-acetyltransferase dependent manner, leading to an increase in T cell migration to infected tissues in response to viral infection. Are they involved in cancer? Which muscarinic receptor and how? How are Inflammation/immunity/life habits related?

# PARTICIPANTS



#### Arnold Levine

Member of the U.S. National Academy of Sciences.

Arnold Levine is Professor at Institute for Advanced Study and Cancer Institute of New Jersey Princeton, New Jersey. He is a widely acclaimed leader in cancer research. In 1979, Levine and others discovered the p53 tumor suppressor protein, a molecule that inhibits tumor development. In 1989 he established the function of p53 as a tu8mor suppressor. In 1998 Levine became the Robert and Harriet Heilbrunn Professor of Cancer Biology and president of Rockefeller University. He established the Simons Center for Systems Biology at the Institute, concentrating on research at the interface of molecular biology and the physical sciences: on

genetics and genomics, polymorphisms and molecular aspects of evolution, signal transduction pathways and networks, stress responses, and pharmacogenomics in cancer biology. Arnold Levine also leads the NSF– sponsored Cancer Convergence Education Network, and focuses on fostering convergence research to produce fundamental insights in the areas of immunology and infectious diseases. In 2017, Levine, with collaborators Benjamin Greenbaum, and Marta Luksza, developed the first mathematical model for predicting patient response to immunotherapy.



#### Gerry Melino

Member of the Lincei Academy and Academia Europaea.

Gerry Melino is Professor of Biochemistry at the University of Rome "Tor Vergata". For 19 years he directed a programme at the Medical Research Council and Leicester and then in Cambridge, UK. He also directed for 5 years the Molecular Pharmacology Centre at Saint Petersburg Institute of Technology. He is Founder & Editor-in-Chief of 3 journals – Cell Death Differentiation (IF 12.1), Cell Death Disease (IF 9.0), and Cell Death Discovery (IF 7.0), as well as a member of several other Editorial Boards and Scientific Advisor for several Governmental Institutions. His training originated in Rome, Italy, where he obtained his M.D. (1978, University of Rome) followed by

clinical specialisations in Paediatrics (1981) and Clinical Oncology (1985); the Ph.D. (1984) was at the University of London, UK, where he became Consultant. His scientific interest are focused on programmed cell death in epidermal, in particular on the p53 family – p63 and p73, in cancer progression.



#### Nikolai Barlev

Professor the Department of Biomedical Sciences, Nazarbaev University in Astana, Kazakhstan, Nick Barlev has obtained his joined PhD degree from Azan State University, Russia and University of Aarhus, Denmark. He did a postdoc on transcription regulation with Shelley L. Berger at the Wistar Institute, Philadelphia. He joined Tufts University, Boston in 2002 as an Assistant Professor to work on the role of lysine-specific post-translational covalent modifications in regulation of tumour suppressor p53. In 2008 he moved to the University of Leicester, UK where his lab worked on various aspects of lysine methylation in p53, E2F1 and other critical transcriptional regulators. In 2015 Dr Barlev became the Head of Gene

Expression Regulation Unit in the Institute of Cytology, Saint Petersburg, Russia and currently direct a research lab in Astana.



#### **Roberto Basili**

Roberto Basili is Full Professor at the Faculty of Engineering of the University of Rome, Tor Vergata. There, he conducts teaching activities in courses such as Web Mining and Retrieval, Databases, and Artificial Intelligence. His research activity, which began in 1990, focuses on problems, methodologies, and technologies of Artificial Intelligence in the areas of Machine Learning, Natural Language Processing (NLP), and Engineering of Natural Language processing systems and Distributed & Web Information Retrieval. He is an author of over 100 publications in scientific journals, International Conference Proceedings, and internationally renowned books. Since 2001, he has been an invited speaker at International Conferences and Workshops in the fields of machine learning for Natural Language Processing, acquisition of ontological knowledge from extensive text collections, and Information Retrieval.



#### Giovanni Blandino

Giovanni Blandino is the Head of Translational Oncology Research Unit at the Regina Elena National Cancer Institute in Rome. Giovanni Blandino is author of over 200 publications and patents. Dr Blandino has made important contributions to the elucidating molecular mechanisms of tumorigenesis and developing innovative anticancer strategies. His current research is focused on the developing of more precise diagnostic approaches to predict cancer progression and prognosis is the key to precision medicine. His Unit mirrors at specific genomic and epigenetic alterations in both solid and hematopoietic malignancies that hold the potential to represent novel cancer biomarkers or druggable targets. This is pursued through

genome wide approaches applied to cell systems, animal models, tissues and biological fluids (ctDNA and non-coding RNAs) of cancer patients



#### Jamie Blundell

Trained as a theoretical physicist at the Cavendish Laboratory, University of Cambridge, he moved to Stanford University in 2012 as a postdoctoral scholar working on the dynamics of clonal evolution with Daniel Fisher, Sasha Levy, Dmitri Petrov and Gavin Sherlock. He joined the Early Cancer Institute in July 2017 and was awarded a UKRI Future Leaders fellowship in September 2019 which funds much of the group's research. His research interests lie in quantitatively understanding somatic evolution in human tissues. He is also the Anthony L. Lyster fellow at Queens' College. Blundell aims to develop a quantitative understanding of somatic evolution in tissues to detect cancer at its earliest stages.



#### Eleonora Candi

#### Member of the Academia Europaea.

Prof Eleonora Candi received her PhD degree at the Department of Experimental Medicine and Biochemical Sciences, University of Rome "Tor Vergata" in 1995. She did her pre- and post-doctoral training, from 1993-1998 at the Skin Biology Branch, NIAMS, National Institute of Health, Bethesda, USA, working under the supervision of Dr PM Steinert on transglutaminases and their substrates. From 1999 to 2001, she received a Telethon Research Fellowship to study the role of transglutaminases in the genetic disease lamellar ichthyosis. In the past two decades, scientific interests of her group have been focused on study of the role of transcription factor

p63, a homolog of p53, and microRNAs in epithelia development and tumour formation. Currently a professor of Biochemistry at University of Rome "Tor Vergata", she is also Editor-in-Chief of a Springer journal *Discover Oncology* as well as editorial board member of multiple international journals.



#### Francesca Croce

Francesca Croce is currently pursuing a doctorate at the University of Vienna, where she specializes in late 17th century Roman art and is a recipient of the Doctoral Fellowship Program of the Austrian Academy of Sciences. Her dissertation "The Divine Master: Raphael and the Works of Giovan Pietro Bellori and Carlo Maratti" focuses on the influence of Raphael on the seventeenth century biographer and artist. Croce's papers have been published in Paragone Arte, the Wiener Jahrbuch für Kunstgeschichte as well as the Anales de Historia del Arte. She holds a master's degree in art

history from the Courtauld Institute of Art, where she wrote her dissertation "Out of the Darkness: Constructing the Seicento Myth of Annibale Carracci", and bachelor's degree in history from Columbia University. Croce has given presentations on the Seicento in the United States and Europe, including at the Universities of London and Vienna, the Institut national d'histoire de l'art and the Columbus Museum of Art.



#### Giannino Del Sal

EMBO (European Molecular Biology Organization) Member.

Prof Giannino del Sal is a Group Leader at International Centre for Genetic Engineering and Biotechnology in Trieste, Italy. His research has been mainly concentrated on the tumour suppressor p53 and its signalling pathway. He discovered new post-translational modifications and sub-cellular localisations of wild type p53, and highlighted the role of missense mutant p53 in controlling the proteasome machinery in cancer. He has received grants from various national and international, public and private, funding bodies, such as the EU, the Italian Ministry for Education University and Research, the Italian Association for Cancer Research

(AIRC), and others. He is member of the editorial board of Journal of Molecular Cell Biology Oxford, and Cell Death and Differentiation; member of the advisory editorial board of EMBO reports; and has been member of the scientific committee of the Italian Association for Cancer Research (AIRC). He has authored over 140 publications among research articles, reviews, opinions and chapters. In recognition of his scientific achievements.



#### Ben Greenbaum

Dr. Greenbaum is the director of Computational Immuno-Oncology within the Computational Oncology Service. After a PhD in theoretical physics from Columbia University he focused on the effect of the innate immune system on viral evolution: his models predicted how the 1918 influenza virus evolved after the pandemic and continued to be cited during Covid-19. Dr. Greenbaum's main research interests have long centered around the fundamental question of self vs non-self discrimination: How does the immune system recognize and target particular molecular patterns and sequences as 'foreign', and how does this affect the evolution of tumors and viruses? Dr. Greenbaum's work is supported by various

federal and philanthropic grants and awards and has contributed to several clinical trials, including a phase II trial to test an inhibitor of repeat elements in colorectal cancer and a phase I trial for an mRNA vaccine against neoantigens in pancreatic cancer.



#### Andrei Gudkov

Andrei V. Gudkov is Professor of Oncology, Senior Vice President, Research Technology and Innovation, and Chair of the Department of Cell Stress Biology at Roswell Park Comprehensive Cancer Center. Dr. Gudkov was graduated from Moscow State University and obtained his academic degrees (PhD in Experimental Oncology and Doctor of Sciences in Molecular Biology) in former Soviet Union. In 1990 joined Department of Genetics at University of Illinois at Chicago (US). Between 2001-2007 he led Department of Molecular Genetics at Cleveland Clinic (Cleveland, Ohio). Since 2007, he is at his current position at Roswell Park Comprehensive Cancer Center in Buffalo, New York. His interests involve anti-

cancer and anti-aging research, radiation biology and mechanisms of inflammation. He authored >250 research articles and founded several biotech companies that develop anticancer and anti-aging drugs based on his inventions.



#### Pierre Hainaut

Pierre Hainaut is a professor in Cancer Biology at University Grenoble Alpes. He graduated from the University of Liège in Belgium. Following postdoctoral positions in France and the United Kingdom (1988-1994), he joined the International Agency for Research on Cancer (IARC, World Health Organization) in 1994, where he held the position of Head of Molecular Carcinogenesis from 1999. Since 2015, he has been directing the Institute for Advanced Biosciences (IAB) in Grenoble, bringing together nearly 300 researchers on the theme of "Epigenetics-Environment-Cellular Plasticity and Cancer." Pierre Hainaut is internationally renowned for his work on mutations in the TP53 gene, the most frequently mutated gene in cancers.

He is particularly known for his research on the mutagenic effects of tobacco, liver cancers, and Li-Fraumeni Syndrome, a form of cancer predisposition caused by the hereditary transmission of TP53 mutations. He is the author of over 400 international publications and several reference books, including a recent Encyclopedia of Cancer.



#### David Lane

Member of the U.S. National Academy of Sciences.

Sir David Lane is professor of tumour suppressor biology at the Department of Microbiology, Tumor and Cell Biology at the Karolinska Institute and the head of the A\*STAR laboratory in Singapore. Sir David is credited with the landmark discovery of p53 and its role in cancer development. As the Chief Scientist of A\*STAR, Lane advises and engages in scientific development across the Biomedical Research Council (BMRC) and the Scientific Engineering Research Council (SERC) at the strategic level. Lane is concurrently the Director of the p53 Laboratory, which primarily focuses on research on protein interactions and how to develop drugs to

inhibit such interactions, using p53 as a model system.



#### Scott Lowe

Member of the U.S. National Academy of Sciences.

Scott Lowe is Chair of the Cancer Biology and Genetics Program in the Sloan Kettering Institute at Memorial Sloan Kettering Cancer Center. Dr. Lowe received his Bachelor's Degree from the University of Wisconsin-Madison and his Ph.D. from the Massachusetts Institute of Technology. He initiated his independent research at Cold Spring Harbor Laboratory, where his group make important contributions to our understanding of the p53 tumour suppressor network, as well as the processes of multi-step carcinogenesis, cellular senescence, and tumour-cell drug resistance. His research group uses genetically engineered mouse models to study how the

genetic alterations in cancer cells contribute to tumorigenesis, alter treatment response, and create molecular vulnerabilities that may be targeted therapeutically.



#### Gigi Lozano

#### Member of the U.S. National Academy of Sciences.

Guillermina (Gigi) Lozano a professor at University of Texas MD Anderson Cancer Center. Dr. Lozano received her BS degree in Biology and Mathematics at the University of Texas Rio Grande Valley. She completed graduate studies at Rutgers University and the University of Medicine and Dentistry of New Jersey, and a postdoctoral fellowship with Dr. Arnold Levine at Princeton University. Dr. Lozano is a member of the National Academy of Sciences, the National Academy of Medicine and the American Academy of Arts and Sciences. She is a renowned geneticist recognized for her studies of the p53 tumor suppressor pathway. Her laboratory

identified a transcriptional activation function for p53. Using mouse models, her team characterized the physiological importance of Mdm2 and Mdm4 proteins as potent inhibitors of p53. The Mdm proteins are over expressed in many cancers that lack p53 mutations presenting an alternate mechanism of eliminating p53 activity. Other mouse models inheriting the most common p53 mutations revealed gain-of-function phenotypes that drive metastases.



#### David Malkin

Dr. Malkin is Professor of Pediatrics and Medical Biophysics in the Faculty of Medicine, University of Toronto. He received his medical degree from the University of Toronto in 1984 and completed postdoctoral research training in molecular genetics at Massachusetts General Hospital, Harvard University, where he discovered the link between germline mutations in the TP53 tumor suppressor gene and the Li-Fraumeni cancer susceptibility syndrome. Dr. Malkin is the Lead of the SickKids Precision Child Health initiative. His research program focuses on genetic and genomic mechanisms of childhood cancer susceptibility which he has explored particularly in the context of TP53 and Li-Fraumeni syndrome. He has

published over 250 peer-reviewed articles and has received several awards recognizing his dedication to clinical care, advocacy, research, medical education and mentorship.



#### Pierluigi Nicotera

Member of the Academia Leopoldina and of the Academia Europaea.

Since 2009, professor Nicotera is Scientific Director and Chairman, German Centre for Neurodegenerative Diseases (DZNE) and Professor of Neurodegeneration, University of Bonn. His main research focus is on molecular mechanisms of cell death and neurodegeneration. Graduated from the University of Pavia, following an early career at the Karolinska Institute with professor Sten Orrenius (1986-1994), he became professor of Toxicology at the University of Konstanz (1995-2001), and then Director at the Medical Research Council, Toxicology Unit (2002-2009).He is

Member of Leopoldina, UK Academy Sciences, Academia Europaea.



#### Giuseppe Novelli

Professor Giuseppe Novelli (PhD) is Head of the Human Genetics Research Unit at The Tor Vergata University of Rome (Italy). Giuseppe Novelli graduated in Biological Sciences in 1981 from the University of Urbino. From 1995 to 1999, he served as an Associate Professor of Human Genetics at the University of Rome Tor Vergata. In 1999, he became a Full Professor of Medical Genetics and in 2013 he became the Rector of this University. Since 2003, Giuseppe Novelli has also been an Adjunct Professor at the University of Arkansas for Medical Sciences, Little Rock, USA. Prof. Novelli's current studies focus on the treatment of hereditary diseases and the development of new drugs and pharmacogenetics. He has coordinated numerous

research projects funded by MIUR, CNR, Ministry of Health, Telethon, AFM, EU FP5, EU FP6, and EU FP7, Ministry of Foreign Affairs, Veronesi Foundation, AIRC, AIFA, ISS, and FFC.



#### **Carol Prives**

Member of the U.S. National Academy of Sciences.

Carol Prives is a Professor of Biology in the Dept of Biological Sciences at Columbia University. She was educated in Canada, receiving her BSc and PhD from McGill University and received postdoctoral training at Albert Einstein College of Medicine and the Weizmann Institute where she became a faculty member. She then joined the Biological Sciences Department at Columbia University where she was named the DaCosta Professor of Biology in 1995 and served as Chair of that department between 2000 and 2004. Her work has focused on the p53 tumor suppressor protein and her group have elucidated aspects of the structure and function of the

p53 protein especially as it relates to its roles as a transcriptional activator. In parallel, her group has examined how cancer related mutant forms of p53 regulate tumorigenesis. Work from her laboratory has also illuminated the functions of the key p53 negative regulators, Mdm2 and MdmX. Dr Prives has served on numerous advisory boards and is also a member of the Editorial Boards of Cell, Genes & Development, Cancer Discovery. Proceedings of the National Academy of Sciences.



## Raul Rabadan

Raul Rabadan is the a Professor at Columbia University. He is the director of the Program for Mathematical Genomics (PMG) and the Center for Topology of Cancer Evolution and Heterogeneity. From 2001 to 2003, Dr. Rabadan was a fellow at the Theoretical Physics Division at CERN, the European Organization for Nuclear Research, in Geneva, Switzerland. In 2003 he joined the Physics Group of the School of Natural Sciences at the Institute for Advanced Study. Previously, Dr. Rabadan was the Martin A. and Helen Chooljian Member at The Simons Center for Systems Biology at the Institute for Advanced Study in Princeton, New Jersey. He has been named one of Popular Science's Brilliant 10 (2010), a Stewart Trust

Fellow (2013), and he received the Harold and Golden Lamport Award at Columbia University (2014). Dr. Rabadan's current interest focuses on uncovering patterns of evolution in biological systems—in particular, RNA viruses and cancer.

# SECOND DAY PARTICIPANTS

#### Massimiliano Agostini

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Massimiliano Agostini is associate professor in Molecular Biology at the University of Rome "Tor Vergata". He obtained his PhD in Clinical and Experimental Pharmacology (Perugia, Italy). In 2007-2014, he worked at the MRC Toxicology Unit, (UK), as PostDoc and then as Senior Investigator. In 2014 worked at TW Mak's laboratory as visiting scientist (Canada). From 2014 to 2019 Visiting Scientist, MRC Toxicology Unit, Cambridge University, UK. Prof Agostini is mainly interested in the characterization of transgenic mice with genetic alterations in the p53 family genes and their targets to understand their effect on development and cancer.

#### Mick Aitken

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Mick is a PhD student in the Rabadan Lab of the Department of Physics at Columbia University. He uses a computational approach to understand and harness the immune system in the context of cancers. Currently, he is interested in quantifying the subspace of peptides covered by an individual's HLA (human leukocyte antigen) repertoire, and the impact of this coverage on clinical variables including cancer risk and response to immunotherapy.

# Danilo Croce

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Danilo Croce is a Tenure-Track Assistant Professor in Computer Science at the University of Rome, Tor Vergata, Faculty of Engineering. He earned a Ph.D. in Informatics Engineering from the same university. His expertise encompasses both theoretical and applied Machine Learning. He primarily focuses on Natural Language Processing, Information Retrieval, and Data Mining. His particular interest lies in innovative kernels for Support Vector Machines, Deep Learning approaches, Transformer-based neural architectures, and Large Language Models. His research is centered on advanced syntactic and semantic processing within the realms of Natural Language Processing and Computer Vision.

# Elena Enzo

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Elena Enzo is Assistant Professor in Biochemistry at the Centre for Regenerative Medicine, University of Modena and Reggio Emilia, Italy. Her research endeavors are primarily centered around elucidating the biochemical pathways governing cell proliferation in cancer and self-renewal in epidermal stem cells. Notably, she has made significant contributions to understanding the interplay between the YAP/TAZ signaling pathway and glycolysis, unveiling their pivotal role as drivers of breast cancers. Leveraging state-of-the-art single-cell transcriptomic approaches, she recently identified FOXM1 as a master regulator of self-renewal in epidermal stem cells. Presently, her research focuses on unraveling the intricate connections between metabolic state, epigenetics, and self-renewal downstream of FOXM1 activity, promising further insights into regenerative medicine applications.

# Xi Fu

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Xi Fu is a 4<sup>th</sup> year PhD student in the Department of Biomedical Informatics at Columbia University, in the laboratory of Dr. Raul Rabadan. Xi is focusing on developing foundational models for transcription regulation and applying them to studying coding and noncoding variants in cancer. Xi received a Bachelor of Science in Cell and Molecular Biology in 2016 and his M.Phil in Computer Science in 2019 from The Chinese University of Hong Kong. During his M.Phil study, he developed a statistical framework for analyzing noncoding regulatory variants using whole-genome sequencing data to study the etiology of Hirschsprung's disease.

# David Hoyos

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David Hoyos is a graduate student in the Tri-Institutional PhD Program in Computational Biology & Medicine at Weill Cornell Medicine, Memorial Sloan Kettering Cancer Center, and The Rockefeller University researching aspects of the immune system, evolution, viruses, and cancer using tools from areas such as physics and information theory. He received his BA in physics from Princeton University with a certificate in Applied and Computational Mathematics as well as Biophysics.

# Hamish MacGregor

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Hamish MacGregor graduated in theoretical physics from the University of Cambridge in 2020. He is jointly supervised by Doug Easton in the Centre for Cancer Genetic Epidemiology on a studentship supported by the <u>ACED alliance.</u> Hamish's PhD project centres around using methods from population genetics to better distinguish germline variants from somatic variants in large collections of blood-derived exomes e.g. UKBiobank or Bridges and understanding how clonal haematopoiesis changed throughout the human lifespan, including childhood.

# Stephen Martis

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Stephen Martis received his PhD in physics from UC Berkeley. He is currently a research fellow at Memorial Sloan Kettering Cancer Center, where he works at the intersection of cancer, the immune system and metabolism.

# Oscar Pundel

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Oscar Pundel is a Postdoctoral Fellow at NYU Langone Health, in the laboratory of Ben Neel, conducting research in syngeneic novel organoid models of high grade serous ovarian carcinoma, analysis of their in vitro intrinsic properties (growth, differentiation, drug responses, etc.) and their in vivo extrinsic responses (TME immune analysis, DNA damage evolution, response to novel therapies, etc.). He received his BS and Master's degrees from the Ecole Polytechnique Federale de Lausanne, in Chemistry and Molecular and Biological Chemistry, respectively, and his PhD in Biophysics from Queen Mary University of London.

# Jean-Baptiste Reynier

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Jean-Baptiste Reynier is a 3<sup>rd</sup> year PhD student in the Department of Biomedical Informatics at Columbia University, where he is advised by Pr. Raul Rabadan. He received his B.S. in genetics and his M.S. in computer science at the University of Chicago. JB is focused on developing computational methods to interrogate cancer immunity."

# Artem Smirnov

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Dr Artem Smirnov is a researcher at University of Rome "Tor Vergata". He received his PhD from the same University in 2017, after which he worked as a postdoctoral fellow in Prof Xin Lu lab at University of Oxford (UK). During that period he studied interplay between p63 and iASPP in skin carcinogenesis as well as p53-dependent regulation of human oncogenic viruses such as EBV. Since 2022 he is a Researcher (RTDa) at University of Rome "Tor Vergata" in Prof Eleonora Candi's lab, where he studies the role of p63 in regulation chromatin accessibility in bladder cancer.

#### Jaiyu Su

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Jiayu Su is a PhD student in Systems Biology at Columbia University working on new computational tools for emerging genomic technologies. Focusing on cancer omics data, he is particularly interested in learning insights from the tumor microenvironment with spatial omics and deciphering the nexus between aging and tumorigenesis.

#### Vinay Swamy

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Vinay Swamy is a 4th year PhD student in the Biomedical Informatics department at Columbia University. Prior to Columbia he received his BS in Biochemistry from the University of California, Los Angeles and worked as a data analyst at the National Eye Institute. His research interests lie in the application of molecular large language models to problems in biology and healthcare.

#### Barbara Wolkowiak

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Barbara Wolkowiak is studying Biological Natural Sciences at Cambridge. She specialised in Genetics, and is currently pursuing a Masters in Systems Biology. She is interested in the role of the immune system in shaping the dynamics of clonal haematopoiesis.

#### Estelle Yao

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Estelle Yao is a computational biology PhD student co-mentored by Drs. Benjamin Greenbaum and Jeffery Ravetch at Memorial Sloan Kettering Cancer Institute and Rockefeller University. She received her Bachelor's and Master's training in math and biology. Her current research focuses on how transposable elements shape the human genome and contribute to cancer immunity.

# Contacts

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#### Giovanni Blandino

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#### Jamie Blundell

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#### Eleonora Candi

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#### Francesca Croce

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#### Giannino Del Sal

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#### Ben Greenbaum

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Cancer Convergence Educational Network (CCEN) & University of Rome "Tor Vergata"

# Symposium on Cancer Challenges

17-19 May 2024 Frascati, Italy

# Program

May 17th	<b>Symposium</b> (5 min flash talks + discussion) Venue: Villa Mondragone
9 <sup>00</sup> -10 <sup>00</sup>	Panel on <b>Dark Genome and Epigenetics: a role for p53?</b> Panelists   Ben Greenbaum (chair), Scott Lowe, Andrei Gudkov, Giuseppe Novelli
10 <sup>00</sup> -11 <sup>00</sup>	Panel on <b>The communication between Immunology, Neurobiology and</b> <b>Cancer</b> Panelists   Pierluigi Nicotera (chair), Gerry Melino
11 <sup>00</sup> -12 <sup>00</sup>	Panel on <b>Al in Cancer Research</b> Panelists   Raul Rabadan (chair), Pierluigi Nicotera, Roberto Basili
12 <sup>00</sup> -12 <sup>15</sup>	Coffee Break
12 <sup>15</sup> -13 <sup>15</sup>	Panel on <b>How does p53 make choices? Life, Repair or Death?</b> Panelists   Gigi Lozano (chair), Giovanni Blandino, Eleonora Candi, Giannino Del Sal, Nick Barlev
13 <sup>15</sup> -14 <sup>30</sup>	Lunch
14 <sup>30</sup> -15 <sup>00</sup>	Art Lecture by Francesca Croce (Vienna): A Scientist's Thirst for Discovery and Baroque Painting
15 <sup>00</sup> -16 <sup>00</sup>	Rector Ceremony, Nathan Levialdi Ghiron Honorary Doctorate to Dr Pierluigi Nicotera, DZNE, Bonn
16 <sup>00</sup> -16 <sup>15</sup>	Coffee Break
16 <sup>15</sup> -17 <sup>15</sup>	Panel on <b>p53: Mutations and Polymorphisms, Li-Fraumeni Syndrome,</b> <b>Metabolism &amp; Tumorigenesis</b> Panelists   Pierre Hainaut (chair), David Malkin, Roberto Basili, Giovanni Blandino, Giannino Del Sal
17 <sup>15</sup> -18 <sup>15</sup>	Panel on <b>The role of p53 in Stem Cells and Aging</b> Panelists   David Lane (chair), Carol Prives, Jamie Blundell
18 <sup>15</sup> -18 <sup>30</sup>	Carol Prives, Ben Greenbaum, Gerry Melino: What are we learning?

	Talks on selected topics
May 18th	Venue: Villa Tuscolana
9 <sup>00</sup> -9 <sup>25</sup>	TP53 variants in the UK Biobank
	Hamish MacGregor
9 <sup>25</sup> -9 <sup>50</sup>	An evolutionary view of transposable elements in shaping TP53 transcriptional
	network
	Ning (Estelle) Yao
9 <sup>50</sup> -10 <sup>15</sup>	p63 targets in bladder cancer Artem Smirnov
10 <sup>15</sup> -10 <sup>40</sup>	<b>p63, ZNF750 cooperation in lipid metabolism</b> Massimiliano Agostini
10 <sup>40</sup> -11 <sup>05</sup>	FOXM1-dependent Histone linker H1B distinguishes between epidermal stem cells and their progeny Elena Enzo
11 <sup>05</sup> -11 <sup>30</sup>	Coffee Break
11 <sup>30</sup> -11 <sup>55</sup>	Looking for evidence of immune surveillance during healthy ageing Barbara Walkowiak
11 <sup>55</sup> -12 <sup>20</sup>	Fundamental immune-oncogenicity trade-offs define driver mutation fitness David Hoyos
	Metabolite availability and antigen affinity can couple to distort the T cell
12 <sup>20</sup> -12 <sup>45</sup>	repertoire
	Stephen Martis
12 <sup>45</sup> -14 <sup>00</sup>	Lunch
14 <sup>00</sup> -14 <sup>25</sup>	Developing a machine learning model of drug response in patient derived tumor cultures
	Vinay Swamy
14 <sup>25</sup> -14 <sup>50</sup>	AI-Driven Transcriptomic Encoders: From Explainable Models to Accurate, Sample- Independent Cancer Diagnostics Danilo Croce
14 <sup>50</sup> -15 <sup>15</sup>	Weakly supervised learning of biological structures in multi-omics data Jaiyu Su
15 <sup>15</sup> -15 <sup>35</sup>	Coffee Break
15 <sup>35</sup> -16 <sup>00</sup>	HLAScope: Quantifying the Peptide Subspace Coverage Advantage in Virus Associated Cancers Mick Aitken
16 <sup>00</sup> -16 <sup>25</sup>	mxTRex: Uncovering T-cell transcriptional programs associated with antigen specificity in single cell genomics Jean Baptiste Reynier
16 <sup>25</sup> -16 <sup>50</sup>	Language models in cancer genetics Xi Fu
16 <sup>50</sup> -17 <sup>15</sup>	Genomic evolution of High Grade Serous Ovarian Carcinoma Oscar Pundel
17 <sup>15</sup> -17 <sup>30</sup>	<b>Conclusive Remarks</b> - Giovanni Blandino, Giannino Del Sal, Eleonora Candi, Gerry Melino
May 19th	Informal Discussions Venue: Villa Tuscolana