CANCER, DEVELOPMENT AND COMPLEXITY (CDAC 2018)

Lake Como School of Advanced Studies - May 22 - 25, 2018

Home

Cancer is a complex disease involving several intertwined phenomena and events, which collude to unleash the tumor cells inherent programs to proliferate, live, and move; thus, it is the malfunction of the biomolecular machinery responsible for the "checks and balances", normally governed by various complex feedback loops among a population of various cell types. Breakdown of this machinery leads to uncontrolled growth of a cell population being selected by evolutionary pressure that ultimately costs the very survival of the host.

Understanding the many intricacies of all these interactions at the subcellular, cellular and tissue levels has greatly benefitted from the ever-improving applications of algorithmic, statistical and mathematical modeling tools. Moreover, during the past 15 years, new measurement technology for gene expression and, more recently, "deep" genome sequence data, have produced vast amount of data, waiting to be analyzed to deliver new interpretations. The design of novel "wet" experiments and appropriately matched algorithmic, statistical and mathematical modeling tools are expected to become the key to successful oncological science and practice.

The Workshop and School on Cancer Development and Complexity seeks to convene researchers from various related disciplines to explore multiple facets of the challenges posed by cancer a "disease of the systems." The workshop will provide opportunities for the researchers to exchange new ideas and viewpoints, forge new collaborations and train the next generation of young scientists.

Participants are encouraged to present their work in two sessions and poster presentations that will be held during the workshop.

The program will provide an introduction to both cancer biology and mathematical and statistical methods used in analyzing the datasets currently being produced by several laboratories around the world. Next the program will provide an opportunity to interact with world renowned cancer and bioinformatics researchers and the chance for attendees to present their current work. Finally, all the attendees will receive a certificate of completion of the School.

School Directors

- **Marco Antoniotti**
  BIMIB, Dipartimento di Informatica, Sistemistica e Comunicazione, Università degli Studi di Milano-Bicocca, Milan, Italy.
- **Bud Mishra**
  Courant Institute of Mathematical Sciences, and Tandon School of Engineering, NYU, New York, NY, USA.

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Lake Como School of Advanced Studies - May 24 - 25, 2018

Schedule

Preliminary schedule as of May 23, 2018.

Tuesday, May 22nd, 2018

- 12:00 onward: Registration
- 13.00: Welcome Address, Aperitif and Lunch
- 14.00: Marco Antoniotti and Bud Mishra: Cancer Development and Complexity
- 15.00: Bud Mishra, Courant Institute of Mathematical Sciences and Tandon School of Engineering, New York University, New York, USA
  [Tutorial]: Self vs Non-self, Information Asymmetry, Signaling Games and Immunology

  I will introduce a mathematical (game theoretic model) of immune systems, with Dendritic and Macrophage playing the roles of sender-receiver pairs and B-cells and T-cells playing the roles of recommender-verifier pairs respectively. I will also delve into the evolution of this complex systems, while distinguishing between jawed and jawless fish. This will help in understanding various issues related to immunotherapy for cancer.

- 16.00: Coffee Break
- 16:30: Abel David González-Pérez, IRB, Barcelona, Spain
  [Tutorial]: Functional annotation of cancer mutations

  We will first define driver mutations in cancer using the Darwinian evolutionary model of tumors. Then, using several computational methods (such as OncodriveFML,) to identify genes under positive selection across cohorts of tumors, we will identify genes driving several malignancies. Then, we will use tools to annotate the functional impact of individual mutations affecting these driver genes, and we will exploit this information as well as accumulated prior knowledge on tumorigenesis to systematically and accurately pinpoint the most likely driver mutations in each cohort. To this end we will employ platforms IntOGen, COSMIC, the cbioportal, the Cancer Genome Interpreter and other platforms. Finally, we will use known and potential biomarkers of anti-cancer drug response to identify clinically actionable mutations in tumors under study. In this endeavor, we will use repositories of biomarkers such as CIViC, cbioportal, and the Cancer Genome Interpreter.
- 17:30: Daily Wrap-up

Wednesday, May 23rd, 2018

- 9:30: Gabriele Dubini, Laboratory of Biological Structure Mechanics, Politecnico di Milano, Milan, Italy
  [Tutorial]: Microfluidic Technologies for Single Cell Manipulation

  Over the past 15 years, the advances in microfluidic technologies have spearheaded the integration of several laboratory functions on a single integrated circuit, the so called 'lab-on-a-chip'. The effective and efficient design of such devices is now possible by means of a combination of numerical simulation, microfabrication technologies and in vitro characterization. In particular, devices for single cell manipulation are now available, which are exploited in many biological fields, including research on cancer.In this tutorial I will give an overview of the physics of the microfluidic environment, will describe the main microfabrication technologies currently adopted, and will address the design issues of microfluidic devices for biotechnological applications.
- 10:30: Coffee Break
- 11:00: Abel David González-Pérez, IRB, Barcelona, Spain
  [Lecture]: Computational genomics at the heart of cancer biology

  In our lab, we use data on genomic mutations in tumors in three main lines of research. First, we study the distribution of mutations across different regions in the genome to understand basic questions about molecular biology, such as the interplay between DNA damage and repair, and other cellular processes. (I will briefly present one example of this basic research.) This helps us build refined models of the expected background mutation rate of different genomic elements across cell types. Comparing these models with the observed mutational patterns of genomic elements across cohorts of tumors, we are then able to detect which of them are under positive selection in the process of tumorigenesis. We go one further step to identify which amongst all the mutations (point mutations and structural variants) of these elements detected in a particular tumor are actually tumorigenic. (I will present our work on unraveling the panorama of driver mutations of more than 2500 tumor whole genomes.) Translating this basic knowledge in ways that may bridge the gap to personalized cancer medicine is the third line of research in the lab. We search for the potential clinical significance of individual driver mutations, and we build tools that assist clinical oncologists in therapeutic decision-making. (I will exemplify our translational research with our work on the immune-phenotypes of solid tumors.)
- 12.00: Charles Cantor, Agena Biosciences, Sequenom, Retrotope and Boston University, USA
  [Lecture]
- 13.00: Lunch break
- 14.00: Bertrand Adanve, Ph.D, Genetic Intelligence, Inc, Co-founder & CEO, USA
  [Lecture]: Improvements in the analysis of population admixture

  Artificial intelligence (AI) holds great promise to precisely classify human ancestry and the genetic causes of complex diseases. We have constructed an unsupervised machine learning paradigm that examines the whole genome as a hyper-dense, nonlinear, multidimensional feature space. Our AI system culminates in neurons that can identify an individual's component genetic heritages, which also provide interesting early data about the distribution of the human population. The system holds great potential to help further other use-cases, including use as a tool to better explore and understand oncogenic processes.
- 15.00: Olivier Elemento, Department of Physiology and Biophysics, Weill Cornell Medical College, New York, USA
  [Tutorial]: Network Analysis
- 16.00: Coffee Break
- 16:30: Participants Presentations

Thursday, May 24th, 2018

- 9:30: Daniele Merico, Director of Molecular Genetics, Deep Genomics Inc., Visiting Scientist, The Centre for Applied Genomics (TCAG) / The Hospital for Sick Children (SickKids), Toronto, Canada
  [Tutorial]: Making sense of cancer somatic SNVs and indels: from variant effects to pathways

  We will review commonly used models and resources for determining variant effects; we will start from gene product annotation using gene models; we will then review the most commonly used models to predict amino acid impact (e.g. SIFT, PolyPhen2, Mutation Assessor, etc…), discuss methodological issues with measuring performance and specific challenges of gain-of-function prediction. Finally, we will briefly review methods for understanding pathway and network-level effects of somatic variants.
- 10:30: Coffee Break
- 11.00:Bud Mishra, Courant Institute of Mathematical Sciences and Tandon School of Engineering, New York University, New York, USA
  [Lecture]: Immune Systems: Genomics
- 12.00: Olivier Elemento, Department of Physiology and Biophysics, Weill Cornell Medical College, New York, USA
  [Lecture]: cancer precision medicine driven by multi-omics, analytics and modeling

  This talk will review the development and implementation of clinical grade (CLIA) whole-exome sequencing based genomic tests for precision cancer medicine and immunotherapy. A novel analytical pipeline will be described that evaluates genomic profiles to unravel the immune landscape of tumors and integrates multi-omics features using machine learning to predict immunotherapy response. Finally, high-throughput single-cell genomic approaches will be presented that dissect the tumor microenvironment and unravel immune repertoires at single-cell resolution.
- 13.00: Lunch
- 14.00: Valentina Boeva, Institut Cochin, Paris, France
  [Tutorial]: Analysis of epigenetics and chromatin states in normal and cancer cells

  I will talk about the role of chromatin modifications in normal and cancer cells: DNA methylation and histone modifications. I will also present the first steps of bioinformatics analysis of ChIP-seq data needed to characterize histone modification profiles.
- 15.00: Participants Presentations
- 16.00: Coffee Break
- 16:30: Participants Presentations
- 19:30: Social Dinner (location: 'Gesumin' Restaurant – via Cinque Giornate 46, Como)

Friday, May 25th, 2018

- 9:30: Valentina Boeva, Institut Cochin, Paris, France
  [Lecture]: Analysis of neuroblastoma super-enhancer landscape identifies two distinct malignant cell types

  We analyzed super-enhancer landscape in 25 neuroblastoma cell lines and six patient-derived mouse xenografts. We detected transcription factors that constitute the core neuroblastoma regulatory circuitries and drive expression of genes determining cell identity in neuroblastoma. Based on the super-enhancer landscape, we defined two neuroblastoma cell identity subtypes. These subtypes have different sensitivity to chemotherapy. Using single cell experiments, we showed that these two epigenetically and transcriptionally different cell identity may coexist within the same patient.
  Reference: Boeva et al, Heterogeneity of neuroblastoma cell identity defined by transcriptional circuitries, Nature Genetics, 2017, 49(9):1408-1413.
- 10:30: Coffee break
- 11.00: Daniele Merico, Director of Molecular Genetics, Deep Genomics Inc., Visiting Scientist, The Centre for Applied Genomics (TCAG) / The Hospital for Sick Children (SickKids), Toronto, Canada
  [Lecture]: Non-coding somatic variant rewiring transcriptional regulation in cancer

  We will examine how difficult it is to predict transcription factor binding changes using in-silico predictors (DeepBind, DeepSEA, etc.) and an allele-specific binding benchmark. We will then review a couple of recent research papers looking at non-coding variants causing transcriptional regulation rewiring in cancer.
- 12.00: Round Table and Wrap-up
- 13.00: Closing lunch

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Speakers

- **Valentina Boeva**
  Institut Cochin, Paris, France
  Valentina Boeva is a group leader at the Institut Cochin / Inserm U1016, Paris. The research objective of her team is to understand the link between genetic and epigenetic changes in cancer and decipher the role of epigenetic modifications in cancer development and progression. The team welcomes both experimental and bioinformatics approaches. Valentina and her group designed and implemented bioinformatics tools in two main areas: (i) Analysis of genomic alterations in cancer genomes: FREEC/Control-FREEC, SVDetect, SV-Bay, ONCOCNV, QuantumClone; and (ii) Analysis of ChIP-seq data: MICSA, HMCan, HMCan-diff and Nebula (http://boevalab.com/tools.html). The team also develops computational techniques for integration of high-throughput data applied to cancer research.
- **Charles Cantor**
  Agena Biosciences, Sequenom, Retrotope and Boston University, USA
  Dr. Charles Cantor is a co-founder, and retired Chief Scientific Officer at SEQUENOM, Inc., the leading provider of noninvasive prenatal diagnostic testing. He consults for a number of biotech companies including SEQUENOM, AgenaBiosciences, Strand Life Sciences, Trovagene, Ann Jema, ProdermIQ, In Silico Biology, and he is executive director of Retrotope. (which he also co-founded) Dr. Cantor is professor emeritus of Biomedical Engineering and of Pharmacology and was the director of the Center for Advanced Biotechnology at Boston University. He is currently adjunct professor of Bioengineering at UC San Diego, adjunct professor of Molecular Biology at the Scripps Institute for Research, distinguished adjunct professor of Physiology and Biophysics at UC Irvine and adjunct professor at the Moscow institute of Physics and Technology. Prior to this, Dr. Cantor held positions in Chemistry and then in Genetics and Development at Columbia University and in Molecular Biology at the University of California at Berkeley. Cantor was educated in chemistry at Columbia College (AB) and at the University of California Berkeley (PhD). Dr. Cantor has been granted more than 60 US patents and, with Paul Schimmel, wrote a three-volume textbook on biophysical chemistry. He also co-authored the first textbook on Genomics titled 'The Science and Technology of the Human Genome Project'. In addition, he has published more than 450 peer-reviewed articles, and is a member of the U.S. National Academy of Sciences. and The National Academy of Inventors. His major scientific accomplishments include the development of pulsed field electrophoresis, immuno-PCR, affinity capture electrophoresis, the earliest uses of FRET to characterize distances in protein complexes and nucleic acids, the standard methods for assaying and purifying microtubule protein, various applications of nucleic acid mass spectrometry, and methods for noninvasive prenatal diagnostics. He is also considered to be one of the founders of the new field of synthetic biology.
- **Gabriele Dubini**
  LaBS, Politecnico di Milano, Milan, Italy
  Gabriele Dubini received his master degree (MSc) in Mechanical Engineering cum laude in 1988 and his PhD degree in Bioengineering in 1993 from Politecnico di Milano, Milan, Italy.
  In 1993 and 1994 he worked as a Research Assistant in the Cardiothoracic Unit of Great Ormond Street Hospital for Children – NHS Trust, London, UK. An Assistant Professor of Thermodynamics and Heat Transfer at the Energy Engineering Department of Politecnico di Milano (1996), he was then appointed Associate Professor (2001) and Full Professor (2007) of Bioengineering at Politecnico di Milano.
  From 2003 to 2007 Gabriele Dubini was the Director of the Laboratory of Biological Structure Mechanics (LaBS, www.labsmech.polimi.it) of Politecnico di Milano. He was a member of the Scientific Panel of the Coordination Centre on NanoBiotechnologies and Nanomedicine at Politecnico di Milano from 2007 to 2012. From 2008 to 2012 he was a member (elected) of the Council of the European Society of Biomechanics (ESB) and the Secretary-General for the 2010-12 biennium. Former Coordinator of the Biological Engineering Section at the Department of Chemistry, Materials and Chemical Engineering 'Giulio Natta' (2013-2017), he has been recently appointed the Deputy Director of the Department.
  Most of Gabriele Dubini's research activity has dealt with experimental and computational Biomechanics. His research has covered a number of topics, such as microcirculation, the hemodynamic optimization of blood circulation after pediatric cardiac surgery procedures, heat and mass transfer in tissues and medical devices, preoperative planning of minimally invasive vascular procedures. His most recent research interests are in the field of the design and characterization of microfluidic devices for medical and biotechnological applications.
- **Olivier Elemento**
  Department of Physiology and Biophysics, Weill Cornell Medical College, New York, USA
  I direct the Englander Institute for Precision Medicine, an Institute that focuses on using genomics and informatics to make medicine more individualized. My research group and I combine Big Data with experimentation and genomic profiling to accelerate the discovery of cancer cures. In cancers, we are elucidating the patterns of aberrant pathway activities, rewiring of regulatory networks and cancer mutations that have occurred in cancer cells. We are also trying to understand how tumors evolve at the genomic and epigenomic level. We use high-throughput sequencing (ChIP-seq, RNA-seq, bisulfite conversion followed by sequencing – specifically RRBS-, ATAC-seq, exome capture and sequencing, single cell RNAseq using DropSeq) to decipher epigenetic mechanisms and regulatory networks at play in malignant cells and study how they affect gene expression. Our research has led to the development of the first New York State approved whole exome sequencing test for oncology, which is now used routinely on patients treated at Weill Cornell Medicine/NewYork Presbyterian Hospital. I have had the privilege to mentor over 15 wonderful Weill Cornell graduate students and postdoctoral fellows.
- **Abel David González-Pérez** IRB, Barcelona, Spain
  Biochemist with a PhD in Bioinformatics, with more than 40 articles published in international peer-reviewed journals. He main expertise area is cancer genomics, with seven years of postdoctoral experience within Dr. Nuria Lopez-Bigas lab. He is currently a Ramon y Cajal fellow and a Research Associate within the lab, which is within the Institute for Research in Biomedicine (IRB Barcelona). He has participated in several international cancer genomics initiatives, such as The Cancer Genome Atlas (TCGA), and the International Cancer Genome Consortium (ICGC), and he is currently part of the scientific committee of the Spanish Group of Breast Cancer Research.
- **Bertrand Adanve** Genetic Intelligence, Inc, New York, USA
  CEO and co-Founder of Genetic Intelligence, a New York-based startup that is pioneering AI-based genetic systems that pinpoint the causal genetic features at the basis of inherited disease in order to bring about curative therapeutics and swift diagnostics for everyone. Bertrand holds a Ph.D in chemistry and bioengineering from Columbia University. His varied experience include leading a residential construction business to pay for college, extensive work with biotech-startup incubator Acidophil, and management consultancy at McKinsey & company. He delights in self-learning including history, AI applications, and distributed systems.
- **Daniele Merico**
  Director of Molecular Genetics, Deep Genomics Inc., Toronto, Canada
  Daniele Merico received his Bachelor's degree in Molecular Biotechnology and his Master's degree in Bioinformatics from Universita di Milano-Bicocca (2003 and 2005, respectively). He then received his Molecular and Cellular Biology PhD from Universita di Milano (2009).

  Daniele Merico was a post-doctoral fellow under the supervision of Drs. Gary D. Bader and Andrew Emili (Donnelly Centre, University of Toronto, Toronto, Canada) from 2009 to 2011. His post-doctoral activity focused on pathway and network analysis of gene expression microarray and proteomics data applied to cardiomiopathy and tumor mouse models.

  Since 2011, Daniele Merico manages the bioinformatics core facility at TCAG (The Centre for Applied Genomics, Hospital for Sick Children, Toronto, Canada), under the direction of Dr. Stephen W. Scherer. As a core facility manager, he is responsible for the next generation sequencing (NGS) analysis pipelines, including human whole exome and whole genome resequencing and variant annotation, RNA-seq, ChIP-seq, methyl-seq, de-novo transcriptome and genome assembly. His current research interests are focused on genome annotation for clinical applications, disease gene discovery for rare disorders, as well as pathway/network analysis of rare genetic variants in autism and schizophrenia.

  Daniele Merico has authored or co-authored 18 peer-reviewed Pubmed-indexed journal articles, 3 peer-reviewed journal articles indexed by other services, as well as 4 peer-reviewed articles published as conference proceedings.

- **Bud Mishra**
  Courant Institute of Mathematical Sciences, Tandon School of Engineering, NYU, New York, USA
  Professor Bud Mishra is an educator, an inventor, and a mentor to technologists, entrepreneurs, and scientists. Professor Mishra founded the NYU/Courant Bioinformatics Group, a multidisciplinary group working on research at the interface of computer science, applied mathematics, biology, biomedicine, and bio/nanotechnologies as well as the Tandon-Online program on Bioinformatics Engineering. He has industrial experience in computer and data science (aiNexusLab, ATTAP, behold.ai, brainiad, Genesis Media, Pypestream, and Tartan Laboratories), finance (Instadat, Pattern Recognition Fund, and Tudor Investment), robotics, and bio/nanotechnologies (Abraxis, Bioarrays, InSilico, MRTech, OpGen, and Seqster).
  Professor Mishra is currently a professor of computer science and mathematics at NYU's Courant Institute of Mathematical Sciences, professor of engineering at NYU's Tandon School of Engineering, professor of human genetics at MSSM Mt. Sinai School of Medicine, visiting scholar in quantitative biology at CSHL Cold Spring Harbor Laboratory, and professor of cell biology at NYU SoM School of Medicine. He has a degree in science from Utkal University, in electronics and communication engineering from IIT, Kharagpur, and MS and PhD degrees in computer science from Carnegie Mellon University. He is a fellow of IEEE, ACM, AAAS, and National Academy of Inventors (NAI), a Distinguished Alumnus of IIT (Kharagpur), and a NYSTAR Distinguished Professor

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Accommodations

A few rooms have been blocked in 3-star **hotels in Como**, with rates ranging from 75 to 120 euros per night (breakfast included), and in a nearby **Hostel**.

The **School Secretariat** will take care of the accommodation of the accepted students who have accomplished the payment of the fee, and who have filled out and sent a suitable **accommodationCDAC2018** before April 10, 2018.

For any help or additional information please contact the Organizing Secretariat:
francesco.camporini@fondazionealessandrovolta.it

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Registration

Registration fees include participation to the school, social events, coffee breaks and school material.

Early registration (until April 1st, 2018): 350.00 EUR
Regular registration (after April 1st, 2018): 400.00 EUR (*)
Daily, on site registration: 100 EUR (social dinner extra)

(*) Participants affiliated with the four Universities supporting the Lake Como School (Milano Statale, Pavia, Milano Bicocca and Insubria) qualify for a 320.00 EUR registration fee.

All fees include VAT.

REGISTRATION ARE CLOSED

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Venue

Lake Como School of Advanced Studies, Villa del Grumello, Como, Italy.

Placed in a central position within Europe, close to four international airports, it is hosted in an outstanding old noble palace located on the shoreline of beautiful Lake Como. The School is an international research facility running short term programs on a wide range of interdisciplinary subjects, sharing a common focus on complex systems. The School attracts leading scholars in different fields including: physics, biology, economics, sociology, geopolitics, education, environmental and development studies, to engage in collaborative research. In small teams, visitors explore questions at the cutting edge of science and knowledge. In a context of globalization and in front of the increasing interaction between various kinds of networks, the analysis of complex systems offers insights into economic development, social cohesion and the environment on many geographical scales.

Venue The school will be held at Villa del Grumello, Via per Cernobbio 11, Como (Italy).

HOW TO GET THERE: http://lakecomoschool.org/contact/travel-info/

Villa del Grumello is 20 min on foot from Como city center – you can also take a bus, lines 6 and 11 (bus stop: "Como Via Regina Piscine Villa Olmo", just after "Villa Olmo").

From the main Train Station (Como S. Giovanni), the nearest bus stop to catch line 6 and 11 is "Piazzale Rocchetto".

View larger map

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Presentations

Here you can find links to the presentations given during CDAC 2018.

Speakers

- Valentina Boeva Analysis of Epigenetics Chromatin States,
  Discovery of Two States of Neuroblastoma
- Cantor The Challenge of Early Cancer Detection via Liquid Biopsies
- Dubini Microfluidics Technologies for Single Cells Manipulations
- Elemento A Cancer Precision Medicine Program
- Merico Optimal Scoring of Variants Altering Transcription Factors,
  Making Sense of Cancer Somatic SNVs and DELs
- Mishra Immune System: Part A,
  Immune System Part B
- Perez-Gonzalez Understanding Cancer Genomes: From Mutational Processes to Tumor Evolution,
  Interpretation of Cancer Genomes in the Clinical Setting

Other Presentations

- Angaroni Optimal Control of Chronic Myeloid Leukemia Treatment
- Antoniotti Reconstructing Cancer Progression Models from Bulk and Single-cell Data with TRaIT
- Ciccolella Inferring Cancer Progression from Single Cell Sequencing while Allowing for Loss of Mutations
- Pellegrini Clustering/Community Detection in Large Protein-Protein Interaction Networks

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- 9:30: Gabriele Dubini, Laboratory of Biological Structure Mechanics, Politecnico di Milano, Milan, Italy
  [Tutorial]: Microfluidic Technologies for Single Cell Manipulation

  Over the past 15 years, the advances in microfluidic technologies have spearheaded the integration of several laboratory functions on a single integrated circuit, the so called 'lab-on-a-chip'. The effective and efficient design of such devices is now possible by means of a combination of numerical simulation, microfabrication technologies and in vitro characterization. In particular, devices for single cell manipulation are now available, which are exploited in many biological fields, including research on cancer.In this tutorial I will give an overview of the physics of the microfluidic environment, will describe the main microfabrication technologies currently adopted, and will address the design issues of microfluidic devices for biotechnological applications.
- 10:30: Coffee Break
- 11:00: Abel David González-Pérez, IRB, Barcelona, Spain
  [Lecture]: Computational genomics at the heart of cancer biology

  In our lab, we use data on genomic mutations in tumors in three main lines of research. First, we study the distribution of mutations across different regions in the genome to understand basic questions about molecular biology, such as the interplay between DNA damage and repair, and other cellular processes. (I will briefly present one example of this basic research.) This helps us build refined models of the expected background mutation rate of different genomic elements across cell types. Comparing these models with the observed mutational patterns of genomic elements across cohorts of tumors, we are then able to detect which of them are under positive selection in the process of tumorigenesis. We go one further step to identify which amongst all the mutations (point mutations and structural variants) of these elements detected in a particular tumor are actually tumorigenic. (I will present our work on unraveling the panorama of driver mutations of more than 2500 tumor whole genomes.) Translating this basic knowledge in ways that may bridge the gap to personalized cancer medicine is the third line of research in the lab. We search for the potential clinical significance of individual driver mutations, and we build tools that assist clinical oncologists in therapeutic decision-making. (I will exemplify our translational research with our work on the immune-phenotypes of solid tumors.)
- 12.00: Charles Cantor, Agena Biosciences, Sequenom, Retrotope and Boston University, USA
  [Lecture]
- 13.00: Lunch break
- 14.00: Bertrand Adanve, Ph.D, Genetic Intelligence, Inc, Co-founder & CEO, USA
  [Lecture]: Improvements in the analysis of population admixture

  Artificial intelligence (AI) holds great promise to precisely classify human ancestry and the genetic causes of complex diseases. We have constructed an unsupervised machine learning paradigm that examines the whole genome as a hyper-dense, nonlinear, multidimensional feature space. Our AI system culminates in neurons that can identify an individual's component genetic heritages, which also provide interesting early data about the distribution of the human population. The system holds great potential to help further other use-cases, including use as a tool to better explore and understand oncogenic processes.
- 15.00: Olivier Elemento, Department of Physiology and Biophysics, Weill Cornell Medical College, New York, USA
  [Tutorial]: Network Analysis
- 16.00: Coffee Break
- 16:30: Participants Presentations

Thursday, May 24th, 2018

- 9:30: Daniele Merico, Director of Molecular Genetics, Deep Genomics Inc., Visiting Scientist, The Centre for Applied Genomics (TCAG) / The Hospital for Sick Children (SickKids), Toronto, Canada
  [Tutorial]: Making sense of cancer somatic SNVs and indels: from variant effects to pathways

  We will review commonly used models and resources for determining variant effects; we will start from gene product annotation using gene models; we will then review the most commonly used models to predict amino acid impact (e.g. SIFT, PolyPhen2, Mutation Assessor, etc…), discuss methodological issues with measuring performance and specific challenges of gain-of-function prediction. Finally, we will briefly review methods for understanding pathway and network-level effects of somatic variants.
- 10:30: Coffee Break
- 11.00:Bud Mishra, Courant Institute of Mathematical Sciences and Tandon School of Engineering, New York University, New York, USA
  [Lecture]: Immune Systems: Genomics
- 12.00: Olivier Elemento, Department of Physiology and Biophysics, Weill Cornell Medical College, New York, USA
  [Lecture]: cancer precision medicine driven by multi-omics, analytics and modeling

  This talk will review the development and implementation of clinical grade (CLIA) whole-exome sequencing based genomic tests for precision cancer medicine and immunotherapy. A novel analytical pipeline will be described that evaluates genomic profiles to unravel the immune landscape of tumors and integrates multi-omics features using machine learning to predict immunotherapy response. Finally, high-throughput single-cell genomic approaches will be presented that dissect the tumor microenvironment and unravel immune repertoires at single-cell resolution.
- 13.00: Lunch
- 14.00: Valentina Boeva, Institut Cochin, Paris, France
  [Tutorial]: Analysis of epigenetics and chromatin states in normal and cancer cells

  I will talk about the role of chromatin modifications in normal and cancer cells: DNA methylation and histone modifications. I will also present the first steps of bioinformatics analysis of ChIP-seq data needed to characterize histone modification profiles.
- 15.00: Participants Presentations
- 16.00: Coffee Break
- 16:30: Participants Presentations
- 19:30: Social Dinner (location: 'Gesumin' Restaurant – via Cinque Giornate 46, Como)

Friday, May 25th, 2018

- 9:30: Valentina Boeva, Institut Cochin, Paris, France
  [Lecture]: Analysis of neuroblastoma super-enhancer landscape identifies two distinct malignant cell types

  We analyzed super-enhancer landscape in 25 neuroblastoma cell lines and six patient-derived mouse xenografts. We detected transcription factors that constitute the core neuroblastoma regulatory circuitries and drive expression of genes determining cell identity in neuroblastoma. Based on the super-enhancer landscape, we defined two neuroblastoma cell identity subtypes. These subtypes have different sensitivity to chemotherapy. Using single cell experiments, we showed that these two epigenetically and transcriptionally different cell identity may coexist within the same patient.
  Reference: Boeva et al, Heterogeneity of neuroblastoma cell identity defined by transcriptional circuitries, Nature Genetics, 2017, 49(9):1408-1413.
- 10:30: Coffee break
- 11.00: Daniele Merico, Director of Molecular Genetics, Deep Genomics Inc., Visiting Scientist, The Centre for Applied Genomics (TCAG) / The Hospital for Sick Children (SickKids), Toronto, Canada
  [Lecture]: Non-coding somatic variant rewiring transcriptional regulation in cancer

  We will examine how difficult it is to predict transcription factor binding changes using in-silico predictors (DeepBind, DeepSEA, etc.) and an allele-specific binding benchmark. We will then review a couple of recent research papers looking at non-coding variants causing transcriptional regulation rewiring in cancer.
- 12.00: Round Table and Wrap-up
- 13.00: Closing lunch

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CANCER, DEVELOPMENT AND COMPLEXITY (CDAC 2018)

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Speakers

- **Valentina Boeva**
  Institut Cochin, Paris, France
  Valentina Boeva is a group leader at the Institut Cochin / Inserm U1016, Paris. The research objective of her team is to understand the link between genetic and epigenetic changes in cancer and decipher the role of epigenetic modifications in cancer development and progression. The team welcomes both experimental and bioinformatics approaches. Valentina and her group designed and implemented bioinformatics tools in two main areas: (i) Analysis of genomic alterations in cancer genomes: FREEC/Control-FREEC, SVDetect, SV-Bay, ONCOCNV, QuantumClone; and (ii) Analysis of ChIP-seq data: MICSA, HMCan, HMCan-diff and Nebula (http://boevalab.com/tools.html). The team also develops computational techniques for integration of high-throughput data applied to cancer research.
- **Charles Cantor**
  Agena Biosciences, Sequenom, Retrotope and Boston University, USA
  Dr. Charles Cantor is a co-founder, and retired Chief Scientific Officer at SEQUENOM, Inc., the leading provider of noninvasive prenatal diagnostic testing. He consults for a number of biotech companies including SEQUENOM, AgenaBiosciences, Strand Life Sciences, Trovagene, Ann Jema, ProdermIQ, In Silico Biology, and he is executive director of Retrotope. (which he also co-founded) Dr. Cantor is professor emeritus of Biomedical Engineering and of Pharmacology and was the director of the Center for Advanced Biotechnology at Boston University. He is currently adjunct professor of Bioengineering at UC San Diego, adjunct professor of Molecular Biology at the Scripps Institute for Research, distinguished adjunct professor of Physiology and Biophysics at UC Irvine and adjunct professor at the Moscow institute of Physics and Technology. Prior to this, Dr. Cantor held positions in Chemistry and then in Genetics and Development at Columbia University and in Molecular Biology at the University of California at Berkeley. Cantor was educated in chemistry at Columbia College (AB) and at the University of California Berkeley (PhD). Dr. Cantor has been granted more than 60 US patents and, with Paul Schimmel, wrote a three-volume textbook on biophysical chemistry. He also co-authored the first textbook on Genomics titled 'The Science and Technology of the Human Genome Project'. In addition, he has published more than 450 peer-reviewed articles, and is a member of the U.S. National Academy of Sciences. and The National Academy of Inventors. His major scientific accomplishments include the development of pulsed field electrophoresis, immuno-PCR, affinity capture electrophoresis, the earliest uses of FRET to characterize distances in protein complexes and nucleic acids, the standard methods for assaying and purifying microtubule protein, various applications of nucleic acid mass spectrometry, and methods for noninvasive prenatal diagnostics. He is also considered to be one of the founders of the new field of synthetic biology.
- **Gabriele Dubini**
  LaBS, Politecnico di Milano, Milan, Italy
  Gabriele Dubini received his master degree (MSc) in Mechanical Engineering cum laude in 1988 and his PhD degree in Bioengineering in 1993 from Politecnico di Milano, Milan, Italy.
  In 1993 and 1994 he worked as a Research Assistant in the Cardiothoracic Unit of Great Ormond Street Hospital for Children – NHS Trust, London, UK. An Assistant Professor of Thermodynamics and Heat Transfer at the Energy Engineering Department of Politecnico di Milano (1996), he was then appointed Associate Professor (2001) and Full Professor (2007) of Bioengineering at Politecnico di Milano.
  From 2003 to 2007 Gabriele Dubini was the Director of the Laboratory of Biological Structure Mechanics (LaBS, www.labsmech.polimi.it) of Politecnico di Milano. He was a member of the Scientific Panel of the Coordination Centre on NanoBiotechnologies and Nanomedicine at Politecnico di Milano from 2007 to 2012. From 2008 to 2012 he was a member (elected) of the Council of the European Society of Biomechanics (ESB) and the Secretary-General for the 2010-12 biennium. Former Coordinator of the Biological Engineering Section at the Department of Chemistry, Materials and Chemical Engineering 'Giulio Natta' (2013-2017), he has been recently appointed the Deputy Director of the Department.
  Most of Gabriele Dubini's research activity has dealt with experimental and computational Biomechanics. His research has covered a number of topics, such as microcirculation, the hemodynamic optimization of blood circulation after pediatric cardiac surgery procedures, heat and mass transfer in tissues and medical devices, preoperative planning of minimally invasive vascular procedures. His most recent research interests are in the field of the design and characterization of microfluidic devices for medical and biotechnological applications.
- **Olivier Elemento**
  Department of Physiology and Biophysics, Weill Cornell Medical College, New York, USA
  I direct the Englander Institute for Precision Medicine, an Institute that focuses on using genomics and informatics to make medicine more individualized. My research group and I combine Big Data with experimentation and genomic profiling to accelerate the discovery of cancer cures. In cancers, we are elucidating the patterns of aberrant pathway activities, rewiring of regulatory networks and cancer mutations that have occurred in cancer cells. We are also trying to understand how tumors evolve at the genomic and epigenomic level. We use high-throughput sequencing (ChIP-seq, RNA-seq, bisulfite conversion followed by sequencing – specifically RRBS-, ATAC-seq, exome capture and sequencing, single cell RNAseq using DropSeq) to decipher epigenetic mechanisms and regulatory networks at play in malignant cells and study how they affect gene expression. Our research has led to the development of the first New York State approved whole exome sequencing test for oncology, which is now used routinely on patients treated at Weill Cornell Medicine/NewYork Presbyterian Hospital. I have had the privilege to mentor over 15 wonderful Weill Cornell graduate students and postdoctoral fellows.
- **Abel David González-Pérez** IRB, Barcelona, Spain
  Biochemist with a PhD in Bioinformatics, with more than 40 articles published in international peer-reviewed journals. He main expertise area is cancer genomics, with seven years of postdoctoral experience within Dr. Nuria Lopez-Bigas lab. He is currently a Ramon y Cajal fellow and a Research Associate within the lab, which is within the Institute for Research in Biomedicine (IRB Barcelona). He has participated in several international cancer genomics initiatives, such as The Cancer Genome Atlas (TCGA), and the International Cancer Genome Consortium (ICGC), and he is currently part of the scientific committee of the Spanish Group of Breast Cancer Research.
- **Bertrand Adanve** Genetic Intelligence, Inc, New York, USA
  CEO and co-Founder of Genetic Intelligence, a New York-based startup that is pioneering AI-based genetic systems that pinpoint the causal genetic features at the basis of inherited disease in order to bring about curative therapeutics and swift diagnostics for everyone. Bertrand holds a Ph.D in chemistry and bioengineering from Columbia University. His varied experience include leading a residential construction business to pay for college, extensive work with biotech-startup incubator Acidophil, and management consultancy at McKinsey & company. He delights in self-learning including history, AI applications, and distributed systems.
- **Daniele Merico**
  Director of Molecular Genetics, Deep Genomics Inc., Toronto, Canada
  Daniele Merico received his Bachelor's degree in Molecular Biotechnology and his Master's degree in Bioinformatics from Universita di Milano-Bicocca (2003 and 2005, respectively). He then received his Molecular and Cellular Biology PhD from Universita di Milano (2009).

  Daniele Merico was a post-doctoral fellow under the supervision of Drs. Gary D. Bader and Andrew Emili (Donnelly Centre, University of Toronto, Toronto, Canada) from 2009 to 2011. His post-doctoral activity focused on pathway and network analysis of gene expression microarray and proteomics data applied to cardiomiopathy and tumor mouse models.

  Since 2011, Daniele Merico manages the bioinformatics core facility at TCAG (The Centre for Applied Genomics, Hospital for Sick Children, Toronto, Canada), under the direction of Dr. Stephen W. Scherer. As a core facility manager, he is responsible for the next generation sequencing (NGS) analysis pipelines, including human whole exome and whole genome resequencing and variant annotation, RNA-seq, ChIP-seq, methyl-seq, de-novo transcriptome and genome assembly. His current research interests are focused on genome annotation for clinical applications, disease gene discovery for rare disorders, as well as pathway/network analysis of rare genetic variants in autism and schizophrenia.

  Daniele Merico has authored or co-authored 18 peer-reviewed Pubmed-indexed journal articles, 3 peer-reviewed journal articles indexed by other services, as well as 4 peer-reviewed articles published as conference proceedings.

- **Bud Mishra**
  Courant Institute of Mathematical Sciences, Tandon School of Engineering, NYU, New York, USA
  Professor Bud Mishra is an educator, an inventor, and a mentor to technologists, entrepreneurs, and scientists. Professor Mishra founded the NYU/Courant Bioinformatics Group, a multidisciplinary group working on research at the interface of computer science, applied mathematics, biology, biomedicine, and bio/nanotechnologies as well as the Tandon-Online program on Bioinformatics Engineering. He has industrial experience in computer and data science (aiNexusLab, ATTAP, behold.ai, brainiad, Genesis Media, Pypestream, and Tartan Laboratories), finance (Instadat, Pattern Recognition Fund, and Tudor Investment), robotics, and bio/nanotechnologies (Abraxis, Bioarrays, InSilico, MRTech, OpGen, and Seqster).
  Professor Mishra is currently a professor of computer science and mathematics at NYU's Courant Institute of Mathematical Sciences, professor of engineering at NYU's Tandon School of Engineering, professor of human genetics at MSSM Mt. Sinai School of Medicine, visiting scholar in quantitative biology at CSHL Cold Spring Harbor Laboratory, and professor of cell biology at NYU SoM School of Medicine. He has a degree in science from Utkal University, in electronics and communication engineering from IIT, Kharagpur, and MS and PhD degrees in computer science from Carnegie Mellon University. He is a fellow of IEEE, ACM, AAAS, and National Academy of Inventors (NAI), a Distinguished Alumnus of IIT (Kharagpur), and a NYSTAR Distinguished Professor

CANCER, DEVELOPMENT AND COMPLEXITY (CDAC 2018)

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Accommodations

A few rooms have been blocked in 3-star **hotels in Como**, with rates ranging from 75 to 120 euros per night (breakfast included), and in a nearby **Hostel**.

The **School Secretariat** will take care of the accommodation of the accepted students who have accomplished the payment of the fee, and who have filled out and sent a suitable **accommodationCDAC2018** before April 10, 2018.

For any help or additional information please contact the Organizing Secretariat:
francesco.camporini@fondazionealessandrovolta.it

CANCER, DEVELOPMENT AND COMPLEXITY (CDAC 2018)

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Registration

Registration fees include participation to the school, social events, coffee breaks and school material.

Early registration (until April 1st, 2018): 350.00 EUR
Regular registration (after April 1st, 2018): 400.00 EUR (*)
Daily, on site registration: 100 EUR (social dinner extra)

(*) Participants affiliated with the four Universities supporting the Lake Como School (Milano Statale, Pavia, Milano Bicocca and Insubria) qualify for a 320.00 EUR registration fee.

All fees include VAT.

REGISTRATION ARE CLOSED

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Venue

Lake Como School of Advanced Studies, Villa del Grumello, Como, Italy.

Placed in a central position within Europe, close to four international airports, it is hosted in an outstanding old noble palace located on the shoreline of beautiful Lake Como. The School is an international research facility running short term programs on a wide range of interdisciplinary subjects, sharing a common focus on complex systems. The School attracts leading scholars in different fields including: physics, biology, economics, sociology, geopolitics, education, environmental and development studies, to engage in collaborative research. In small teams, visitors explore questions at the cutting edge of science and knowledge. In a context of globalization and in front of the increasing interaction between various kinds of networks, the analysis of complex systems offers insights into economic development, social cohesion and the environment on many geographical scales.

Venue The school will be held at Villa del Grumello, Via per Cernobbio 11, Como (Italy).

HOW TO GET THERE: http://lakecomoschool.org/contact/travel-info/

Villa del Grumello is 20 min on foot from Como city center – you can also take a bus, lines 6 and 11 (bus stop: "Como Via Regina Piscine Villa Olmo", just after "Villa Olmo").

From the main Train Station (Como S. Giovanni), the nearest bus stop to catch line 6 and 11 is "Piazzale Rocchetto".

View larger map

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Presentations

Here you can find links to the presentations given during CDAC 2018.

Speakers

- Valentina Boeva Analysis of Epigenetics Chromatin States,
  Discovery of Two States of Neuroblastoma
- Cantor The Challenge of Early Cancer Detection via Liquid Biopsies
- Dubini Microfluidics Technologies for Single Cells Manipulations
- Elemento A Cancer Precision Medicine Program
- Merico Optimal Scoring of Variants Altering Transcription Factors,
  Making Sense of Cancer Somatic SNVs and DELs
- Mishra Immune System: Part A,
  Immune System Part B
- Perez-Gonzalez Understanding Cancer Genomes: From Mutational Processes to Tumor Evolution,
  Interpretation of Cancer Genomes in the Clinical Setting

Other Presentations

- Angaroni Optimal Control of Chronic Myeloid Leukemia Treatment
- Antoniotti Reconstructing Cancer Progression Models from Bulk and Single-cell Data with TRaIT
- Ciccolella Inferring Cancer Progression from Single Cell Sequencing while Allowing for Loss of Mutations
- Pellegrini Clustering/Community Detection in Large Protein-Protein Interaction Networks