



Cancer development and complexity

May 24-27, 2016 – Lake Como School of Advanced Studies

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Home

Lake Como Workshop and School on Cancer Development and Complexity 2016
May 24 – May 27, 2016 – Villa del Grumello , Como, ITALY
website: <https://cdac.lakecomoschool.org/>

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 Evolution and Complexity convenes 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.

**Workshop and School on
Cancer, Development and Complexity**

**Villa del Grumello
Como**

May 24 – May 27, 2016

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Keynote speakers

Oliva Alberti
Diatech Pharmacogenetics
Italy

Antonina Mitrofanova
Department of Health
Informatics, Rutgers University
USA

Charles Cantor
Agena Biosciences, Sequenom,
Exatropes and Boston University
USA

Bud Mishra
Courant Institute of
Mathematical Sciences, NYU
USA

Giulio Caravagna
School of Informatics
University of Edinburgh, UK

Andrea Sottoriva
The Institute of Cancer
Research, UK

Francesca De Micheli
University of Trento
Italy

Rory Stark
Cancer Research UK
UK

Pietro Liò
University of Cambridge
UK

Giovanni Tonon
San Raffaele Scientific
Institute, Italy

School Directors
Marco Antoniotti
University of Milan-Bicocca, Italy
Bud Mishra
NYU, USA

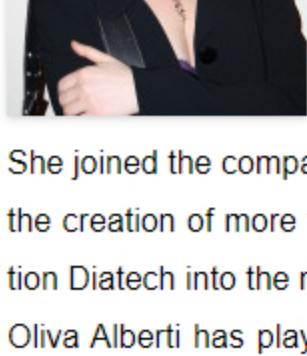
Local organization
Alex Graudenzi
(IBFM-CNR)
Giancarlo Mauri
(University of Milan-Bicocca)
Daniela Ramazzotti
(University of Milan-Bicocca)
Nadia Tassinari
(Fondazione Alessandro Volta)

Registration and Contacts
<http://cdac.lakecomoschool.org>
cdacinfo@disco.unimib.it



Keynote Speakers

Oliva Alberti, CEO Diatech Pharmacogenetics srl



She joined the company in 1998 and was appointed to CEO in 2004. She was actively supporting the creation of more than 7 sister and controlled companies helping to better structure and position Diatech into the molecular diagnostic market.

Oliva Alberti has played a critical role in support the company's growth in the field of molecular diagnostics.

From 1998 to 2014 she operated like project manager into developing the projects financed to the company by the Italian Ministry for University and Research as well as the Industrial once, she was also supporting the filing of the JEV project that the company was presenting to EU in 2002 and the Horizon 2020 project that has been approved by EU in 2015.

She has over 15 years of experience in the biotechnology industry.

Summary, From life science to molecular diagnostics: a tailored approach

Diagnostic laboratories face a major challenge in being able to provide rapid, sensitive and state of the art molecular tests. We developed a novel mass spectrometry multiplexed genotyping solution named Myriapod® to concurrently assess single nucleotide polymorphisms in most clinically relevant cancer gene.

The CE IVD system has been developed taking into consideration the diagnostic needs of the laboratories, the usability inside a routine diagnostic environment and it is a complete solution that includes instruments, accessories, software and reagents.

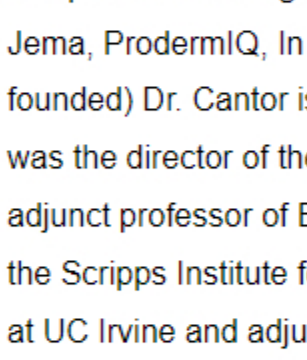
To evaluate and validate the systems, the research and development activities have been performed systematically addressing sensitivity, specificity, and reproducibility of our platform.

Our Myriapod® solution is a high throughput and robust tool, allowing genotyping for targeted therapy selection with a practical turnaround time of 8 working hours.

The system can provide an immediate, accurate and cost effective multiplex approach for clinically relevant gene mutation analysis using the state of the art technology in mutation analysis in multiplexing Mass Spectrometry.

Charles Cantor, PhD, Agena Biosciences, Sequenom, Retrotopo and

Boston University, USA



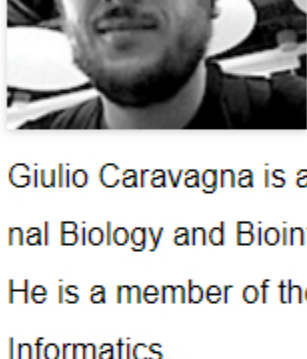
Dr. Charles Cantor is a co-founder, and retired Chief Scientific Officer at SEQUENOM, Inc., the leading provider of noninvasive prenatal diagnostic testing. He consults for a number of biotech companies including SEQUENOM, AgenaBiosciences, Strand Life Sciences, Trovogene, Ann Jerns, ProdermiQ, In Silico Biology, and he is executive director of Retrotopo, (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.

Title: sensitive detection of low levels of cancer- specific DNA sequence differences

Brief summary: For various reasons mutations that determine the properties and drug responsiveness of tumors are often present in only trace amounts in clinical samples such as fine needle biopsies, plasma or urine. A number of sensitive methods exist to detect these low levels of specific sequences, but even these are compromised when only a few molecules of the desired analytes are present, because experiments are then subject to stochastic noise. New strategies that attempt to bypass stochastic noise are under development, and these may increase detection sensitivity enough to allow, some day, pre symptomatic detection of cancer.

Giulio Caravagna, PhD, School of Informatics, University of

Edinburgh, UK



Giulio Caravagna is a Research Associate in the Laboratory of Machine Learning for Computational Biology and Bioinformatics run by Guido Sanguinetti at the University of Edinburgh, UK.

He is a member of the Institute of Adaptive and Neural Computation, located within the School of Informatics.

Before, he was a Postdoctoral Research Fellow at Milano-Bicocca Bioinformatics and at the National Research Council, Italy.

He has a PhD in Computer Science from the University of Pisa.

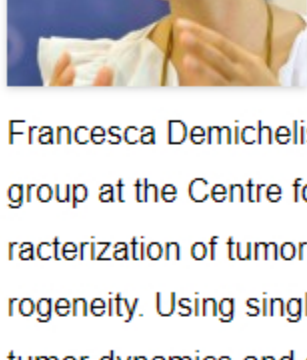
Summary.

Computational approaches are becoming key to automatically identify explanatory models of how (epi)genomic events are choreographed in cancer initiation and development. Such models shed new lights on the evolutionary nature of cancer, possibly allowing to understand the dramatic heterogeneity and temporality of the disease.

Presently, the increasing availability of next generation sequencing data are creating the ground for successful applications of such techniques, both at the individual and the population level.

In this talk, I will present a general overview of approaches to extract such models from data. Thus I will focus on techniques inspired by recent works relating causality and probability theory. I will present a versatile and modular pipeline to extract ensemble-level progression models from cross-sectional sequenced cancer genomes, and discuss its application to colorectal cancer. I will briefly discuss various proposed techniques to solve the same problem from multiple biopsy and single-cell data as well.

Francesca Demichelis, Università degli Studi di Trento, Trento, Italy

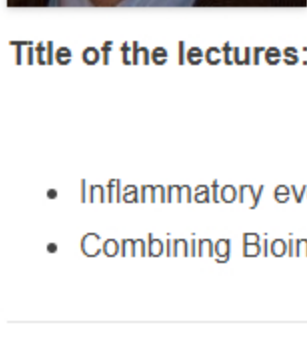


Francesca Demichelis, PhD, is expert in the area of Cancer Genomics. Dr. Demichelis' research group at the Centre for Integrative Biology at the University of Trento, Italy, focuses on the characterization of tumor evolution and progression through the study of intra- and inter-tumor heterogeneity. Using single base level information from tissue biopsies or circulating DNA (plasma), tumor dynamics and evolution maps are charted to inform on patient's status and treatment response. Dr. Demichelis also studies the impact of inherited polymorphisms, including structural variants, within transcriptionally active regulatory regions of the genome on the initiation of hormone regulated cancer phenotypes. The research group is involved in consortia studies including The Cancer Genome Atlas (TCGA) and Stand Up 2 Cancer International PCF Dream Team. Dr. Demichelis has received support from the European Research Committee (ERC), Department of Defense (USA), the National Cancer Institute (NCI), and the Prostate Cancer Foundation. She trained at the University of Trento (Physics Department, Information and Communication Technology PhD School), did her post-doc at Brigham and Women's Hospital/Harvard Medical School in Boston, and led her own laboratory at Weill Cornell Medicine (NY) between 2007-2011 before moving to Centre for Integrative Biology at the University of Trento.

Summary

Understanding treatment resistance is emerging as a critical hurdle for precision medicine in cancer care. We exploit single base resolution data and allele-specific analysis to reconstruct tumor evolution charts and to quantify intra- and inter-tumor molecular heterogeneity. These approaches proved useful in identifying potential mechanisms of resistance to AR (androgen receptor) directed therapies in prostate cancer. Specifically, we found evidence of the emergence of an alternative 'AR-indifferent' cell state through divergent clonal evolution as a mechanism of treatment resistance in advanced disease. Translating this new information to a biomarker assay readily applicable in the clinical setting requires the implementation of high performing non-invasive tests. We will discuss technical aspects related to the detection of somatic structural variants in the circulation of cancer patients' during treatment.

Pietro Liò, University of Cambridge, Cambridge, UK

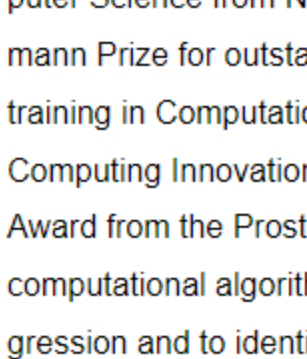


Title of the lectures:

- Inflammatory events and cancer: a statistical Bioinformatics perspectives.
- Combining Bioinformatics and cancer survival analysis.

Antonina Mitrofanova, Department of Health Informatics, Rutgers

University, Newark (NJ), USA



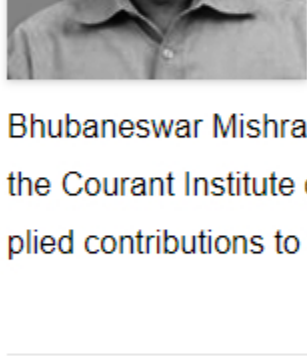
Antonina Mitrofanova is an Assistant Professor and Director of Biomedical Informatics Research in the Department of Health Informatics at Rutgers University. Antonina received her PhD in Computer Science from New York University, with the Best Dissertation Award and the Henning Biermann Prize for outstanding contribution to Education at NYU. She completed her PostDoctoral training in Computational Systems Biology at Columbia University, where she was a recipient of Computing Innovation Fellowship from the National Science Foundation and Young Investigator Award from the Prostate Cancer Foundation. At Rutgers, Antonina's lab develops and applies computational algorithms to elucidate transcriptional and epigenetic mechanisms of cancer progression and to identify optimal therapeutic strategies to target specific cancer malignancies.

Summary, Computational Approaches to Investigate Mechanisms of Progression and Drug Response in Human Cancer.

Complexity of human cancer is driven by the coordinated activation and inactivation of multiple genes, which makes the identification of causal drivers of cancer progression a daunting challenge. Although animal models are often used to study mechanisms of cancer progression and evaluate new cancer therapies, the accurate extrapolation of animal studies to human cancer has been difficult. I will present novel cross-species systems biology algorithms that identify conserved regulatory programs between human and mouse cancer models and inform on therapeutic strategies for human patients with the most aggressive disease. These algorithms identify causal gene "drivers" of aggressive cancer, which may also serve as biomarkers to categorize patients with poor prognosis. We have generated complementary human and mouse prostate cancer gene regulatory networks (interactomes) assembled from molecular profiles of human tumors and genetically engineered mouse models. Our computational systems biology network-based approaches and subsequent experimental validation have elucidated a synergistic interaction of two genes, FOXM1 and CENPF, that drives prostate cancer aggressiveness and is a robust prognostic indicator of cancer outcome. I will demonstrate that these identified drivers are excellent candidates for targeted therapeutics, especially for patients with aggressive prostate cancer. Furthermore, I will describe an innovative computational algorithm to identify drugs and drug combinations that inhibit the transcriptional activity of these molecular drivers. Experimental validation confirms high efficacy of the top predicted drug combination for inhibiting tumorigenesis in mouse and human prostate cancer models. Although these approaches have been specifically applied to prostate cancer, they also address issues of broad general relevance for the prognosis, diagnosis, and treatment of human disease.

Bud Mishra, Courant Institute of Mathematical Sciences and Tandon

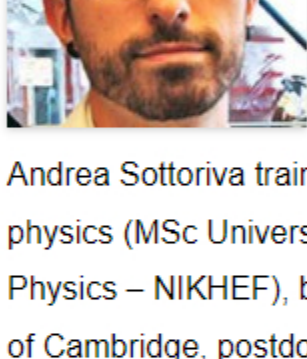
School of Engineering, NYU, New York, USA



Bhubaneswar Mishra (or Bud Mishra) is an Indian American computer scientist and professor at the Courant Institute of Mathematical Sciences of New York University. He is known for his applied contributions to bioinformatics, cybersecurity, and computational finance.

Andrea Sottoriva, Centre for Evolution and Cancer, The Institute of

Cancer Research, London, UK



Andrea Sottoriva trained in computer science (BSc University of Bologna) and computational physics (MSc University of Amsterdam and National Institute for Nuclear and High-Energy Physics – NIKHEF), before switching to computational biology and bioinformatics (PhD University of Cambridge, postdoc University of Southern California).

He now leads the Evolutionary Genomics and Modelling team within the Centre for Evolution and Cancer at The Institute of Cancer Research in London.

His research focuses on using multi-disciplinary approaches based on high-throughput genomics and mathematical modelling to understand cancer as a complex system driven by evolutionary principles. The goal of his team is to identify those patient-specific rules that regulate tumour evolution in individual patients, in order to predict the future course of the disease.

Talk: Functional versus non-functional intra-tumour heterogeneity

Despite extraordinary efforts to profile cancer genomes, interpreting the vast amount of genomic data in the light of cancer evolution remains challenging. In particular, although genomic intra-tumour heterogeneity (ITH) has become a hot topic in cancer, determining how much of it is actually functional and clinically relevant remains an open question. Here we will present a null model of genomic ITH that can be applied to next-generation sequencing data from human malignancies. This mathematical framework is based on neutral evolution and allows identifying which tumours are characterized by complex evolutionary dynamics, such as clonal selection and cooperation, and which ones do not. Importantly, reanalyzing cancer genomic data within the neutral framework allowed the measurement, in each individual patient, of both the *in vivo* mutation rate and the timing of mutations. This result provides a new way to interpret existing cancer genomic data and to discriminate between functional and non-functional ITH.

Rory Stark, Principal Bioinformatics Analyst – Cancer Research UK,

Cambridge Institute (Univ. of Cambridge)



Dr. Rory Stark is the Principal Bioinformatics Analyst at the University of Cambridge, where he leads the core analysis team at Cancer Research UK's Cambridge Institute. He has been working extensively with next-generation, high-throughput sequencing technologies since 2007, when he helped establish the CRUK sequencing facility and associated core bioinformatics group. He is most interested in the analysis of transcriptional regulatory elements such as transcription factor binding and epigenetic marks. Besides supervising and performing analyses of experimental datasets for breast, prostate, and colon cancer, he has developed a number of computational tools including DiffBind, a popular Bioconductor package for differential binding analysis of ChIP-seq data.

Dr. Stark's history in the commercial sector includes founding several Silicon Valley start-ups, joining Microsoft after they acquired NetCarta, an Internet software company he started in 1994. As a Group Manager at Microsoft he was involved in technology transfer between research and development, ultimately overseeing the development of speech recognition platforms and products. Dr. Stark's academic degrees cover a range of computational sciences, including a BA in Computer and Information Science

(UCSC), MSc in Cognitive Science (Edinburgh), PhD in Artificial Intelligence (Edinburgh/Sussex), and an MPhil from the Cambridge Computational Biology Institute, where he now also lectures.

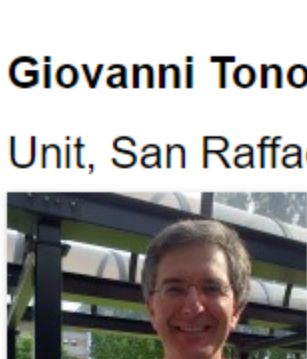
Talks: Demo: Overview of Bioconductor for analysis of high-throughput cancer experiments (60 minutes)

Lecture: Analysis of regulatory protein binding dynamics in cancer: (60 minutes)

Practical: differential binding analysis (45 minutes)

Giovanni Tonon, MD PhD, Head, Functional Genomics of Cancer

Unit, San Raffaele Scientific Institute, Milan Italy



Dr. Giovanni Tonon is the Director of the Center for Translational Genomics and Bioinformatics and of the Functional Genomics of Cancer Unit at the San Raffaele Scientific Institute. He has a long-standing interest in the identification of cancer genes and pathways through cytogenetic and bioinformatic approaches, the elucidation of their oncogenic mechanism and the translation of these results in novel therapies. He has contributed to the identification of cancer genes in multiple myeloma, lung cancer and colon cancer, and of tumor-related pathways such as MYC in glioma and mitochondria in telomere dysfunction.

Summary: Synthetic Lethal Approaches Exploiting DNA Damage DNA damage in cancer fosters heterogeneity, increasing the evolutionary diversity of cancer cells. Based on recent findings, we argue that subset of patients, and potentially of cells within a tumor, present genomically unstable cells that are particularly apt to enhance the clonal pool and as such should be preferentially targeted. We have identified synthetic lethality approaches exploiting DNA damage thus inducing apoptosis in these particularly aggressive yet frail cells.



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Program

CDAC 2016	Tue May 24	Wed May 25	Thu May 26	Fri May 27	
09:00		Charles Cantor	Pietro Liò	Andrea Sottoriva	09:00
10:00		Oliva Alberti	Pietro Liò	Andrea Sottoriva	10:00
11:00		Coffee break	Coffee break	Coffee break	11:00
11:30		Antonina Mitrofanova	Giulio Caravagna	Francesca Demichelis	11:30
12:30	Registration	Antonina Mitrofanova	Giulio Caravagna	Round table	12:30
13:30	Lunch break	Lunch break	Lunch break	Lunch break	13:30
14:30	Welcome by Bud Mishra and Marco Antoniotti	Participants' presentation	Rory Stark		14:30
15:30	Rory Stark	Participants' presentation	Rory Stark		15:30
16:30	Coffee break	Coffee break	Coffee break		16:30
16:45	Giovanni Tonon	Francesca Demichelis			16:45
17:45	Giovanni Tonon				17:45
			Social Dinner @ Ristorante Sociale, Via Rodari, 6 - Como		20.00

Download the full program at this [link](#).

Slides

- Rory Stark
- Giovanni Tonon
- Charles Cantor
- Oliva Alberti
- Antonina Mitrofanova
- Francesca Demichelis
- Pietro Liò
- Giulio Caravagna
- Andrea Sottoriva



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Organizing Committee

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, NYU, New York, NY, USA.

Local Organization

Alex Graudenzi (CNR)

Giancarlo Mauri (BIMIB)

Daniele Ramazzotti (BIMIB)

Nadia Tansini (Fondazione Alessandro Volta)

Institutions

* **BIMIB**, Dipartimento di Informatica, Sistemistica e Comunicazione, Università degli Studi di Milano Bicocca, Milan, Italy (<http://bimib.disco.unimib.it>)

* **Fondazione Alessandro Volta**, Como, Italy (<http://fondazionealessandrovolta.it>)

* **Lake Como School of Advanced Studies**, Como, Italy (<http://lakecomoschool.org>)



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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/>



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Registration

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

Early registration (until April 30th, 2016): 320,00 EUR

Regular registration (after April 30th, 2016): 400,00 EUR

Daily, on site registration: 90,00 EUR

All fees include VAT.

Students and Post-docs of the four Universities supporting the Lake Como Schools (Milano Statale, Pavia, Milano Bicocca and Insubria) automatically qualify for a further fee reduction.

TO REGISTER, PLEASE FILL IN THE FORM BELOW:

Registrations are closed.



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Accommodation

The first registrants may ask to be hosted directly at the Guesthouse of Villa Del Grumello (in a shared accommodation) for an additional cost of 37.00 EUR V.A.T. included, per night up to capacity (10 places).

The accommodation can be paid on site at the check in – accommodation is available from May 23rd (arrival day) to May 27th/28th (departure date), 2016.

A list of local hotels will be provided soon. For any help or additional information: please contact the Organizing Secretariat email: (nadia.tansini@fondazionealessandrovolta.it)



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Contacts

For enquiries about the scientific aspects of the school, please contact Marco Antoniotti
(antoniotti.marco@disco.unimib.it)

For enquiries about the venue of the school, travel, accommodation, and registration procedure,
please contact Nadia Tansini
(nadia.tansini@fondazionealessandrovolta.it) at Fondazione Alessandro Volta, Como.



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Como**

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Charles Cantor
Agena Biosciences, Sequenom,
Ratcliffe and Boston University
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Bud Mishra
Courant Institute of
Mathematical Sciences, NYU
USA

Giulio Caravagna
School of Informatics
University of Edinburgh, UK

Andrea Sottoriva
The Institute of Cancer
Research, UK

Francesca De Micheli
University of Trento
Italy

Rory Stark
Cancer Research UK
UK

Pietro Liò
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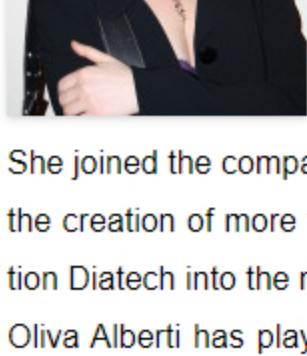
Local organization
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(Fondazione Alessandro Volta)

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<http://cdac.lakecomoschool.org>
cdacinfo@disco.unimib.it



Keynote Speakers

Oliva Alberti, CEO Diatech Pharmacogenetics srl



She joined the company in 1998 and was appointed to CEO in 2004. She was actively supporting the creation of more than 7 sister and controlled companies helping to better structure and position Diatech into the molecular diagnostic market.

Oliva Alberti has played a critical role in support the company's growth in the field of molecular diagnostics.

From 1998 to 2014 she operated like project manager into developing the projects financed to the company by the Italian Ministry for University and Research as well as the Industrial once, she was also supporting the filing of the JEV project that the company was presenting to EU in 2002 and the Horizon 2020 project that has been approved by EU in 2015.

She has over 15 years of experience in the biotechnology industry.

Summary, From life science to molecular diagnostics: a tailored approach

Diagnostic laboratories face a major challenge in being able to provide rapid, sensitive and state of the art molecular tests. We developed a novel mass spectrometry multiplexed genotyping solution named Myriapod® to concurrently assess single nucleotide polymorphisms in most clinically relevant cancer gene.

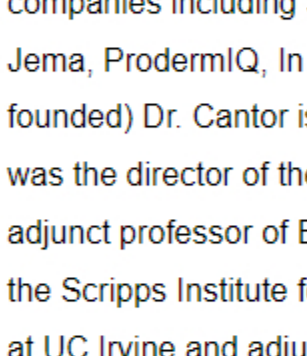
The CE IVD system has been developed taking into consideration the diagnostic needs of the laboratories, the usability inside a routine diagnostic environment and it is a complete solution that includes instruments, accessories, software and reagents.

To evaluate and validate the systems, the research and development activities have been performed systematically addressing sensitivity, specificity, and reproducibility of our platform.

Our Myriapod® solution is a high throughput and robust tool, allowing genotyping for targeted therapy selection with a practical turnaround time of 8 working hours.

The system can provide an immediate, accurate and cost effective multiplex approach for clinically relevant gene mutation analysis using the state of the art technology in mutation analysis in multiplexing Mass Spectrometry.

Charles Cantor, PhD, Agena Biosciences, Sequenom, Retrotopo and Boston University, USA

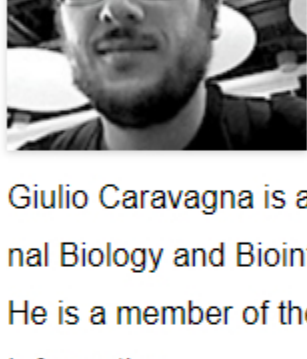


Dr. Charles Cantor is a co-founder, and retired Chief Scientific Officer at SEQUENOM, Inc., the leading provider of noninvasive prenatal diagnostic testing. He consults for a number of biotech companies including SEQUENOM, AgenaBiosciences, Strand Life Sciences, Trovogene, Ann Jerns, ProdermiQ, In Silico Biology, and he is executive director of Retrotopo, (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.

Title: sensitive detection of low levels of cancer- specific DNA sequence differences

Brief summary: For various reasons mutations that determine the properties and drug responsiveness of tumors are often present in only trace amounts in clinical samples such as fine needle biopsies, plasma or urine. A number of sensitive methods exist to detect these low levels of specific sequences, but even these are compromised when only a few molecules of the desired analytes are present, because experiments are then subject to stochastic noise. New strategies that attempt to bypass stochastic noise are under development, and these may increase detection sensitivity enough to allow, some day, pre symptomatic detection of cancer.

Giulio Caravagna, PhD, School of Informatics, University of Edinburgh, UK



Giulio Caravagna is a Research Associate in the Laboratory of Machine Learning for Computational Biology and Bioinformatics run by Guido Sanguinetti at the University of Edinburgh, UK.

He is a member of the Institute of Adaptive and Neural Computation, located within the School of Informatics.

Before, he was a Postdoctoral Research Fellow at Milano-Bicocca Bioinformatics and at the National Research Council, Italy.

He has a PhD in Computer Science from the University of Pisa.

Summary.

Computational approaches are becoming key to automatically identify explanatory models of how (epi)genomic events are choreographed in cancer initiation and development.

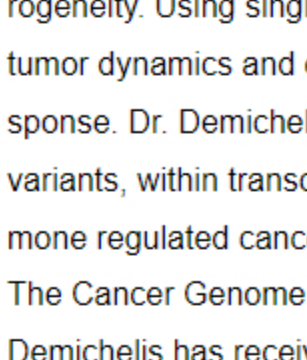
Such models shed new lights on the evolutionary nature of cancer, possibly allowing to understand the dramatic heterogeneity and temporality of the disease.

Presently, the increasing availability of next generation sequencing data are creating the ground for successful applications of such techniques, both at the individual and the population level.

In this talk, I will present a general overview of approaches to extract such models from data. Thus I will focus on techniques inspired by recent works relating causality and probability theory. I will present a versatile and modular pipeline to extract ensemble-level progression models from cross-sectional sequenced cancer genomes, and discuss its application to colorectal cancer.

I will briefly discuss various proposed techniques to solve the same problem from multiple biopsy and single-cell data as well.

Francesca Demichelis, Università degli Studi di Trento, Trento, Italy

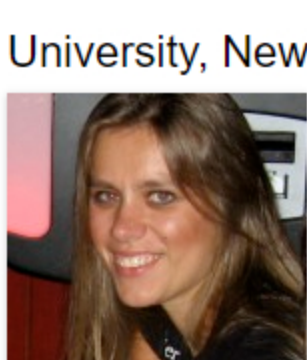


Francesca Demichelis, PhD, is expert in the area of Cancer Genomics. Dr. Demichelis' research group at the Centre for Integrative Biology at the University of Trento, Italy, focuses on the characterization of tumor evolution and progression through the study of intra- and inter-tumor heterogeneity. Using single base level information from tissue biopsies or circulating DNA (plasma), tumor dynamics and evolution maps are charted to inform on patient's status and treatment response. Dr. Demichelis also studies the impact of inherited polymorphisms, including structural variants, within transcriptionally active regulatory regions of the genome on the initiation of hormone regulated cancer phenotypes. The research group is involved in consortia studies including The Cancer Genome Atlas (TCGA) and Stand Up 2 Cancer International PCF Dream Team. Dr. Demichelis has received support from the European Research Committee (ERC), Department of Defense (USA), the National Cancer Institute (NCI), and the Prostate Cancer Foundation. She trained at the University of Trento (Physics Department, Information and Communication Technology PhD School), did her post-doc at Brigham and Women's Hospital/Harvard Medical School in Boston, and led her own laboratory at Weill Cornell Medicine (NY) between 2007-2011 before moving to Centre for Integrative Biology at the University of Trento.

Summary

Understanding treatment resistance is emerging as a critical hurdle for precision medicine in cancer care. We exploit single base resolution data and allele-specific analysis to reconstruct tumor evolution charts and to quantify intra- and inter-tumor molecular heterogeneity. These approaches proved useful in identifying potential mechanisms of resistance to AR (androgen receptor) directed therapies in prostate cancer. Specifically, we found evidence of the emergence of an alternative 'AR-indifferent' cell state through divergent clonal evolution as a mechanism of treatment resistance in advanced disease. Translating this new information to a biomarker assay readily applicable in the clinical setting requires the implementation of high performing non-invasive tests. We will discuss technical aspects related to the detection of somatic structural variants in the circulation of cancer patients' during treatment.

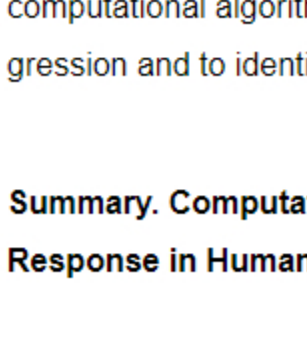
Pietro Liò, University of Cambridge, Cambridge, UK



Title of the lectures:

- Inflammatory events and cancer: a statistical Bioinformatics perspectives.
- Combining Bioinformatics and cancer survival analysis.

Antonina Mitrofanova, Department of Health Informatics, Rutgers University, Newark (NJ), USA

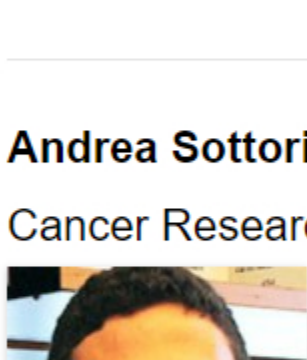


Antonina Mitrofanova is an Assistant Professor and Director of Biomedical Informatics Research in the Department of Health Informatics at Rutgers University. Antonina received her PhD in Computer Science from New York University, with the Best Dissertation Award and the Henning Biermann Prize for outstanding contribution to Education at NYU. She completed her PostDoctoral training in Computational Systems Biology at Columbia University, where she was a recipient of Computing Innovation Fellowship from the National Science Foundation and Young Investigator Award from the Prostate Cancer Foundation. At Rutgers, Antonina's lab develops and applies computational algorithms to elucidate transcriptional and epigenetic mechanisms of cancer progression and to identify optimal therapeutic strategies to target specific cancer malignancies.

Summary, Computational Approaches to Investigate Mechanisms of Progression and Drug Response in Human Cancer.

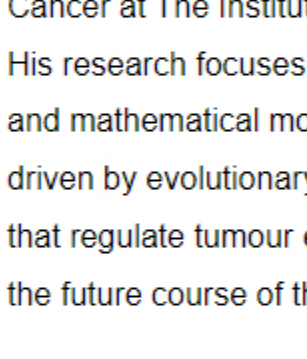
Complexity of human cancer is driven by the coordinated activation and inactivation of multiple genes, which makes the identification of causal drivers of cancer progression a daunting challenge. Although animal models are often used to study mechanisms of cancer progression and evaluate new cancer therapies, the accurate extrapolation of animal studies to human cancer has been difficult. I will present novel cross-species systems biology algorithms that identify conserved regulatory programs between human and mouse cancer models and inform on therapeutic strategies for human patients with the most aggressive disease. These algorithms identify causal gene "drivers" of aggressive cancer, which may also serve as biomarkers to categorize patients with poor prognosis. We have generated complementary human and mouse prostate cancer gene regulatory networks (interactomes) assembled from molecular profiles of human tumors and genetically engineered mouse models. Our computational systems biology network-based approaches and subsequent experimental validation have elucidated a synergistic interaction of two genes, FOXM1 and CENPF, that drives prostate cancer aggressiveness and is a robust prognostic indicator of cancer outcome. I will demonstrate that these identified drivers are excellent candidates for targeted therapeutics, especially for patients with aggressive prostate cancer. Furthermore, I will describe an innovative computational algorithm to identify drugs and drug combinations that inhibit the transcriptional activity of these molecular drivers. Experimental validation confirms high efficacy of the top predicted drug combination for inhibiting tumorigenesis in mouse and human prostate cancer models. Although these approaches have been specifically applied to prostate cancer, they also address issues of broad general relevance for the prognosis, diagnosis, and treatment of human disease.

Bud Mishra, Courant Institute of Mathematical Sciences and Tandon School of Engineering, NYU, New York, USA



Bhubaneswar Mishra (or Bud Mishra) is an Indian American computer scientist and professor at the Courant Institute of Mathematical Sciences of New York University. He is known for his applied contributions to bioinformatics, cybersecurity, and computational finance.

Andrea Sottoriva, Centre for Evolution and Cancer, The Institute of Cancer Research, London, UK



Andrea Sottoriva trained in computer science (BSc University of Bologna) and computational physics (MSc University of Amsterdam and National Institute for Nuclear and High-Energy Physics – NIKHEF), before switching to computational biology and bioinformatics (PhD University of Cambridge, postdoc University of Southern California).

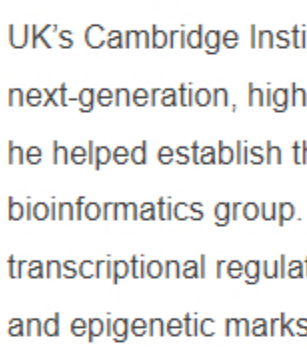
He now leads the Evolutionary Genomics and Modelling team within the Centre for Evolution and Cancer at The Institute of Cancer Research in London.

His research focuses on using multi-disciplinary approaches based on high-throughput genomics and mathematical modelling to understand cancer as a complex system driven by evolutionary principles. The goal of his team is to identify those patient-specific rules that regulate tumour evolution in individual patients, in order to predict the future course of the disease.

Talk: Functional versus non-functional intra-tumour heterogeneity

Despite extraordinary efforts to profile cancer genomes, interpreting the vast amount of genomic data in the light of cancer evolution remains challenging. In particular, although genomic intra-tumour heterogeneity (ITH) has become a hot topic in cancer, determining how much of it is actually functional and clinically relevant remains an open question. Here we will present a null model of genomic ITH that can be applied to next-generation sequencing data from human malignancies. This mathematical framework is based on neutral evolution and allows identifying which tumours are characterized by complex evolutionary dynamics, such as clonal selection and cooperation, and which ones do not. Importantly, reanalyzing cancer genomic data within the neutral framework allowed the measurement, in each individual patient, of both the *in vivo* mutation rate and the timing of mutations. This result provides a new way to interpret existing cancer genomic data and to discriminate between functional and non-functional ITH.

Rory Stark, Principal Bioinformatics Analyst – Cancer Research UK, Cambridge Institute (Univ. of Cambridge)



Dr. Rory Stark is the Principal Bioinformatics Analyst at the University of Cambridge, where he leads the core analysis team at Cancer Research UK's Cambridge Institute. He has been working extensively with next-generation, high-throughput sequencing technologies since 2007, when he helped establish the CRUK sequencing facility and associated core bioinformatics group. He is most interested in the analysis of

transcriptional regulatory elements such as transcription factor binding and epigenetic marks. Besides supervising and performing analyses of experimental datasets for breast, prostate, and colon cancer, he has developed a number of computational tools including DiffBind, a popular Bioconductor package for differential binding analysis of ChIP-seq data.

Dr. Stark's history in the commercial sector includes founding several Silicon Valley start-ups, joining Microsoft after they acquired NetCarta, an Internet software company he started in 1994. As a Group Manager at Microsoft he was involved in technology transfer between research and development, ultimately overseeing the development of speech recognition platforms and products. Dr. Stark's academic degrees cover a range of computational sciences, including a BA in Computer and Information Science

(UCSC), MSc in Cognitive Science (Edinburgh), PhD in Artificial Intelligence (Edinburgh/Sussex), and an MPH from the Cambridge Computational Biology Institute, where he now also lectures.

Giovanni Tonon, MD PhD, Head, Functional Genomics of Cancer Unit, San Raffaele Scientific Institute, Milan Italy



Dr. Giovanni Tonon is the Director of the Center for Translational Genomics and Bioinformatics and of the Functional Genomics of Cancer Unit at the San Raffaele Scientific Institute. He has a long-standing interest in the identification of cancer genes and pathways through cytogenetic and bioinformatic approaches, the elucidation of their oncogenic mechanism and the translation of these results in novel therapies. He has contributed to the identification of cancer genes in multiple myeloma, lung cancer and colon cancer, and of tumor-related pathways such as MYC in glioma and mitochondria in telomere dysfunction.

Summary Synthetic Lethal Approaches Exploiting DNA Damage DNA damage in cancer fosters heterogeneity, increasing the evolutionary diversity of cancer cells. Based on recent findings, we argue that subset of patients, and potentially of cells within a tumor, present genomically unstable cells that are particularly apt to enhance the clonal pool and as such should be preferentially targeted. We have identified synthetic lethality approaches exploiting DNA damage thus inducing apoptosis in these particularly aggressive yet frail cells.



Cancer development and complexity

May 24-27, 2016 – Lake Como School of Advanced Studies

Program

CDAC 2016	Tue May 24	Wed May 25	Thu May 26	Fri May 27	
09:00		Charles Cantor	Pietro Liò	Andrea Sottoriva	09:00
10:00		Oliva Alberti	Pietro Liò	Andrea Sottoriva	10:00
11:00		Coffee break	Coffee break	Coffee break	11:00
11:30		Antonina Mitrofanova	Giulio Caravagna	Francesca Demichelis	11:30
12:30	Registration	Antonina Mitrofanova	Giulio Caravagna	Round table	12:30
13:30	Lunch break	Lunch break	Lunch break	Lunch break	13:30
14:30	Welcome by Bud Mishra and Marco Antoniotti	Participants' presentation	Rory Stark		14:30
15:30	Rory Stark	Participants' presentation	Rory Stark		15:30
16:30	Coffee break	Coffee break	Coffee break		16:30
16:45	Giovanni Tonon	Francesca Demichelis			16:45
17:45	Giovanni Tonon				17:45
			Social Dinner @ Ristorante Sociale, Via Rodari, 6 - Como		20.00

Download the full program at this [link](#).

Slides

- Rory Stark
- Giovanni Tonon
- Charles Cantor
- Oliva Alberti
- Antonina Mitrofanova
- Francesca Demichelis
- Pietro Liò
- Giulio Caravagna
- Andrea Sottoriva



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Organizing Committee

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, NYU, New York, NY, USA.

Local Organization

Alex Graudenzi (CNR)

Giancarlo Mauri (BIMIB)

Daniele Ramazzotti (BIMIB)

Nadia Tansini (Fondazione Alessandro Volta)

Institutions

* **BIMIB**, Dipartimento di Informatica, Sistemistica e Comunicazione, Università degli Studi di Milano Bicocca, Milan, Italy (<http://bimib.disco.unimib.it>)

* **Fondazione Alessandro Volta**, Como, Italy (<http://fondazionealessandrovolta.it>)

* **Lake Como School of Advanced Studies**, Como, Italy (<http://lakecomoschool.org>)



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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/>



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Registration

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

Early registration (until April 30th, 2016): 320,00 EUR

Regular registration (after April 30th, 2016): 400,00 EUR

Daily, on site registration: 90,00 EUR

All fees include VAT.

Students and Post-docs of the four Universities supporting the Lake Como Schools (Milano Statale, Pavia, Milano Bicocca and Insubria) automatically qualify for a further fee reduction.

TO REGISTER, PLEASE FILL IN THE FORM BELOW:

Registrations are closed.



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Accommodation

The first registrants may ask to be hosted directly at the Guesthouse of Villa Del Grumello (in a shared accommodation) for an additional cost of 37.00 EUR V.A.T. included, per night up to capacity (10 places).

The accommodation can be paid on site at the check in – accommodation is available from May 23rd (arrival day) to May 27th/28th (departure date), 2016.

A list of local hotels will be provided soon. For any help or additional information: please contact the Organizing Secretariat email: (nadia.tansini@fondazionealessandrovolta.it)



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Contacts

For enquiries about the scientific aspects of the school, please contact Marco Antoniotti
(antoniotti.marco@disco.unimib.it)

For enquiries about the venue of the school, travel, accommodation, and registration procedure,
please contact Nadia Tansini
(nadia.tansini@fondazionealessandrovolta.it) at Fondazione Alessandro Volta, Como.