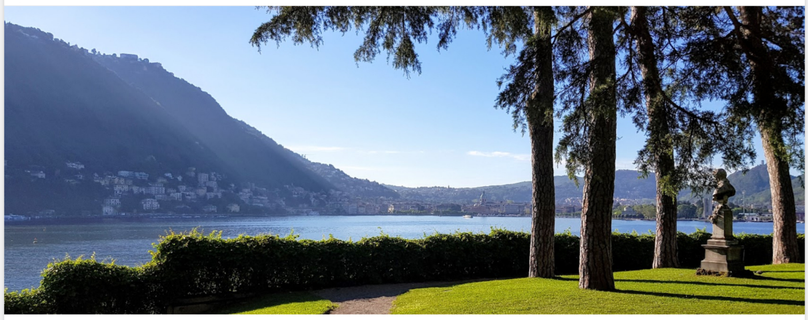
School on Cancer Development and Complexity (CDAC 2021)

Lake Como School of Advanced Studies, - May 24-28, 2021



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.

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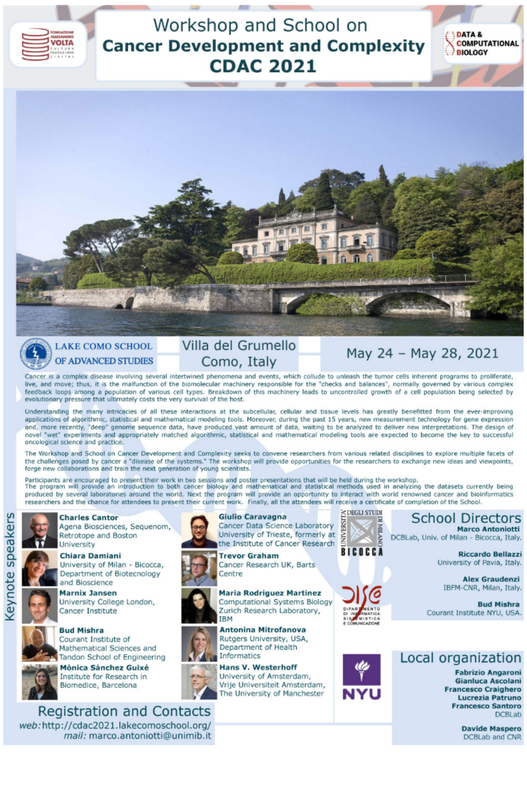

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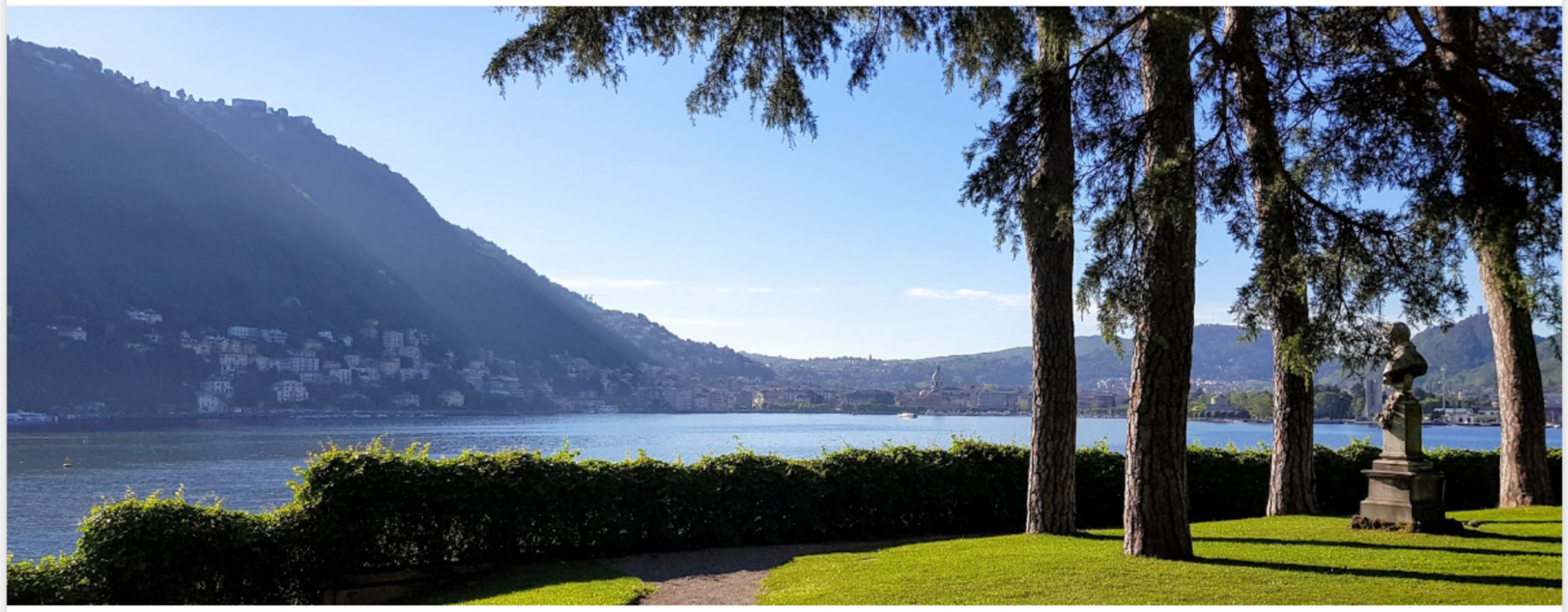

Speakers

Charles Cantor
Emeritus, Boston University, USA.
Talk:
New techniques and methods that will impact the understanding and the management of cancer (Part I & II)

Giulio Caravagna
Università degli studi di Trieste, IT.
Talk:
Model-based interpretation of cancer whole genome sequencing data: from subclonal populations to evolutionary trajectories (part I & II)

Chiara Damiani
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Talk:
Data integration to unravel cancer metabolic variation and regulation (part I & II)

Trevor Graham
Queen Mary University of London, UK.
Talk:
1.Measuring evolutionary dynamics of human tumours

Marnix Jansen
University College London, UK.
Talk: TBD.

María Rodríguez Martínez
Computational Systems Biology Zurich Research Laboratory, IBM, Switzerland
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Understanding the determinants to T cell receptor binding in cancer immunotherapies (part I & II)

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Antonina Mitrofanova
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Mònica Sánchez-Guixé,
Institute for Research in Biomedicine, Spain.
Talks:
1. IntOGen: from data repositories to cancer driver gene discovery
2. Genomic analysis of rare pediatric cancer cases with secondary neoplasms

Hans Westerhoff,
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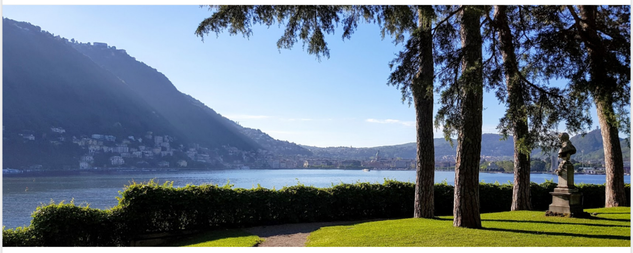

Program

Preliminary Schedule

Time (UTC+2)	Mon May 24	Tue May 25	Wed May 26	Thu May 27	Fri May 28
9:00 - 10:30		Mònica Sánchez-Guixé (*Tutorial*)	Trevor Graham (*Lecture*)	María Rodríguez-Martínez (*Lecture*)	Hans Westerhoff (*Lecture*)
10.30 - 10.45	**Welcome**	**Break**	**Break**	**Break**	**Break**
10:45 - 12:15	Trevor Graham (*Tutorial*)	Giulio Caravagna (*Tutorial*)	Giulio Caravagna (*Lecture*)	Marnix Jansen (*Lecture*)	Chiara Damiani (*Lecture*)
12:15 - 13:45	Hans Westerhoff (*Tutorial*)	Marco Pellegrini (*Partecipants' talks*)	Shadi Shafighi (*Partecipants' talks*)	Bruno Galuzzi (*Partecipants' talks*)	**Open discussion**
13:45 - 14:30	**Lunch break**	**Lunch break**	**Lunch break**	**Lunch break**	
14:30 - 16:00	Bud Mishra (*Lecture*)	Chiara Damiani (*Tutorial*)	Charles Cantor (*Lecture*)	Mónica Sánchez-Guixé (*Lecture*)	
16:00 - 17:30	RxCovea (*joint meeting*)			Antonina Mitrofanova (*Lecture*)	

CDAC 2021 schedule (downloadable PDF)

Preliminary Talks Titles and Abstracts

Charles Cantor

"New techniques and methods that will impact the understanding and the management of cancer"

Cancers generally become increasingly heterogeneous as they develop. They accumulate point mutations, DNA rearrangements and eventually massive chromosomal abnormalities. Cancers also remodel their chromatin through epigenetic changes, presumably to try to create and maintain a less differentiated phenotype than their tissue of origin. To understand cancer, we must understand how the heterogeneity originates and develops. To manage cancer efficiently, we must be able to detect it before the level of heterogeneity makes a curative treatment nearly impossible.

Show More

Giulio Caravagna

"Model-based interpretation of cancer whole genome sequencing data: from subclonal populations to evolutionary trajectories"

In these two lectures we will discuss the fundamental problem of interpreting cancer growth and evolution from WGS data. We will discuss the main problems in assessing data quality, reliable subclonal deconvolution estimates integrating population genetics and machine learning, and comparing evolution across different patients. The lectures will present the theory underlying some recently developed models to this purpose, and will show how to run these analyses on real data. Attendants are invited to follow the practical parts of the lectures on their computer (programming will be done in R).

Chiara Damiani

"Data integration to unravel cancer metabolic variation and regulation"

The excessive genetic heterogeneity of cancer cells and the general failure of somatic mutation calling in supporting the identification of effective cancer treatments have fostered an increasing interest towards cancer metabolism. Cell metabolism is indeed the most obvious product of the interplay between genetic and environmental factors. Moreover, the metabolic requirements of highly proliferating cells markedly differ from those of quiescent ones. Yet, cancer cells cope with these requirements heterogeneously, as they are exposed to different levels of nutrients in time and space. The specific metabolic program of a cell cannot be deduced from currently accessible omics data, unless different omics are opportunely integrated with one another and with mathematical models. In the first part of this talk the basics of computational modeling of metabolism are presented, along with some demo.

In the second part of the talk a recent work is presented that dissects the regulation of cancer metabolism, by integrating transcriptomics and metabolomics data into constraint-based and kinetic models. Recent advancements on the characterization of intra-tumor metabolic heterogeneity from single-cell RNA-seq data are also reported.

Trevor Graham

Tutorial: "Using mechanistic mathematical models to explore cancer genomes"

Cancer genomes are rich sources of information about the dynamical process of tumour evolution. Arguably the most common approach to mining this information is find patterns in the data, and then post-hoc propose the process that produced these patterns. An alternative approach is propose an evolutionary model up-front and use inference to ask how well the model is supported by the data. Here, we will discuss these two approaches and explore some of the challenges (and interesting aspects) of constructing mathematical models of tumour genomic evolution. I hope this will be an interactive session with lots of discussion.

Lecture: "Measuring evolutionary dynamics of human tumours"

As tumours grow, each cell within the tumour independently accumulates new mutations. The pattern of genetic heterogeneity between tumour cells (intra-tumour heterogeneity – ITH) is read out of the evolutionary dynamics of cancer growth. Here I will discuss our work to mathematically model ITH and parameterise these models using genomic data. We show how positive and negative (immune-mediated) selection and neutral evolution shapes pattern of ITH and report the frequency of these evolutionary patterns across cancer types. We explore the influence of spatial processes on the detectability of evolutionary dynamics.

Marnix Jansen

María Rodríguez-Martínez

"Understanding the determinants to T cell receptor binding in cancer immunotherapies"

The activity of the adaptive immune system depends on the recognition of foreign antigens by T cells by their specific T cell receptors (TCRs). A correct understanding of the determinants that govern the binding of T cells to cancer neo-antigens is crucial to design better immunotherapies, distinguished by more effective binding profiles and less cross-reactive effects.
Our group has recently developed TITAN, a multi-modal deep learning model that predicts the binding affinity between TCRs and epitopes, outperforming the state of the art in this difficult task. Interestingly, TITAN allows to study independently the generalization capabilities to new TCRs and/or epitopes, which previous models have struggled with.
Furthermore, to enhance the interpretability of the predictions, TITAN exploits interpretable attention mechanisms that selectively highlight the patterns in the TCR and epitope sequence that are more important to make the prediction. In parallel, we are investigating the use of alternative techniques to enhance prediction transparency, for instance, based on the use of probabilistic graphical models. This is an example of how the combined used of AI and traditional mathematical approaches can result in more performant models able to make great strides into a multitude of fields, including prediction of autoantigens in autoimmune diseases, development of immunotherapies for cancer, or vaccine design.

Bud Mishra

"Variant(Stranger)/Scariant(Danger) Games: Cancer 2 Covid & Back"

Antonia Mitrofanova

"Pathway-centric approaches to uncover interpretable markers of treatment response in cancer patients"

Identification of functional cancer markers requires in-depth understanding of complexity of mechanisms that govern its initiation, progression, and therapeutic response. We have developed a series of computational algorithms that utilize pathway-centric approaches to identify markers, which constitute functional units for elucidation of interpretable mechanisms of treatment resistance and potential therapeutic targeting. We have demonstrated that these approaches are superior compared to black-box methods and gene-level analysis alone. When applied to tamoxifen resistance in ER+ breast cancer, chemotherapy resistance in lung and colorectal adenocarcinoma, pathway-centric approaches demonstrated their robustness, high accuracy, and superior ability to predict treatment response. Our predictions were independent of overall disease aggressiveness and not affected by common co-variates. To further elucidate the complexity of upstream pathway-centric regulation, we coupled our approaches with transcriptional regulatory network inference, opening an avenue for precision therapeutic targeting. We propose that prioritization of patients using interpretable pathway-based markers is central to personalized therapeutic planning and improved cancer course and outcomes.

Mònica Sánchez-Guixé

Tutorial: "Genomic analysis of rare pediatric cancer cases with secondary neoplasms"

The discovery of cancer driver genes is key to understand the molecular processes causing cancer and to ultimately define treatment strategies in the clinics. The Barcelona Biomedical Genomics (BBG) group has developed IntOGen [1] (intogen.org), a tool for the discovery of cancer driver genes. We have gathered somatic mutations from publicly available data repositories, collecting a total of 28 076 samples in 221 different cohorts across 66 different cancer types. IntOGen pipeline receives the collected genomic data for each cohort and applies 7 different methods for driver identification. The candidate drivers identified by each method are then systematically combined creating a highly reliable list of candidate driver genes per cohort. In the current release, 568 cancer driver genes have been identified. Furthermore, mutational features from these cancer genes can be used to train BoostDM [2] (cancergenomeinterpreter.org), another framework developed by the BBG. This machine learning model classifies which somatic point mutations bear the capacity of driving tumorigenesis, and is able to robustly predict the driver capacity of all potential single nucleotide variants along the gene sequences across different tumor types, generating the first in silico saturation mutagenesis of cancer genes.

1. Martínez-Jiménez F, Muiños F, Sentís I, Deu-Pons J, Reyes-Salazar I, Arnedo-Pac C, et al. A compendium of mutational cancer driver genes. Nat Rev Cancer. 10 de agosto de 2020;1-18.
2. Muiños F, Martinez-Jimenez F, Pich O, Gonzalez-Perez A, Lopez-Bigas N. In silico saturation mutagenesis of cancer genes. bioRxiv. 9 de junio de 2020;2020.06.03.130211.

Lecture: "IntOGen: from data repositories to cancer driver gene discovery"

Cancer mutations can originate from many carcinogenic sources. Several mutational processes in cancer have been described, like the mutational events caused by cancer therapy [1], where some chemotherapeutic agents have been linked to the development of treatment-related AMLs. Still, many rare pediatric secondary neoplasms need to be further characterized to determine the origin of their tumorigenesis. In this study, we aim to uncover the driver events behind pediatric cancer samples with rare secondary neoplasms. In collaboration with Sant Joan de Déu Barcelona Children's Hospital, we have performed WGS on tumor samples from 6 pediatric patients that have developed a secondary neoplasm with major clinical differences from their primary. First, we have applied mutation calling pipelines (snvs, small indels, copy number alterations and structural variants) to accurately annotate all genomic alterations, and have reconstructed the evolutionary events for each patient. To identify possible cancer predisposition, we have thoroughly analyzed germline alterations, and then carefully checked for common events between both tumors that could point to a case of early embryo clone expansion or mosaicism. Finally, we dissected the mutational signatures for each tumor and analyzed the implication of cancer therapy on the development of the second neoplasm.

1. Pich, O, Muiños, F, Lolkema, MP et al. The mutational footprints of cancer therapies. Nat Genet 51, 1732–1740 (2019). https://doi.org/10.1038/s41588-019-0525-5

Hans Westerhoff

"What if exception rules?"

Molecules in solution are a mess: they diffuse, roll, and bump into one another. How come then that (almost) every time a human is born, it develops two arms, two legs and two eyes? Or, that every time we inject glucose into a cell, it develops a transient reduction of NAD to NADH (visible by fluorescence)? Or that a culture of mammalian cells growing on a surface stops growing when they touch each other?

I will remind you of three grand paradoxes of the dynamic molecular world. The first is that dynamic worlds strive towards 'chaos' and that precisely by doing so, they end up in order. This 'order' is the rule, and the 'chaos' is the plethora of exceptions around it. Because most systems in and around us consist of lots of molecules, this preference for rules is so strong that we mostly observe those systems as 'deterministic', i.e. as completely determined by rules. It is these rules that one reads on Wikipedia and in the textbooks of physics and chemistry.

Show More

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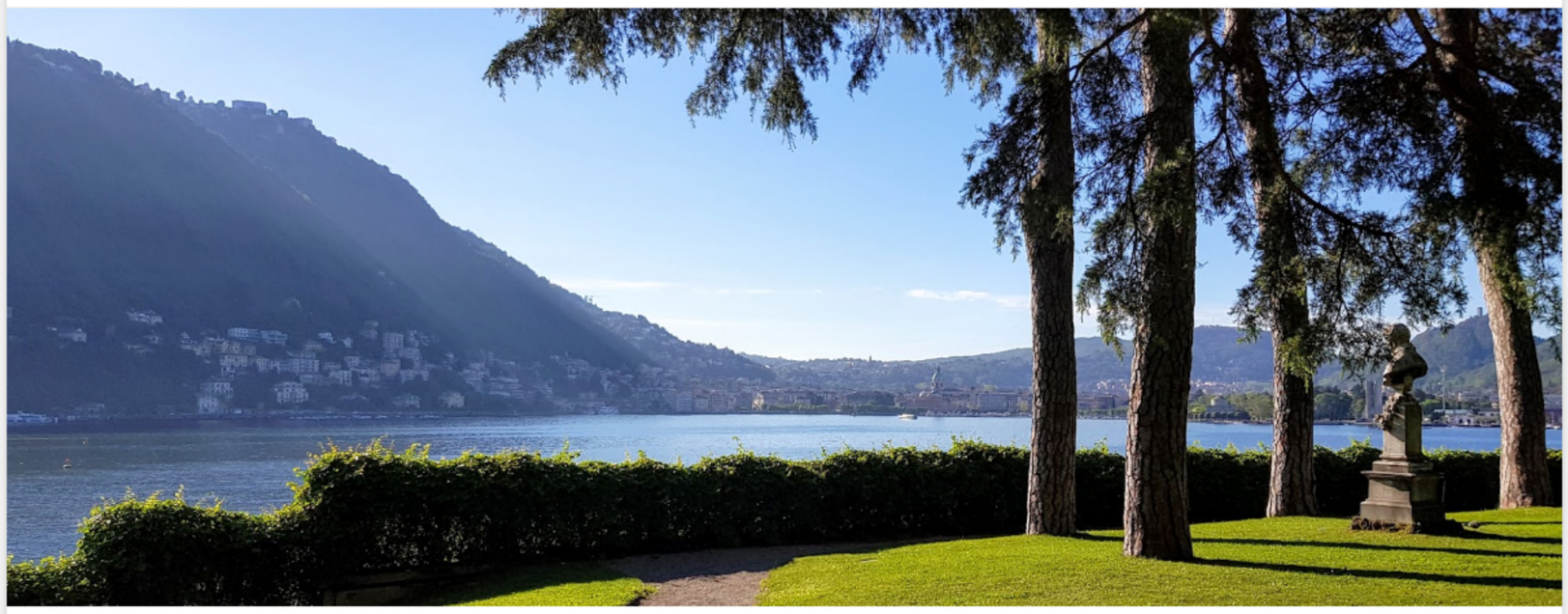

Registration

Registration fee is for the online, virtual event.

Registration: 75 EUR, online (All fees include VAT.)

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Postal code

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Payment information (required)

Registration fees

○ fee

Would you like to give a presentation of your work during the school?:

○ Yes ○ No

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CDAC 2021 Registration fees

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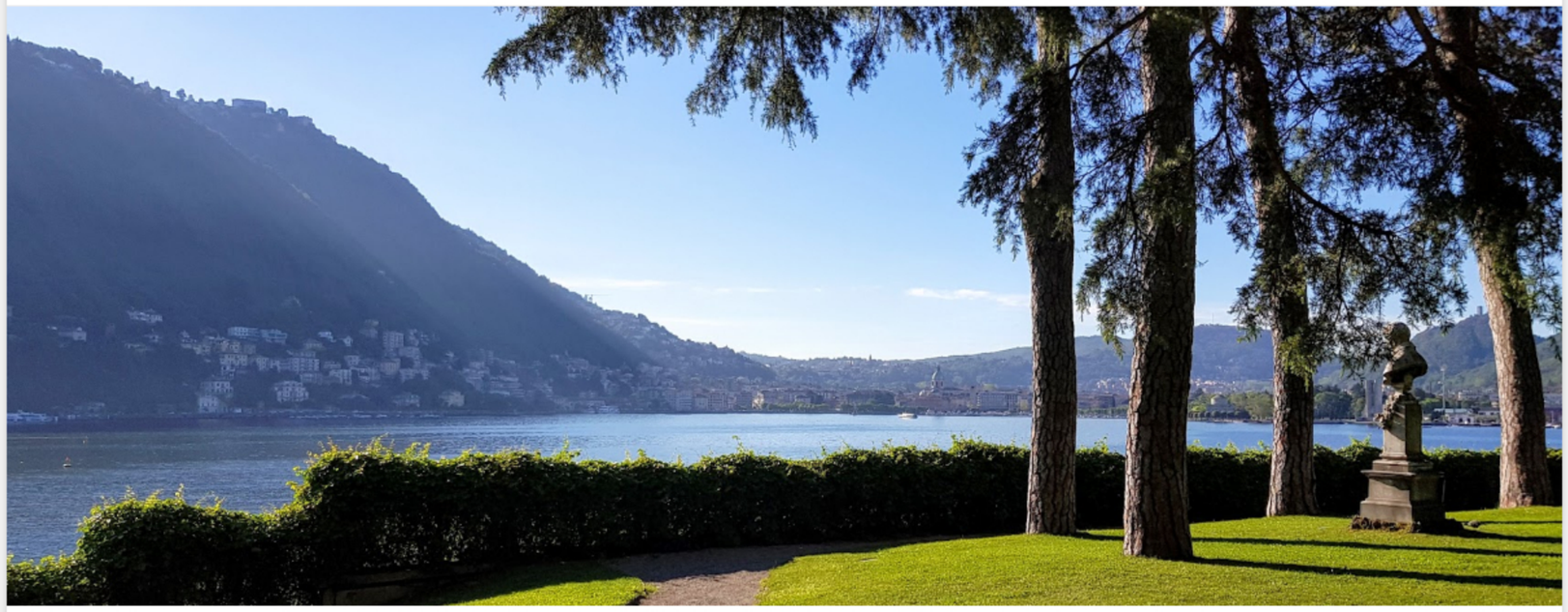
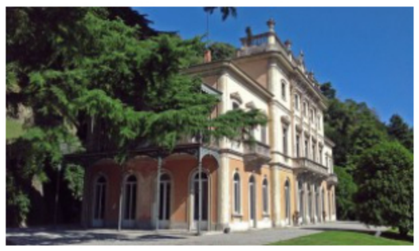


Venue

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.

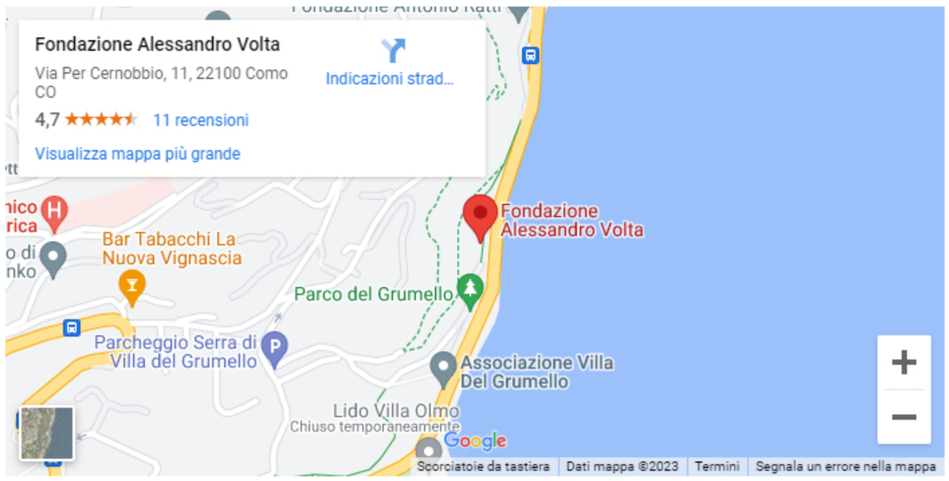


Venue: The school will be held at Villa del Grumello, Via per Cernobbio 11, Como (Italy).

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".



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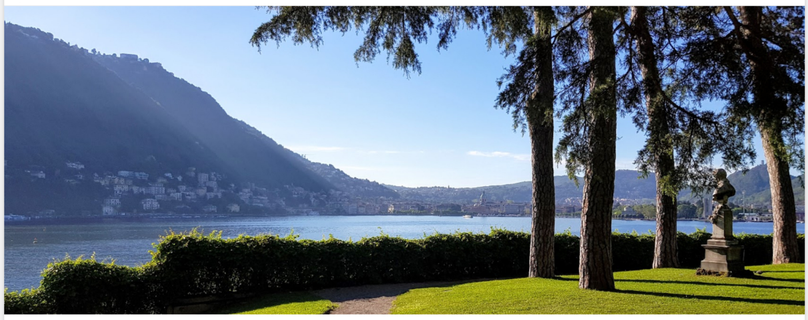

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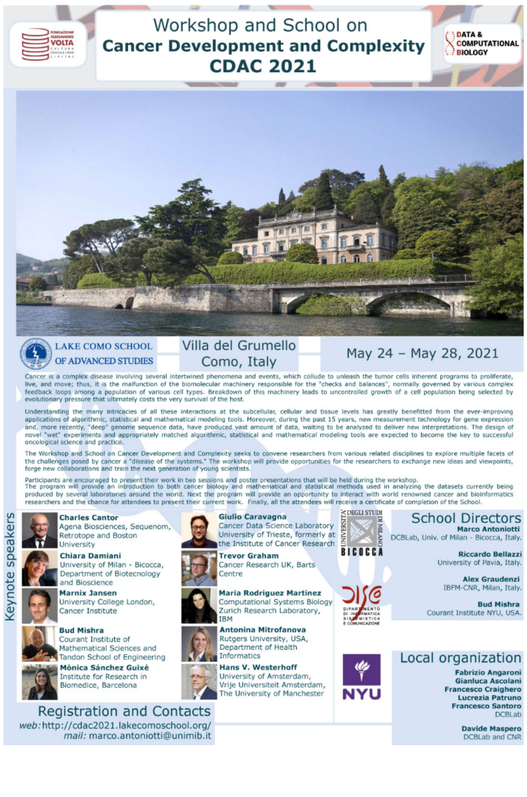

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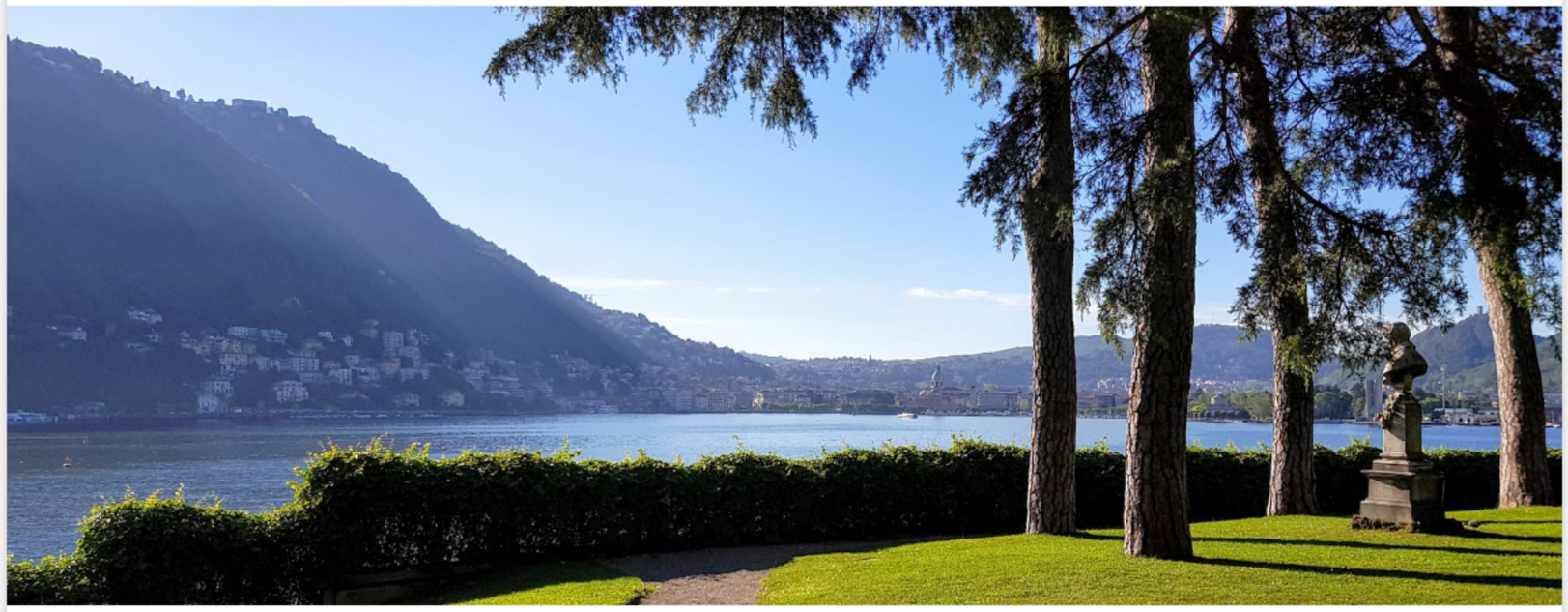

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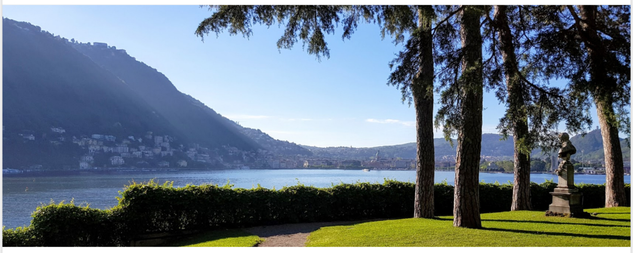

Program

Preliminary Schedule

Time (UTC+2)	Mon May 24	Tue May 25	Wed May 26	Thu May 27	Fri May 28
9:00 - 10:30		Mònica Sánchez-Guixé (*Tutorial*)	Trevor Graham (*Lecture*)	María Rodríguez-Martínez (*Lecture*)	Hans Westerhoff (*Lecture*)
10.30 - 10.45	**Welcome**	**Break**	**Break**	**Break**	**Break**
10:45 - 12:15	Trevor Graham (*Tutorial*)	Giulio Caravagna (*Tutorial*)	Giulio Caravagna (*Lecture*)	Marnix Jansen (*Lecture*)	Chiara Damiani (*Lecture*)
12:15 - 13:45	Hans Westerhoff (*Tutorial*)	Marco Pellegrini (*Partecipants' talks*)	Shadi Shafighi (*Partecipants' talks*)	Bruno Galuzzi (*Partecipants' talks*)	**Open discussion**
13:45 - 14:30	**Lunch break**	**Lunch break**	**Lunch break**	**Lunch break**	
14:30 - 16:00	Bud Mishra (*Lecture*)	Chiara Damiani (*Tutorial*)	Charles Cantor (*Lecture*)	Mónica Sánchez-Guixé (*Lecture*)	
16:00 - 17:30	RxCovea (*joint meeting*)			Antonina Mitrofanova (*Lecture*)	

CDAC 2021 schedule (downloadable PDF)

Preliminary Talks Titles and Abstracts

Charles Cantor

"New techniques and methods that will impact the understanding and the management of cancer"

Cancers generally become increasingly heterogeneous as they develop. They accumulate point mutations, DNA rearrangements and eventually massive chromosomal abnormalities. Cancers also remodel their chromatin through epigenetic changes, presumably to try to create and maintain a less differentiated phenotype than their tissue of origin. To understand cancer, we must understand how the heterogeneity originates and develops. To manage cancer efficiently, we must be able to detect it before the level of heterogeneity makes a curative treatment nearly impossible.

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Giulio Caravagna

"Model-based interpretation of cancer whole genome sequencing data: from subclonal populations to evolutionary trajectories"

In these two lectures we will discuss the fundamental problem of interpreting cancer growth and evolution from WGS data. We will discuss the main problems in assessing data quality, reliable subclonal deconvolution estimates integrating population genetics and machine learning, and comparing evolution across different patients. The lectures will present the theory underlying some recently developed models to this purpose, and will show how to run these analyses on real data. Attendants are invited to follow the practical parts of the lectures on their computer (programming will be done in R).

Chiara Damiani

"Data integration to unravel cancer metabolic variation and regulation"

The excessive genetic heterogeneity of cancer cells and the general failure of somatic mutation calling in supporting the identification of effective cancer treatments have fostered an increasing interest towards cancer metabolism. Cell metabolism is indeed the most obvious product of the interplay between genetic and environmental factors. Moreover, the metabolic requirements of highly proliferating cells markedly differ from those of quiescent ones. Yet, cancer cells cope with these requirements heterogeneously, as they are exposed to different levels of nutrients in time and space. The specific metabolic program of a cell cannot be deduced from currently accessible omics data, unless different omics are opportunely integrated with one another and with mathematical models. In the first part of this talk the basics of computational modeling of metabolism are presented, along with some demo.

In the second part of the talk a recent work is presented that dissects the regulation of cancer metabolism, by integrating transcriptomics and metabolomics data into constraint-based and kinetic models. Recent advancements on the characterization of intra-tumor metabolic heterogeneity from single-cell RNA-seq data are also reported.

Trevor Graham

Tutorial: "Using mechanistic mathematical models to explore cancer genomes"

Cancer genomes are rich sources of information about the dynamical process of tumour evolution. Arguably the most common approach to mining this information is find patterns in the data, and then post-hoc propose the process that produced these patterns. An alternative approach is propose an evolutionary model up-front and use inference to ask how well the model is supported by the data. Here, we will discuss these two approaches and explore some of the challenges (and interesting aspects) of constructing mathematical models of tumour genomic evolution. I hope this will be an interactive session with lots of discussion.

Lecture: "Measuring evolutionary dynamics of human tumours"

As tumours grow, each cell within the tumour independently accumulates new mutations. The pattern of genetic heterogeneity between tumour cells (intra-tumour heterogeneity – ITH) is read out of the evolutionary dynamics of cancer growth. Here I will discuss our work to mathematically model ITH and parameterise these models using genomic data. We show how positive and negative (immune-mediated) selection and neutral evolution shapes pattern of ITH and report the frequency of these evolutionary patterns across cancer types. We explore the influence of spatial processes on the detectability of evolutionary dynamics.

Marnix Jansen

María Rodríguez-Martínez

"Understanding the determinants to T cell receptor binding in cancer immunotherapies"

The activity of the adaptive immune system depends on the recognition of foreign antigens by T cells by their specific T cell receptors (TCRs). A correct understanding of the determinants that govern the binding of T cells to cancer neo-antigens is crucial to design better immunotherapies, distinguished by more effective binding profiles and less cross-reactive effects.
Our group has recently developed TITAN, a multi-modal deep learning model that predicts the binding affinity between TCRs and epitopes, outperforming the state of the art in this difficult task. Interestingly, TITAN allows to study independently the generalization capabilities to new TCRs and/or epitopes, which previous models have struggled with.
Furthermore, to enhance the interpretability of the predictions, TITAN exploits interpretable attention mechanisms that selectively highlight the patterns in the TCR and epitope sequence that are more important to make the prediction. In parallel, we are investigating the use of alternative techniques to enhance prediction transparency, for instance, based on the use of probabilistic graphical models. This is an example of how the combined used of AI and traditional mathematical approaches can result in more performant models able to make great strides into a multitude of fields, including prediction of autoantigens in autoimmune diseases, development of immunotherapies for cancer, or vaccine design.

Bud Mishra

"Variant(Stranger)/Scariant(Danger) Games: Cancer 2 Covid & Back"

Antonia Mitrofanova

"Pathway-centric approaches to uncover interpretable markers of treatment response in cancer patients"

Identification of functional cancer markers requires in-depth understanding of complexity of mechanisms that govern its initiation, progression, and therapeutic response. We have developed a series of computational algorithms that utilize pathway-centric approaches to identify markers, which constitute functional units for elucidation of interpretable mechanisms of treatment resistance and potential therapeutic targeting. We have demonstrated that these approaches are superior compared to black-box methods and gene-level analysis alone. When applied to tamoxifen resistance in ER+ breast cancer, chemotherapy resistance in lung and colorectal adenocarcinoma, pathway-centric approaches demonstrated their robustness, high accuracy, and superior ability to predict treatment response. Our predictions were independent of overall disease aggressiveness and not affected by common co-variates. To further elucidate the complexity of upstream pathway-centric regulation, we coupled our approaches with transcriptional regulatory network inference, opening an avenue for precision therapeutic targeting. We propose that prioritization of patients using interpretable pathway-based markers is central to personalized therapeutic planning and improved cancer course and outcomes.

Mònica Sánchez-Guixé

Tutorial: "Genomic analysis of rare pediatric cancer cases with secondary neoplasms"

The discovery of cancer driver genes is key to understand the molecular processes causing cancer and to ultimately define treatment strategies in the clinics. The Barcelona Biomedical Genomics (BBG) group has developed IntOGen [1] (intogen.org), a tool for the discovery of cancer driver genes. We have gathered somatic mutations from publicly available data repositories, collecting a total of 28 076 samples in 221 different cohorts across 66 different cancer types. IntOGen pipeline receives the collected genomic data for each cohort and applies 7 different methods for driver identification. The candidate drivers identified by each method are then systematically combined creating a highly reliable list of candidate driver genes per cohort. In the current release, 568 cancer driver genes have been identified. Furthermore, mutational features from these cancer genes can be used to train BoostDM [2] (cancergenomeinterpreter.org), another framework developed by the BBG. This machine learning model classifies which somatic point mutations bear the capacity of driving tumorigenesis, and is able to robustly predict the driver capacity of all potential single nucleotide variants along the gene sequences across different tumor types, generating the first in silico saturation mutagenesis of cancer genes.

1. Martínez-Jiménez F, Muiños F, Sentís I, Deu-Pons J, Reyes-Salazar I, Arnedo-Pac C, et al. A compendium of mutational cancer driver genes. Nat Rev Cancer. 10 de agosto de 2020;1-18.
2. Muiños F, Martinez-Jimenez F, Pich O, Gonzalez-Perez A, Lopez-Bigas N. In silico saturation mutagenesis of cancer genes. bioRxiv. 9 de junio de 2020;2020.06.03.130211.

Lecture: "IntOGen: from data repositories to cancer driver gene discovery"

Cancer mutations can originate from many carcinogenic sources. Several mutational processes in cancer have been described, like the mutational events caused by cancer therapy [1], where some chemotherapeutic agents have been linked to the development of treatment-related AMLs. Still, many rare pediatric secondary neoplasms need to be further characterized to determine the origin of their tumorigenesis. In this study, we aim to uncover the driver events behind pediatric cancer samples with rare secondary neoplasms. In collaboration with Sant Joan de Déu Barcelona Children's Hospital, we have performed WGS on tumor samples from 6 pediatric patients that have developed a secondary neoplasm with major clinical differences from their primary. First, we have applied mutation calling pipelines (snvs, small indels, copy number alterations and structural variants) to accurately annotate all genomic alterations, and have reconstructed the evolutionary events for each patient. To identify possible cancer predisposition, we have thoroughly analyzed germline alterations, and then carefully checked for common events between both tumors that could point to a case of early embryo clone expansion or mosaicism. Finally, we dissected the mutational signatures for each tumor and analyzed the implication of cancer therapy on the development of the second neoplasm.

1. Pich, O, Muiños, F, Lolkema, MP et al. The mutational footprints of cancer therapies. Nat Genet 51, 1732–1740 (2019). https://doi.org/10.1038/s41588-019-0525-5

Hans Westerhoff

"What if exception rules?"

Molecules in solution are a mess: they diffuse, roll, and bump into one another. How come then that (almost) every time a human is born, it develops two arms, two legs and two eyes? Or, that every time we inject glucose into a cell, it develops a transient reduction of NAD to NADH (visible by fluorescence)? Or that a culture of mammalian cells growing on a surface stops growing when they touch each other?

I will remind you of three grand paradoxes of the dynamic molecular world. The first is that dynamic worlds strive towards 'chaos' and that precisely by doing so, they end up in order. This 'order' is the rule, and the 'chaos' is the plethora of exceptions around it. Because most systems in and around us consist of lots of molecules, this preference for rules is so strong that we mostly observe those systems as 'deterministic', i.e. as completely determined by rules. It is these rules that one reads on Wikipedia and in the textbooks of physics and chemistry.

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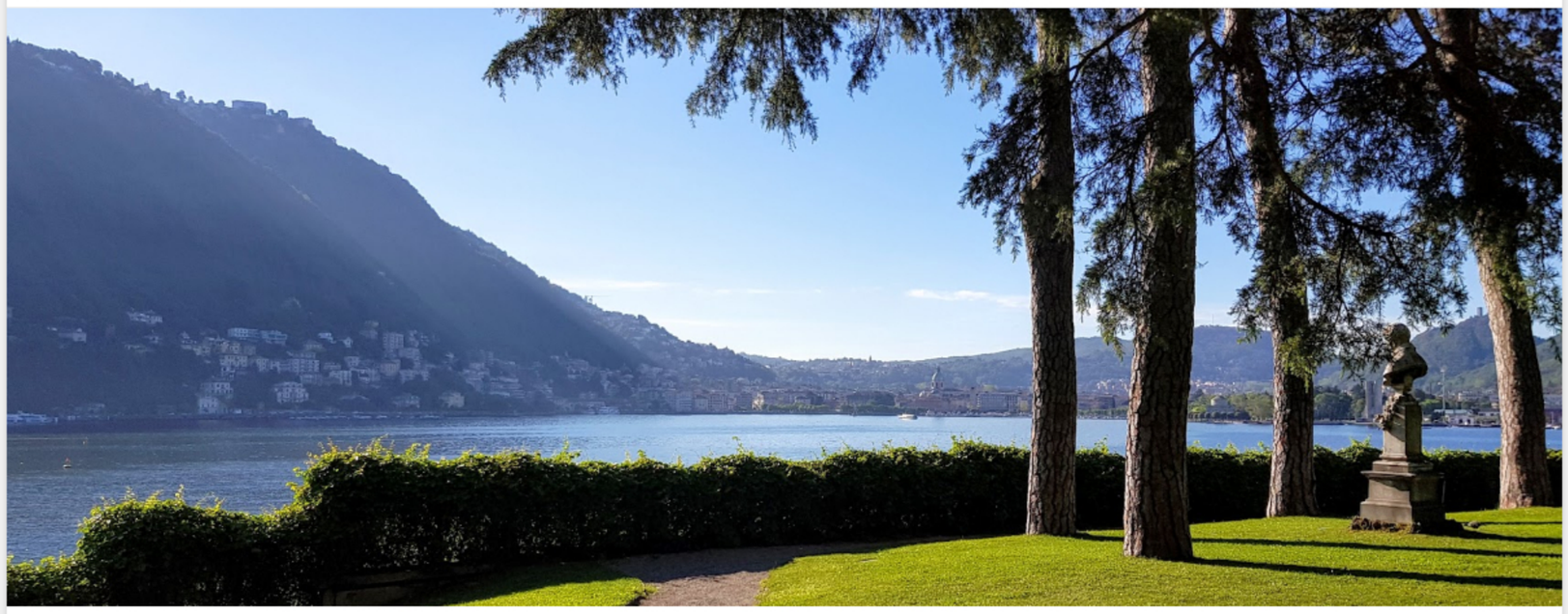
School on Cancer Development and Complexity (CDAC 2021)

Lake Como School of Advanced Studies, - May 24-28, 2021



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Registration fee is for the online, virtual event.

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CDAC 2021 Registration fees

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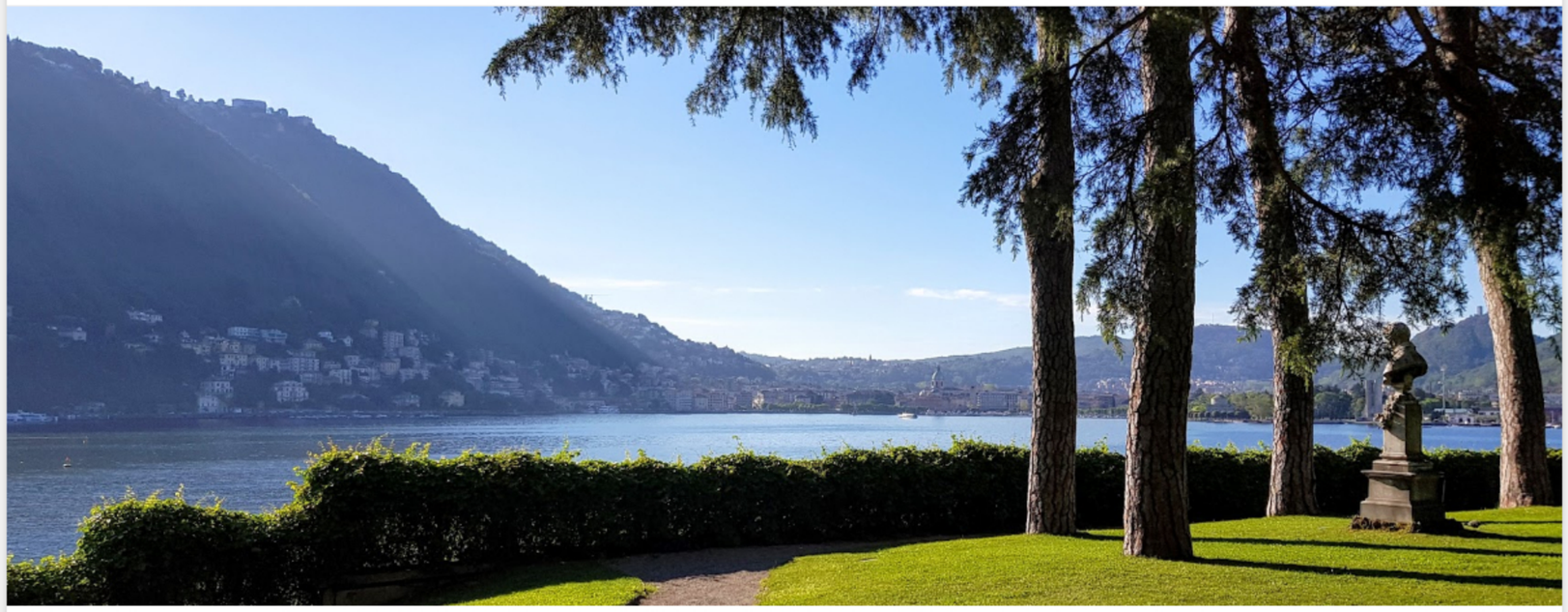
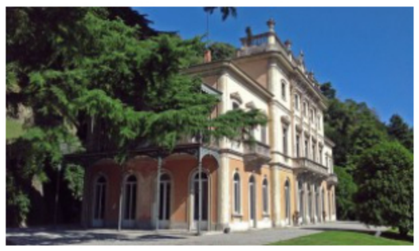


Venue

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.

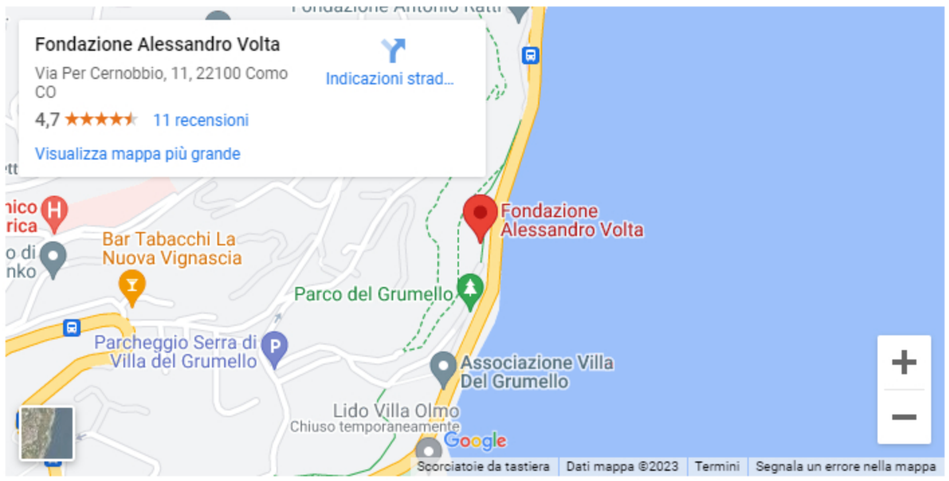


Venue: The school will be held at Villa del Grumello, Via per Cernobbio 11, Como (Italy).

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".



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