Keynote Speakers and Lectures

Charles Cantor (Agena Biosciences, Sequenom, Retrotope and Boston University, USA)

Tutorial: Is precision medicine possible?

Research: Sensitive detection of low levels of cancer-specific DNA sequence difference

---

Philippe Gorry (GREThA UMR CNRS 5113, Université de Bordeaux, France)

Tutorial: Pharma Competitive Intelligence for Dummies

Pharma-biotech industry is facing a changing world with many market challenges. In that context, technology scouting is evolving toward pharma competitive intelligence and would take advantage of the information flow during the drug R&D cycle times. Use of open sources databases for drug R&D milestone and versatile data visualization tool can help to visualize trends across market, bringing real-time clinical data, across geographies and demographics. It could help biotech startups as well academic laboratories to manages flow of competitive intelligence information, learn about new technologies in the market, that could to benefit research laboratories by improving discovery platforms or by identifying public-private partnership opportunities.

Research Topic: "Economic Dimensions of Precision Medicine in Oncology"

Precision medicine is a new paradigm for disease treatment and prevention, taking in account genes, environment, and lifestyle for each patient. In oncology, it is the use of genomic information about person's tumor in order to individualize treatments. It is rapidly gaining prominence in OECD countries, and it is supported by the pharma industry, moving from blockbuster to niche buster drug model, with the support of the Orphan Drug legislation. Today, the increased availability of targeted therapies with their high cost, and their use for chronic disease, raises a debate about accessibility, cost-effectiveness, and reimbursement. So, if precision medicine approaches become part of routine healthcare, paying for precision drugs would be a future challenge by checking traditional models of health protection systems. We will take advantage of on-going research on the Orphan Drug market to explore the economics dimensions of niche buster drug model on innovation dynamics, intellectual property protections, R&D return on investment and welfare impact.

Marcin Imielinsky (Weill Cornell Medical College, Cornell University, New York, USA)

Tutorial: Deciphering junctions, copy number, and walks in cancer whole genomes with linked-reads

The altered structure of cancer DNA can be represented as a genome graph of nodes representing reference genomic intervals (DNA alleles) and edges representing junctions (3-5 phosphodiester bonds). A subset of edges in the genome graph are variant– representing signed pairs of genomic locations that were previously distant (e.g. in the reference genome) and are made adjacent (e.g. in a cancer) through DNA breakage and fusion. The copy number and rearrangement states of cancer genomes are constrained by junction balance, a constraint that arises from from the physical intuition that every copy of every (non-telomeric) interval in the genome must have a left and a right neighbor. In practical terms, junction balance requires the copy number of nodes in the genome graph to be consistent with the copy number of incoming and outgoing edges. I demonstrate how this inference can be performed on standard cancer whole genome sequencing (WGS) data through the analysis of read depth subject to junction balance constraints. We implement this robustly as a mixed-integer quadratic program optimization (JaBbA, https://github.com/mskilab/JaBbA) which also allows for loose ends that represent missing junctions (e.g. rearrangements occurring in unamappable genomic regions) and result in copy number changes unaccounted for by

Cancer Development And Complexity 2017

Lake Como School of Advanced Studies, May 23 - 26, 2017

Home | Keynote Speakers and Lectures | Program | Accommodation | Registration | Venue

Venue

The school will be held in the facilities offered by the Fondazione Alessandro Volta, Como (Italy), and specifically at Villa del Grumello, a nice villa close to Como: the center of the town can be reached in a ten minutes walk along the border of the lake.

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

Cancer Development And Complexity 2017. < Back to Lake Como School of Advanced Studies

Tutorial: "A user's guide to subclonal reconstruction"

Research topic: "Reconstructing the evolutionary history of cancers using DNA-seq data"

Ben Raphael (Princeton University, Princeton, USA)

Tutorial: Identification of Cancer Genes, Pathways, and Networks

A key challenge in interpretation of cancer genome sequencing data is to distinguish driver mutations responsible for cancer development from random passenger mutations. We will survey a number of computational approaches to predict driver mutations. These include: (1) methods to identify recurrently mutated genes across cohorts of cancer genomes/exomes; (2) approaches that examine clustering of mutations in pathways and interaction networks; (3) algorithms that consider correlations between mutations including mutual exclusivity and co-occurrence. We will demonstrate how these approaches have been used in a number of large-scale cancer sequencing projects.

Research: Algorithms for Inferring Evolution and Migration of Tumors

Cancer is an evolutionary process driven by somatic mutations that accumulate in a population of cells that form a primary tumor. In later stages of cancer progression, cells migrate from a primary tumor and seed metastases at distant anatomical sites. I will describe algorithms to reconstruct this evolutionary process from DNA sequencing data of tumors. These algorithms address challenges that distinguish the tumor phylogeny problem from classical phylogenetic tree reconstruction, including challenges due to mixed samples and complex migration patterns.

Andrea Sottoriva (The Institute of Cancer Research, London, UK)

Research: "Quantifying clonal selection in human cancer using next-generation sequencing data"

Recent studies have identified prevalent subclonal architectures within many cancer types. However, the temporal evolutionary dynamics that produce these subclonal architectures remain largely unknown. Although we can detect subclones in cancer, measuring what these subclones are doing remains challenging. We developed a computational model of tumour evolution based on branching processes that allows measuring the dynamics of clonal selection using high throughput sequencing data from bulk cancer cell populations. Application of our method to high-depth sequencing data from gastric and lung cancers revealed that detectable subclones consistently emerged early during tumour growth and had considerably large fitness advantages (>20% growth advantage). Our quantitative framework provides new insight into the evolutionary history of cancers by facilitating the measurement of fundamental evolutionary parameters in individual patients.

Tutorial: "Evolutionary modelling and Bayesian inference on cancer genomic data"

Genomics has revolutionized cancer research and has led to the generation of astonishing amounts of data. Such large-scale multidimensional datasets contain an overwhelming amount of information that is often hard to make sense of. In particular, there is the need to integrate genomic information into a solid mechanistic framework based on cancer evolution that allows understanding what has happened in individual patients over time (the big hidden variable in cancer). In evolutionary biology, mathematical modeling and in particular population genetics have helped making sense of genetic data for decades, however such wealth of literature is often underexploited in cancer. In this tutorial we present the use of established statistical inference frameworks, in particular Approximate Bayesian Computation, that allow integrating complex mathematical and computational models of tumour evolution with commonly available genomic data, offering unprecedented insight into the dynamics of cancer evolution.

Simon Tavaré (Cancer Research UK, Cambridge, UK)

Tutorial: "An introduction to Approximate Bayesian Computation"

Research: "How to study tumours in 3.5D"