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Mathematical and Computational Oncology

First International Symposium, ISMCO 2019 Lake Tahoe, NV, USA, October 14–16, 2019 Proceedings

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Preface

It is with great pleasure that we welcome you to the proceedings of the First International Symposium on Mathematical and Computational Oncology (ISMCO 2019), which was held in Lake Tahoe, Nevada, USA (October 14–16, 2019).

The purpose of ISMCO is to provide a common interdisciplinary forum for mathematicians, scientists, engineers, and clinical oncologists throughout the world to present and discuss their latest research findings, ideas, developments, and applications in mathematical and computational oncology. Despite significant advances in the understanding of the principal mechanisms leading to various cancer types, less progress has been made toward developing patient-specific treatments. Advanced mathematical and computational models could play a significant role in examining the most effective patient-specific therapies. ISMCO aspires to enable the forging of stronger relationships among mathematics and physical sciences, computer science, data science, engineering, and oncology with the goal of developing new insights into the pathogenesis and treatment of malignancies.

The program included eight oral sessions, one special track, one tutorial, three invited talks, and seven keynote presentations. We received 30 submissions from which we accepted 19 submissions (7 papers and 12 abstracts) for oral presentation. This LNCS volume includes only the papers accepted for presentation; all abstracts accepted for presentation appeared in an online volume of Frontiers (link is provided on the ISMCO website).

All submissions were reviewed with an emphasis on the potential to contribute to the state of the art in the field. Selection criteria included accuracy and originality of ideas, clarity and significance of results, and presentation quality. The review process was quite rigorous, involving three independent blind reviews followed by several days of discussion. During the discussion period we tried to correct anomalies and errors that might have existed in the initial reviews. Despite our efforts, we recognize that some papers worthy of inclusion may have not been included in the program. We offer our sincere apologies to authors whose contributions might have been overlooked.

Organizing ISMCO for the first time was rewarding but also challenging due to the diverse background and interests of the targeted audience. Although significant advances have been made in various fields individually, it is evident now more than ever that new challenges in oncology can only be addressed by truly transcending disciplinary boundaries. Effectively bridging the gap among physical sciences, computer science, engineering, data science, and oncology is an absolute necessity in the hope of making significantly more progress in the fight against cancer.

Many contributed to the success of ISMCO 2019. First and foremost, we are grateful to the Steering, Organizing, and Program Committees; they strongly welcomed, supported, and promoted the organization of this new meeting. Second, we are deeply indebted to the keynote speakers who warmly accepted our invitation to talk at ISMCO 2019; their reputation in mathematical and computational oncology added

significant value to and excitement to the meeting. Next, we wish to thank the invited speakers, the authors who submitted their work to ISMCO 2019 and the reviewers who helped us to evaluate the quality of the submissions. It was because of their contributions that we succeeded in putting together a technical program of high quality. Finally, we would like to express our appreciation Springer-Verlag, Frontiers, and the International Society for Computational Biology (ISCB) for sponsoring ISMCO 2019.

We sincerely hope that ISMCO 2019 offered participants opportunities for professional growth. We look forward to many more successful meetings in mathematical and computational oncology.

September 2019

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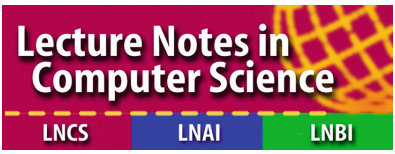

Keynote Talks

Breast Cancer Genomics: Tackling Complexity with Functional Genomics and Patient-Derived Organoids

Ron Bose

Washington University School of Medicine, USA

Abstract. Breast cancer is a heterogeneous disease with multiple molecular subtypes and three major clinical subtypes: hormone receptor positive, HER2 positive, and triple negative breast cancer. These three clinical subtypes are very important because they determine the drugs used for patient treatment. Cellular, molecular, and genomic understanding of breast cancer has resulted in new treatments for breast cancer. In 2019, the FDA approved an oral PIK3CA inhibitor for PIK3CA mutated, hormone receptor positive, Stage IV breast cancer and immunotherapy for triple negative, Stage IV breast cancer. Major challenges facing future research on breast cancer and other cancers are: (1) Interpreting genome sequencing results to better understand the effects and significance of new or under-characterized mutations, and (2) having platforms for rapid biological testing of hypotheses. I will provide examples of how my laboratory is trying to address both of these challenges.

High Dimensional Unsupervised Approaches for Dealing with Heterogeneity of Cell Populations and Proliferation of Algorithmic Tools

Yuval Kluger

Yale University School of Medicine, USA

Abstract. Revealing the clonal composition of a single tumor is essential for identifying cell subpopulations with metastatic potential in primary tumors or with resistance to therapies in metastatic tumors. Bulk sequencing technologies provide only an overview of the aggregate of numerous cells. We propose an evolutionary framework for deconvolving data from a bulk genome-wide experiment to infer the composition, abundance and evolutionary paths of the underlying cell subpopulations of a tumor. With advances in high throughput single cell techniques, we can in principle resolve these issues. However, these techniques introduce new challenges such as analyzing datasets of millions of cells, batch effects, missing values etc. We provide several algorithmic solutions for some of these challenges. Finally, a key challenge in bioinformatics is how to rank and combine the possibly conflicting predictions of several algorithms, of unknown reliability. We provide new mathematical insights of striking conceptual simplicity that explain mutual relationships between independent classifiers/algorithms. These insights enable the design of efficient, robust and reliable methods to rank the classifiers performances and construct improved predictions in the absence of ground truth.

Career Development Opportunities: The Government Can Help!

Susan Perkins

National Cancer Institute, USA

Abstract. The National Cancer Institute is committed to the training and support of the next generation of cancer researchers. The NCI funds training at extramural institutions across the nation, using funding mechanisms that include fellowships, career development awards, and institutional training grants. This session will provide a broad overview of this wide range of opportunities, with an emphasis on some new NCI programs for early-stage investigators, as well as some tips and tools for applicants.

Bringing Math into the Clinic: Mathematical Oncology at City of Hope

Russell Rockne

City of Hope, USA

Abstract. In this keynote lecture, I will provide vignettes of applications of mathematical modeling aimed at use in the clinic within the Division of Mathematical Oncology at City of Hope. I will focus on the use of non-invasive imaging (MRI, PET) to calibrate and validate patient-specific mathematical models of cancer growth and response to therapy. Applications include primary brain tumors and breast cancer, with therapeutic applications including cell-based therapies, radiation therapy, and combination therapies. I will provide a forward-looking view of Mathematical Oncology at City of Hope and present clinical challenges that may be addressed with mathematical modeling.

Application of Functional Genomics to Oncology Practice: Opportunities, Successes, Failures and Barriers

Panos Anastasiadis and George Vasmatzis

Mayo Clinic, USA

Abstract. Radical improvement in cancer care can be accomplished by individualizing patient management via the application of genomics and functional model systems into clinical practice. Recent breakthroughs in immunotherapy (i.e. checkpoint inhibitors) and targeted therapies (i.e. NTRK inhibitors) have shown that therapy of advanced cancers might become agnostic to the organ of origin, arguing for a more individualized approach to patient care. Emerging genomics technologies, data integration and visualization platforms are powerful tools to determine the state of the individual's tumor and point to tailored treatments. Furthermore, an efficient combination of comprehensive genomics with 3D microcancer functional model systems can further refine treatment decisions. However, applying such disruptive technologies in clinical practice is not trivial. Regulatory, financial and clinical barriers will be discussed.

Recognition of Non-synonymous Somatic Mutations by Tumor Infiltrating Lymphocytes (TIL) in Metastatic Breast Cancer

Nikos Zacharakis

National Cancer Institute, USA

Abstract. Adoptive transfer of tumor infiltrating lymphocytes (TIL) can mediate long-term durable regression in patients with metastatic melanoma, a type of cancer which is characterized by a high number of mutated genes and pronounced lymphocytic infiltrate. Common epithelial cancers, including breast cancer, express far fewer somatic mutations than melanoma and the level of reactive TIL is limited. This pilot study investigated the ability to identify personalized non-synonymous somatic mutations in metastatic breast cancer lesions, to grow TIL that recognize the products of these mutations, and to adoptively transfer these TIL into patients with metastatic breast cancer, refractory to other treatments. Metastatic and primary tumor lesions from thirty one patients with breast cancer were studied in the Surgery branch, NCI, NIH and all of them were found to contain and express mutated genes (range: 4-1788 , median: 99). TIL recognized at least one (range: 1-10, median: 3) mutated product in 21 of 32 the patients (66%). Five evaluable patients with metastatic breast cancer, refractory to prior multiple lines of treatment, were treated with enriched mutation-reactive TIL in our ongoing pilot clinical trial. The immunogenicity of mutations in the majority of the patients with metastatic breast cancer can be the platform for an adoptive T cell transfer therapeutic approach targeting those mutated genes.

Inferring Tumor Evolution from Bulk and Single-cell Sequencing Data

Ben Raphael

Princeton University, USA

Abstract. Cancer is an evolutionary process driven by somatic mutations that accumulate in a population of cells. These mutations provide markers to infer the ancestral relationships between cells of a tumor, to describe populations of cells that are sensitive/resistant to treatment, or to study migrations between a primary tumor and distant metastases. However, such phylogenetic analyses are complicated by specific features of cancer sequencing data such as heterogeneous mixtures of cells present in bulk tumor sequencing data, undersampling in single-cell sequencing data, and large-scale genome rearrangements. In this talk, I will describe algorithms to address several problems in tumor evolution including: the inference of seeding patterns of metastases; the identification of copy number aberrations and whole-genome duplications in multi-sample sequencing data; and the integrated analysis of single-nucleotide mutations and copy number aberrations in single-cell sequencing data.

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