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ÉCOLE NORMALE SUPÉRIEURE

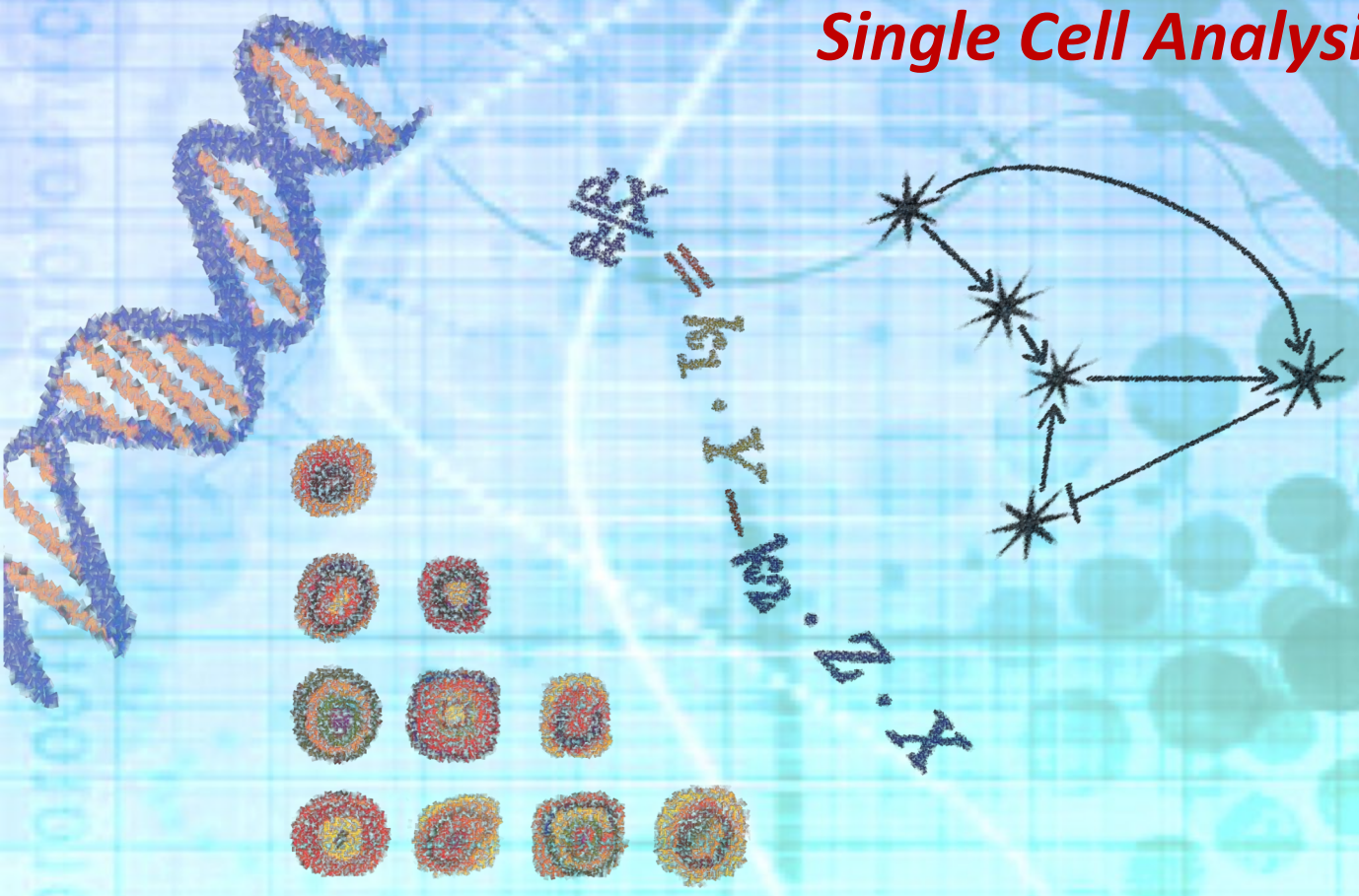
institutCurie

September 23-28 2019

2nd course

Computational Systems Biology of Cancer

Single Cell Analysis



Institut Européen de Finance Louis Bachelier

OWKIN

SERVIER

CRC Press Taylor & Francis Group

Google

CRI

NOVARTIS

Together, let's beat cancer

training.institut-curie.org

Course information

-Venue
BDD Amphithéâtre, Biologie du Développement building (BDD)
Institut Curie - Centre de Recherche
11-13 rue Pierre et Marie Curie, 75005 Paris

-Registration desk
Open from Monday, September 23rd on 8.30 in the BDD hall

-Attendance of all events during the course is mandatory
Each Master, PhD and post-doc participant must sign in the presence form twice a day

-**Certificate of course attendance**
Will be issued according to presence signatures and distributed at the end of the course

-**Posters**
Location
BDD Annexes 1-3. Posters are permanently accessible for viewing and discussions.

Posters placement and removal
Odd numbers: Placed during the first coffee break and lunch break on Monday, September 23rd and removed after the Poster Session 2 on Tuesday, September 24th

Even numbers: Placed during the first coffee break and lunch break on Wednesday, September 25th and removed after the Poster Session 4 on Thursday, September 26th

Authors are requested to stand near their posters during the poster sessions
Odd numbers

POSTER SESSION 1	Monday, September 23rd	16.00-17.00
POSTER SESSION 2	Tuesday, September 24th	17.00-18.00

Even numbers

POSTER SESSION 3	Wednesday, September 25th	17.00-18.00
POSTER SESSION 4	Thursday, September 26th	16.30-17.30

-Internet access
Network: Curie_Events
Login: Tetrameles*45D

-Marie Curie museum and garden visit options
The free-of-charge visits will take place during lunch breaks on Wed-Fri September 25th - 27th.
All interested persons are asked to subscribe at the reception desk.
The groups will be called and guided to the museum from the BDD Hall.

- Best presentations prizes (sponsored by CRC press)
Friday 27th at 18.00-18.30

-Coffee/tea and lunches
Provided in the BDD hall

-Welcome reception
Monday 23th at 17.30-19.00 at Chez Marie (follow support persons)

-Farewell cocktail
Friday 27th at 18.30-21.00 at Chez Marie (follow support persons)

-Badges recycling
Return your badge in the end of the course

-Find the right person to ask for help
Persons with badges “ASSISTANCE”

-Organizers

Emmanuel BARILLOT	Institut Curie - INSERM U900, FR
Inna KUPERSTEIN	Institut Curie - INSERM U900, FR
Vassili SOUMELIS	Institut Curie - INSERM U932, FR
Denis THIEFFRY	IBENS - ENS, FR
Thomas WALTER	MINES - ParisTech, FR

-Scientific committee

Laurence CALZONE	Institut Curie - INSERM U900, FR
Tatiana POPOVA	Institut Curie - INSERM U830, FR
Andrei ZINOVYEV	Institut Curie - INSERM U900, FR

2nd Course on Computational Systems Biology of Cancer - September 23-28, 2019

A Training Unit International Course - Open conferences (in blue or orange)

Monday, September 23th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 1: Pathway databases for single cell research** Chairs: Emmanuel Barillot	
08:50 09:00	**Training Unit and Emmanuel Barillot** Institut Curie, Paris, France	Welcome and opening remarks
09:00 10:00	**Loredana Martignetti** *Didactic introductory lecture* Imagine Insitut, Paris, France	**Approaches in computational single cell genomics data analysis**
10:00 10:30	COFFEE/TEA BREAK (BDD Hall) AND POSTERS PLACEMENT (odd numbers, BDD, Annexes 1-3)	
10:30 11:30	**Augustin Luna** Harvard Medical School, Boston, USA	**Pathway Commons resource for single cell data analysis and network-based interpretation**
11:30 12:30	**Flash presentations of projects by post-docs**	7 minutes/presentation
12:30 13:30	LUNCH (BDD Hall) AND POSTERS PLACEMENT (odd numbers, BDD, Annexes 1-3)	
Monday, September 23th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 2: Visualization and interpretation of single cell cancer data** Chairs: Vassili Soumelis	
13:30 14:30	**Reinhard Schneider** LCSB, Belval, Luxembourg	**Data integration and knowledge management in Biomedicine**
14:30 15:30	**Flash presentations of projects by post-docs and PhD students**	7 minutes/presentation and 4 minutes/presentation
15:30 16:00	COFFEE/TEA BREAK (BDD Hall)	
16:00 17:00	POSTER SESSION 1 (odd numbers, BDD Annexes 1-3)	Master student's journal club - session 1 (BDD Amphithéâtre)
17:30 19:00	**WELCOME RECEPTION (Chez Marie)**	

Tuesday, September 24th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 3: Single cell omics data analysis in tumor heterogeneity studies (1)** Chairs: Denis Thieffry	
09:00 10:00	**Julio Saez-Rodriguez** EMBL-EBI, Hinxton, UK	**Pathway-based analysis of single-cell data**
10:00 10:30	COFFEE/TEA BREAK (BDD Hall)	
10:30 11:30	**Luca Pinello** Harvard Medical School, Boston, USA	**Single Cell Trajectory Reconstruction Exploration and Mapping of omics data**
11:30 12:30	**Flash presentations of projects by PhD students**	4 minutes/presentation
12:30 13:30	LUNCH (BDD Hall)	
Tuesday, September 24th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 4: Single cell omics data analysis in tumor heterogeneity studies (2)** Chairs: Denis Thieffry	
13:30 14:30	**Thomas Höfer** Deutsches Krebsforschungszentrum, Heidelberg, Germany	**Tumorigenesis driven by aberrant stem cell dynamics**
14:30 15:30	**Andrew Teschendorff** UCL, London, UK	**Towards the quantification of Waddington's epigenetic landscape at the single-cell level**
15:30 16:00	COFFEE/TEA BREAK (BDD Hall)	
16:00 17:00	**Ioannis Xenarios** UNIL, Lausanne, Switzerland	**Cellular decision process using single data to build up cellular automata of differentiations and responses**
17:00 18:00	POSTER SESSION 2 (odd numbers, BDD Annexes 1-3)	Master student's journal club - session 2 (BDD Amphithéâtre)

Wednsday, September 25th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris		**Session 5: Exploring tumor microenvironment using single cell data (1)** Chairs: Laurence Calzone
09:00 10:00	**Denis Thieffry** IBENS-ENS, Paris, France	**Qualitative dynamical modeling of T-helper cell differentiation and reprogramming**
10:00 10:30	COFFEE/TEA BREAK (BDD Hall) AND POSTERS PLACEMENT (even numbers, BDD, Annexes 1-3)	
10:30 11:30	**Veronique Thomas-Vaslin** Sorbonne University, Paris, France	**Systems biology for cell proliferation quantification and modeling of lymphocyte dynamics: T-cell heterogeneity dynamics across aging and genetic origins**
11:30 12:00	**Flash presentations of projects by PhD students**	4 minutes/presentation
12:00 13:30	LUNCH (BDD Hall), POSTERS PLACEMENT (even numbers, BDD, Annexes 1-3) AND VISIT OF MARIE CURIE MUSEUM (Group 1)	
Wednsday, September 25th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris		**Session 6: Exploring tumor microenvironment using single cell data (2)** Chairs: Tatiana Popova
13:30 14:30	**Vassili Soumelis** INSERM, Paris, France	**Immune cell diversity in cancer: of concepts, subsets, states and single cells**
14:30 15:30	**Leïla Perié** Institut Curie, Paris, France	**Family matters: the role of single cell families in hematopoiesis**
15:30 16:00	COFFEE/TEA BREAK (BDD Hall)	
16:00 17:00	**Jérome Galon** Cordeliers Research Center, Paris, France	**Integrative cancer immunology and immune contexture**
17:00 18:00	POSTER SESSION 3 (even numbers, BDD Annexes 1-3)	Master student's journal club - session 3 (BDD Amphithéâtre)

Thursday, September 26th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 7: Tumor genetics and epigenetics** Chairs: Inna Kuperstein	
09:00 10:00	**Flash presentations of projects by PhD students**	4 minutes/presentation
10:00 10:30	COFFEE/TEA BREAK (BDD Hall)	
10:30 11:30	**Estelle Duprez** CRCM, Marseille, France	**Epigenetic and gene expression profiling for patient stratification and biomarker discovery**
11:30 12:30	**Talks selected from abstracts**	10 minutes/presentation
12:30 13:30	LUNCH (BDD Hall) and VISIT OF MARIE CURIE MUSEUM (Group 2)	
Thursday, September 26th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 8: Treatment response prediction and patient stratification** Chairs:Andrei Zinovyev	
13:30 14:30	**Lodewyk Wessels** National Cancer Institute, Amsterdam, The Netherlands	**Interactions and drug response prediction in cancer**
14:30 15:30	**Kathleen Marchal** Ghent University, Ghent, Belgium	**Integrative network-based analysis for subtyping and cancer driver identification**
15:30 16:00	COFFEE/TEA BREAK (BDD Hall)	
16:00 16:30	**Antoine de Weck** *Pharma talk* Novartis, Basel, Switzerland	**Functional screening for Target Identification and Drug Discovery**
16:30 17:30	POSTER SESSION 4 (even numbers, BDD Annexes 1-3)	Master student's journal club - session 4 (BDD Amphithéâtre)

Friday, September 27th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 9: Multi-level single cell omics data analysis** Chairs: Vassili Soumelis	
09:00 10:00	**Andrei Zinovyev** Institut Curie, Paris, France	**Epigenetic tumor heterogeneity at single cell level**
10:00 10:30	COFFEE/TEA BREAK (BDD Hall)	
10:30 11:30	**Peter Kharchenko** Keynote Marie Curie Seminar Harvard Medical School, Boston, USA	**Integrative analysis of large single-cell RNA-seq collections**
11:30 12:00	**Philip Stegmaier** *Pharma talk* geneXplain, Wolfenbüttel, Germany	**Combining Single Cell and Upstream Analysis to Infer Molecular Mechanisms of Cancer**
12:00 12:30	**Talks selected from abstracts**	10 minutes/presentation
12:30 14:30	LUNCH (BDD Hall) and VISIT OF MARIE CURIE MUSEUM (Groups 3, 4)	
Friday, September 27th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris	**Session 10: Bioimage informatics for single cell data cancer research** Chairs: Thomas Walter	
14:30 15:30	**Thomas Walter** Centre for Computational Biology, MINES ParisTech, Paris, France	**Bioimage analysis for single cell analysis and spatial transcriptomics**
15:30 16:30	**Talks selected from abstracts**	10 minutes/presentation
16:30 17:00	Coffee break (BDD Hall)	
17:00 18:00	**Ido Amit** The Weizmann Institute of Science, Rehovot, Israel	**The power of ONE: Immunology in the age of single cell genomics**
18:00 18:30	**Closing remarks, prizes for flash presentations and posters**	
18:30 21:00	**FAREWELL COCKTAIL (Chez Marie)**	

Saturday, September 28th BDD Amphithéâtre, 11-13 rue Pierre & Marie Curie, 75005 Paris		**CAREER DEVELOPMENT WORKSHOP**
10:00 10:15	**Furtado Ana Rita** The training Unit of Institut Curie, Paris, France	**The general trends of career paths in academy**
10:15 10:30	**Emmanuel Barillot** Institut Curie, Paris, France	**Career in a Bioinformatics Core Facility**
10:30 10:45	**Denis Thieffry** IBENS-ENS, Paris, France	**CV and profile writing: what recruiters like and dis-like**
10:45 11:00	**Vassili Soumelis** Institut Curie-INSERM, Paris, France	**Working at the interface between academic research and hospital**
11:00 11:30	BRUNCH (BDD Hall)	
11:30 11:45	**Laura Cantini** IBENS-ENS-CNRS, Paris, France	**How I got here: a young researcher career journey**
11:45 12:00	**Urszula Czerwińska** Consultante Data Scientist, Saegus, Paris, France	**From systems biology to data science**
12:00 12:15	**Philip Stegmaier** GeneXplain, Wolfenbüttel, Germany	**Career and Life in Bioinformatics SMEs**
12:15 12:30	**Valérie Devillaine** Communication department of Pollinis, Medscape and Institut Curie, Paris, France	**Science as seen by the pen - scientific journalism**
12:30 13:30	**PANEL DISCUSSION WITH SPEAKERS (BDD Amphithéâtre)**	
13:30 14:50	**COFFEE/TEA (BDD Hall) AND INDIVIDUAL ROUND TABLE DISCUSSIONS (BDD, Annexes 1-3)** Students discuss career paths face-to-face with invited speakers	
14:50 15:00	**CLOSURE OF THE COURSE (BDD Amphithéâtre)**	

Posters and oral presentations schedule

Poster #	Surname	Name	Presentation date	Presentation time	Presentation title
1	SAHU	Divya	23. 09	11.30-11.40	GATA3-knockout favors reprogramming from adrenergic to mesenchymal identity in neuroblastoma
2	TIMPERI	Eleonora	23. 09	11.40-11.50	Analysis of tumor associated macrophage heterogeneity at single cell level in triple negative breast cancer
3	MADELEINE	Noelly	23. 09	11.50-12.00	Vitamin K influences therapeutic resistance in melanoma
4	PICHOL-THIEVEND	Cathy	23. 09	12.00-12.10	Tracking glioblastoma mechanisms of radioresistance via single cell transcriptomics and live imaging
5	ZHOU	Zhicheng	23. 09	12.10-12.20	Benign islet autoimmunity and type 1 diabetes: differential gene expression profiling of islet-reactive T lymphocytes in type 1 diabetic and healthy donors
6	RODRIGUEZ MIER	Pablo	23. 09	12.20-12.30	Ignoring the optimal set of tissue-specific metabolic networks can bias the interpretation of data
7	VAZQUEZ JIMENEZ	Aaron	23. 09	14.30-14.40	Phenotypic heterogeneity analysis in breast cancer MCTS through single-cell RNAseq
8	PREVEDELLO	Giulio	23. 09	14.40-14.50	Multiplexed division tracking dyes for proliferation-based clonal lineage tracing
9	TOSELLO	Jimena	23. 09	14.50-15.00	Understanding Treg accumulation in human cancer: a technological approach
10	VILLAR	Javiera	23. 09	15.00-15.05	Identifying novel molecular regulators of human monocyte differentiation
11	ITURRI TORREA	Lorea	23. 09	15.05-15.10	Building a differentiation tree of Erythro-Myeloid Progenitor (EMP)-derived haematopoiesis
12	CHEN	Weiyan	23. 09	15.10-15.15	Single-cell landscape in mammary epithelium reveals bipotent-like cells associated with breast cancer risk and outcome
13	HARI	Kishore	23. 09	15.15-15.20	Decoding the role of network topology in Epithelial Mesenchymal Plasticity
14	GUREGHIAN	Vincent	23. 09	15.20-15.25	Mining the role of the non-coding genome in drug resistance mechanisms in melanoma
15	GUERRERO	José	24. 09	11.30-11.35	Crosstalk of the circadian cycle and the mTORC1 pathway
16	TSIRVOULI	Eirini	24. 09	11.35-11.40	Multiscale Logical Model Simulations for Data Analysis and Experimental Design
17	TOURÉ	Vasundra	24. 09	11.40-11.45	Knowledge management and data extraction of causal statements for logical modeling
18	ORVIETO	Antonio	24. 09	11.45-11.50	Parameter estimation in large scale dynamical systems, with applications to biology
19	HIROSUE	Shoko	24. 09	11.50-11.55	Single Cell RNA Seq Analysis of ccRCC Using Conditional Inducible Mouse Model
20	SCHNEIDER	Michael	24. 09	11.55-12.00	scAbsolute: overcoming unidentifiability in calling absolute copy number in single cells
21	SINGH	Urminder	24. 09	12.00-12.05	Methods and Tools for Integrative Analysis of Big Heterogeneous RNA-Seq Datasets
22	DOW	Michelle	24. 09	12.05-12.10	Genomics characterization of response to immunotherapy via MHC machinery genes
23	ZHANG	Mengying	24. 09	12.10-12.15	Modeling of Warburg Effect Theory and Computational Response Prediction of Combination Treatment in a Xenograft Model of Colorectal Cancer
24	MATEK	Christian	24. 09	12.15-12.20	Using Deep Learning for recognition of malignant cell morphologies in blood smears
25	KAKOICHENKOVA	Alekandra	24. 09	12.20-12.25	The development of personalized vaccines for the treatment of breast cancer based on IVT-RNA
26	WANG	Weitao	NA	NA	Genome-Wide Identification of Early-Firing Human Replication Origins by Optical Replication Mapping (poster only)
27	PARDO	Jérémie	25. 09	11.30-11.35	Sequential reprogramming of biological network
28	PANKAEW	Saran	25. 09	11.35-11.40	Modelling PTEN and TCR signaling network in thymocytes
29	HÉRAULT	Léonard	25. 09	11.40-11.45	Modeling the aging of the hematopoietic stem cell
30	BUCHET	Samuel	25. 09	11.45-11.50	Learning biological systems as dynamical discrete systems
31	BONNET	Raphael	25. 09	11.50-11.55	Study and prediction of relapses for pediatric T-Acute Lymphoblastic Leukemia through Next-Gen sequencing

Posters and oral presentations schedule

Poster #	Surname	Name	Presentation date	Presentation time	Presentation title
32	WANG	Yunfeng	26. 09	09.00-09.05	A replicability study in large cohorts of lung cancer using DEkupl
33	CANCILA	Gabriele	26. 09	09.05-09.10	Insights into microRNA network in Medulloblastoma
34	VIBERT	Julien	26. 09	09.10-09.15	Analysis of cellular heterogeneity in liposarcoma by single-cell RNA-seq
35	METOIKIDOU	Christina	26. 09	09.15-09.20	Single-cell analysis of anti-tumor immune responses in NSCLC patients
36	LOBON IGLESIAS	Maria J	26. 09	09.20-09.25	Impact of Smarcb1 loss on the development of mouse brain : a single-cell approach to study the cell of origin of Atypical Teratoid Rhabdoid Tumor
37	MORVAN	Micks	26. 09	09.25-09.30	Multilayer modelling in immuno-oncology
38	AMBLARD	Elise	26. 09	09.30-09.35	A classifier for single-cell RNAseq data
39	LIU	Jing	26. 09	09.35-09.40	Molecular characterisation of retinoblastoma
40	MENSSOURI	Naoual	26. 09	09.40-09.45	Mechanisms of resistance to therapies targeting the androgen receptor pathway in prostate cancer
41	PIAU	Olivier	26. 09	09.45-09.50	Developmental mechanisms underlying the production of hematopoietic stem cells from human induced pluripotent stem cells
42	ZHAI	Yunhao	26. 09	09.50-09.55	Quantitative Interactomics in Primary T Cells Provides a Rationale for Concomitant PD-1 and BTLA Coinhibitor Blockade in Cancer Immunotherapy
43	PROMPSY	Pacome	26. 09	11.30-11.45	High Throughput Single Cell ChIP-seq
44	NADALIN	Francesca	26. 09	11.45-12.00	Single-cell RNA-Seq of dendritic cell precursors highlights cell-specific transcriptional reprogramming upon HIV-1 infection
45	THIRANT	Cécile	26. 09	12.00-12.15	Neuroblastoma tumor heterogeneity and cellular plasticity
45a	DOSTALOVA	Anna	26. 09	12.15-12.30	Learning from the single-cell level transcriptome for immuno-oncology biomarker and target discovery (talk only)
46	BLUM	Yuna	27. 09	12.00-12.15	Unravelling cancer heterogeneity through molecular deconvolution approaches
47	FLORESCU	Ana Maria	27. 09	12.15-12.30	Identification of a T cell population associated to response to immune checkpoint blockade using scRNAseq data
48	BHALSHANKAR	Jaydutt	27. 09	15.30-15.45	Assessing intratumor heterogeneity and clonal evolution in Neuroblastoma through single-cell DNA sequencing
49	DELAHAYE	Fabien	27. 09	15.45-16.00	Epigenetic Response to Early Stress in the context of metabolic and age-related diseases
50	ZHITNYAK	Irina	27. 09	16.00-16.15	Early events in actin cytoskeleton dynamics and E-cadherin-mediated cell-cell adhesion during epithelial-mesenchymal transition
51	NAZAROV	Petr	27. 09	16.15-16.30	Independent component analysis of single cell RNA-seq data: from batch effect correction to biological processes
52	LA PAGLIA	Laura	NA	NA	miRNA therapeutics based on pathway logic circuits (poster only)
53	MOLKENOV	Askhat	NA	NA	Insights into genomic variants and admixture genetics of 120 whole-exomes of Kazakh individuals (poster only)

Master's journal club presentations schedule

September 23th			
Camille LE SCAO	Katherine SHERAN	16.00-16.20	RNA velocity of single cells *La Manno et. al. Nature 2018*
Nikola ZAREVSIK	Divvya RAMESH	16.20-16.40	Single-cell entropy for accurate estimation of differentiation potency from a cell's transcriptome *Teschendorff & Enver Nat Commun 2017*
Choudhury SUBHAM	Aditya KULKARNI	16.40-17.00	A microfluidics platform for combinatorial drug screening on cancer biopsies *Eduati et. al. Nat Commun 2018*
September 24th			
Valerie MARCH	Lara BÜCHER	17.00-17.20	Single-Cell Map of Diverse Immune Phenotypes in the Breast Tumor Microenvironment *Azizi et. al. Cell 2018*
Claire LANSONNEUR	Emile GASSER	17.20-17.40	Fundamental properties of unperturbed haematopoiesis from stem cells in vivo *Busch et. al. Nature 2015*
Clément HUA	James JOHN	17.40-18.00	Polylox barcoding reveals haematopoietic stem cell fates realized in vivo *Pei et. al. Nature 2017*
September 25th			
Bojana DEJLIC	Dorian BOCHATON	17.00-17.20	Mathematical Modelling of Molecular Pathways Enabling Tumour Cell Invasion and Migration *Cohen et.al. PLoS Comput Biol 2015*
Léa BAUDRE	Julie SEGENI	17.20-17.40	Logical model specification aided by model-checking techniques: application to the mammalian cell cycle regulation *Traynard et. al. Bioinformatics 2016*
Raphael NERE	Humbeline VAUCELLE	17.40-18.00	Modelling the onset of senescence at the G1/S cell cycle checkpoint *Mombach et. al. BMC Genomics 2014*
September 26th			
Artemiy POLOZHINTSEV		16.30-16.50	Batch effects in single-cell RNA- sequencing data are corrected by matching mutual nearest neighbors *Haghverdi et. al. Nat Biotechnol 2018*
Alexandre PELLETIER	Mihai CRACIUN	16.50-17.10	Optimal-Transport Analysis of Single-Cell Gene Expression Identifies Developmental Trajectories in Reprogramming *Schiebinger et. al. Cell 2019*
Melissa SAICHI	Javier FERNANDEZ SEGURA	17.10-17.30	CellMinerCDB for Integrative Cross-Database Genomics and Pharmacogenomics Analyses of Cancer Cell Lines *Rajapakse et. al. iScience 2018*
Maryna CHEPELEVA	Mahfuza AKTER	17.30-17.50	Identifying Epistasis in Cancer Genomes: A Delicate Affair *van de Haar et.al. Cell. 2019*

Pathway Commons: A Resource for Sequencing Data Analysis and Network-Based Interpretation

Augustin Luna
Harvard Medical School

Abstract:

Participants will be introduced to the Pathway Commons (pathwaycommons.org) resource along with a collection of related software tools for understanding cancer-related sequencing data and exploiting therapeutic opportunities. Pathway Commons integrates data from public pathway and interaction databases. The knowledge base is comprised of genetic, signaling, drug-target, and physical interactions involving proteins, drugs, metabolites, and nucleic acids. Data is disseminated in a uniform fashion using the Biological Pathway Exchange (BioPAX) representation and additionally, made available in a number of formats, including: the Simple Interaction Format (SIF)/gene set (GMT) formats and the Systems Biology Graphical Notation Markup Language (SBGNML) for visualization. Integrated analysis using the Pathway Commons dataset is simplified using packages provided in a number of programming languages, such as R using the paxtoolsr package. And a number of algorithms have been developed making use of Pathway Commons to aid researchers in: 1) simplifying the results of enrichment analyses, 2) understanding the overlap between experimental and known molecular interactions, and 3) utilizing complementary information (e.g., genetic alterations) to identify novel molecular relationships. Sophisticated representations of enrichment and pathway analysis results can be created in Cytoscape and accompanying web applications. Additional resources will also be introduced to identify clinically actionable opportunities and leverage existing large-scale pharmacogenomics datasets that together with Pathway Commons can help researchers in answering key questions in cancer biology and the related therapeutic implications.

Bio:

Augustin Luna is a Research Associate at Harvard Medical School and Dana-Farber Cancer Institute in Boston. Luna received his B.S. in Biomedical Engineering from the Georgia Institute of Technology in 2005 and his Ph.D. from Boston University through a joint program with the National Cancer Institute in 2013.

His research makes use of molecular networks to analyze changes in cellular processes in response to stimuli (e.g., drug response) and alterations through statistical and mechanistic models. He has been involved in the development of pathway data standards, including: the Biological Pathway Exchange (BioPAX) and Systems Biology Graphical Notation (SBGN) formats. These have been the basis of his work with the Pathway Commons team that seeks to aggregate molecular interactions from partner databases. His recent studies have been as part of The Cancer Genome Atlas (TCGA) on pan-cancer analyses of pathways identifying clinically actionable opportunities and CellMinerCDB; a cross-database pharmacogenomics platform of cancer cell line data.

Data Integration and Knowledge Management In Biomedicine

Reinhard Schneider

Luxembourg Centre for Systems Biomedicine

Abstract:

The talk will discuss the IT, data management and knowledge management challenges in systems Biomedicine. I will present the Minerva platform for knowledge management in the context of diseases.

Bio:

Prof. Dr. Reinhard Schneider is heading the Bioinformatics Core facility at the Luxembourg Centre for Systems Biomedicine (LCSB) and since 2017 the ELIXIR node in Luxembourg. Between 2004-2010 he was Team Leader at the European Molecular Biology Laboratory (EMBL) in Heidelberg, where he led the "Data Integration and Knowledge Management" group. Before he was co-founder and CIO in LION bioscience AG and CEO of LION bioscience Research Inc., Cambridge, Massachusetts, establishing an IT based knowledge management system for Bayer. Till 1997 he was a postdoc in the biocomputing department at the EMBL, where he studied various aspects of protein structures and became an expert in HPC. He received his Ph.D. in biology at the University of Heidelberg and has over 180 research papers published with over 11 thousand citations. He is a member of the board of Directors of the International Society for Computational Biology where he served 7 years as treasurer. He is also involved in several start-ups in Luxembourg and Germany.

Pathway-Based Analysis of Single-Cell Data

Julio Saez-Rodriguez

Institute for Computational Biomedicine, Heidelberg University

Abstract:

In this presentation I will discuss various strategies to analyse single cell data by using prior knowledge. This knowledge describes pathways as well as regulatory processes, and can be used to extract informative features from single-cell RNA data. Using the prior knowledge we can also build dynamic logic models from single-cell data, either RNA or proteomic data, by fitting a prior knowledge network to the data at hand. The approaches will be illustrated in cases of relevance for cancer understanding and treatment.

Bio:

Julio Saez-Rodriguez is Professor of Medical Bioinformatics and Data Analysis at the Faculty of Medicine of the University of Heidelberg. He is an affiliated member of Sage-Bionetworks and a director of the DREAM challenges to crowdsource systems biology.

He obtained his PhD in 2007 at the University of Magdeburg and the Max-Planck-Institute. He was a postdoctoral fellow at Harvard Medical School and M.I.T., and a Scientific Coordinator of the NIH-NIGMS Cell Decision Process Center. From 2010 until 2015 he was a group leader at EMBL-EBI with a joint appointment in the EMBL Genome Biology Unit in Heidelberg, as well as a senior fellow at Wolfson College (Cambridge). From 2015 to 2018 he was professor of Computational Biomedicine at the RWTH University Medical Hospital in Aachen, Germany. His group develops and applies computational methods to acquire a functional understanding of signaling networks and their deregulation in disease, and to apply this knowledge to develop novel therapeutics. To this end, his group collaborates closely with experimental groups and pharmaceutical companies. More information at www.saezlab.org

Single Cell Trajectory Reconstruction Exploration and Mapping of Omics Data

Luca Pinello

MGH/Harvard Medical School

Abstract:

Single-cell transcriptomic assays have enabled the de novo reconstruction of lineage differentiation trajectories, along with the characterization of cellular heterogeneity and state transitions. Several methods have been developed for reconstructing developmental trajectories from single-cell transcriptomic data, but efforts on analyzing single-cell epigenomic data and on trajectory visualization remain limited. Here we present STREAM, an interactive pipeline capable of disentangling and visualizing complex branching trajectories from both single-cell transcriptomic and epigenomic data. First, I will set the stage presenting the basic concepts of how to build a trajectory inference approach from scratch (a cookbook perspective). Then I will describe the method behind STREAM - a novel Elastic Principal Graph implementation (ElPiGraph), followed by a detailed discussion of how to visualize the learned trajectory and how to discover branch-specific genes, or genes differentiating between trajectory branches. We will close off with examining what we have learned so far and what the future directions and challenges are.

Bio:

Luca is an Assistant Professor at Massachusetts General Hospital and Harvard Medical School. He received his BA, MA and PhD in Computer Science and Mathematics from the University of Palermo in Italy. During his postdoctoral research at Dana-Farber Cancer Institute/Harvard School of Public Health, he studied the role of chromatin structure in gene regulation and developed computational methods for single cell analysis and epigenomics. His research program uses computational approaches to systematically analyze the sources of variation that affect gene regulation: epigenetic variation, genetic variation and (single-cell) gene expression variability. He is actively involved in the single-cell community and he is part of the Human Cell Atlas initiative, proposing computational strategies to reconstruct developmental trajectories (http://stream.pinellolab.org). He also developed computational tools to quantify and visualize the outcome of CRISPR genome editing experiments, that are nowadays the standard the facto for the community (http://crispresso2.pinellolab.org).

Tumorigenesis driven by aberrant stem cell dynamics

Thomas Höfer

Division of Theoretical Systems Biology, German Cancer Research Center Heidelberg

Abstract:

Oncogenic mutations are the hallmark of most human cancers. Such mutations are regularly found in normal tissues, so their occurrence does not imply neoplasia. Rather, it is thought that a tumor can be initiated when mutations that confer selective advantage to self-renewing cells reach fixation. To understand how this occurs, we are studying the dynamics of tissue renewal and how mutations accumulate in this process. To this end, we develop computational approaches to infer, from clonal cell markers such as DNA barcodes or somatic mutations, how stem cell clones grow, mutate, compete, disappear or persist. I will focus on hematopoiesis and the development of acute lymphoblastic leukemia

Bio:

Thomas Höfer heads the Division of Theoretical Systems Biology at the German Cancer Research Center and is professor at Heidelberg University. Following his studies of biophysics, he obtained his PhD in mathematical biology from the University of Oxford, where he was Jowett Senior Scholar at Balliol College from 1994-96. After postdocs at the MPI for Physics of Complex Systems in Dresden and at the College de France, he was junior professor at Humboldt University Berlin from 2002-2007. His research 'puts time into the equation' by developing data-driven mathematical models for the dynamics of molecular networks and cellular differentiation pathways. Areas of interest include hematopoiesis, immunology and cancer cell cycles. Thomas serves editorial roles for several journals, among them the European Journal of Immunology, Current Opinion in Systems Biology and PLoS Computational Biology, and coordinates systems-biology consortia on cancer research and antiviral immunity.

Towards the Quantification of Waddington's Epigenetic Landscape at The Single-Cell Level.

Andrew Teschendorff

CAS-MPG PICB and UCL London

Abstract:

Over 50 years ago Waddington proposed a simple epigenetic landscape model of cellular differentiation, yet currently we still lack detailed quantitative models to represent this landscape. Single-cell approaches, notably scRNA-Seq, is rapidly altering our understanding of cellular development and differentiation processes, whilst also offering us an unprecedented opportunity to begin building more quantitative systems-biological models. In this talk, I will review a number of statistical methods that have been proposed to model different aspects of Waddington's landscape. On the one hand, I will describe methods for estimating differentiation potency at the single-cell level (i.e. the height in Waddington's landscape), with an emphasis on a marker-free systems biology method that we have developed, based on the concept of signalling entropy. I will show how and why this computational method can estimate single-cell potency fairly robustly, even in high dropout rate scRNA-Seq data, and importantly that it also works on bulk samples, a key requirement for mathematical consistency. Furthermore, it will be shown how the method also works in the cancer context, allowing putative cancer stem-cell and drug resistant single-cell phenotypes to be identified. Theoretical and computational details will be covered with illustrative example applications, for instance the identification of a novel single-cell bipotent phenotype in the mammary epithelium that correlates with basal breast cancer risk and outcome. In the second part of the talk, I will describe methods for estimating regulatory activity in scRNA-Seq data, and highlight the significant challenges of reverse-engineering regulatory networks from high-dropout rate data. It will be shown how an alternative hybrid approach that leverages the power of large-scale bulk RNA-Seq datasets, can significantly improve the inference of regulatory activity at the single cell level, even for minor cell-types. It will be shown how application of this method to scRNA-Seq data from the tumor microenvironment can lead to key systems-biological insights underlying carcinogenesis.

Bio:

Andrew Teschendorff trained as a Theoretical Physicist, first at the University of Edinburgh with Peter Higgs and later at Cambridge University, where he obtained his PhD. He entered the field of Statistical Cancer Genomics in 2003, first at the University of Cambridge and later at University College London. He currently holds an appointment as a PI at the CAS-MPG Partner Institute for Computational Biology in Shanghai and as a CAS-Royal Society International Newton Fellow at the UCL Cancer Institute in London. His broad research interest is in Statistical Cancer Epigenomics and Cancer System-omics. He has published over 125 papers, is Associate Editor for Genome Biology, Epigenomics, BMC Systems Biology and Scientific Reports, and reviews regularly for journals like Nature, NEJM, Science, Nature Methods and Genome Biology. He is the recipient of various academic awards, including the Tait Medal and Robert Schlapp Prize in Physics, the Jennings Prize, a Cambridge-MIT Initiative Award, an Isaac Newton Trust Award, a Wellcome Trust VIP Award, and a CAS Visiting Professorship. He holds 2 patents on Risk Prediction in Cancer.

Cellular Decision Process Using Single Data to Build Up Cellular Automata of Differentiations And Responses.

Ioannis Xenarios

CHUV-UNIL-LICR-Genome Center

Abstract:

The aim of the presentation will to be to describe several modeling and simulation methods that have been developed over the last decades. These use several underlying principle but ultimately provides a computational solution to a "what happens if" that all biologists and clinician are after. Single cell biology opens up an area of data that is unprecedented and mixing modeling and simulation with such kind of data what my talk and course will provide. Example will be taken from several laboratories around the world not only my own research to demonstrate where the community is going.

Bio:

I am trained as an immunologist from the LICR and then did a postdoctoral fellow in bioinformatics and computational biology in UCLA under supervision of David Eisenberg. During 8 years I developed computational biology and bioinformatics group within the Serono company and later on for the last 11 years leading Swiss-Prot and Vital-IT at the SIB Swiss Institute of Bioinformatics. Since end of 2018 I am now leading the data analytics platform of the Genome Center in Geneva (on the former campus of Serono) and lead the Hi-TIDE CompBio research activities within the Ludwig Institute of Cancer Research at the CHUV/UNIL Lausanne.

Qualitative dynamical modeling of T-helper cell differentiation and reprogramming.

Denis Thieffry
IBENS

Abstract:

The balance between different T-helper sub-types of, in particular between Th17 and Treg, has been associated with central processes linked to anti-tumoral response. In this chapter, taking advantage of a previously published logical model of T-helper cell differentiation, we explore the possibilities to reach these lineages from naïve cells and to reprogram differentiated cells into alternative phenotypes. For this, we combine several powerful formal approaches and software tools to analyse a logical model containing a hundred components. To ease the recourse to different tools and ensure reproducibility, we have gathered the relevant tools in a Docker image, and chain all the analyses in an executable and editable Python Jupiter notebook. This notebook covers the computation of asymptotic cell behaviour (stable states and approximations of more complex, cyclic attractors), state and stable state reachability, along with stochastic simulations. From a biological point of view, focusing on the differentiation of Th17 and Treg subsets, we hereby compute the conditions required and the probability of each these T-helper subtypes, and we further predict and analyse the effect of micro-environmental perturbations enabling the reprogramming of immuno-supressive Treg into pro-inflammatory Th17.

Bio:

Denis THIEFFRY IS Professor of Systems Biology at the Ecole Normale Supérieure (ENS). He has obtained his Ph.D in 1993 at the Free University of Brussels, under the direction of René THOMAS. In between, he spent seven years of postdocs in Mexico (UNAM, 1995-1997), Germany (MPI, Berlin, 1997-1998) and Belgium (Univ. Ghent, 1998-2000), and was appointed as full Professor of Bioinformatics at the University of Aix-Marseille in France (2000-2010).

Associate Editor of PLoS Computational Biology, BMC Systesm Biology & Biosystems, member of the F1000 Faculty (computational biology / systems biology), as well of various scientific committees related to computational biology, DT has published over 140 articles and book chapters, mostly in international journals, proceedings or books.

Denis Thieffry currently heads the interdisciplinary Master in Life Science at ENS/PSL and a research team dedicated to Computational Systems Biology at IBENS (https://www.ibens.ens.fr/?rubrique27&lang=en).

Systems Biology For Cell Proliferation Quantification And Modeling Of Lymphocyte Dynamics:
T-Cell Heterogeneity Dynamics Across Aging And Genetic Origins.

Véronique Thomas-Vaslin
INSERM

Abstract:

Cell proliferation is the common characteristic of all biological systems, but the quantification, modeling and control of cell proliferation remains a challenge of systems biology. Understanding cell proliferation dynamics requires specific experimental methods and mathematical modelling. This concerns the heterogeneity of T cell populations that continuously differentiate in the immune system, and modify their renewal and fluxes across tissues in response to perturbations and aging. Then, lymphocyte sensitivity to depletion of dividing cell and their recovery post-depletion have allowed us to quantify and model lymphocyte dynamics and renewal. Moreover, following the in vivo staining of cells to reveal their progression across the cell cycle phases, we revealed the heterogeneity of cell populations according to their states and phenotypes, and quantified the percentage of dividing cells and dead cells. Our investigation is based upon single-cell multi-parameter flow cytometry analysis thereby revealing the active incorporation in DNA of a thymidine analogue during S phase after pulse-chase experiments, versus cell DNA content. A generic mathematical model that simulates through ODEs and state-transition diagrams the evolution of single cell behavior during the experiment allows us to fit our data, to estimate proliferation rates and mean cell cycle phase durations in sub-populations. Our model is flexible and can be used with various pulse/chase experiments and even for other cell types.

We revealed the heterogeneity of lymphocyte proliferation, and signatures of T-cell population dynamics through their differentiation from the thymus to the spleen, across aging of the organism and dependent on the genetic origins.

Bio:

PhD in Immunology, researcher at CNRS she founded the “Integrative Immunology: Differentiation, Diversity, Dynamics” team and the ImmunoComplexiT network to better understand “Complex Systems”.

From experimental investigation in murine models, she developed systems immunology to model T cell dynamics by mathematical and computational approaches.

https://immunocomplexit.wordpress.com/an-overwiew-on-modelling-t-lymphocyte-dynamics-from-physiology-to-perturbations-of-immune-system/

Studying Intratumoral Heterogeneity at Single Cell Level

Vassili Soumelis
Hôpital St Louis

Abstract:

The definition of cell types and subsets initially started with morphological features. This led to a cellular taxonomy that is still valid as of today. Molecular markers analyzed by in situ immuno-histology, and subsequently flow cytometry, added to the resolution in cell subset definition. The availability of single cell Omics technologies now enables to characterize individual cells based on hundreds of variables/molecular markers. Analyzing very large number of cells, based on large-scale datasets, and in increasingly diversified organs and anatomic locations, revealed a broad diversity of cellular phenotypes. This is now raising questions on the interpretation and biological meaning of these cellular populations: do they correspond to new bona fide cell types or subsets? Do they correspond to environmentally-driven cell states? Are they associated to specific and significant functional specialization? Do they have a role in the pathogenesis of various human diseases. We will discuss these questions in relation to immune cell diversity, through knowledge obtained by controlled in vitro studies, ex vivo analysis of steady state immune cell populations, and ex vivo analysis of tumor tissue. We will more particularly focus on dendritic cell and T cell diversity, in human blood and breast cancer. We will try to illustrate the power and utility of single cell approaches as discovery tools, but also the importance of subsequent validation and functional studies, which are often lacking from published studies. Finally, we will discuss the limits of increasing granularity in describing individual cells, in systems where the main functions are most of the time accomplished by the collective action of groups of cells.

Bio:

V. Soumelis is a Professor of Immunology at the Paris University, and a practicing physician at the Hôpital St Louis hematology department. He is the director of the INSERM Unit HIPI "Human Immunology, Pathophysiology, Immunotherapy" at the St Louis Research Institute (IRSL). He is an expert in human immunology and tissue inflammation in cancer, allergy, and auto-immunity. His interdisciplinary team has built a strong interface between immunology, systems biology, and bioinformatics. Some applications have been the large-scale study of signal integration by immune cells, and the mapping of immune cell diversity in inflammatory conditions, including cancer. V. Soumelis coordinated the bioinformatics in a EU FP7 network on allergy and autoimmunity. In 2011, he obtained an ERC consolidator grant to study the integrative biology of human dendritic cells. He is a currently global coordinator of the EU H2020 project ImmunAID "Immunome consortium on Auto-Inflammatory Diseases", and coordinates bioinformatics and data integration in the IMI project ImmuCAN on human tumor microenvironment.

Family Matters: The Role of Single Cell Families in Hematopoiesis

Leïla Perié
Institut Curie

Abstract:

How heterogeneous systems of cells constituting multicellular organisms establish, organize and achieve coordination persists as a central question in natural sciences. Whereas stochastic gene or protein expressions have clearly demonstrated their role in cellular heterogeneity and are widely studied (Wang and Bodovitz, 2010), the role of cell heterogeneity in the organization of multicellular organisms has been less interrogated. Addressing this question requires adequate tools that quantitatively study ensembles of cells individually rather than group of cells.

My research aims at addressing cell heterogeneity in dynamical and complex systems of cells using the hematopoietic system as a model of study. Strikingly hematopoietic cells (immune cells, platelets and red blood cells) compose over 90% of total human cells and correspond to approximately ten trillions of cells (Sender R, 2016). More importantly they all originate from the same cells, the hematopoietic stem cells (HSC), through a process called hematopoiesis. In addition, as immune and blood cells have a short life span (from hours to months) and can response to perturbations like infections, this process is highly dynamical. It is therefore an interesting and challenging model to study differentiation in a complex system at the single cell level.

To achieve this, we combine different experimental and mathematical/computational approaches of genealomics to study hematopoiesis in vivo. Genealomics use high throughput sequencing methods to track the descendant of individual cells. For example cellular barcoding is one of the genealomic approaches used by my lab. It simultaneously traces the in vivo differentiation of individual cells, allowing to reconstitute the relationship between cell lineages with single cell resolution. In this seminar, I will introduce the different genealomics methods, their experimental and computational challenges. I will also discuss some of our recent results using genealomics in hematopoiesis.

Bio:

Leïla Perié was trained in food science as an undergrad, she then obtained a PhD in immunology performing experimental work. As a postdoc, she worked at the Schumacher's lab (NKI, Amsterdam) for the experimental part and at the de Boer's lab (Utrecht University) for the theoretical part. She has started in 2015 a junior group at the Curie Institute in Paris. Her lab is interested in understanding the hematopoietic tree at the single level and combines different experimental and mathematical/computational approaches of lineage tracing to study hematopoiesis. She won several prestigious grants (ATIP-Avenir, ERC) and awards (prix Bettencourt-Schueller, prix Paoletti from CNRS).

Integrative Cancer Immunology And Immune Contexture

Jerome Galon
INSERM

Abstract:

To-date, the evaluation of the prognosis of cancer patients relied on the anatomic extent of tumor (TNM-classification). However, this classification provides limited prognostic information and does not predict response to therapy. We redefined cancer by integrating the immune system to transfer cutting-edge medicine to the patients. We have previously shown that tumors from human colorectal cancer with a high-density of infiltrating memory and effector-memory T-cells are less likely to disseminate to lymphovascular and perineural structures and to regional lymph-nodes. We also demonstrated the critical tumor-microenvironment parameters determining the dissemination to distant metastasis. We found that the combination of immune parameters associating the nature, the density, the functional immune orientation and the location of immune cells within the tumor was essential to accurately define the impact of the local host-immune reaction on patients' prognosis. We defined these parameters as the "immune contexture". We characterized the immune landscape within human tumors, and showed the importance of several adaptive immune cells. We described the immunophenotype and antigenome associated with immune escape mechanisms and demonstrated mechanisms associated with pre-existing and proliferating intratumoral T-cells. Based on the immune contexture, a standardized, simple and powerful digital-pathology-based immune stratification-system, termed "Immunoscore", was delineated having a prognostic power superior to that of the currently used cancer staging-system. Tumor invasion parameters were statistically dependent on the host-immune reaction. A worldwide consortium validated the prognostic value of the consensus Immunoscore, using a standardized-assay. We have demonstrated the significant role of Immunoscore and immunoediting in affecting metastatic dissemination. We hence proposed a "parallel immune selection model" of tumor evolution incorporating the effects of the immune system in shaping and driving metastatic spread. Thus, tumor progression, invasion and recurrence are dependent on pre-existing immunity and on Immunoscore. Further analyses revealed a large inter- and intra-metastatic immune heterogeneity. Nonetheless, even when measured on a single biopsy, the Immunoscore held a prognostic value and was surpassing the accuracy of PD-L1 expression. The same study revealed how Immunoscore and T and B cell score (TB score) from the least-infiltrated metastasis are the most associated with survival. Finally, novel concepts underpinning tumor evolution will be advocated.

Bio:

Specialized in the fields of immunology and cancer, Jérôme Galon is Research Director at INSERM, heading the Laboratory of Integrative Cancer Immunology at the Cordeliers Research Center in Paris, France. He is associate Director and co-founder of European Academy of Tumor Immunology (EATI), board member of Society for Immunotherapy of Cancer (SITC). His work on the comprehensive analysis of the tumor-microenvironment and the role of T-cells in human cancer led to the demonstration of the importance of adaptive pre-existing immunity in human cancer, and the concept of cancer immune-contexture. He pioneered the Immunoscore. He is the co-founder of HalioDx company and the Chairman of its scientific council. His contributions have been recognized with numerous awards, including the William B. Coley Award, an international prize which honors the best scientists in the fundamental and cancer immunology, and Award from the National Academy of Science, and from the National Academy of Medicine.

Single-cell RNA-seq analysis of hematopoietic stem cell aging: towards prediction for hematological malignancy susceptibility

Estelle Duprez
INSERM-CNRS-AMU

Abstract:

Hematopoietic stem cells (HSCs) represent a rare population of cells, residing in the Bone Marrow (BM) at the top of hematopoietic hierarchy. The defining characteristics of hematopoietic stem cells (HSCs) are their capacity for self-renewal and multipotent differentiation, which allow them to maintain homeostasis throughout an organism's life span. The hematopoietic system deteriorates with age and numerous changes occurring in both humans and mice have been reported, including reduced production of red blood cells and lymphocytes as well as a relative increase in the production of myeloid cells. This age-related myeloid-biased differentiation results in a reduction in the number of adaptive immune cells that promotes immunosenescence and an increase of myeloid malignancies.
Thus, aging hematopoiesis could be viewed as the result of selection pressure that promotes alterations in the composition of HSC clones endowed with rather stable functional characteristics. However, it is unclear if the functionalities of different HSC clones are fixed, or if they diversify as the number of HSCs expands. It is also currently unknown if this clonal expansion would favor the development of a pre-leukemic clone with a particular signature.
To address these questions we have developed mouse models that harbors accelerated HSC aging phenotype and increased susceptibility to hematological malignancies. To unveil how HSC clonal selection is orchestrated during aging and is linked to cell malignant transformation, we have generated single-cell transcriptome data from these models. I will present the strategies and computational methods developed to analyze and profile the transcriptional diversification that occurs in individual HSCs as they differentiate in aged and preleukemic conditions. I will discuss how theses data can be used to predict myeloid malignancy susceptibility and disease evolution.

Bio:

ESTELE DUPREZ (DR2 CNRS**)**
Now:Team leader of the Team: Epigenetic factors in normal and malignant hematopoiesis, CRCM, IPC, U-1068 INSERM, UMR 7258 CNRS, Aix Marseille University.

Diplomas:
1995- Doctorat de l'université PARIS XI. Mention très honorable avec félicitations du jury
2008-HDR de Aix-Marseille Université

Past

- 1995-PhD fellow, Unité INSERM U-301 Hôpital St Louis, PARIS.
  Financial support: Bourse MRT, Bourse ARC.
- 1996-1997-Postdoctoral fellow, Paul Freemont Lab Imperial Cancer Research Fund, London.
  Financial support: Bourse "Capital Humain et Mobilité" de la CE.
- 1998-1999-Chargé de recherche (CR2) CNRS. INSERM U-496, Hopital Saint-Louis, Paris.
- 1999-2002-Détachement, Division of Hematology/ Oncology Harvard Institute of Medicine, Boston, USA, Dan Tenen Lab.
- 2003-2010-Chargé de recherche (CR1) Mickael Sieweke lab. Centre d'Immunologie de Marseille Luminy.
- **Expertise**: Cancer, Leukemia, hematopoiesis, Transcription, Epigenetics

Interactions and drug response prediction in cancer

Lodewyk Wessels
NKI, Amsterdam

Abstract:

Recent studies of the tumor genome seek to identify cancer pathways as groups of genes in which mutations are epistatic with one another or, specifically, "mutually exclusive". Here, we show that most mutations are mutually exclusive not due to pathway structure but to interactions with disease subtype and tumor mutation load. In particular, many cancer driver genes are mutated preferentially in tumors with few mutations overall, causing mutations in these cancer genes to appear mutually exclusive with numerous others. Researchers should view current epistasis maps with caution until we better understand the multiple cause-and-effect relationships among factors such as tumor subtype, positive selection for mutations, and gross tumor characteristics including mutational signatures and load.

Cell lines and patient-derived xenografts (PDX) have been used extensively to understand the molecular underpinnings of cancer. While core biological processes are typically conserved, these models also show important differences compared to human tumors, hampering the translation of findings from pre-clinical models to the human setting. In particular, employing drug response predictors generated on data derived from pre-clinical models to predict patient response, remains a challenging task. As very large drug response datasets have been collected for pre-clinical models, and patient drug response data is often lacking, there is an urgent need for methods that efficiently transfer drug response predictors from pre-clinical models to the human setting. We show that cell lines and PDXs share common characteristics and processes with human tumors. We quantify this similarity and show that a regression model cannot simply be trained on cell lines or PDXs and then applied on tumors. We developed PRECISE, a novel methodology based on domain adaptation that captures the common information shared amongst pre-clinical models and human tumors in a consensus representation. Employing this representation, we train predictors of drug response on pre-clinical data and apply these predictors to stratify human tumors. We show that the resulting domain-invariant predictors show a small reduction in predictive performance in the pre-clinical domain but, importantly, reliably recover known associations between independent biomarkers and their companion drugs on human tumors.

Bio:

Lodewyk Wessels leads the Computational Cancer Biology group at the Netherlands Cancer Institute in Amsterdam, The Netherlands. His group focuses on developing computational and experimental approaches to understand treatment response in preclinical models and patients. Dr Wessels received his M.Sc. and Ph.D. both from the Department of Electronic and Computer Engineering, University of Pretoria, South Africa. From 1993 to 1997 he was a member of the Center for Spoken Language Understanding at the Oregon Graduate School of Science and Technology. In 1997 he joined the Faculty of Electrical Engineering, Mathematics and Computer Science at the Delft University of Technology and was appointed assistant professor in 2002. In 2006 he became a faculty member at the Netherlands Cancer Institute in Amsterdam, The Netherlands. He was appointed chair of Computational Cancer Biology at the Delft University of Technology in 2012 and in 2016 as Deputy Director Research of the Netherlands Cancer Institute.

Integrative Network-Based Analysis for Cancer Driver Identification

Kathleen Marchal
Ghent University

Abstract:

Mining cohorts of cancer genomes offers the potential to identify driver genes or pathways. A key challenge in the identification of driver genes is their distinction from genes carrying neutral mutations and/or aberrations that do not cause tumorigenesis or any other cancer related phenotype.

Gene-centric methods prioritize drivers by making use of one or more of gene specific properties, such as whether genes in a cohort are more frequently mutated than expected by chance, either throughout the gene or at specific functional or clustered sites and whether genes are enriched in aberrations with high functional impact.

While gene-centric methods are ideal to identify drivers with a clear statistical signal they often are less suited to identify the more rarely mutated genes (long tail of rarely mutated genes). A promising approach for recovering infrequent drivers are network based methods. These methods assume that cancer is a disease of disturbed pathways. Typically a pathway can become aberrant in different ways and hence different patients can carry different mutations while exhibiting the same tumor phenotype. By searching for recurrently mutated pathways rather than genes, the power of the analysis increases while individual mutations can still be prioritized as long as they are part of a larger pathway. Analysis of large public datasets illustrated the importance of such network-based approaches in identifying driver pathways, rare driver genes and subtypes.

Besides their ability to dig in the long tail of rare drivers, networks offer a natural way of integrating different types of omics data. We will illustrate with a few examples the power of fully integrated network models in prioritizing rare mutations that can be coupled to a functional and/or a clinical phenotype.

Bio:

Kathleen Marchal (http://bioinformatics.psb.ugent.be/DBN/) is associate Professor at the Dept. of Plant Biotechnology & Bioinformatics and at the Dept. of Information Technology, (IDLab, IMEC) at Ghent University. Her lab focuses on developing computational methods for the analysis, integration and interpretation of systems biology and systems genetics data. The group's research has contributed to the development of methods for motif-detection, network inference, and network-based data interpretation. Since 2013 the group's interest is in the use of network methods for integrative genotype-phenotype mapping with a major focus on clonal systems. The group is member of the International Cancer Genome Consortium (ICGC)-PAWG network analysis group.

Functional screening for Target Identification and Drug Discovery

Antoine de Weck

Novartis Institutes for BioMedical Research

Abstract:

The systematic translation of cancer genomic data into knowledge of tumor biology and therapeutic opportunities remains challenging. This effort has been greatly aided by robust preclinical model systems, such as the Cancer Cell Line Encyclopedia (CCLE), for which detailed genetic annotation has been generated. However, a comprehensive mapping of cancer dependencies has lagged behind.

Firstly I will present Project DRIVE, a large-scale RNAi screen in which viability effects of mRNA knockdown were assessed for 7,837 genes in 398 cancer cell lines. Secondly I will compare RNAi and CRISPR screens and show evidence that CRISPR-based screens have a significantly lower false-negative rate compared with RNAi-based screens, but have specific liabilities particularly in the interrogation of regions of genome amplification. I will describe computational means to correct for this artifact in order to leverage the full information available in CRISPR screens.

Time permitting I will show results leveraging transposon-based functional screens to elucidate mechanism of resistance to HDM201, an MDM2-TP53 protein-protein interaction inhibitor.

Bio:

Antoine is a computational biology team leader at the Novartis Institutes for BioMedical Research, where he joined the oncology department in 2013. Before that he completed his PhD with Prof. J. Ragoussis and Prof. F. Buffa at the University of Oxford, which he joined as part of the Life Science Interface Doctoral Training Centre. He holds a degree in physics from the ETH Zürich.

Studying Intratumoral Heterogeneity at Single Cell Level

Andrei Zinovyev
Institut Curie

Abstract:

Single cell measurements change the modern biology due to bringing the 'Big Data'-related approaches and challenges to the studies of normal physiology and diseases such as cancer. A number of novel computational methods and paradigms have emerged to deal with complexity of single cell genomic and epigenomic data. In this lecture, I will overview several methods for dealing with large and complex single-cell datasets, with a particular focus on studying intratumoral heterogeneity and the properties of tumor microenvironment. I will present our recent single cell study of heterogeneity of tumors of Ewing sarcoma, starting from characterizing the cell cycle-independent transcriptional program of EWS/FLI-1 oncogene in inducible cell line and finishing by the analysis of patient derived xenografts profiled with 10x Genomics platform. Our study shows that the tumors of Ewing sarcoma are characterized by intratumoral heterogeneity strongly associated with activity of the EWS/FLI-1 oncogene, with existence of tumor cell subpopulations characterized by specific biological properties.

Bio:

Andrei Zinovyev graduated in Theoretical Physics, Cosmology from the Physics department of Krasnoyarsk State University, obtained PhD in Computer Science in 2001 at Institute of Computational Modeling of Russian Academy of Science, and habilitated in Biology at École Normale Supérieure, Paris, in 2014. He was a postdoctoral researcher in bioinformatics at Institut des Hautes Etudes Scientifiques, Bures-sur-Yvette, from 2001 to 2004. From 2005 he coordinates the Computational Systems Biology of Cancer group (part of INSERM U900 since 2008) at Institut Curie, Paris. His research interests are systems biology of cancer, developing methods of machine learning and their application to omics data, developing software for computational biology and data dimension reduction. Author of 3 books, including "Computational Systems Biology of Cancer" textbook and more than 90 articles in computational biology and bioinformatics, cancer biology, mathematical chemistry, machine learning.

Integrative Analysis of Large Single-Cell RNA-Seq Collections

Peter Kharchenko
Harvard Medical School

Abstract:

Single-cell RNA-seq methods are being increasingly applied in complex study designs, which involve measurements of many samples, commonly spanning multiple individuals, conditions, or tissue compartments. Joint analysis of such extensive, and often heterogeneous, sample collections requires a way of identifying and tracking recurrent cell subpopulations across the entire collection. Here we describe a flexible approach, called Conos (Clustering On Network Of Samples), that relies on multiple plausible inter-sample mappings to construct a global graph connecting all measured cells. The graph can then be used to propagate information between samples and to identify cell communities that show consistent grouping across broad subsets of the collected samples. Conos results enable investigators to balance between resolution and breadth of the detected subpopulations. In this way, it is possible to focus on the fine-grained clusters appearing within more similar subsets of samples, or analyze coarser clusters spanning broader sets of samples in the collection. Such multi-resolution joint clustering provides an important basis for downstream analysis and interpretation of sizeable multi-sample single-cell studies and atlas-scale collections.

Bio:

Peter Kharchenko, Ph.D, is the Gilbert S. Omenn Associate Professor of Biomedical Informatics the Harvard Medical School. His lab specializes in developing statistical and computational methods for analysis of high-throughput assays, including transcriptional, epigenetic and genetic analysis. Dr. Kharchenko has received his Ph.D from the Biophysics program at Harvard University, under the mentorship of George Church. He then conducted his postdoctoral training with Peter Park at the Harvard Medical School, focusing on analysis of epigenetic regulation in model organisms and mammalian tissues.

Combining Single Cell and Upstream Analysis to Infer Molecular Mechanisms of Cancer

GeneXplain

Abstract:

The geneXplain platform is an online toolbox and workflow management system for a broad range of bioinformatic and systems biology applications. Its goal is to provide research scientists, groups, as well as larger organizations a comprehensive data management and analysis system for all their scientific projects and research tasks. Integrated tools and databases place an emphasis on the analysis of molecular networks, particularly gene regulatory and signal transduction networks, using (multi-)omic experimental data. Several of the novel workflows make use of the "Upstream Analysis" approach [1-3] that enables causal analysis of gene regulatory changes by step-wise inference of transcription and signal transduction regulators. Our demonstration will describe the "Upstream Analysis" and show how it is used to facilitate inference of drug targets as well as regulatory feedback loops integrating gene expression with other types of experimental data. We are going to conclude with an introduction of the recently developed, fully automatic tool called Genome Enhancer (my-genome-enhancer.com) that allows to perform complete analysis of multiple sets of various patient multi-omics data, identify key drug targets of the pathology and suggest potential therapeutic compounds.

Bio:

Philip Stegmaier studied biochemistry and biotechnology at the Technical University Braunschweig and has over 15 years of experience in the bioinformatics industry where he took on a variety of positions. His research has focused on the computational analysis of gene regulation and cellular signaling networks as well as interpretation of systems biology data and much of his career was dedicated to development of software platforms for bioinformatics analysis. Currently, Philip Stegmaier is IT Director of geneXplain GmbH and Manager of Software & Technology Development.

Machine Learning and Computer Vision for bioimage analysis – Applications to single cell analysis and the study of RNA localization

Thomas Walter

Mines ParisTech, PSL Research University / Institut Curie

Abstract:

While we have the technologies and computational tools to analyze entire genomes, transcriptomes and proteomes, the computational description of phenotypes resulting from this molecular basis is still lagging behind. Yet, the quantitative description of the diverse aspects of the phenome is a prerequisite for understanding the complex genotype-phenotype relationships in living systems. As compared to omics techniques, microscopy-based assays provide us with excellent tools to study complementary aspects of living systems, such as morphological phenotypes, spatial arrangements and organization at different scales. High Content Screening (HCS) is a tool to explore these phenotypic aspects in response to gene silencing or perturbation experiments at a large scale, involving tens to hundreds of thousands of experiments in a single project. The study of stained tissue slides in histopathology allows us to study the cellular and tissular changes in response to disease.

The computational methods of choice to analyze these large and complex data sets are usually based on Computer Vision. Computer Vision typically integrates many aspects of images and has the potential to map them to a biologically meaningful description by supervised or unsupervised learning. In my lecture, I will introduce the principles of Machine Learning applied to images and explain the challenges and opportunities of deep learning in this context. While I will briefly describe several applications, I will mostly focus on the field of RNA localization, where we aim at understanding the mechanisms of spatial regulation of gene expression. Indeed, we can visualize individual transcripts in cells and tissues by single molecule Fluorescence in situ Hybridization (smFISH), allowing to see how transcripts of a given gene spatially distribute inside the cell. These imaging data pose interesting and challenging questions for the computational analysis, too. In particular, I will show how we can use image simulation in order to overcome the need for large annotated data sets which is currently considered to be a major obstacle for the use of the latest generation of machine learning and computer vision methods.

Bio:

Thomas Walter is a researcher in the field of image analysis and computer vision applied to biology. After having received his PhD from Mines ParisTech in 2003 (Centre for Mathematical Morphology), he joined Jan Ellenberg's lab at the EMBL Heidelberg, where he worked on computational analysis of High Content Screening. In 2012, he moved to the Centre for Computational Biology of Mines ParisTech and the Bioinformatics Unit (U900) of the Curie Institute, where he lead a team on Bioimage Analysis. Since 2018, he is director of the Centre for Computational Biology (Mines ParisTech) and codirector of the department "Cancer and Genome: Bioinformatics, Biostatistics, Epidemiology of Complex Systems" (Institut Curie / Mines ParisTech / INSERM).

The power of ONE: Immunology in the age of single cell genomics

Ido Amit

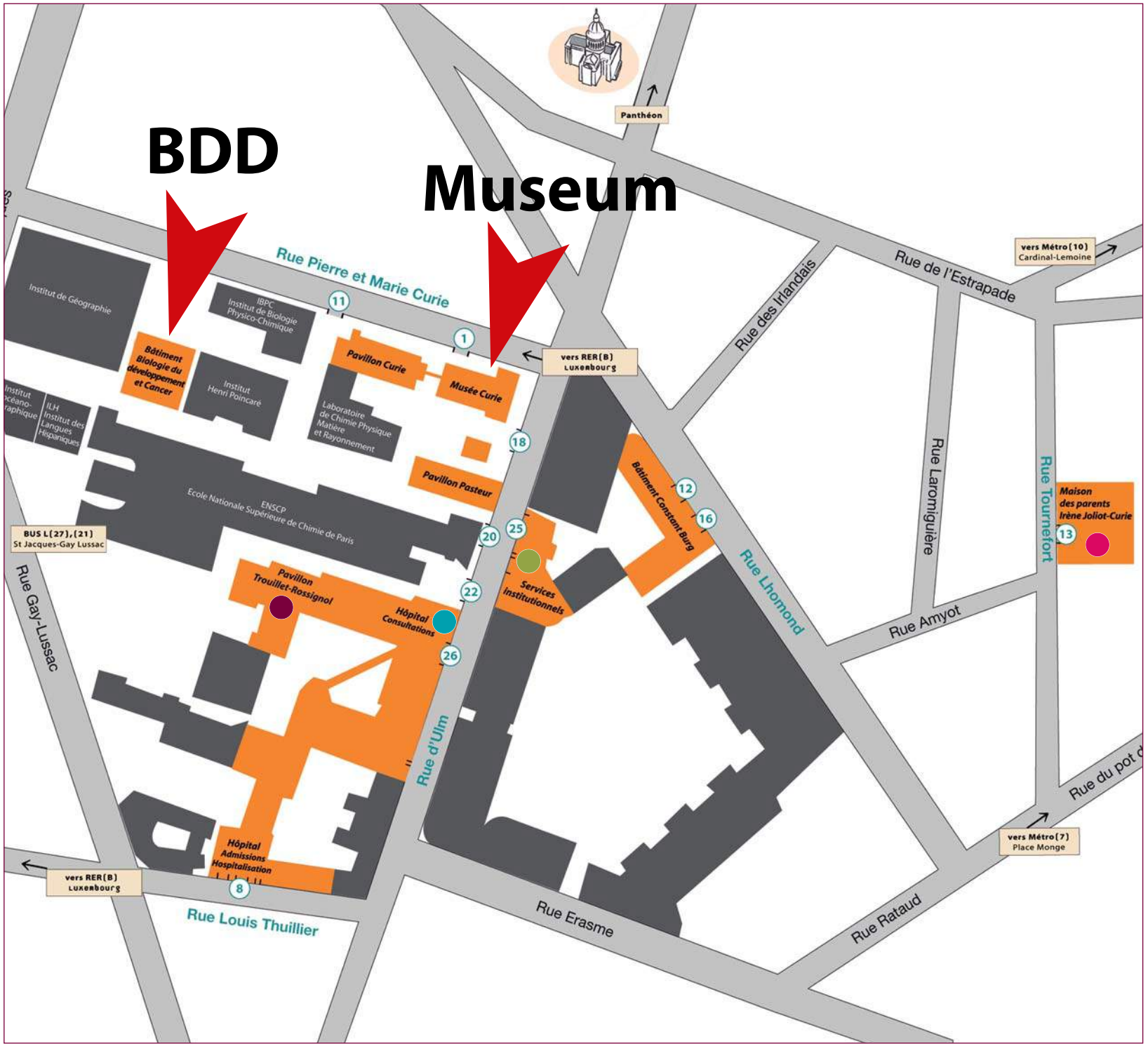
Weizmann Institute of Science

Abstract:

The immune system is a complex, dynamic and plastic network composed of various interacting cell types that are constantly sensing and responding to environmental cues. From very early on, the immunology field has invested great efforts and ingenuity to characterize the various immune cell types and elucidate their functions. However, accumulating evidence indicates that current technologies and classification schemes are limited in their ability to account for the functional heterogeneity of immune processes. Single cell genomics hold the potential to revolutionize the way we characterize complex immune cell assemblies and study their spatial organization, dynamics, clonal distribution, pathways, and crosstalk. This emerging field can greatly affect basic and translational research of the immune system. I will discuss how recent single cell genomic studies are changing our perspective of various immune related pathologies from cancer to neurodegeneration. Finally, I will consider recent and forthcoming technological and analytical advances in single cell genomics and their potential impact on the future of immunology research and immunotherapy.

Bio:

Prof. Ido Amit earned his PhD in biological regulation at the Weizmann Institute of Science in 2007. For four years, he was a postdoctoral fellow at the Broad Institute of Harvard University and the Massachusetts Institute of Technology, before joining the Weizmann Institute in 2011. Ido Amit is a Professor at the Immunology Department at the Weizmann Institute of Science. His lab pioneered single cell genomic technologies and their application to characterize the immune system. Amit's research answers some of the most fundamental questions in immunology which are being translated into innovate new targets for immunotherapy in autoimmune diseases, neurodegeneration and cancer. Prof. Amit is a leader in the field of immunogenomics, aimed at detecting and engineering genome sequences that are essential for the function of the immune system in physiology and disease.



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