RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

Martin Schaefer

* Name & Surname

* Affiliation IEO

PHD PROJECT DETAILS

* Title of the proposed project

The cancer code: unraveling selection across the cancer genome and epigenome

* Short description of the project (up to 300 words)

Cancer is driven by alterations across all molecular layers - from single-nucleotide mutations to epigenetic changes and large-scale genomic rearrangements. While our understanding of point mutations and their contribution to the phenotypic hallmarks of cancer has grown considerably over the last two decades, much less is known how epigenetic changes and copy number alterations of genomic regions contribute to cancer initiation and progression. In addition, we understand little about the evolutionary forces shape these changes - and what do they reveal about cancer's vulnerabilities?
In this project, we are looking for a computational PhD student to decode the cancer genome and epigenome through the lens of tumor evolution. You will develop models that identify novel drivers of carcinogenesis by combining methods from population genetics, machine learning, and network biology. The ultimate goal is a systems-level understanding of how diverse molecular alterations act together to transform healthy into cancer cells.
The successful candidate will work closely with other members of our lab, as well as with experimental and clinical collaborators. This environment offers the opportunity to translate computational insights into real-world biomedical applications.
In particular, the project will:
- Identify genomic and epigenomic alterations under selection in late-stage tumors.
- Investigate how copy number changes and epigenetic reprogramming enable adaptation to the metastatic niche.
- Explore how selection pressures can expose therapeutic vulnerabilities.
This work builds on our recent studies, including Heery and Schaefer (NAR, 2021) and Alfieri, Caravagna and Schaefer (Nat Comm, 2023).

* Indicate the main research area for the project described above Computational biology

If needed indicate a second research area for the project described above Cancer Biology

* Provide up to 3 key words for project:

Computational cancer biology; tumor evolution; cancer driver genes

YOUR LABORATORY ACTIVITIES DETAILS

* Main topic/s of the lab

Identifying and quantification of selection in tumor evoltuion; epigenetic drivers; role of copy number alterations in cancer; network biology

* Short description of the lab activity (up to 500 words)

Our lab is a computational biology group focused on understanding how molecular alterations - ranging from point mutations to epigenetic modifications and large-scale copy number changes - drive tumor evolution. Our research aims to identify and quantify the forces of selection acting on cancer genomes and epigenomes, with the goal of uncovering novel drivers of carcinogenesis and therapeutic vulnerabilities.
Cancer progression is an evolutionary process. Tumor cells acquire molecular changes that confer selective advantages, allowing them to outcompete their neighbouring cells, adapt to challenging microenvironments, and metastasize to distant organs. While point mutations have been studied extensively, the role of epigenetic changes and copy number alterations in this adaptive landscape remains less well understood. Our lab is particularly interested in these underexplored layers of cancer biology and how they contribute to the emergence and progression of tumors.
We develop and apply computational models rooted in population genetics, network biology, and machine learning to disentangle the complex signals of positive and negative selection in cancer. By integrating multi-omics datasets, we aim to build a systems-level understanding of how different types of molecular alterations interact within molecular networks to drive cancer evolution.
A central interest of our work is the interplay between the tumor and its microenvironment. We study how selective pressures shape the tumor genome, and conversely, how tumor cells modify their environment to promote survival, immune evasion, and metastasis. This bidirectional relationship is key to identifying cancer vulnerabilities that can be targeted therapeutically.
Our lab maintains close collaborations with experimental and clinical groups, enabling us to validate computational predictions and ensure biological and clinical relevance.

* Recent bibliography (max 5 references)

Blumenthal DB, Lucchetta M, Kleist L, Fekete SP, List M, Schaefer MH. Emergence of power law distributions in protein-protein interaction networks through study bias. eLife. (2024) Dec 11;13:e99951.

Alfieri, F, Giulio C, Schaefer MH. Cancer genomes tolerate deleterious coding mutations through somatic copy number amplifications of wild-type regions. Nature Communications 14.1 (2023): 3594.

Sambruni G, Macandog AD, Wirbel J, Cagnina D, Catozzi C, Dallavilla T, Borgo F, Fazio N, Fumagalli-Romario U, Petz W, Manzo T, Ravenda S, Zeller G, Nezi L, Schaefer MH. Location and condition based reconstruction of colon cancer microbiome from human RNA sequencing data. Genome Medicine 15.1 (2023): 32.f

Hernandez-Alias X, Benisty H, Radusky LG, Serrano L, Schaefer MH. Using protein-per-mRNA differences among human tissues in codon optimization. Genome Biology 24.1 (2023): 1-20.

Heery R, Schaefer MH. DNA methylation variation along the cancer epigenome and the

identification of novel epigenetic driver events. Nucleic acids research 49.22 (2021): 12692-12705.

* Group composition: total members, and roles distribution (PhD, postdoc, technician, etc.)

One postdoc, two PhD students, three master students

Institutional page link

https://www.research.ieo.it/research-and-technology/principal-investigators/martin-schaefer/

Lab website link, if any

https://www.schaeferlab.org/

Social media links, if any

If you prepare a video to promote your lab/project, please include the link below

https://www.youtube.com/watch?v=CZkQmMb1g60&t=2012s