Decoding the Cancer Genome: A Patient-Centric Journey from Telomere to Telomere

Challenge

- Roughly 90% of tumours exhibit aneuploidy, where cancer cells have extra or missing chromosomes.
- Aneuploidy often results from structural abnormalities in chromosomes such as deletions, insertions, and inversions, accounting for most varying bases in the human genome. It can serve as a prognostic marker and potential treatment insights, depending on context and cancer type.
- Among the broad spectrum of structural variants (SVs) driving tumorigenesis, a relevant subset escapes discovery using short-read sequencing due to technical difficulties with respect to their discovery and characterization.
- Robust and innovative methods are necessary to discover and characterize the extent, origin, and functional consequences of SVs in the context of cancer but also in germline and across the vast landscape of aging.

Technology

Our research provides methods for (epi)genome profiling and insights into complex rearrangements underlying genetic phenomena. We combine long-read sequencing (e.g. Oxford Nanopore Technologies, ONT) and diverse omics and imaging approaches, to investigate the molecular mechanisms behind human phenotypes linked to genetic variation complexities[1]. This includes the completion of human genome variation maps using strand-specific and single-molecule DNA sequencing techniques (e.g. Strand-seq). Our focus encompasses both assembly techniques and the analysis of individual cell karyotypes. Our experimental methods extend to tissues and organoids, where we pioneer data science techniques, including machine learning for high-dimensional single-cell data and connecting genetic variation with patient phenotypes. We've developed various computational methods such as scTRIP[2], a computational framework combining read depth, template strand, and haplotype phase to detect SVs at the single-cell level. We also identify and describe associations between disease-causing copy number variants (CNVs) and recurrent inversion hotspots. We are establishing a comprehensive human genome database, aiming to enhance the scalability of cancer research. We use this database to train our karyotyping tools for genetic rearrangement analysis and adjust our approaches in long-read sequencing. Our expertise extends to sequence inheritance and evolution within cell lineages, with a particular emphasis on cancer, where we hold a prominent position as global leaders.

Internal EMBLEM Reference

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Key Inventors

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Applications

- **Precision Medicine:** Ensuring accurate and stringent karyotype depiction as quality control for CRISPR-*Cas* engineered cells before their reintroduction to the patient. Improving diagnosis, prognosis, and tailored therapeutic interventions. Detecting disease-associated SVs for early diagnosis and risk assessment. Prediction and analysis of drug resistance in pathogens and cancer cells…
- **Pharmaceutical Industry:** Enhancing drug development by targeting specific genetic variations…
- **Advanced Cancer Therapies**: Single-cell strand sequencing methods for comprehensive SVs analysis…
- **Biotechnology:** Enhancing cells engineer e.g. for synthetic biology and bioproduction…

References

[1] https://doi.org/10.1016/j.xgen.2023.100281

[2] https://doi.org/10.1038/s41587-019-0366-x

[3] https://doi.org/10.1016/j.cell.2022.04.017

Software

- High-throughput sequencing
  - CopySeq
  - DELLY
  - PEMer
- Sequence Analysis
  - BreakSeq
  - scTRIP
  - scNova
- Miscellaneous
  - BreakPtr

Keywords

Cancer
Aging
Chromosomal Rearrangement
Single Cell
Mosaicism
Karyotyping
Cell Therapy
Long Read Sequencing

Benefits

- Scalable methods
- Modular tools
- Comprehensive workflow
- Innovative processes
- Custom-tailored designs

Seeking:

☒ Collaborations

☒ Commercial partners

Intellectual Property

☒ Know-how based

☒ Copyright

Commercial Opportunity

We wish to extend the potential of our diagnostic and prognostic tools in the fields of cancer and aging by joining forces with experts from various sectors such as microfluidics or geriatrics.

Our services are available to everyone, and we offer special rates for academics and SMEs.

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