Somatic Mutation Signatures for Lineage Tracing, Tissue Homeostasis, and Human Development

Challenge

Understanding how human tissues develop, maintain homeostasis, accumulate somatic mutations, and transition toward disease remains a major hurdle across biomedical research and biotechnology. Key challenges include:

- Reconstructing human developmental and tissue lineage histories from somatic mutations across ages
- Quantifying somatic mutation accumulation to understand aging, disease predisposition, and tissue-level selection dynamics.
- Characterizing cell-type–specific mutational processes in normal and diseased tissues.
- Linking developmental origins to cancer risk and identifying early developmental precursors of malignancies.
- Integrating large-scale somatic mutation datasets across tissues, individuals, and species.
- Innovating new computational approaches for novel data types including single cell DNA sequencing and spatial DNA sequencing

The research of Dr. Tim Coorens provides high-resolution, mutation-based lineage tracing tools and frameworks that address these foundational biological and clinical challenges.

Technology

Dr. Coorens' work develops computational approaches to reconstruct human tissue dynamics from somatic mutations, enabling unprecedented insights into:

- **Somatic Mutation Landscapes in Normal Tissues**
  Using a variety of genome sequencing approaches, including single cell DNA sequencing spatial sequencing and duplex sequencing, the technology identifies and interprets somatic variant patterns across normal human tissues to quantify clonal architecture, mutational burdens, and selective pressures.

- **High-Resolution Human Developmental Phylogenies**
  A novel computational pipeline infers developmental lineage trees spanning from early embryogenesis to adulthood, derived from extensive somatic mutation profiles across tissues. Insights into embryogenesis can even be derived from mutations in tissues of aged individuals, and does not require human prenatal material.

- **Cross-Species Developmental Genomics**
  Through the Human and Non-Human Primate Developmental GTEx Project, the technology establishes a comparative framework for understanding human development and tissue maturation.

- **Mutation-Based Detection of Disease Precursors**
  Mutation signatures reveal embryonic origins of childhood cancers, as demonstrated in Wilms tumor studies. This offers novel diagnostic potential for early-stage developmental lesions.

Key Features: Whole-genome–scale mutation calling and filtering, down to single-cell resolution - Lineage inference and phylogenetic reconstruction algorithms - Mutational pattens and molecular clocks based across human tissues - Cross-species comparative genomics resources

Internal EMBLEM Reference

2026-029

Key Inventors

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Applications

- **Pharmaceutical R&D:** Tissue lineage reconstruction for toxicity testing, tissue turnover analysis, and early detection of treatment-induced mutagenesis.
- **Diagnostics & Precision Medicine:** Mutation-based biomarkers for early cancer detection and developmental disorder assessment.
- **Biotechnology, Genomics & Tools Development:** Software and computational platforms for somatic mutation analysis.
- **Aging & Regenerative Medicine:** Quantitative assessment of clonal dynamics and tissue repair mechanisms.
- **Comparative Genomics & Model Systems:** Tools for evaluating conservation of developmental pathways across species.

Benefits

- **Non-invasive lineage reconstruction** via naturally occurring somatic mutations
- **High sensitivity** to low-frequency clonal populations
- **Applicable across tissues, ages, and species**
- **Scalable** to large sequencing datasets
- **Clinically relevant insights** into developmental origins of disease

Software

The research described supports computational pipelines for:

- Mutation calling and filtering and phylogenetic reconstruction, including the **Sequoia** toolkit (https://github.com/TimCoorens/Sequoia)
- Clonal dynamics modelling
- Cross-tissue mutational comparison

Keywords

Somatic mutations
Lineage tracing
Developmental genomics
#Tissue homeostasis
Clonal architecture
Mutational signatures
Embryogenesis
Cancer precursors
Comparative genomics
Gastric epithelium
Primate development
Single-cell genomics
Whole-genome sequencing

Further Reading

[1] https://doi.org/10.1038/s41586-025-08708-6
[2] https://doi.org/10.1038/s41586-024-08244-9
[3] https://doi.org/10.1038/s41586-021-03790-y
[4] https://doi.org/10.1038/s41586-021-03345-1
[5] https://doi.org/10.1126/science.aax1323

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Intellectual Property

☒ Know-how based

☒ Copyright

Commercial Opportunity

Opportunities include licensing, co-development, sponsored research, and computational method integration.

Seeking:

☒ Collaborations

☒ Commercial partner

☒ Licensing

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