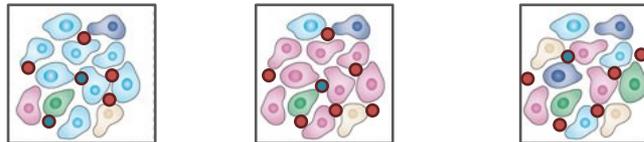
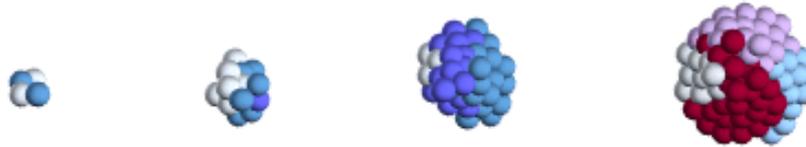
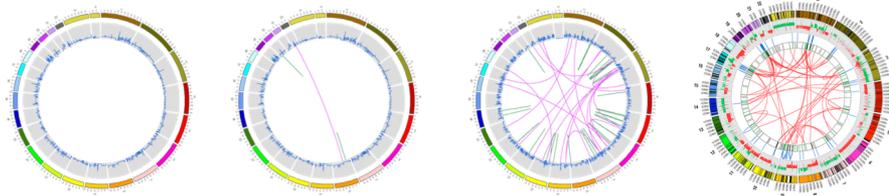
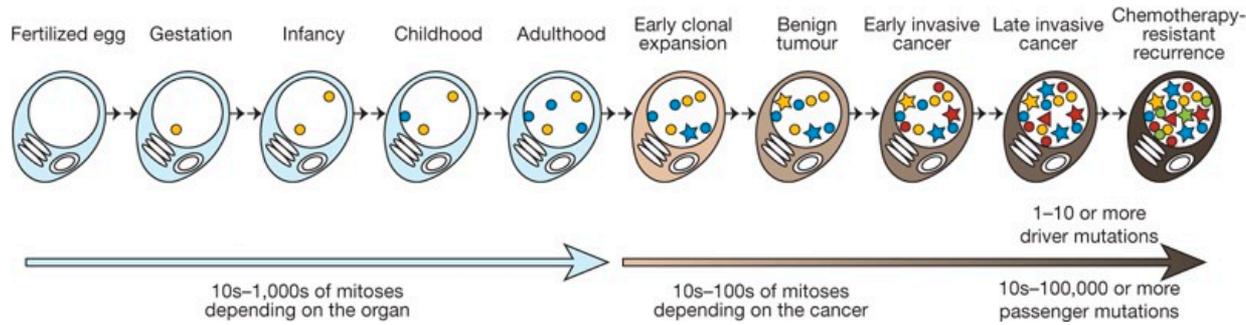


Inference of tumor growth dynamics using genomic data

Subhajyoti De, PhD

Rutgers Cancer Institute
Rutgers, the State University of New Jersey

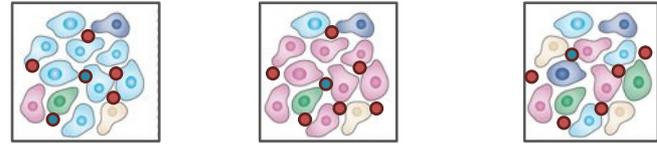
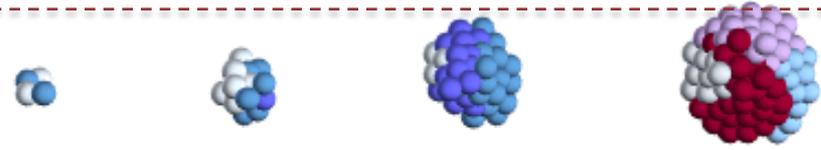
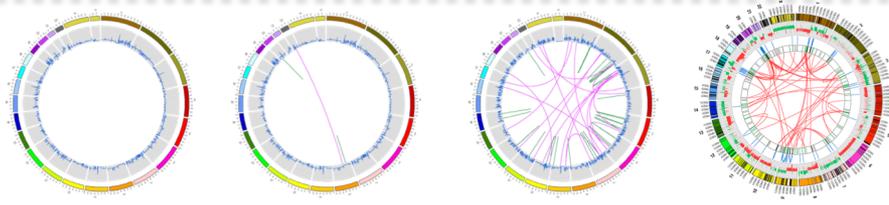
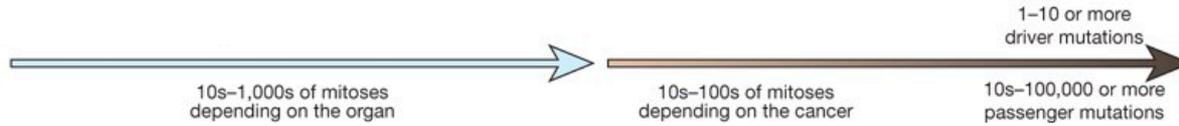
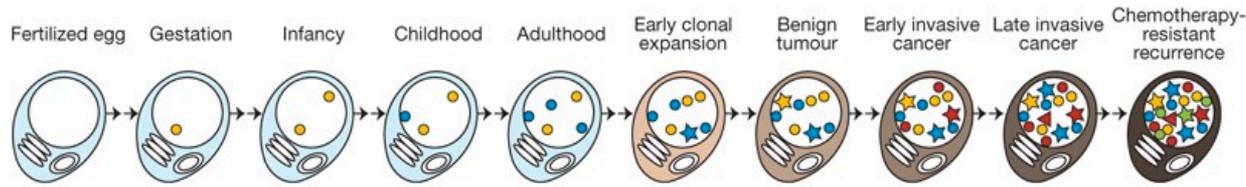
Overview



Cancer Evolution

- Genome-level evolution in cancer
- Cell population-level evolution in cancer
- Microenvironment-level evolution in cancer

Overview

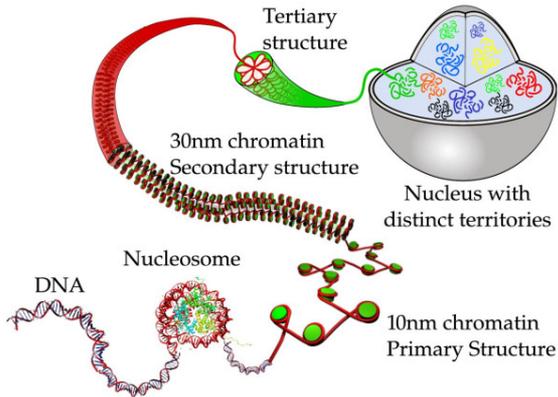


Cancer Evolution

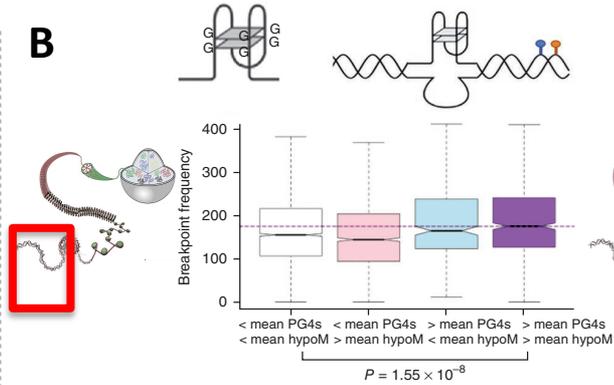
- Genome-level evolution in cancer
- Cell population-level evolution in cancer
- Microenvironment-level evolution in cancer

Genome-level evolution

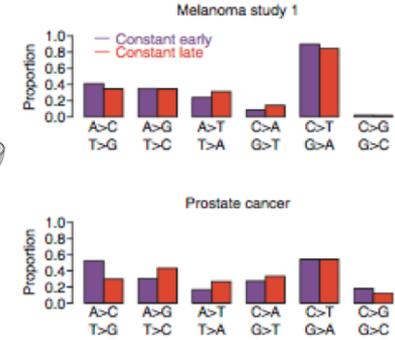
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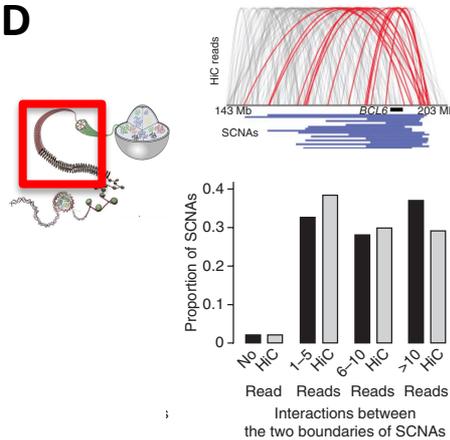
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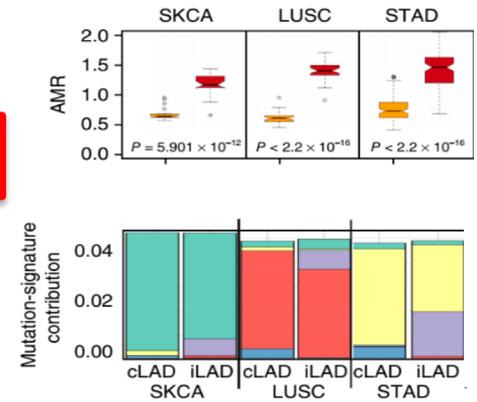
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D



E



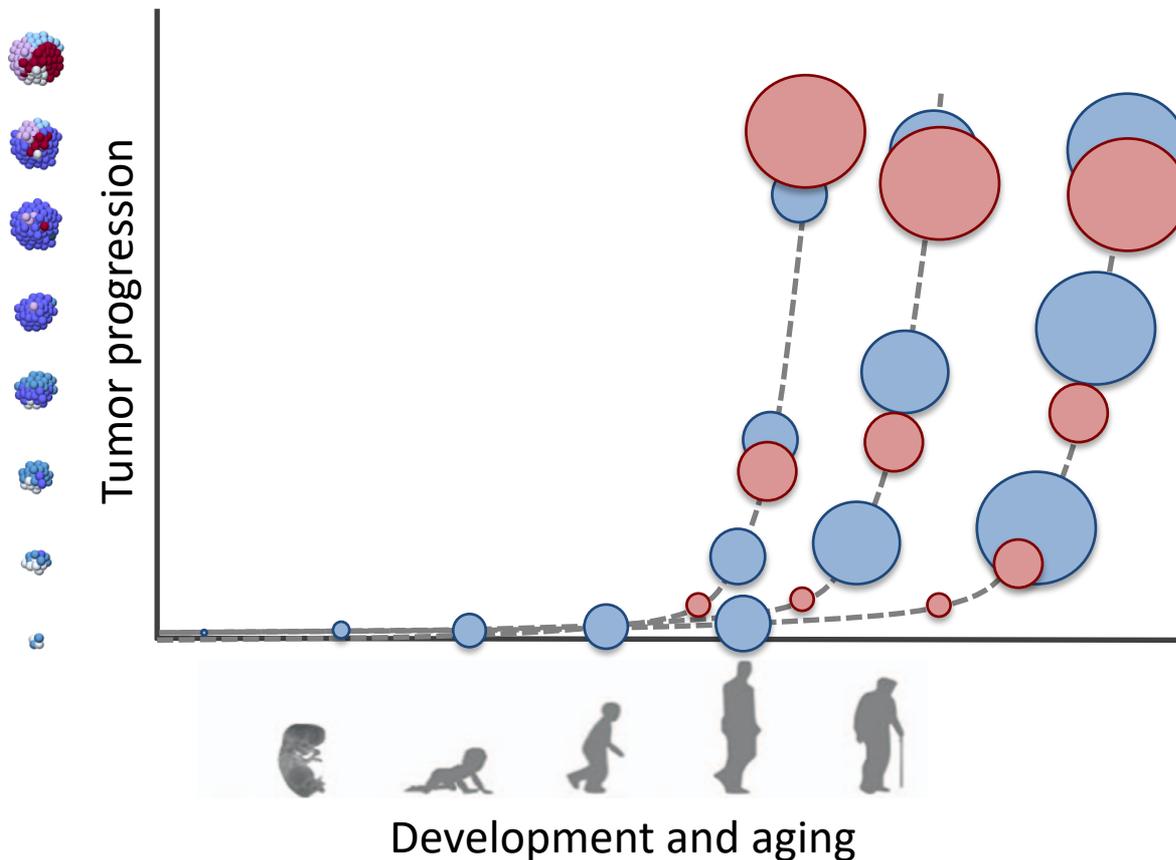
De et al. Nature Str Mol Biol. 2011

Liu, De, Michor, Nature Comm. 2013

De et al., Nature Biotech. 2011

Smith, ..., De, Nature Str Mol Biol. 2017

Genomic alterations and tumor evolution



Point mutations with
clock-like signatures

Complex rearrangements

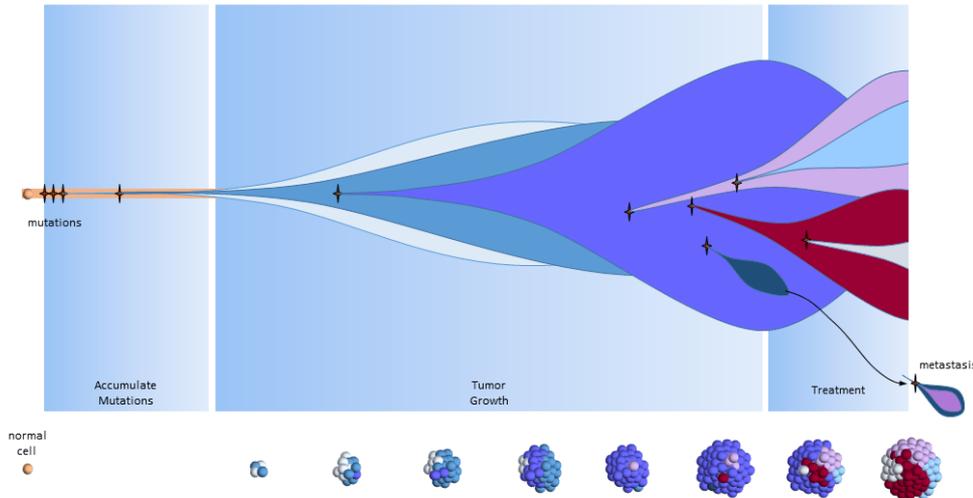
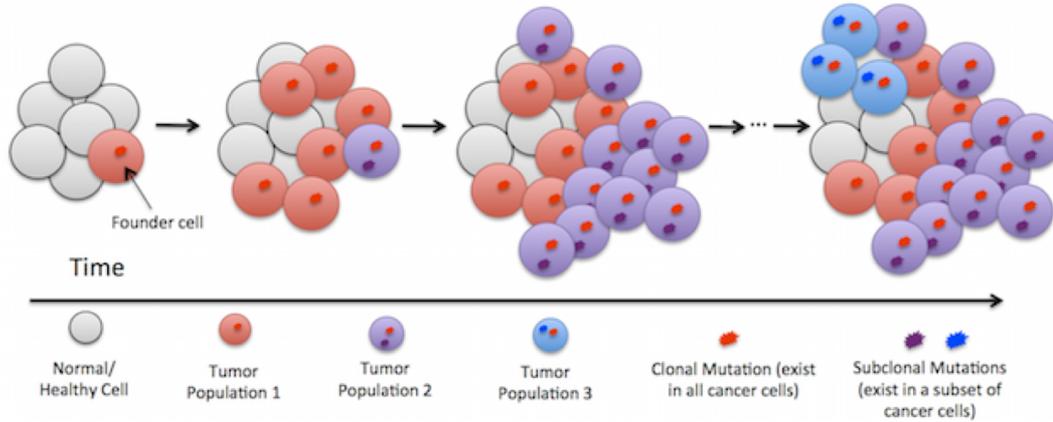
Mutation Signature SBS8
(late replication error)

Alexandrov et al. Nature Genet, 2014

Yadav et al. Nucleic Acids Res. 2016

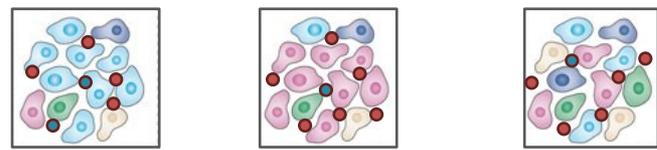
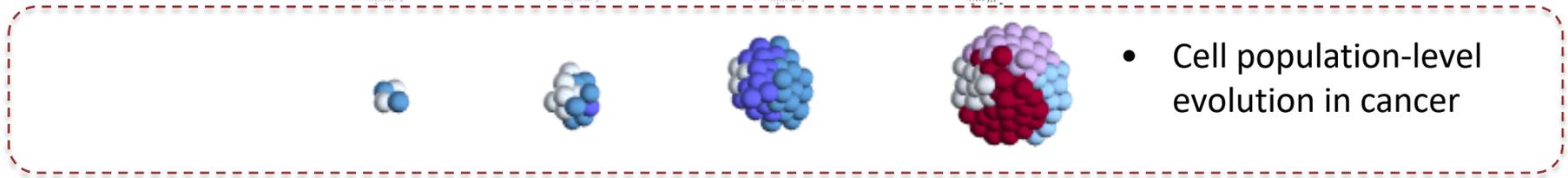
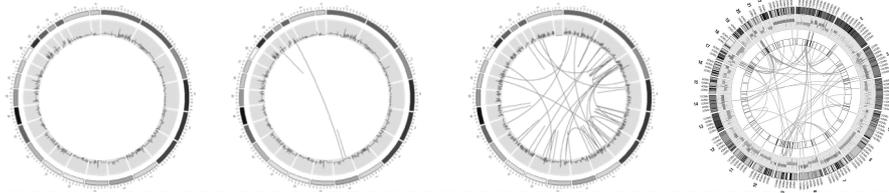
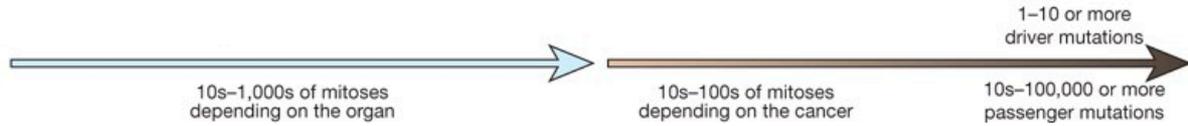
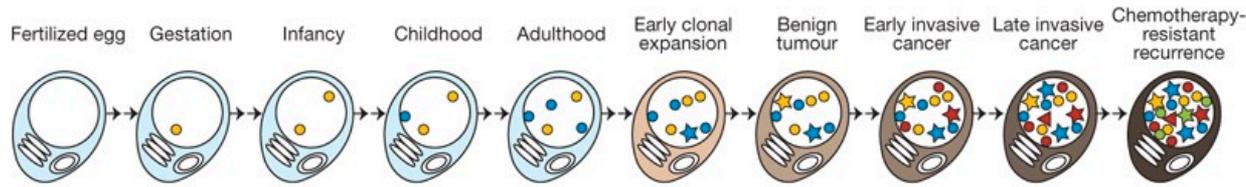
Singh et al. Comm Biol. 2020

Overview



- Genome-level evolution in cancer
- Cell population-level evolution in cancer

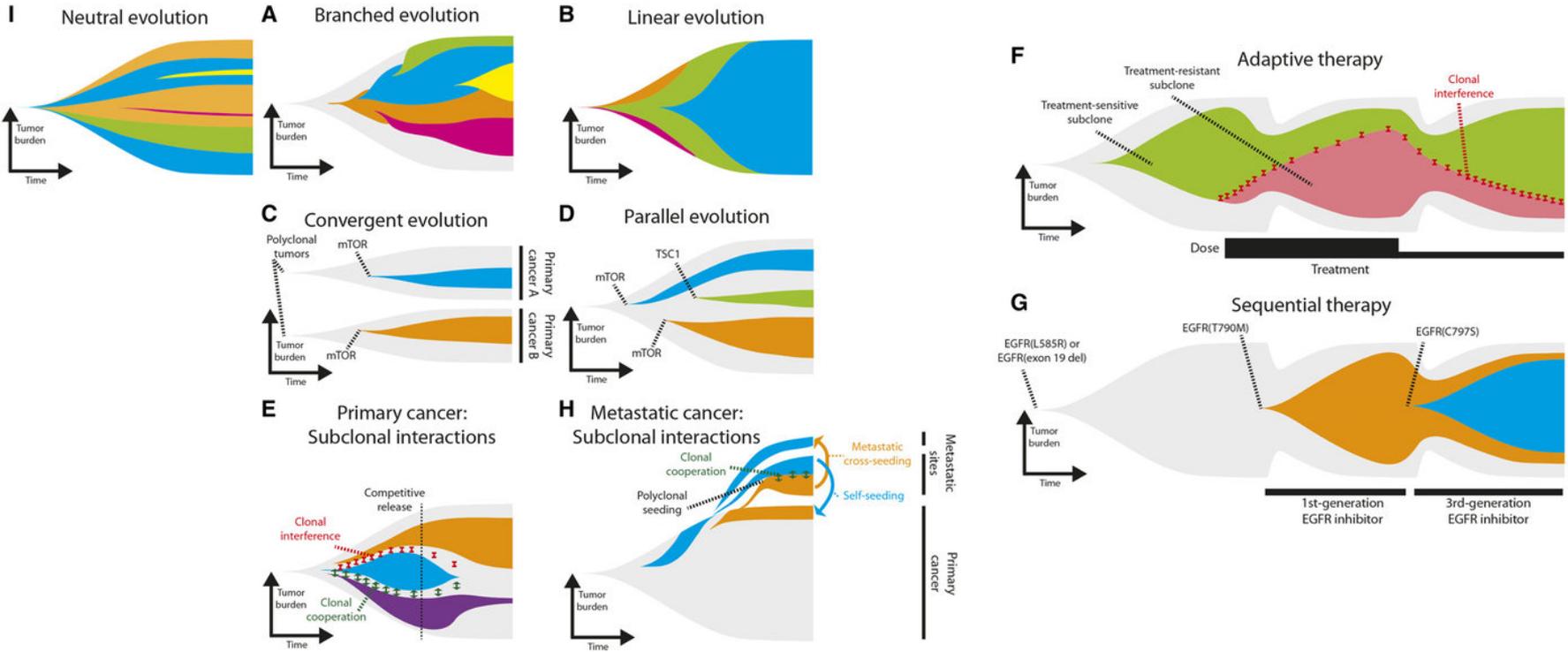
Overview



Cancer Evolution

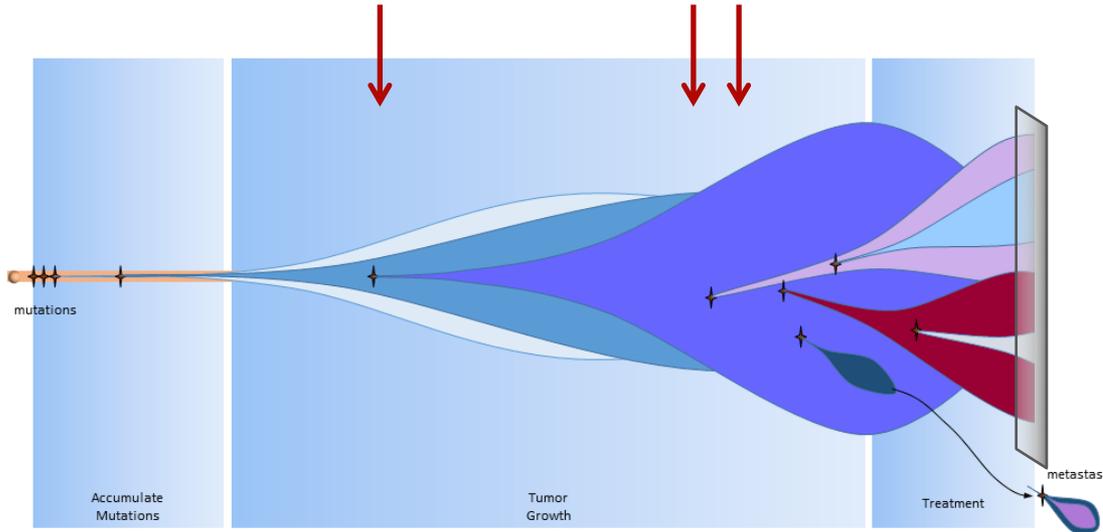
- Genome-level evolution in cancer
- Cell population-level evolution in cancer
- Microenvironment-level evolution in cancer

Cell population-level evolution in cancer



Venkatesan & Swanton, 2016
De & Ganesan, 2017

Motivation



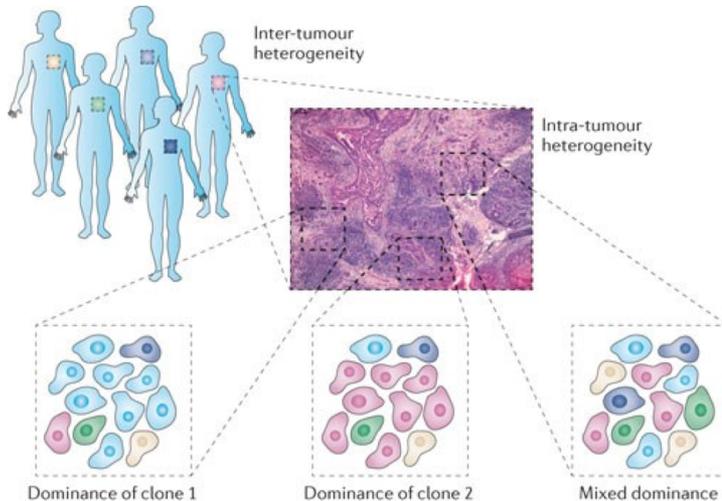
Diagnosis represents a snapshot late during tumor evolution.

True mutational history and clonal makeup are unknown.

Impact of acquired driver mutations is not 'always' well understood.

Intra-tumor spatial heterogeneity and limited sampling can bias the observations

Pathological markers (e.g. mitotic index) do not provide information about past characteristics of tumor cells, and different subclones therein.



Overall Goal and Aims

To develop a framework to estimate subclonal growth rates in tumors using emerging genomic approaches, and then estimate selective advantage conferred by selected oncogenic drivers during tumor progression.

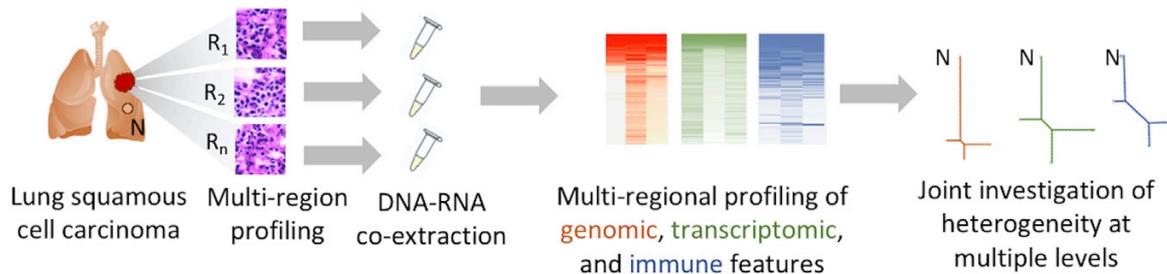
Specific Aims

Aim-1: Develop a genomic approach to quantify subclonal growth rates in heterogeneous tumors.

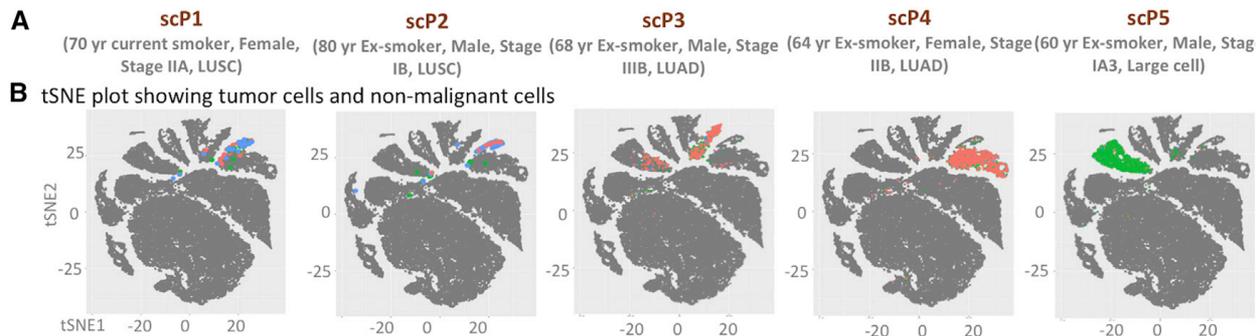
Aim-2: Quantify growth advantage conferred by subclonal oncogenic mutation in human cancers.

Team: De, *Computational cancer genomics*; Carpizo, *Surgical oncology*; Riedlinger, *Pathology and imaging*; Wang: *Biostatistics*.

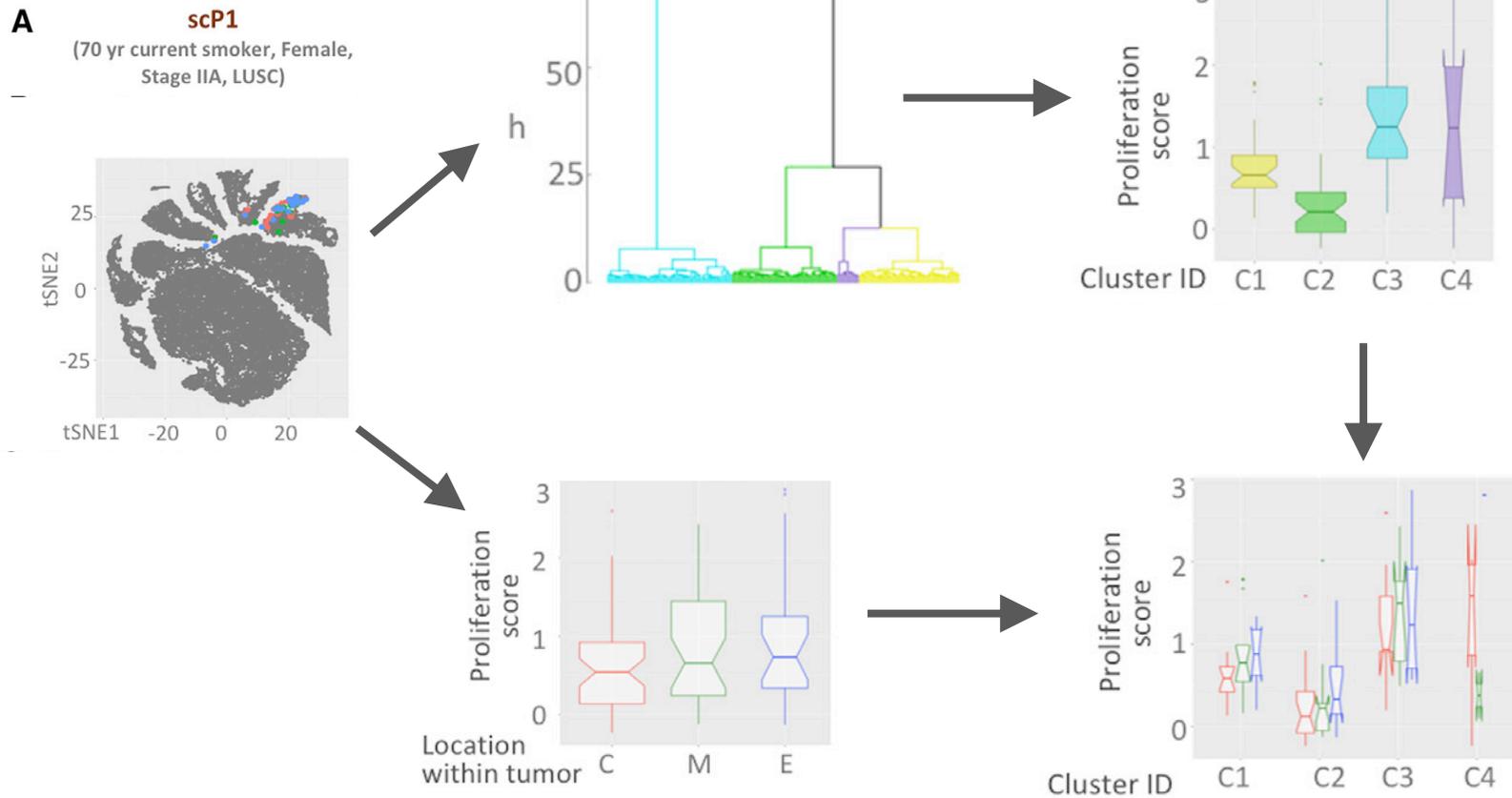
Bulk multi-region sequencing



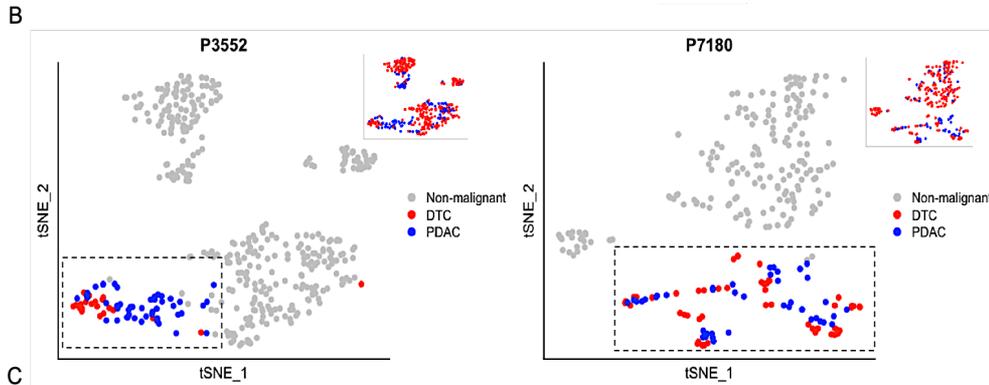
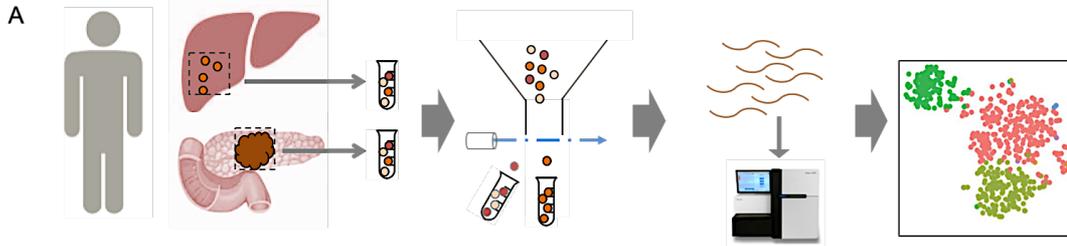
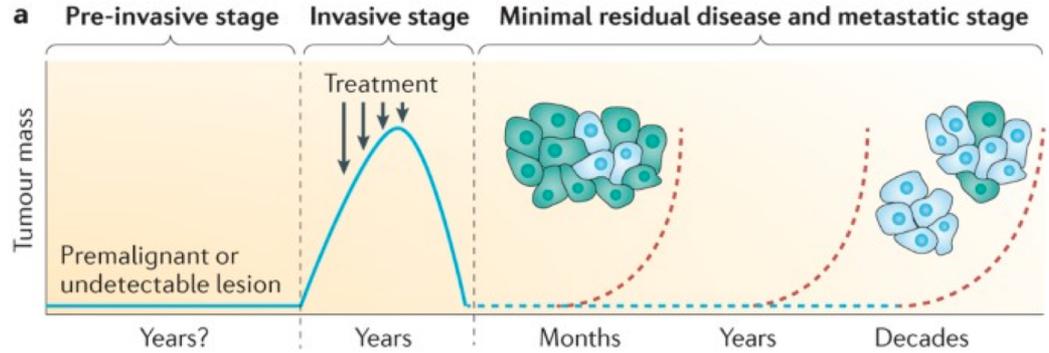
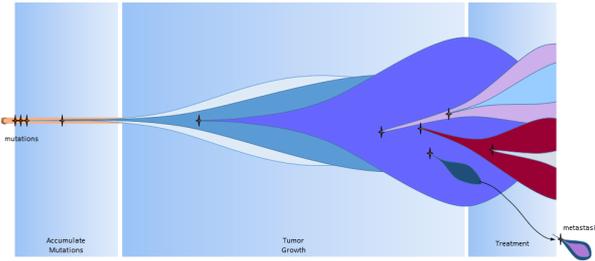
Analysis of single cell multi-region sequencing



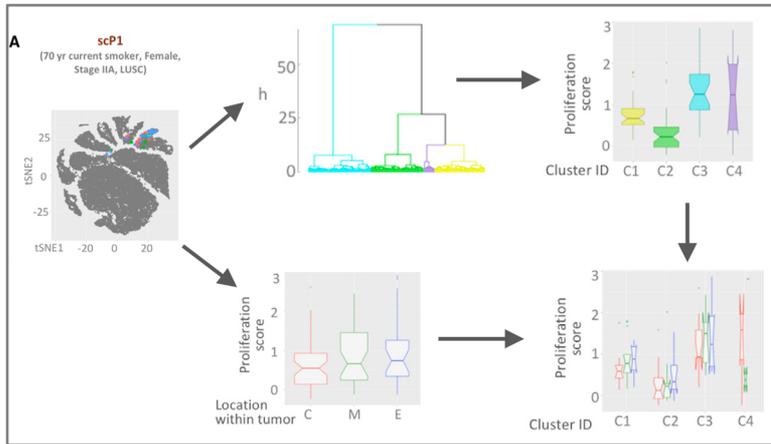
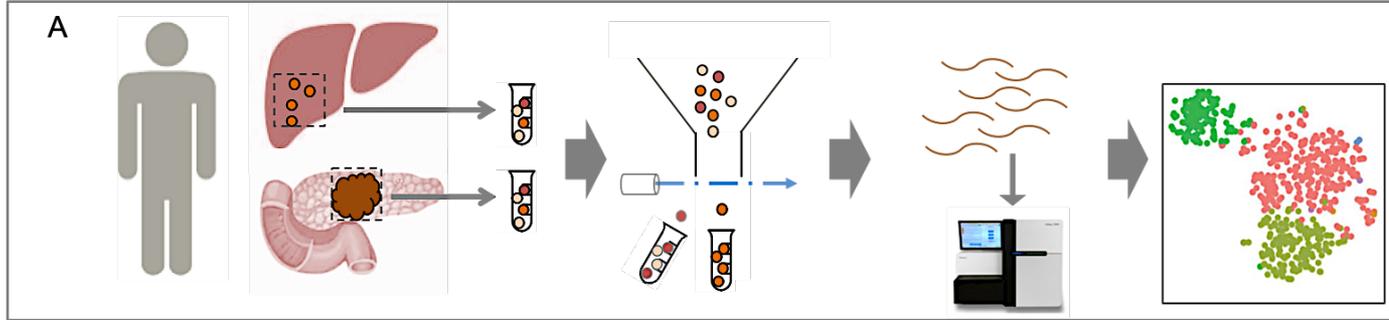
Analysis of single cell multi-region sequencing



Single cell sequencing to study pancreatic cancer evolution



Progress report so far ...



Challenges, opportunities, and collaboration with ITCR community

- Reliable mutation calling from single cell data
- Reliable clonal reconstruction from single cell data
- Non-genetic determinants of cell population growth
- Epistasis, clonal cooperation and competition
- Applying the frameworks to other cancers