

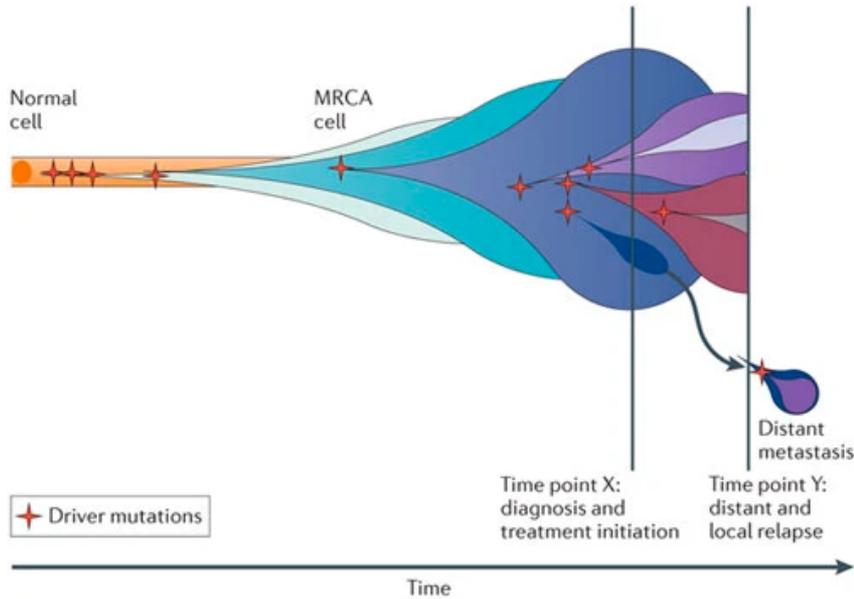


Ongoing evolutionary dynamics in cancer

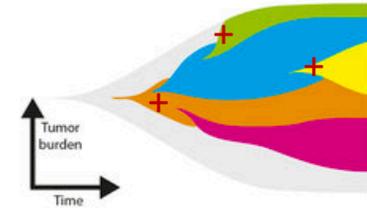


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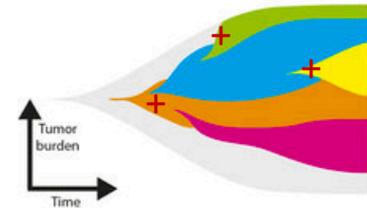
Dynamics of somatic evolution in cancer



Mode of evolution and effects of driver mutations

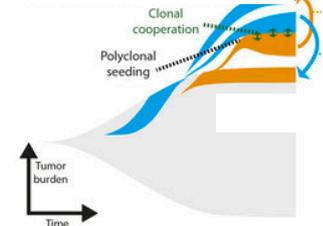


Cancer stemness and clonal dynamics

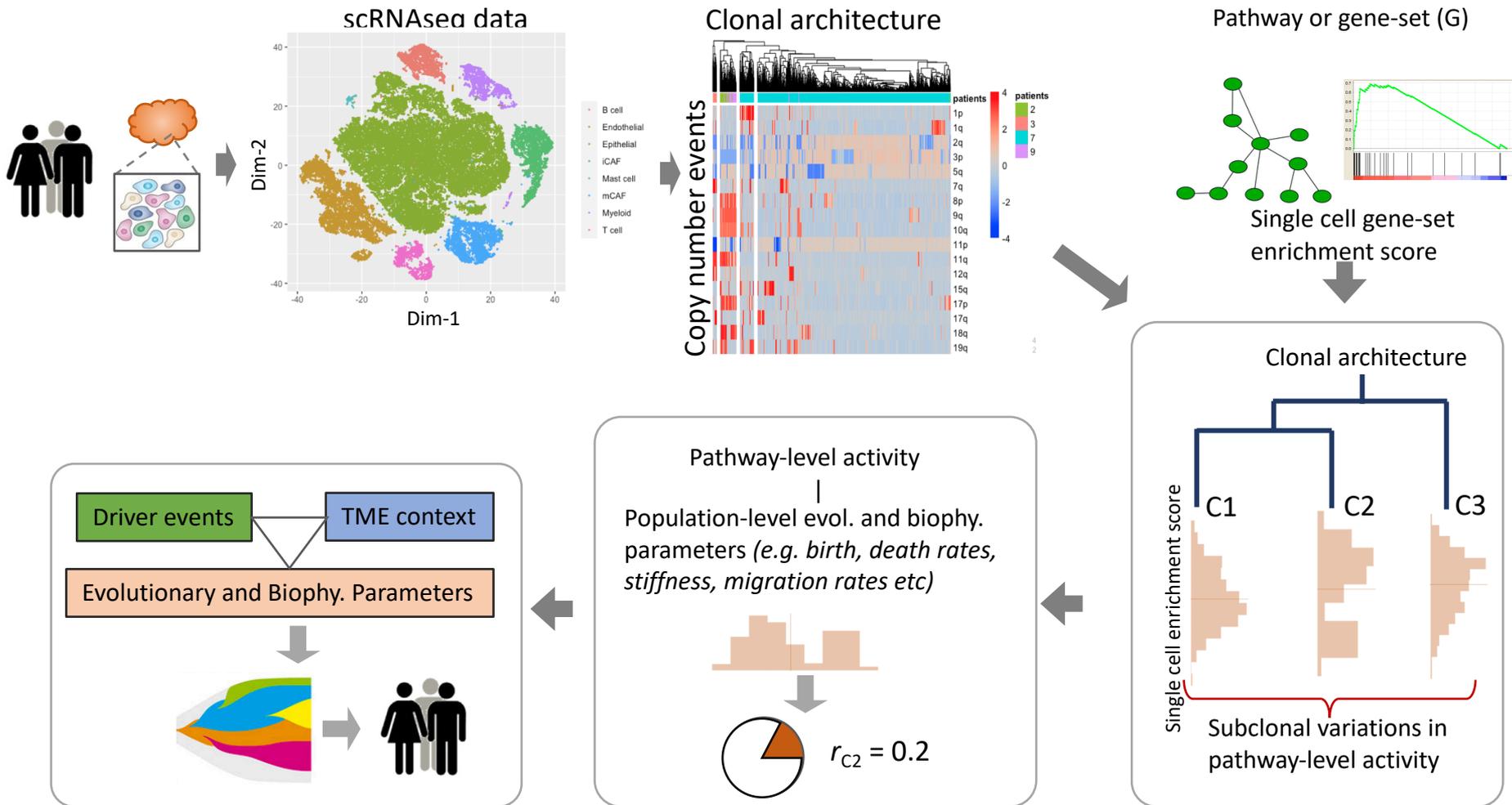


Microenvironment, metastasis, and treatment

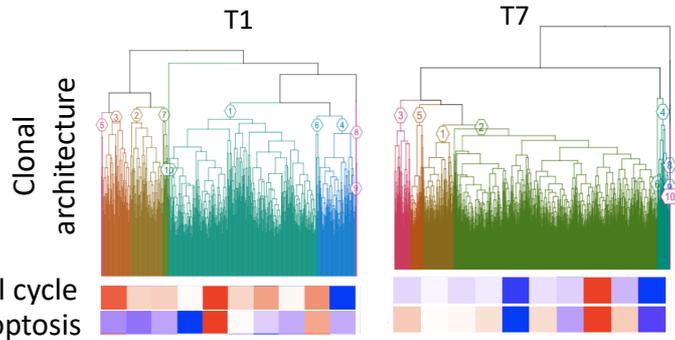
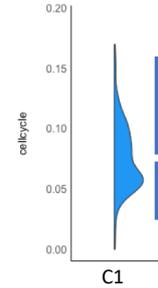
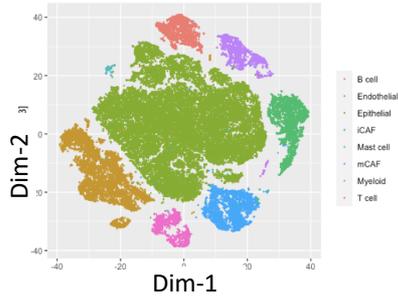
TME interactions in primary tumor and metastasis



Parameter Estimation for Modeling Somatic Evolution in Cancer (PEMSEC)



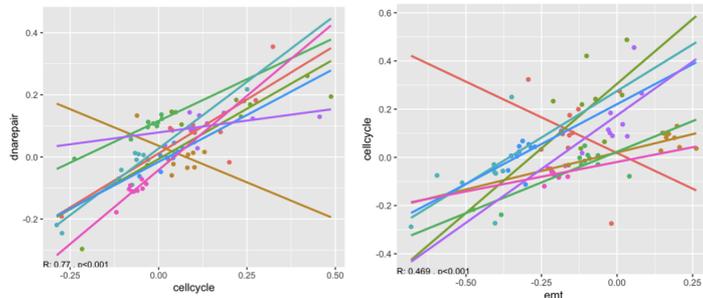
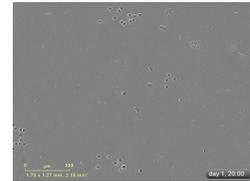
PEMSEC : modes of cancer evolution



Replicating fraction (f) -> Birth rate: r
 Apoptotic and necrotic fraction (k) -> Death rate: d

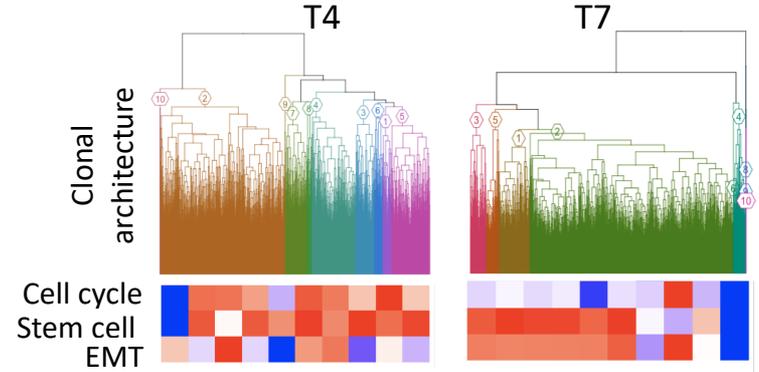
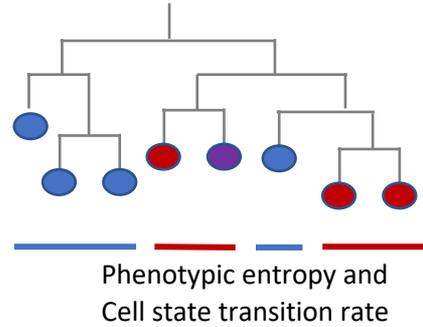
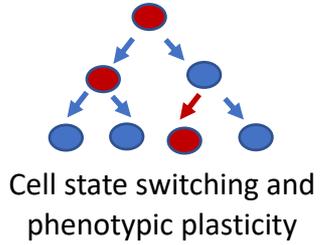
Mode of evolution: Test for neutrality in ongoing clonal dynamics

Validation

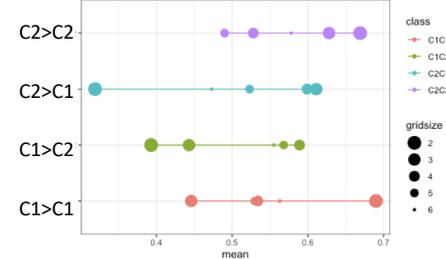
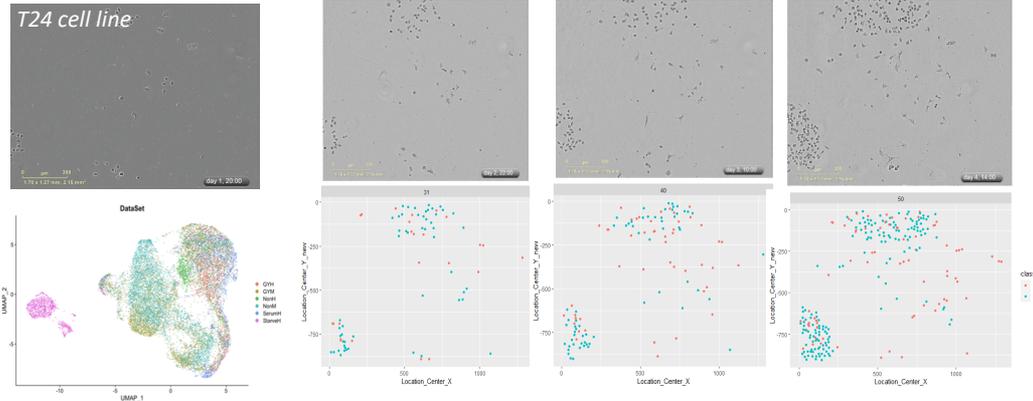


- Differences in the activity of the pathways associated with proliferation, cell death etc between subclones.
- Subclonal pathway-level scores collectively consistent and aligned with cancer hallmarks.
- Inference on the modes of tumor evolution and association with subclonal driver events.

PEMSEC : impact of phenotypic plasticity on evolutionary parameters

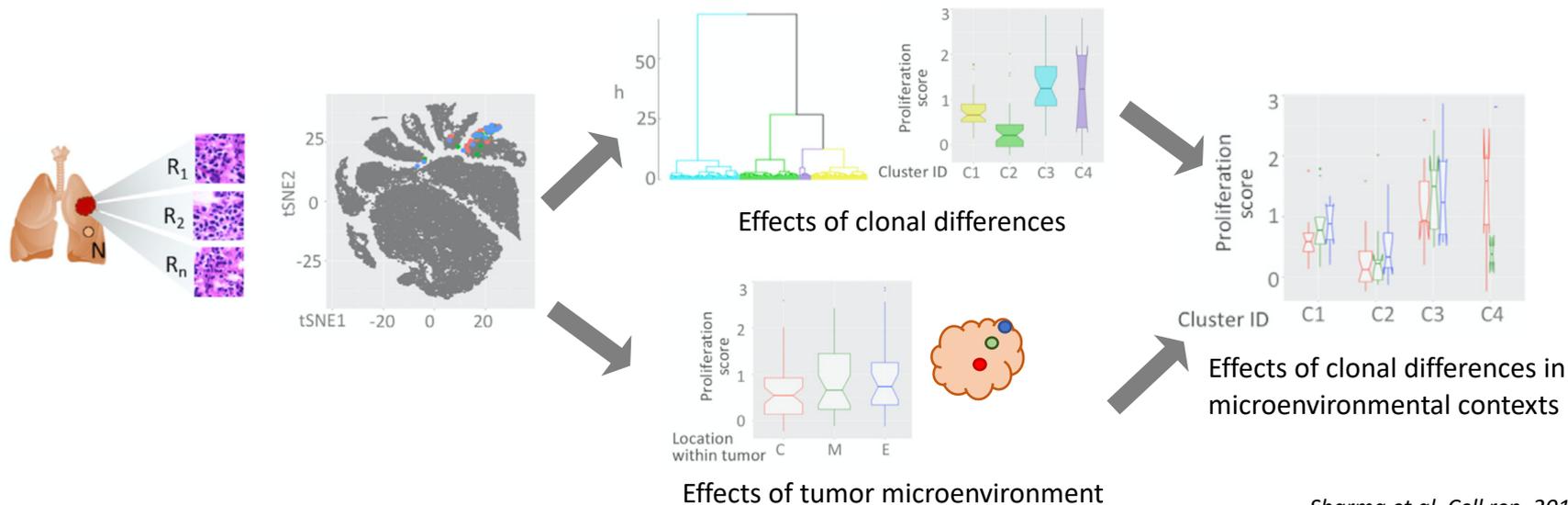


In vitro clonal evolution model: infer the cell state transition rate from transcriptomic data



C1: Stem cell / holoclone
C2: Differentiated cell / meroclone

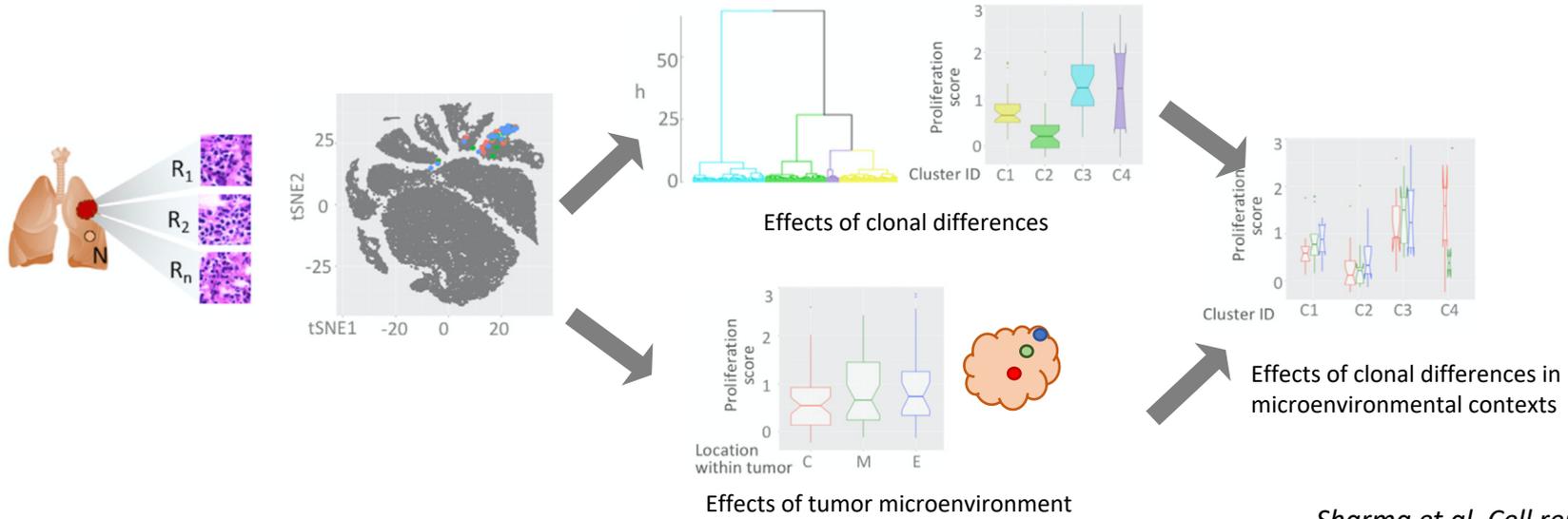
PEMSEC : effects of tumor microenvironment on evolutionary parameters



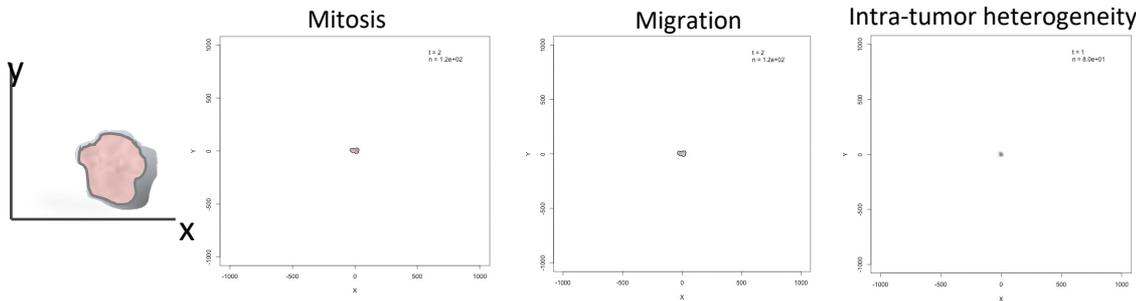
Sharma et al. Cell rep, 2019

- Proportions of variance explained by clonal and microenvironmental attributes.
- Effects of microenvironmental makeups on cancer hallmarks.
- Revisiting inferences on neutral evolution and clonal dynamics under selection.

PEMSEC : effects of tumor microenvironment on evolutionary parameters



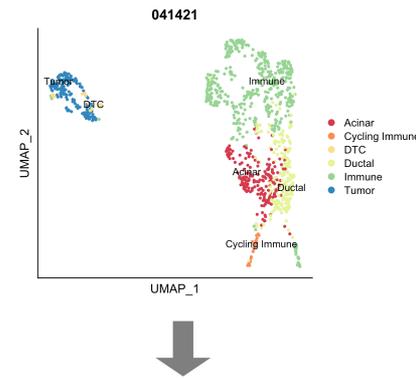
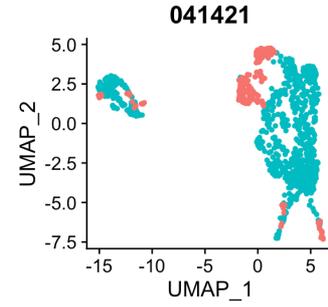
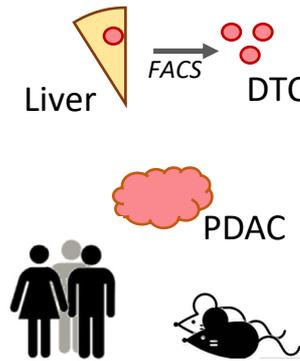
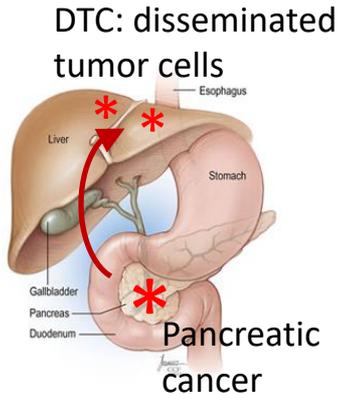
Sharma et al. Cell rep, 2019



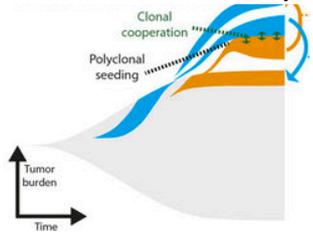
Modeling tumor growth based on inferred estimates of tumor evolutionary dynamics

- Microenvironmental contexts influence clonal fitness and overall makeups of intra-tumor spatial heterogeneity

PEMSEC : evolutionary parameters in metastatic contexts



Evolutionary properties in the primary and metastatic sites may differ



Cellular states, biophysical and evolutionary parameters vary between primary tumor and metastatic contexts.

Non-stationarity of the mode of evolution:
Modes of cancer evolution and parameters may be dynamically modulated by cellular states and microenvironment contexts.

PDAC
 PDAC DTC
 Ductal cells

