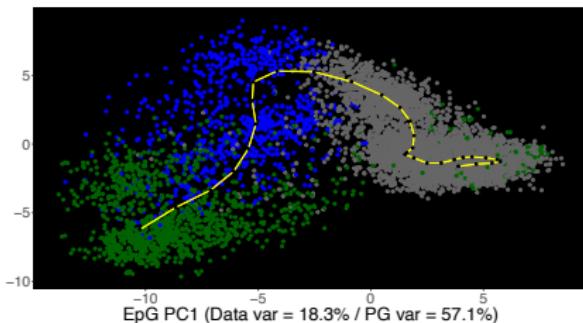
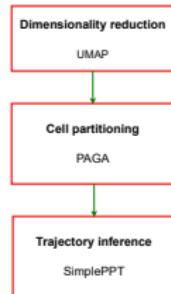
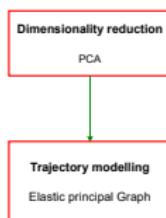


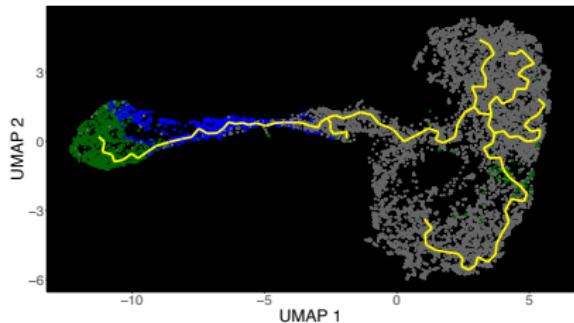
Trajectory Inference Analysis

EPIGraph
Albergante et al. (2020)

Monocle3
Cao et al. (2019); Wolf et al. (2019)



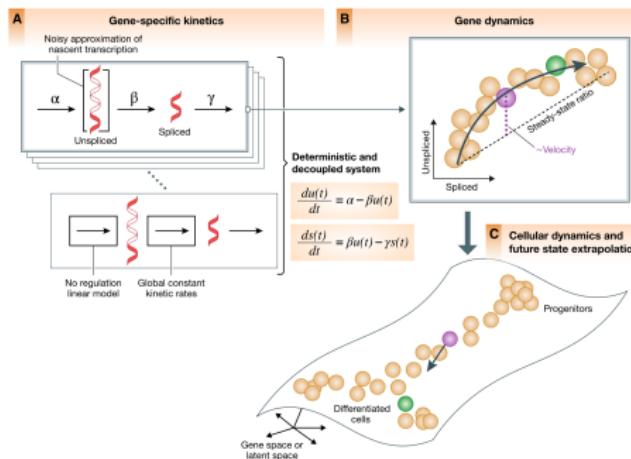
Cell Type
Cycling cells
hypoxic-inflammatory response (HIR)
Neuronal Progenitor Like 1
Neuronal Progenitor Like 2
Non-Neuronal
Undifferentiated



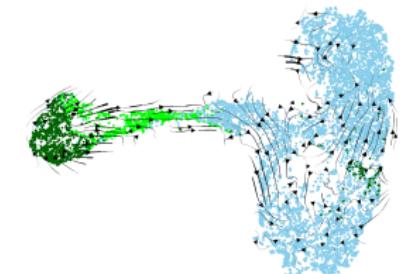
RNA velocity analysis to identify the trajectory root



Bergen et al. (2020)



Bergen et al. (2021)



latent time

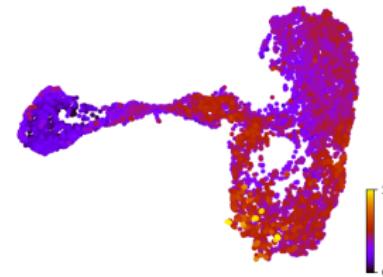
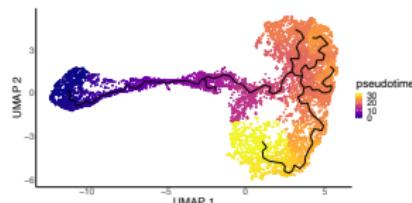


Figure: Monocle3 pseudotime



Cell differentiation state

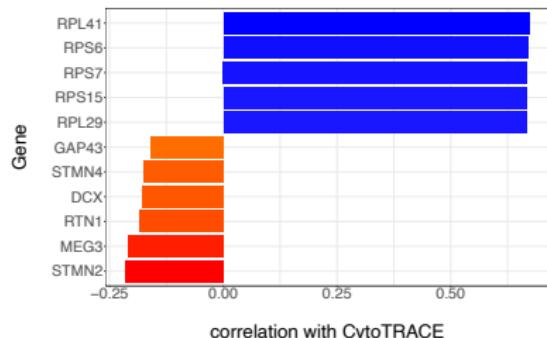
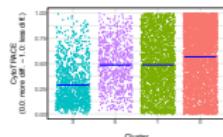
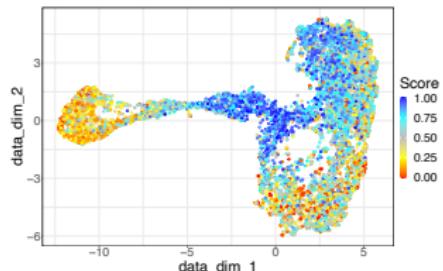
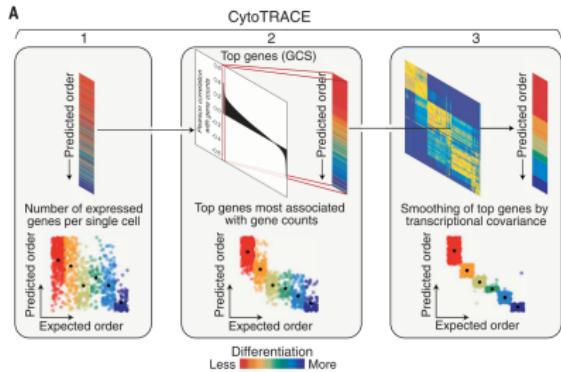
RESEARCH ARTICLE

RESEARCH METHODS

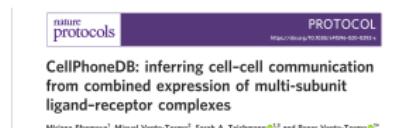
Single-cell transcriptional diversity is a hallmark of developmental potential

Gunsagar S. Gulati^{1,2*}, Shaheen S. Sikandar^{3*}, Daniel J. Wesche³, Anoop Manjunath³, Anjan Bharadwaj³, Mark J. Berger^{2†}, Francisco Ilagan¹, Angera H. Kuo¹, Robert W. Hsieh¹, Shang Cai³, Maider Zabala^{1,‡}, Ferenc A. Scheeren⁴, Neethan A. Lobo^{1,‡}, Dalong Qian¹, Feiqiao B. Yu⁵, Frederick M. Dirbas⁶, Michael F. Clarke^{1,7}, Aaron M. Newman^{1,8§}

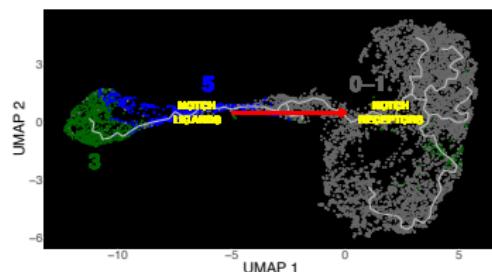
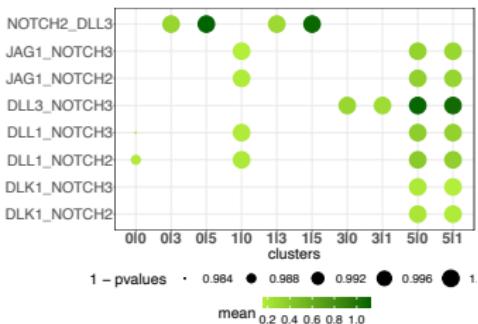
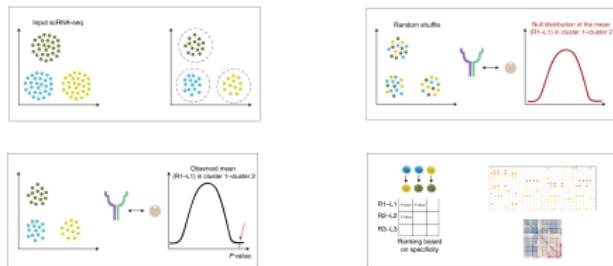
Gulati et al. (2020)



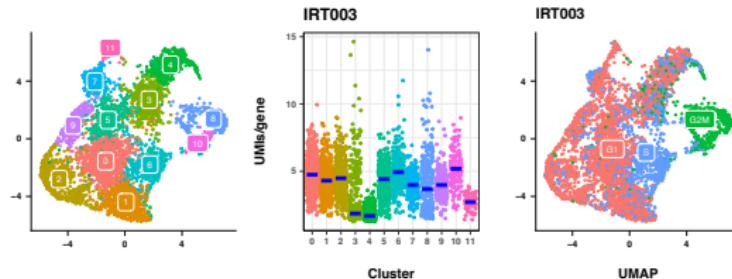
Ligand-receptor interaction analysis



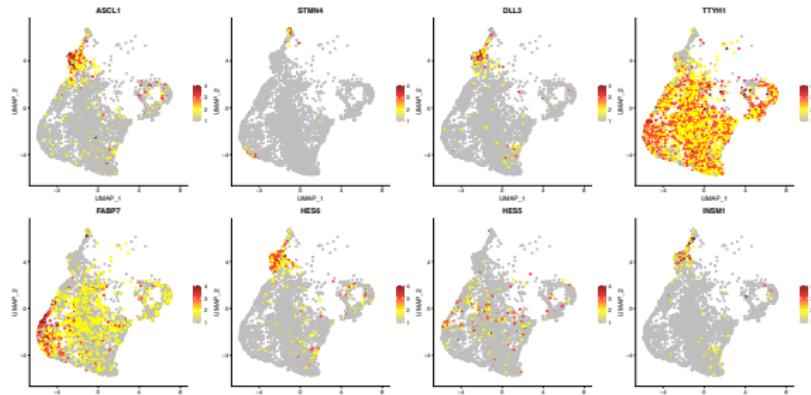
Efremova et al. (2020)



New sample (IRT003) shows similar heterogeneity



Expression of ATRT-SHH signature genes



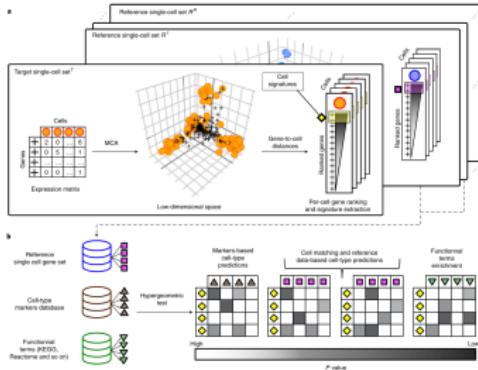
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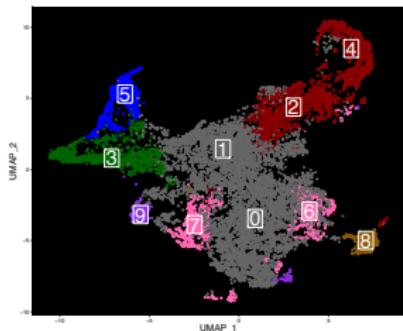
Gene signature extraction and cell identity recognition at the single-cell level with Cell-ID

Akira Cortal¹, Lorredore Mortiglieri¹, Emanuele Sis¹ and Antonio Rausell^{1,2,3}

Cortal et al. (2021)



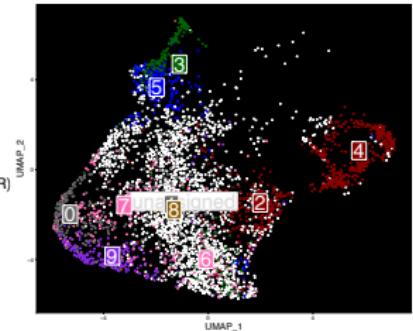
integrated INI254,INI255,INI267



Cell Type

- Cycling cells
- hypoxic-inflammatory response (HIR)
- Neuronal Progenitor Like 1
- Neuronal Progenitor Like 2
- Non-Neuronal
- Undifferentiated

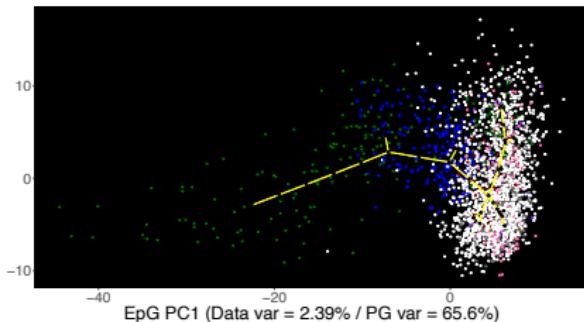
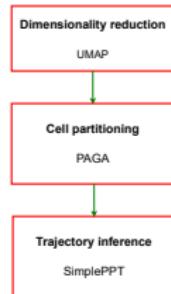
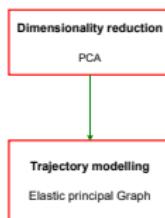
IRT003



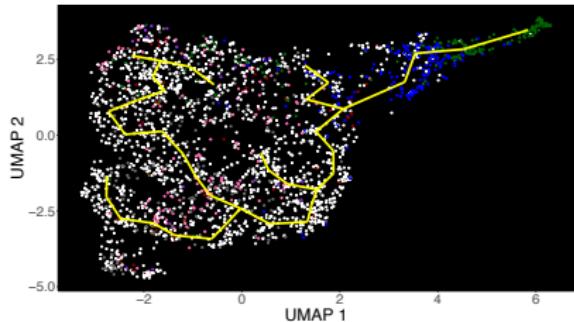
Trajectory Inference Analysis on IRT003

EPIGraph
Albergante et al. (2020)

Monocle3
Cao et al. (2019); Wolf et al. (2019)



Cell Type
Cycling cells
hypoxic-inflammatory response (HIR)
Neuronal Progenitor Like 1
Neuronal Progenitor Like 2
Non-Neuronal
Undifferentiated



Cell differentiation state of IRT003

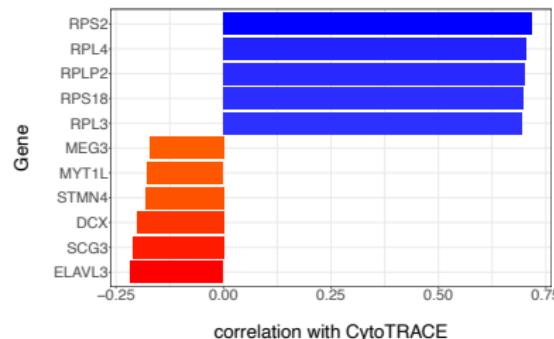
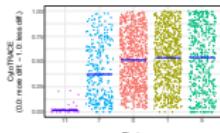
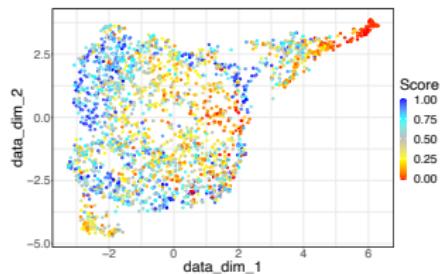
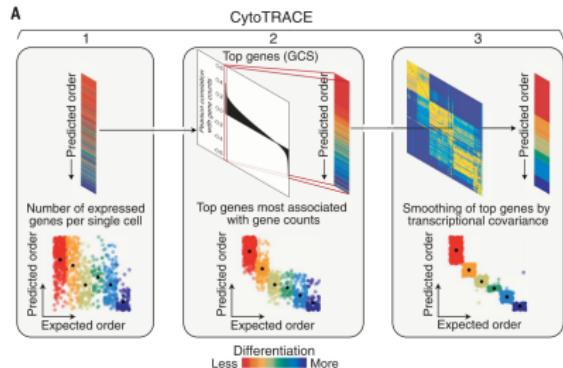
RESEARCH ARTICLE

RESEARCH METHODS

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Gulati et al. (2020)



CAL-ATRT from public data shows similar heterogeneity

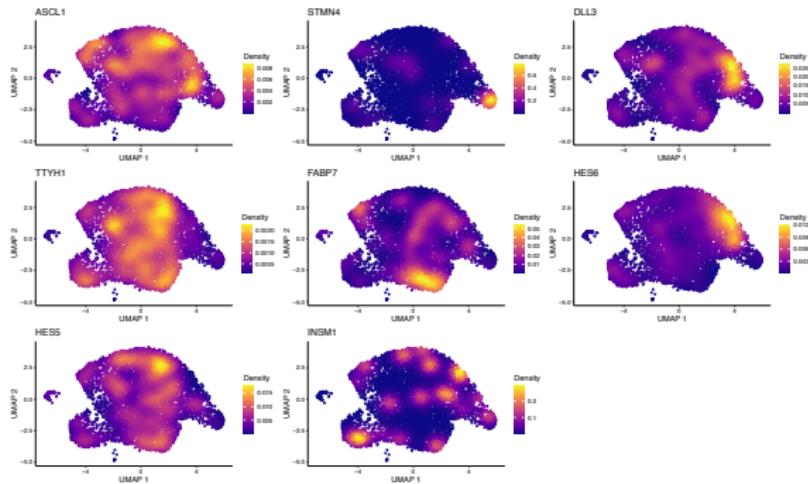
Stalled developmental programs at the root of pediatric brain tumors

Selin Jessa^{○1,2}, Alexis Blanchet-Cohen^{○1}, Brian Krug^{○1}, Maria Vladouli^{○1,5}, Marie Coutelier^{○1,3},
Damien Faury^{○4*}, Brice Poreau^{○1,6}, Nicolas Du Jay^{○1,7}, Steven Hebert^{○1}, Jean Monlong^{○1,8},
W. Todd Farmer^{○1,9}, Laura K. Donovan^{○1,6}, Yixing Hu^{○1,2}, Melissa K. McConechy^{○1}, Florence M. G. Cavalli^{○1,5},
Leonie G. Mikael^{○2}, Benjamin Eliezam^{○1,3}, Maxime Richer^{○1,3}, Andréa Allaire^{○1}, Alexander G. Well^{○1,10},
Jeffrey Atkinson^{○1}, Jean-Pierre Farmer^{○1}, Roy W. R. Dudley^{○1,6}, Valérie Larouche^{○1}, Louis Crevier^{○1,11},
Steffen Albrecht^{○1}, Mariella G. Fillin^{○1}, Hervé Saletot^{○1,7}, Pierre-Eric Lutz^{○1,12,13}, Corina Nagy^{○1,13},
Gustavo Turecki^{○1,2,13}, Santiago Costantino^{○1,14}, Peter B. Dirks^{○1,6,15}, Keith K. Mura^{○1,16},
Guillaume Bourque^{○1,6,17}, Jiamnis Ragoussis^{○1,18}, Livia Garzia^{○1,17}, Michael D. Taylor^{○1,8,19,20,21,22,23,24},
Nada Jabado^{○1,6,24} and Claudia L. Kleinman^{○1,24}

Jessa et al. (2019)

- ▶ ATRT sample from the CAL region
- ▶ single nuclei data

Expression of ATRT-SHH gene markers
(*Nebulosa R package*)



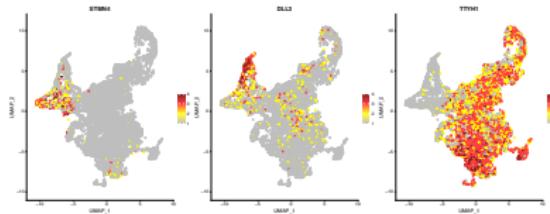
Transcriptional intratumoral heterogeneity of CAL-ATRT

integrated

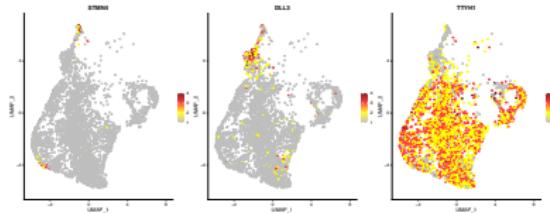
INI254

INI255

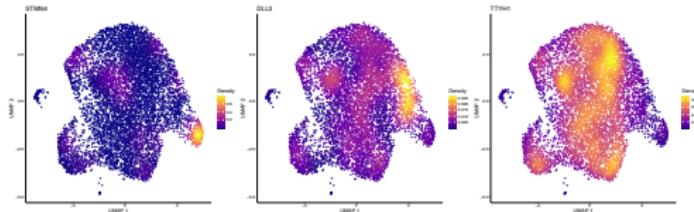
INI267



InnoRT003



ATRT5



Conclusion

- ▶ Transcriptional intratumoral heterogeneity of ATRT SHH/SHH CAL-ATRT
- ▶ Neuronal progenitors identified as putative cells of origin of CAL-ATRT
- ▶ Dedifferentiation process and NOTCH signaling may be involved in CAL-ATRT tumor development
- ▶ On-going validation with cell lines and mouse models

M.-J. Lobon-Iglesias, M. Andrianteranagna, Z.-Y. Han et al.
(submitted in Nature Communication)