

Metastatic Cancer Genomics

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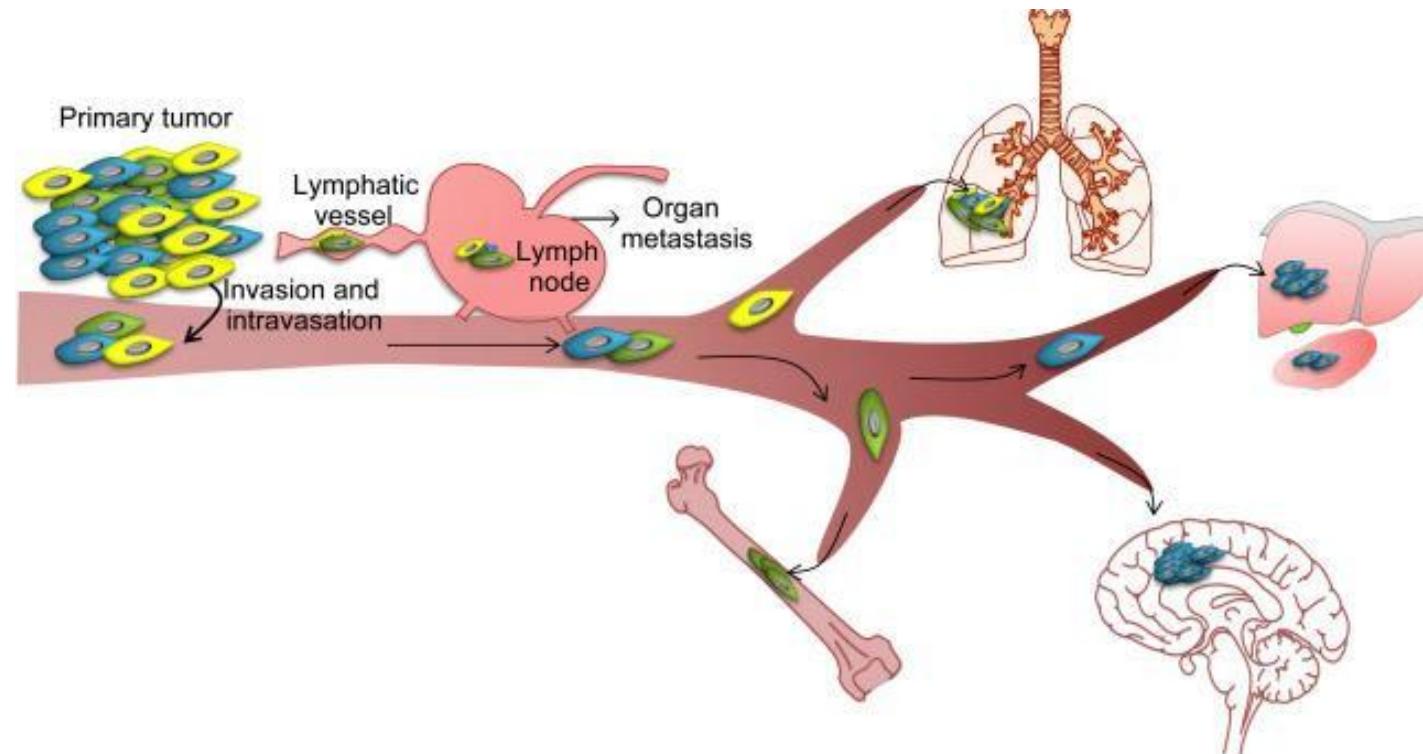
27/4/2025

Cancer metastasis

Primary tumor



Second organ



Zubair and Ahmad, Introduction to Cancer Metastasis, 2017

Seed and Soil Hypothesis

Lancet, 1889



Stephen Paget (1855-1926)



Primary tumor → Metastatic Site

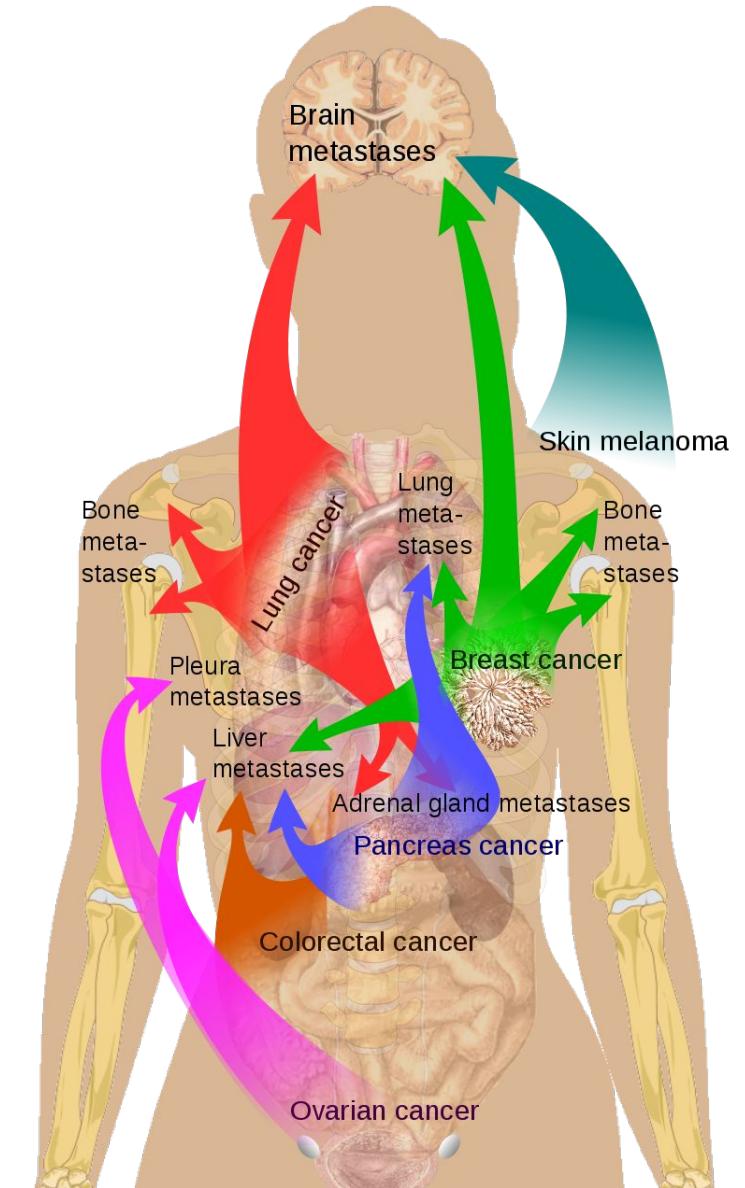
Random processes in metastasis



Primary tumor

progress

Random
metastasis

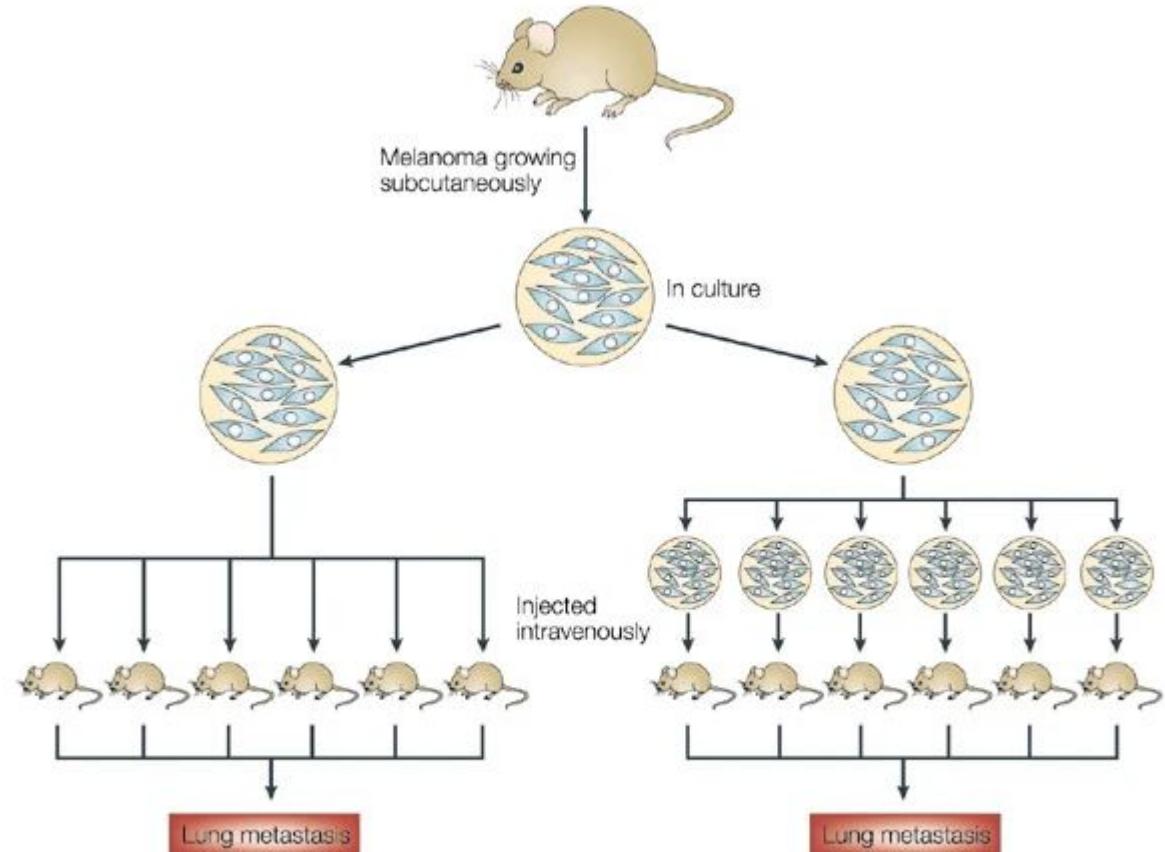


James Ewing (1866-1943)

Non-random processes in metastasis



Isaiah Fidler, MD Anderson



Nature Reviews | Cancer

Fidler, I. The pathogenesis of cancer metastasis: the 'seed and soil' hypothesis revisited. Nat Rev Cancer 3, 453–458 (2003). 10.1038/nrc1098

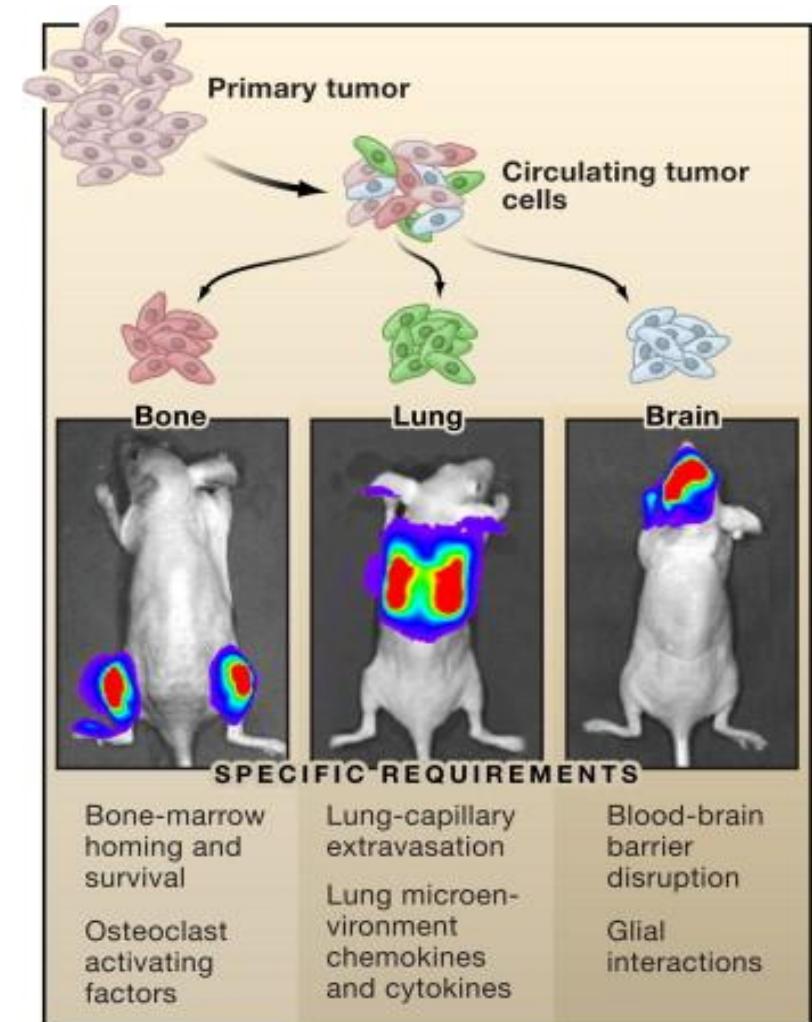
Non-random processes in metastasis



Primary tumor

Molecular signal
→

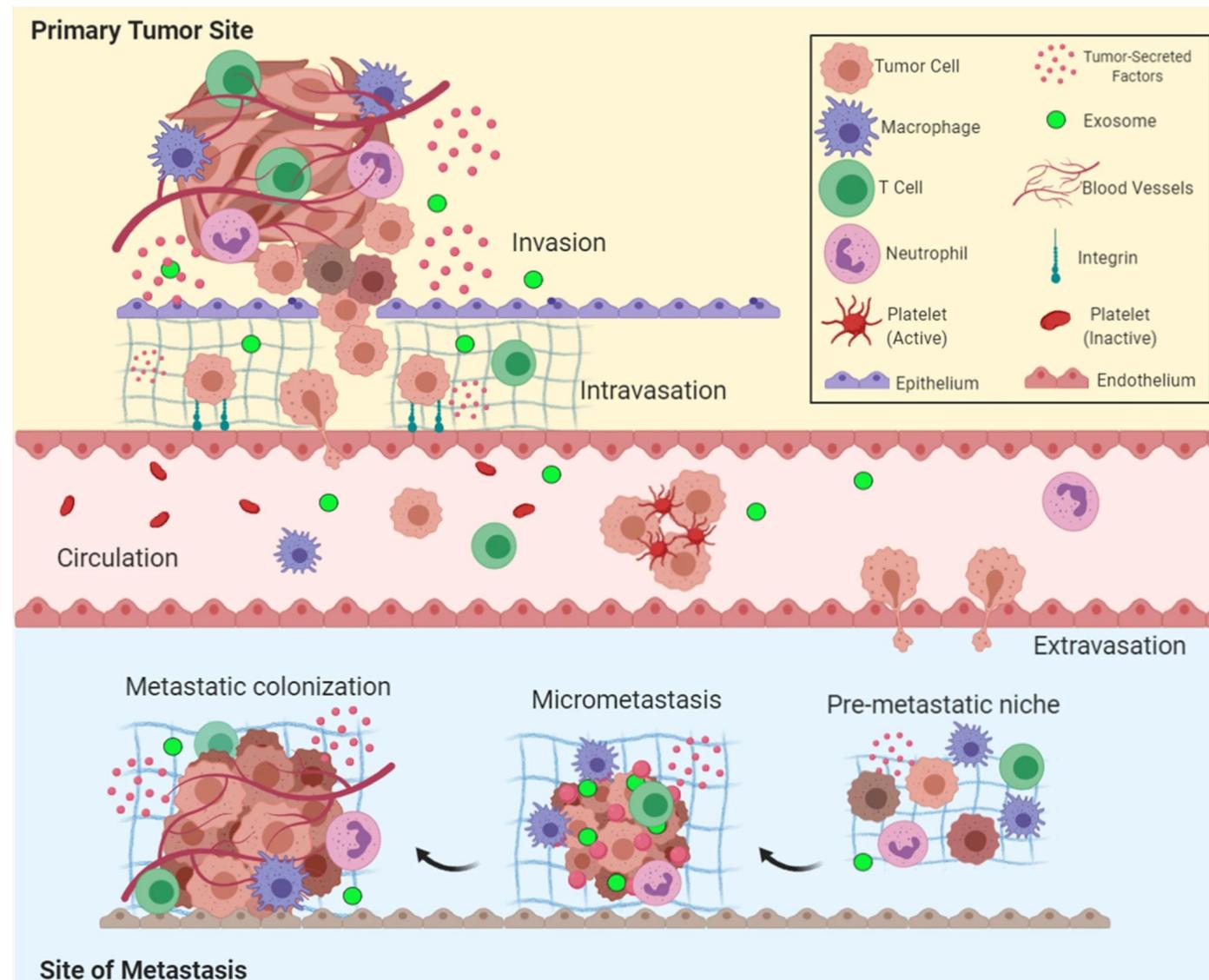
Tissue specific
metastasis



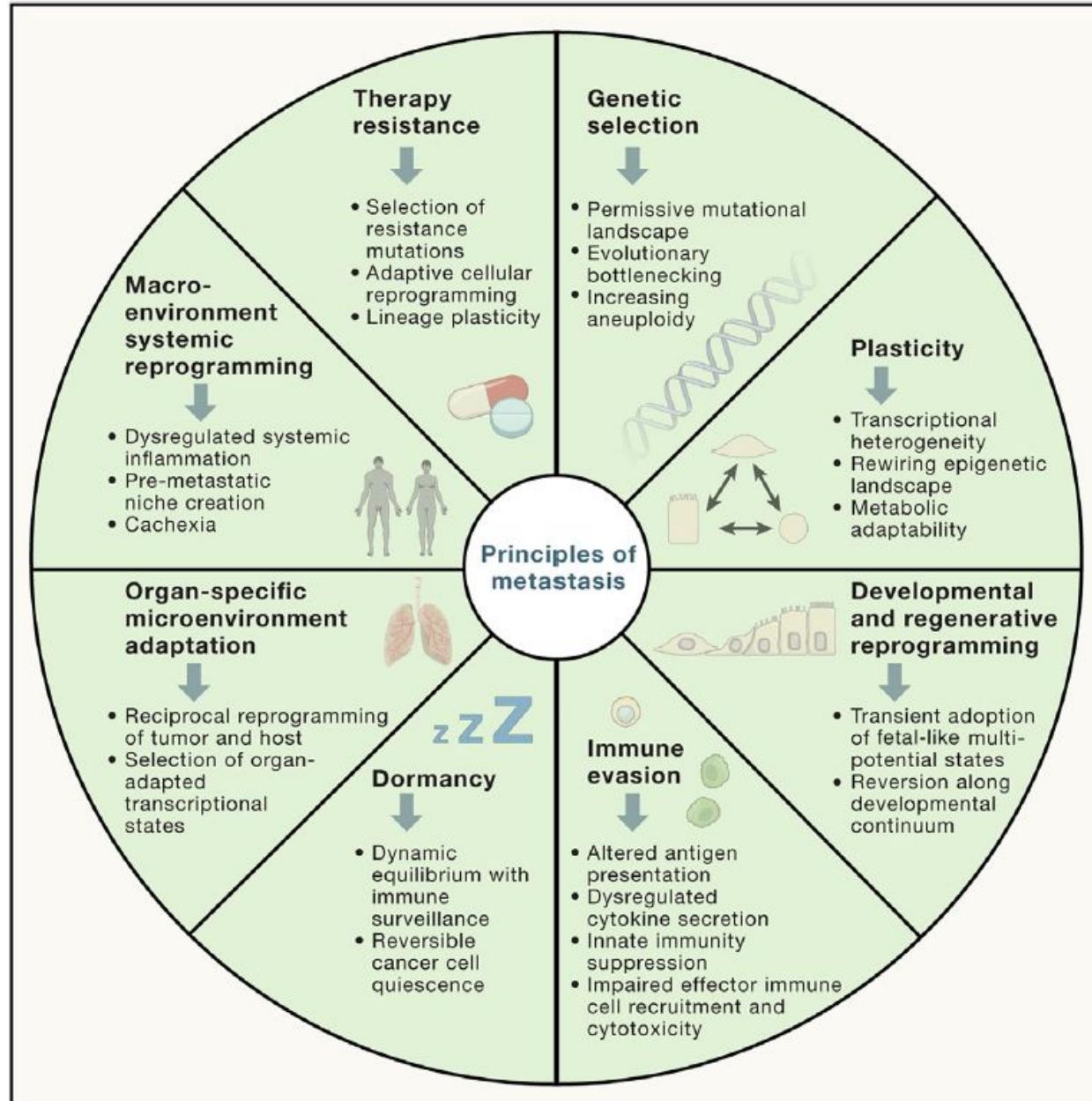
Joan Massague (MSKCC)

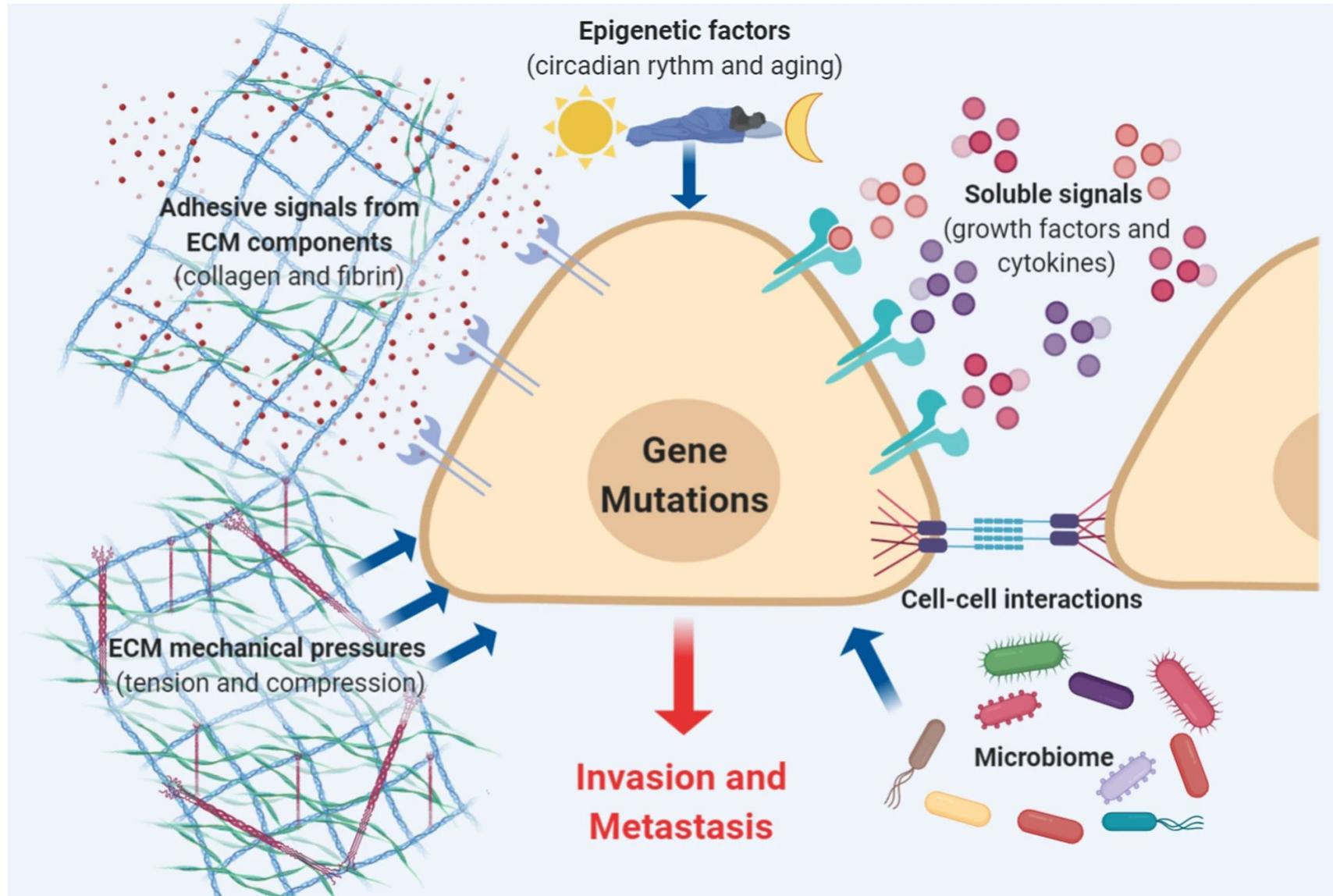
Gupta and Massague, 2006, Cell

The main steps in the formation of a metastasis

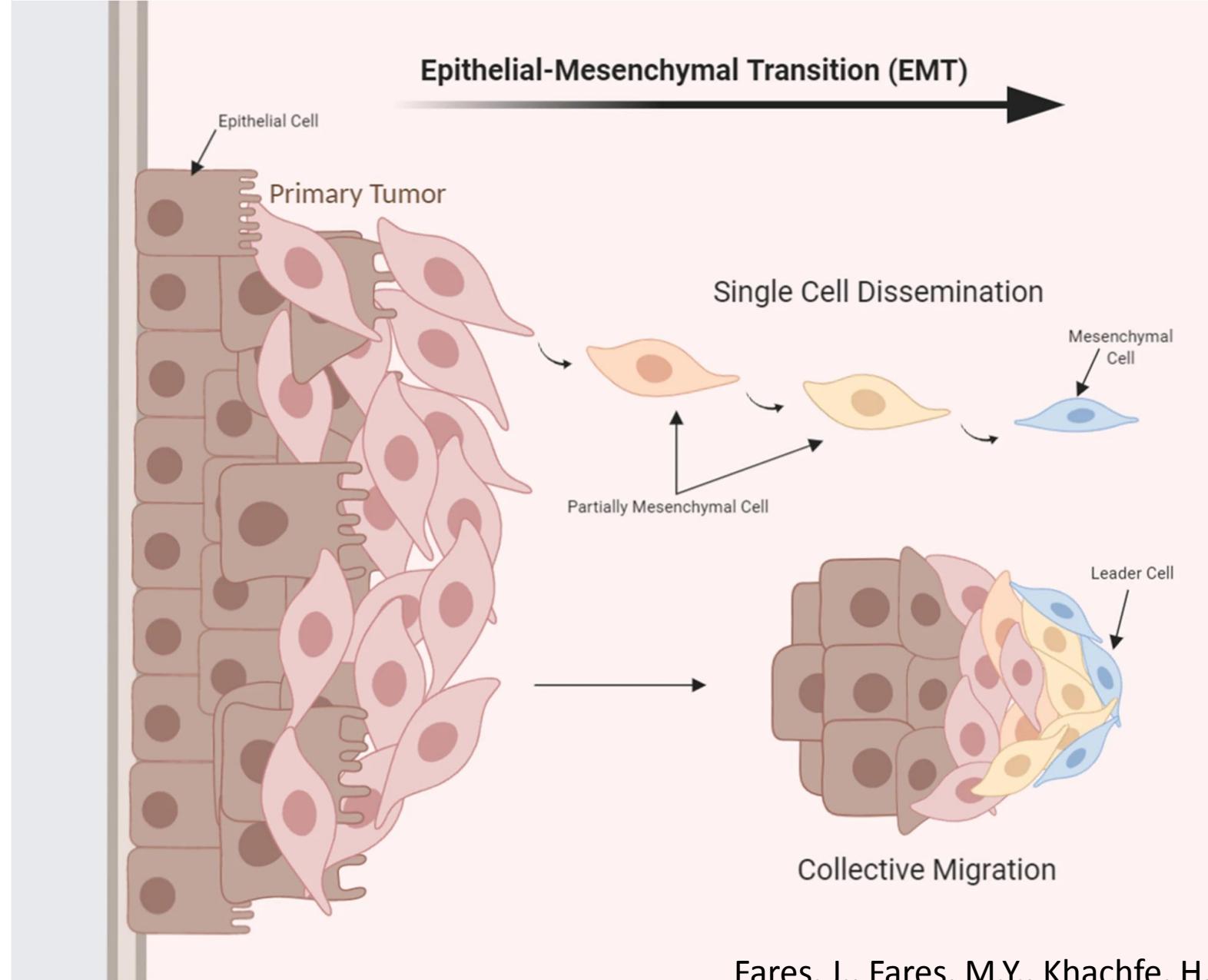


Fares, J., Fares, M.Y., Khachfe, H.H. et al. Molecular principles of metastasis: a hallmark of cancer revisited. *Sig Transduct Target Ther* 5, 28 (2020). 10.1038/s41392-020-0134-x



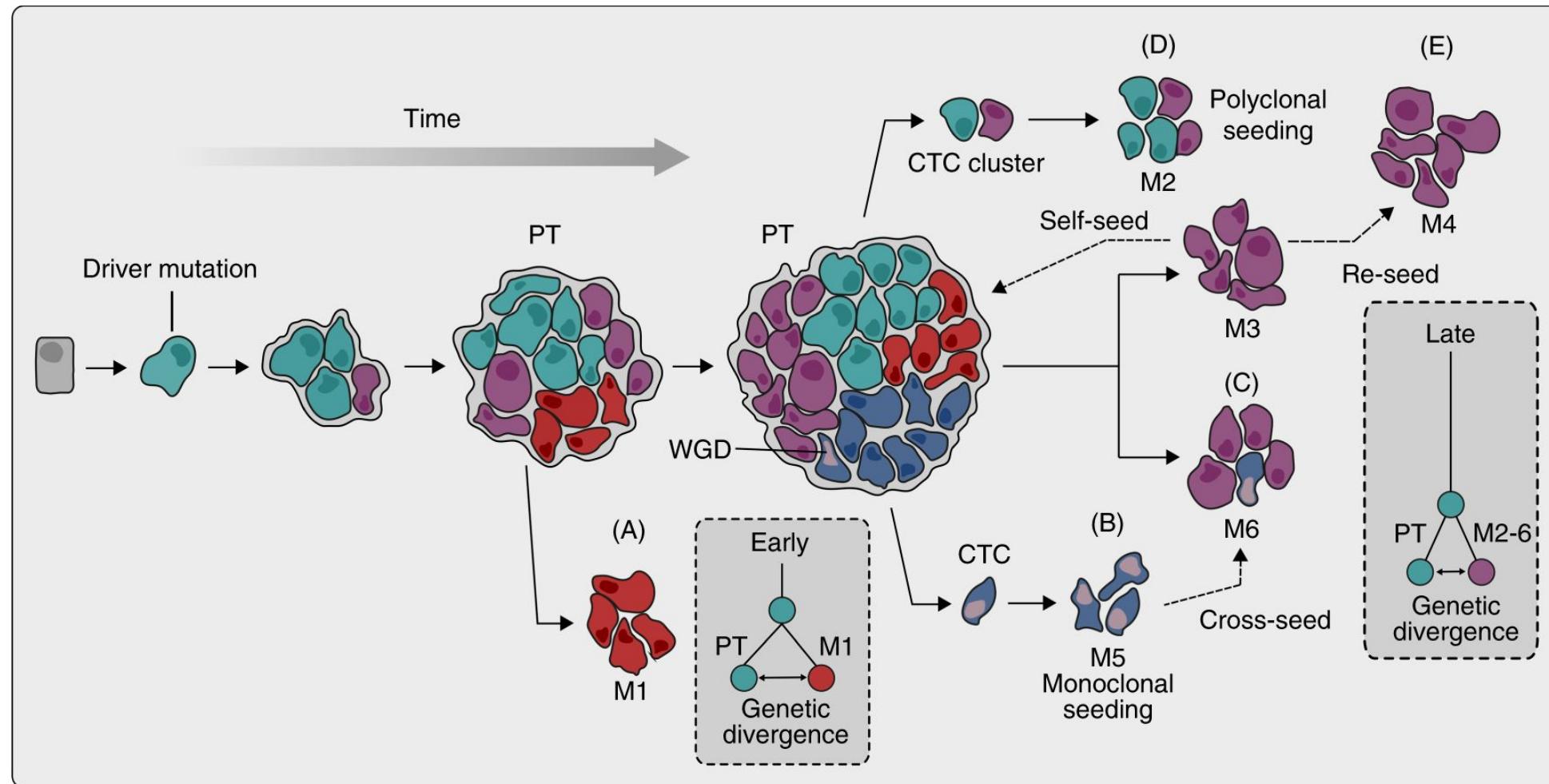


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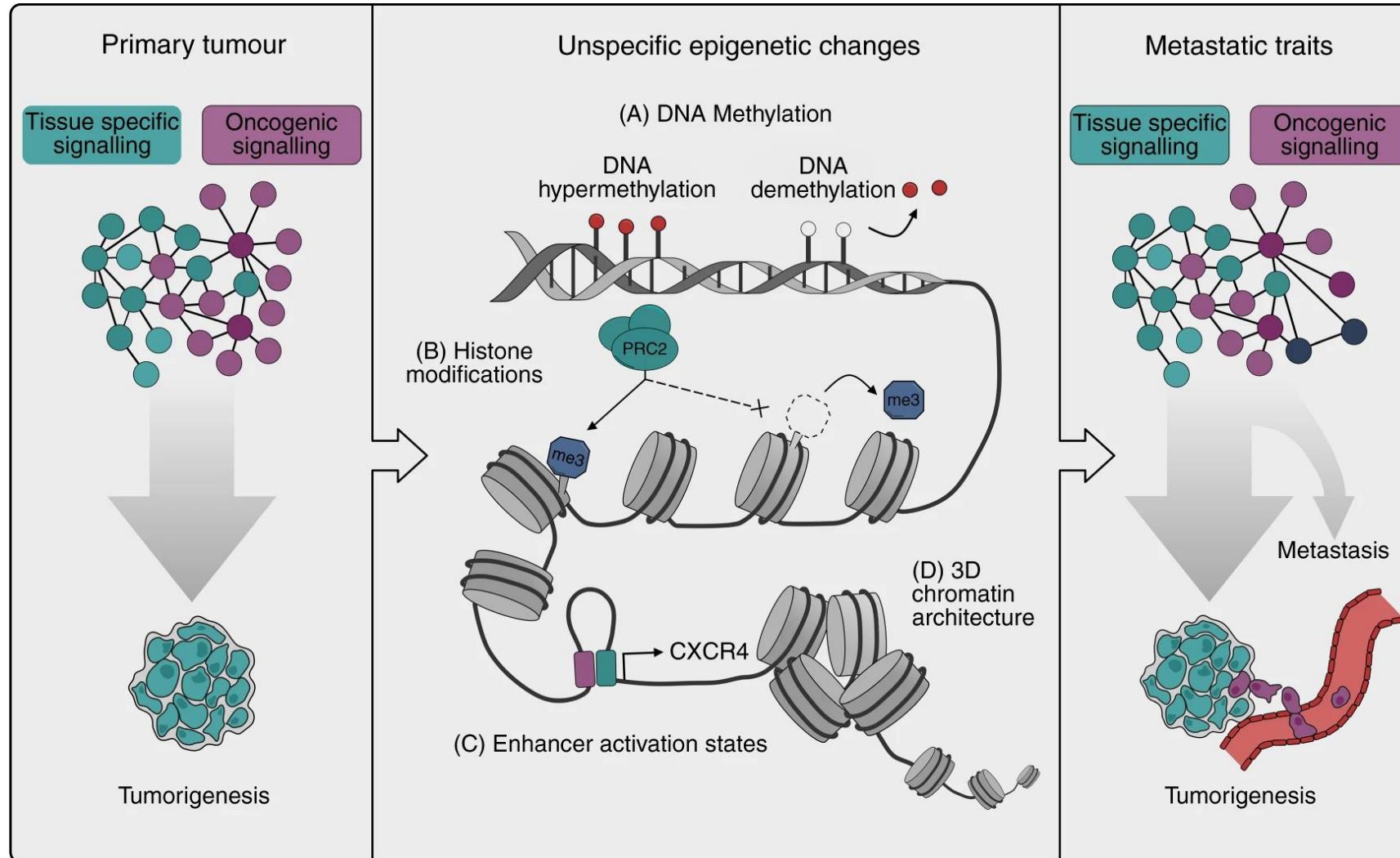
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Complex temporal patterns and trajectories of metastatic dissemination



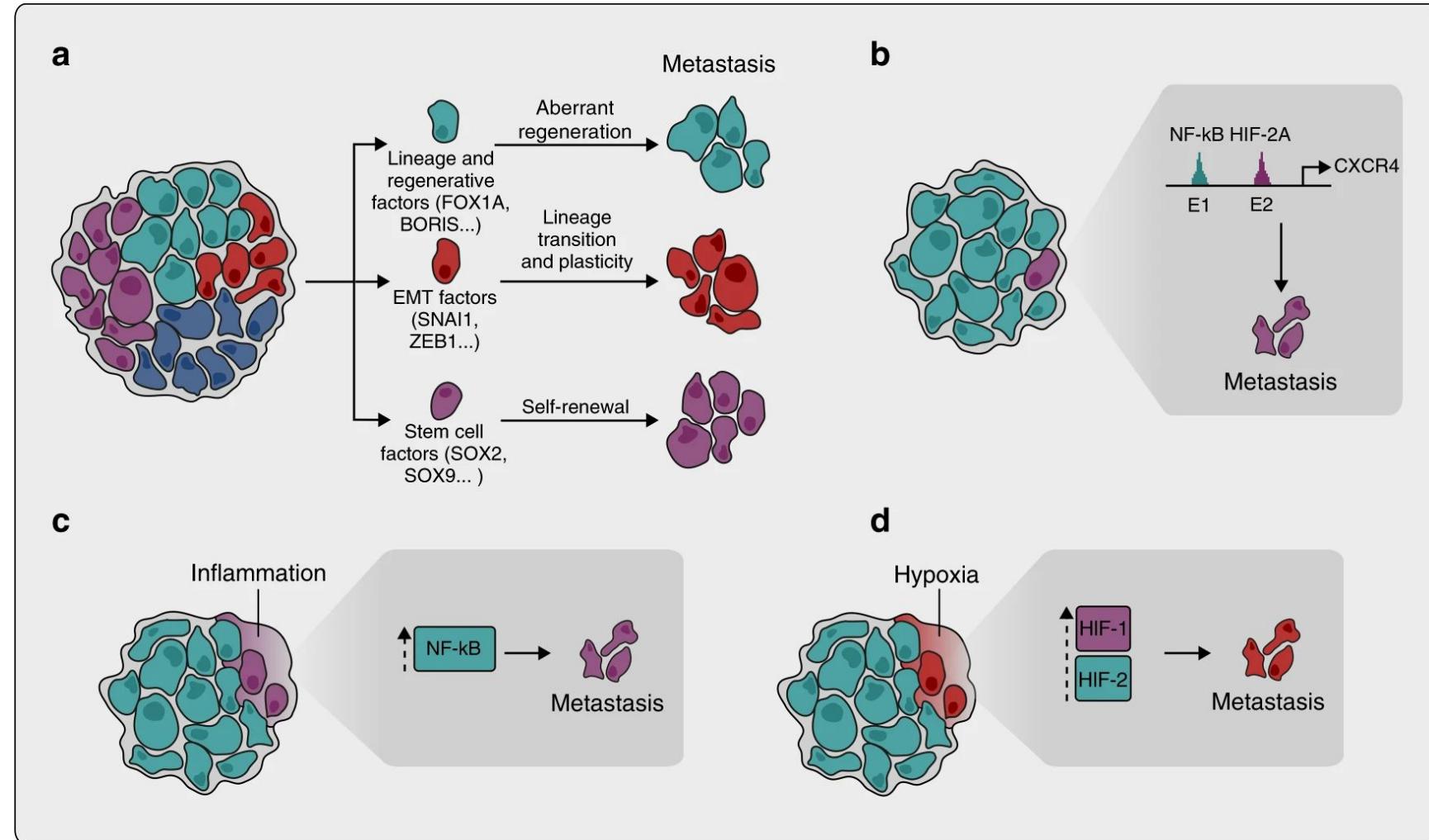
Patel, S.A., Rodrigues, P., Wesolowski, L. et al. Genomic control of metastasis. *Br J Cancer* 124, 3–12 (2021).
10.1038/s41416-020-01127-6

Epigenetic mechanisms alter oncogenic signalling in support of metastasis



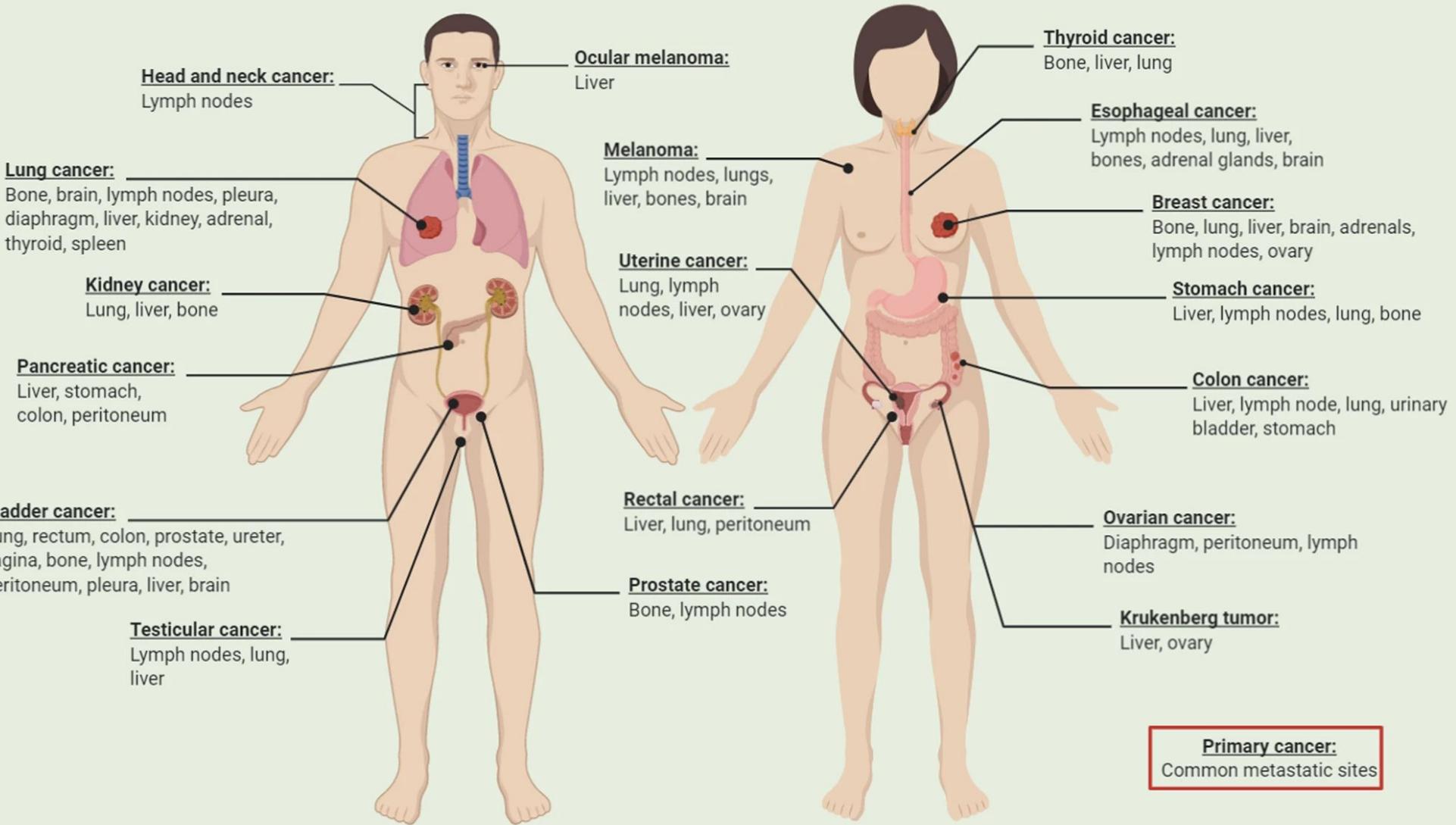
Patel, S.A., Rodrigues, P., Wesolowski, L. et al. Genomic control of metastasis. *Br J Cancer* 124, 3–12 (2021).
10.1038/s41416-020-01127-6

Metastatic transcriptional programmes.

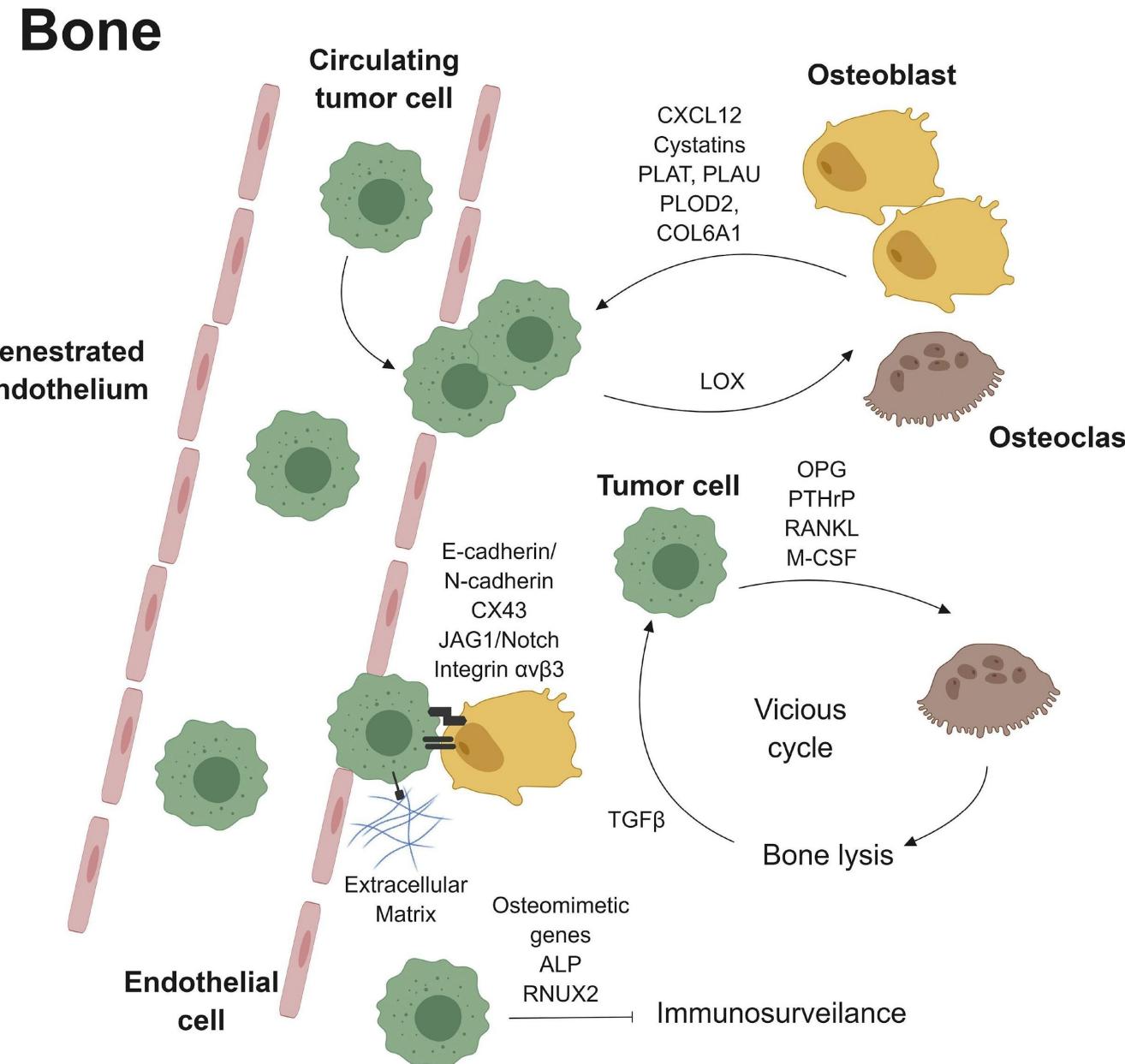


Patel, S.A., Rodrigues, P., Wesolowski, L. et al. Genomic control of metastasis. *Br J Cancer* 124, 3–12 (2021).
10.1038/s41416-020-01127-6

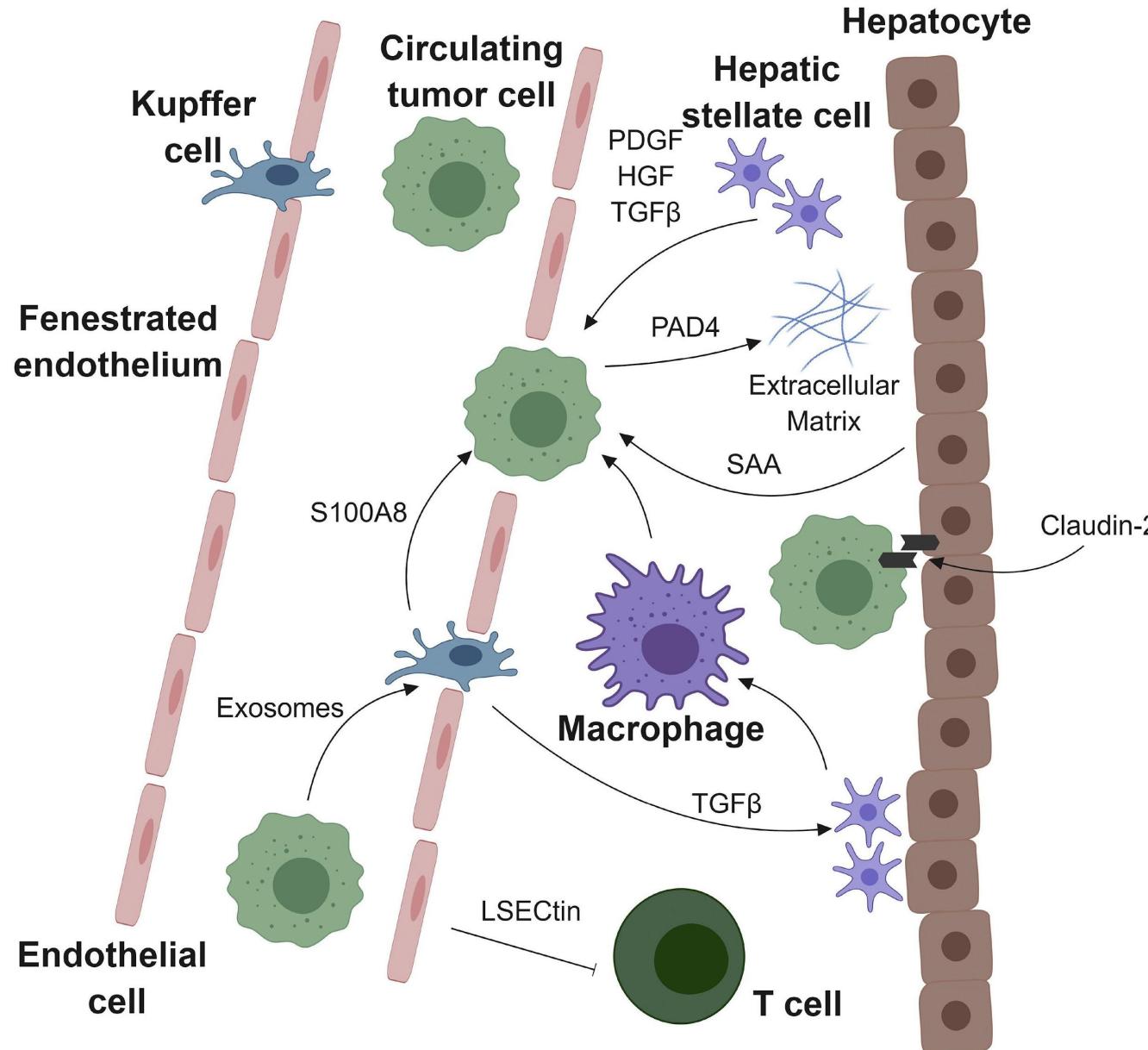
Metastatic Organotropism

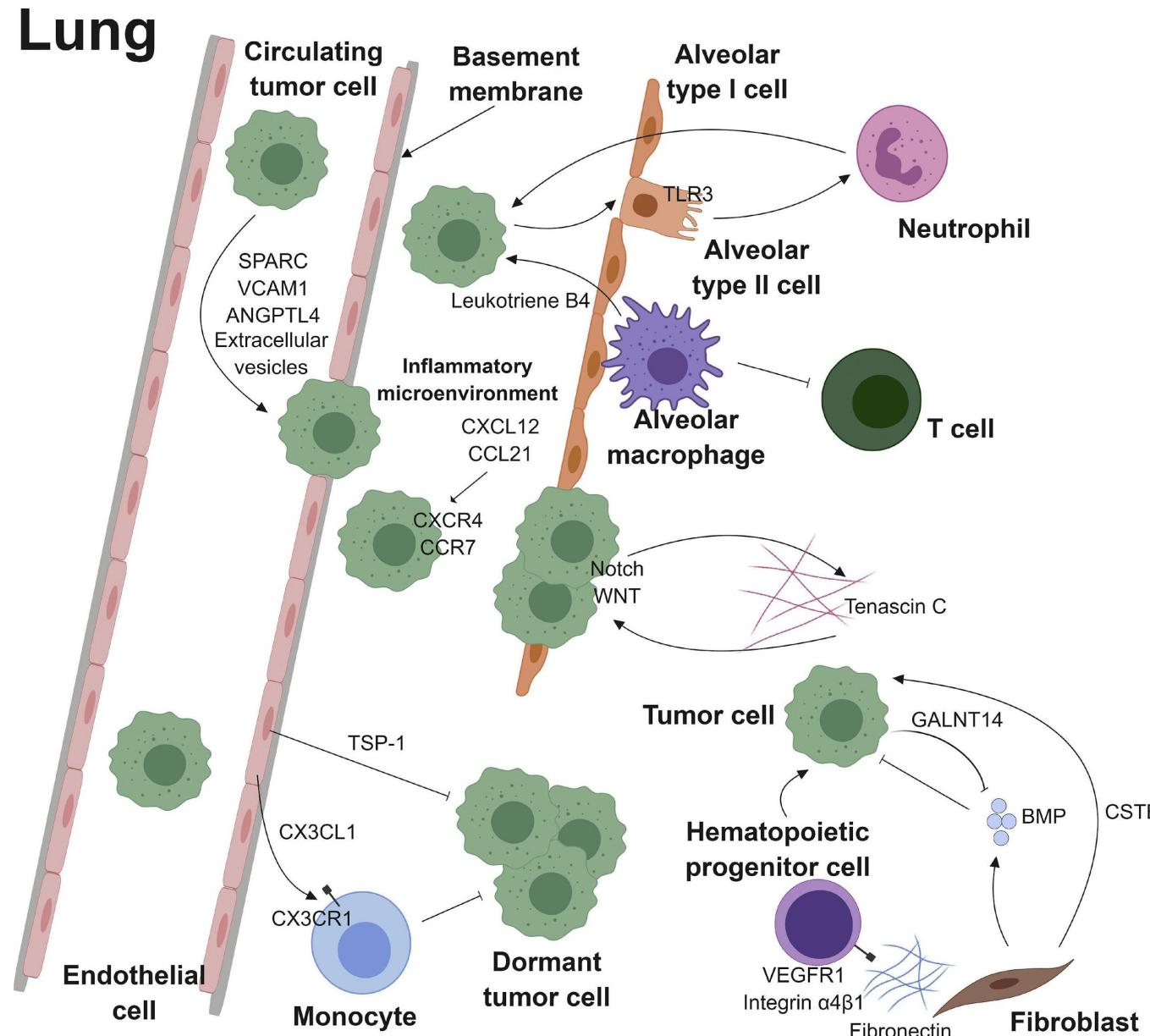


Fares, J., Fares, M.Y., Khachfe, H.H. et al. Molecular principles of metastasis: a hallmark of cancer revisited. Sig Transduct Target Ther 5, 28 (2020). 10.1038/s41392-020-0134-x

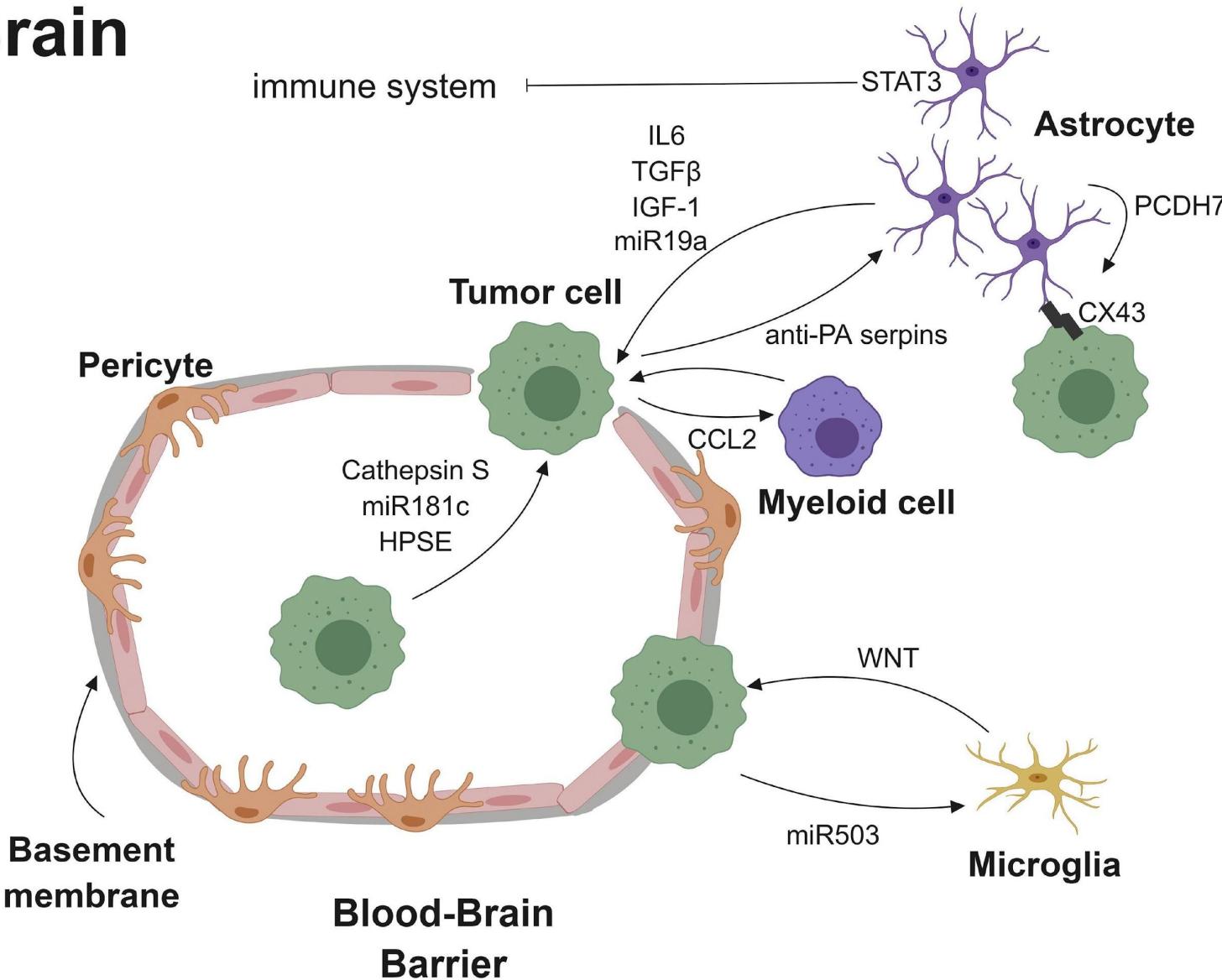


Liver

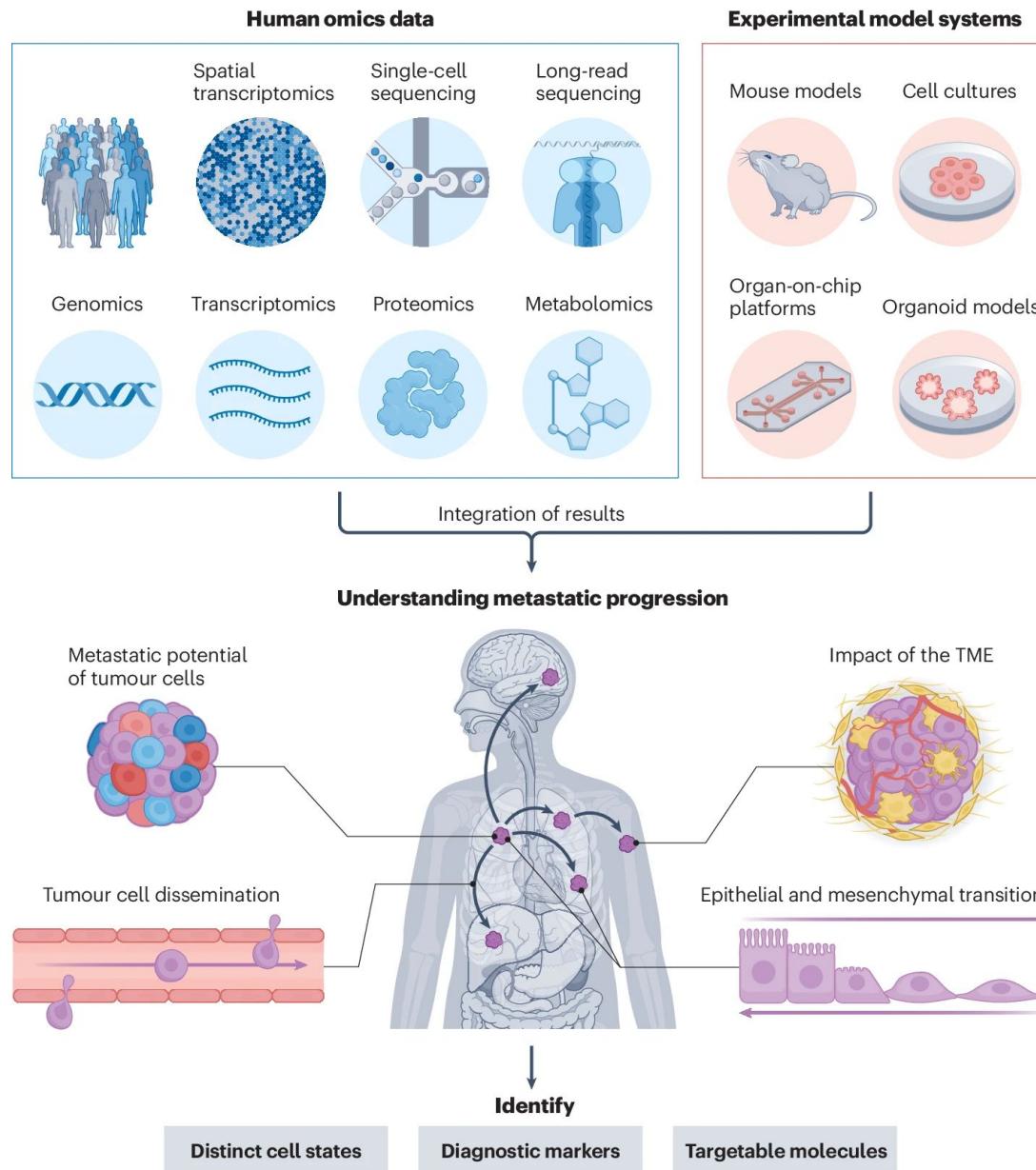




Brain



Overview of the synergism between omics analyses and experimental models in metastasis research.

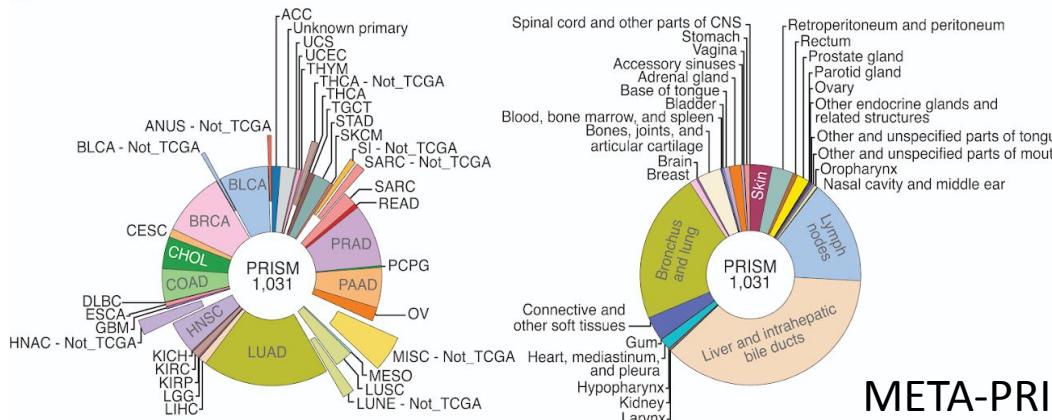


Leung, M.M., Swanton, C. & McGranahan, N. Integrating model systems and genomic insights to decipher mechanisms of cancer metastasis. *Nat Rev Genet* (2025).
10.1038/s41576-025-00825-2

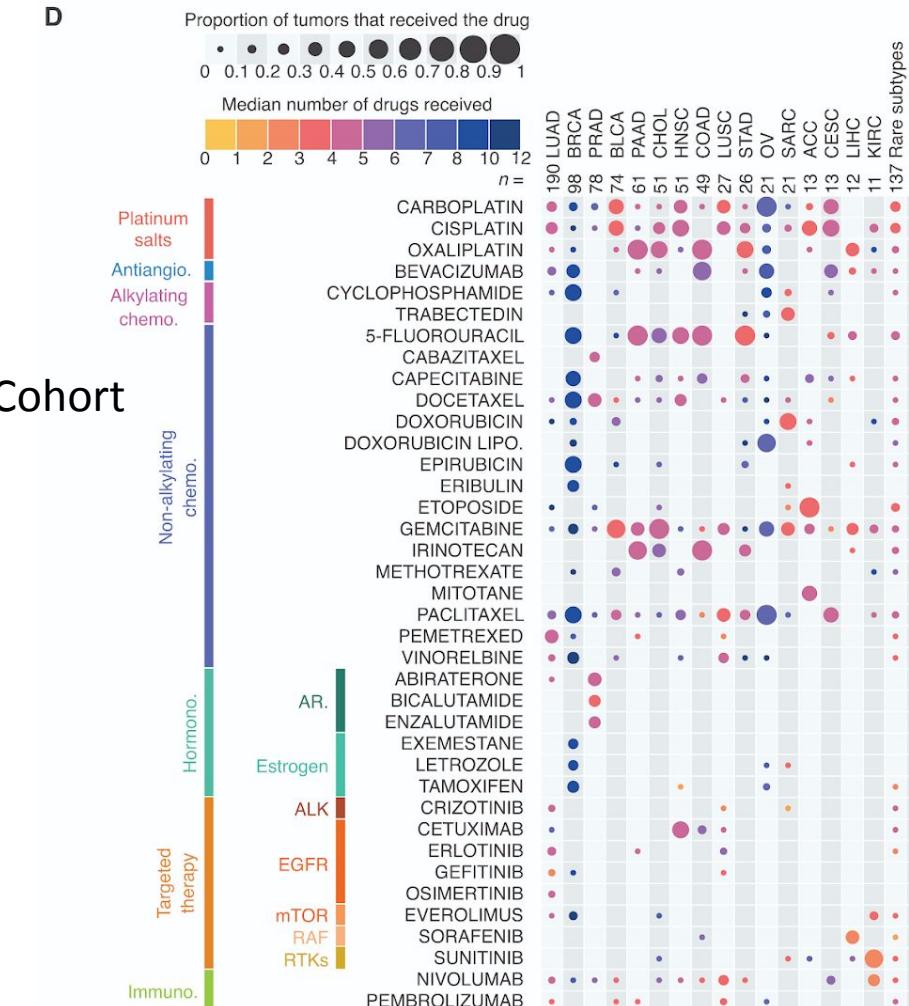
Integrative Pan-Cancer Genomic and Transcriptomic Analyses of Refractory Metastatic Cancer

Yoann Pradat ; Julien Viot ; Andrey A. Yurchenko ; Konstantin Gunbin ; Luigi Cerbone ; Marc Deloger ;
Guillaume Grisay ; Loic Verlingue ; Véronique Scott ; Ismael Padoleau ; Leonardo Panunzi ; Stefan Michiels ;
Antoine Hollebecque ; Gérôme Jules-Clément ; Laura Mezquita ; Antoine Lainé ; Yohann Loriot ; Benjamin Besse ;
Luc Friboulet ; Fabrice André ; Paul-Henry Cournède ; Daniel Gautheret ; Sergey I. Nikolaev

A

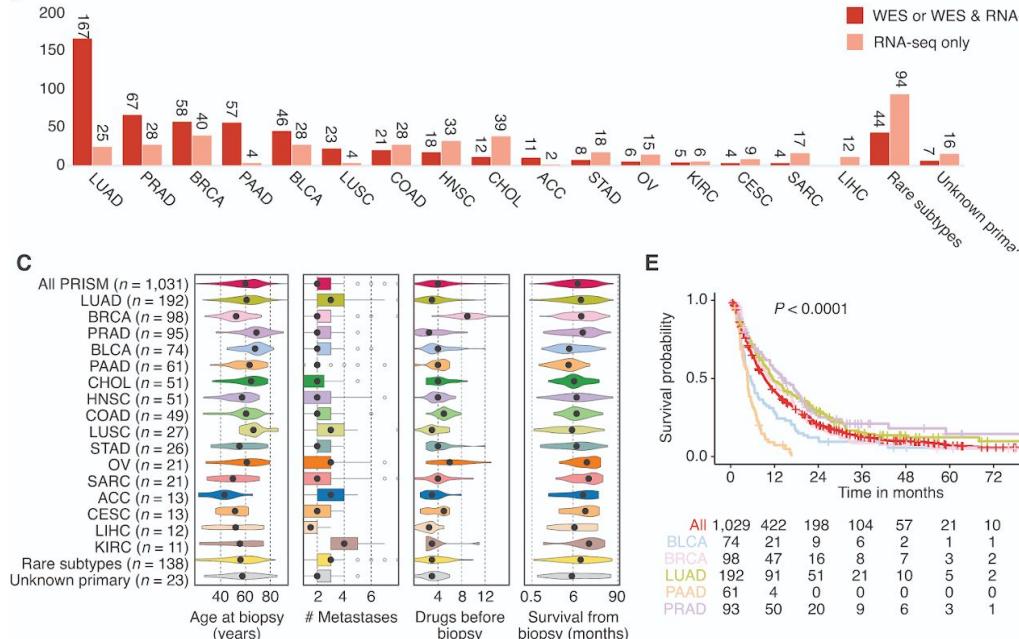


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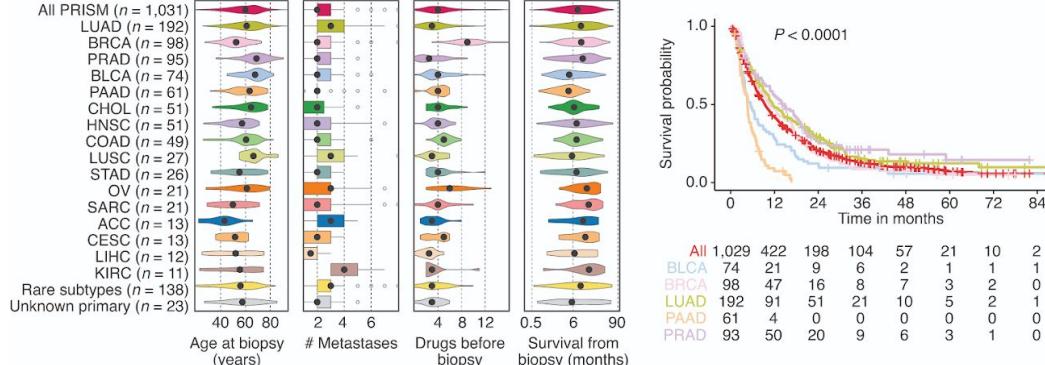


META-PRISM Cohort

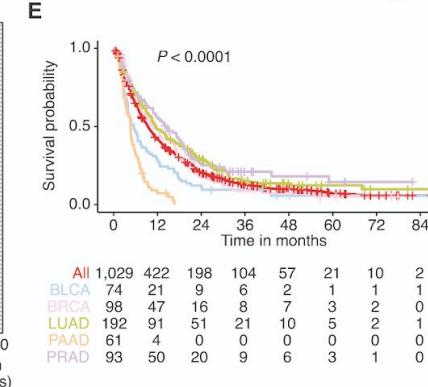
B



C

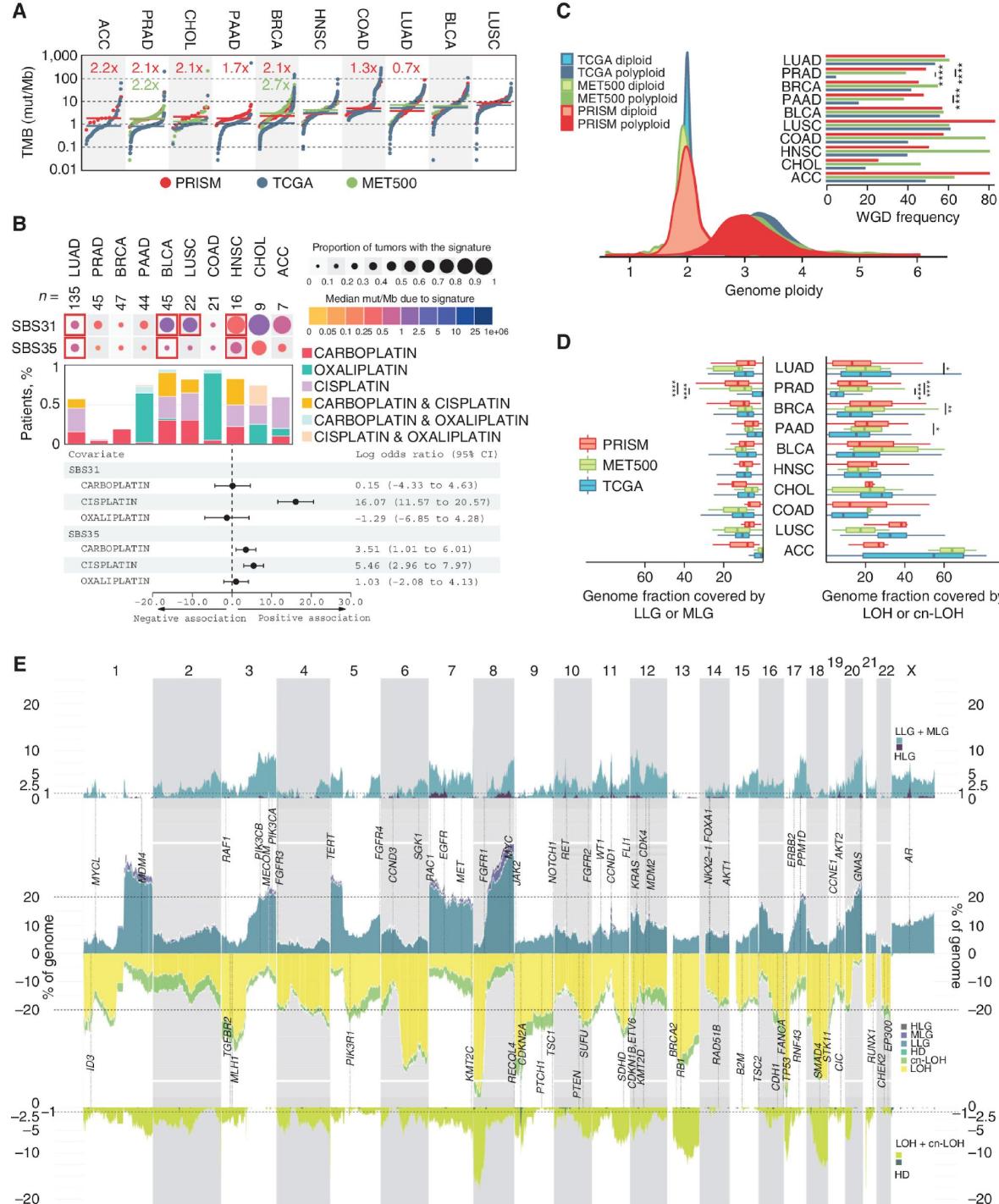


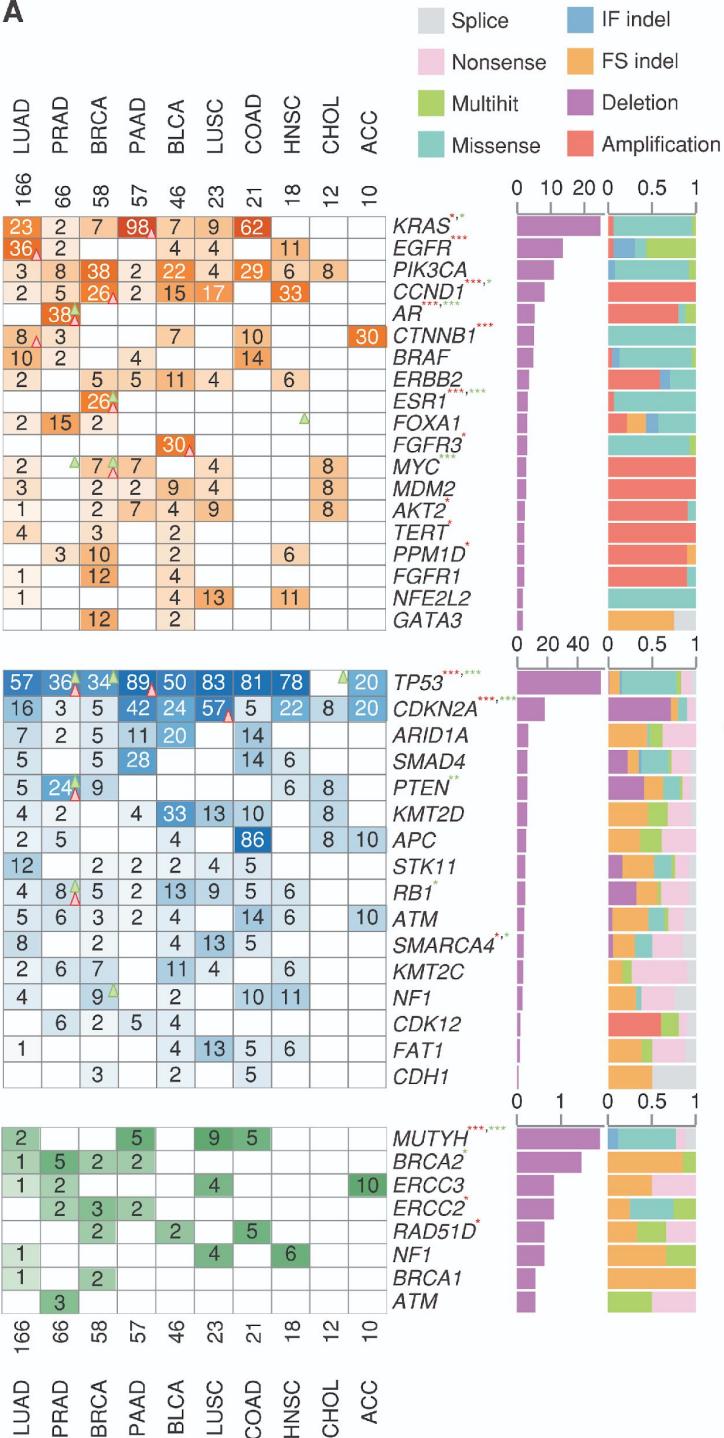
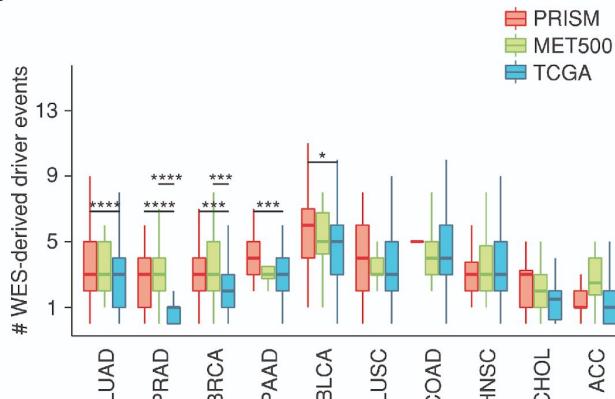
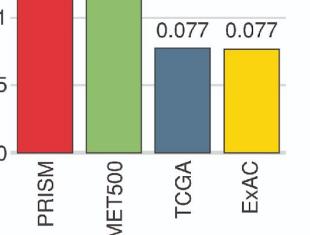
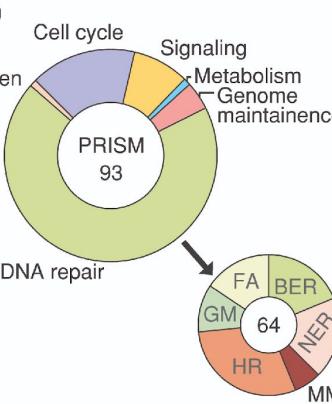
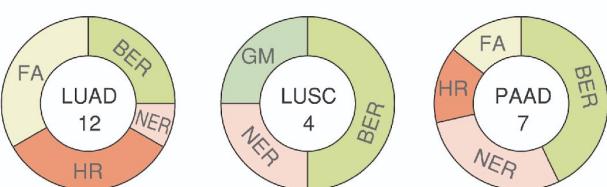
E



Cancer Discov (2023) 13 (5): 1116–1143.

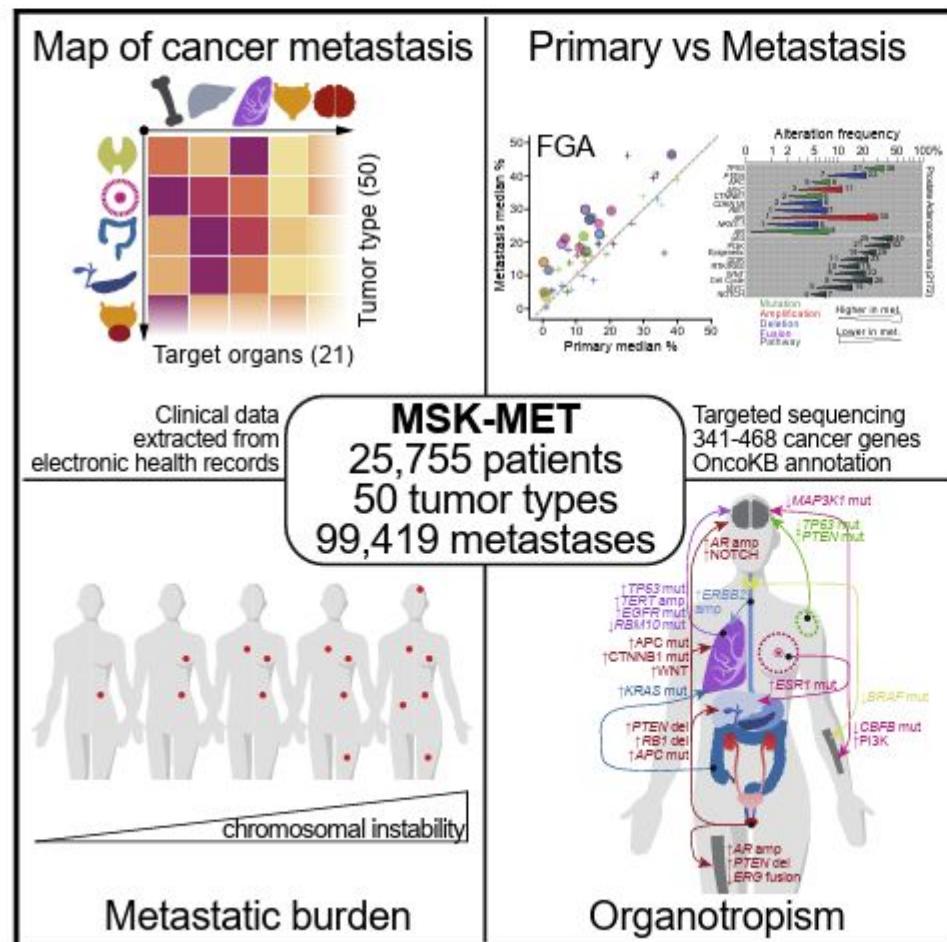
<https://doi.org/10.1158/2159-8290.CD-22-0966>



A**B****C****D****E**

Genomic characterization of metastatic patterns from prospective clinical sequencing of 25,000 patients

Graphical abstract



Authors

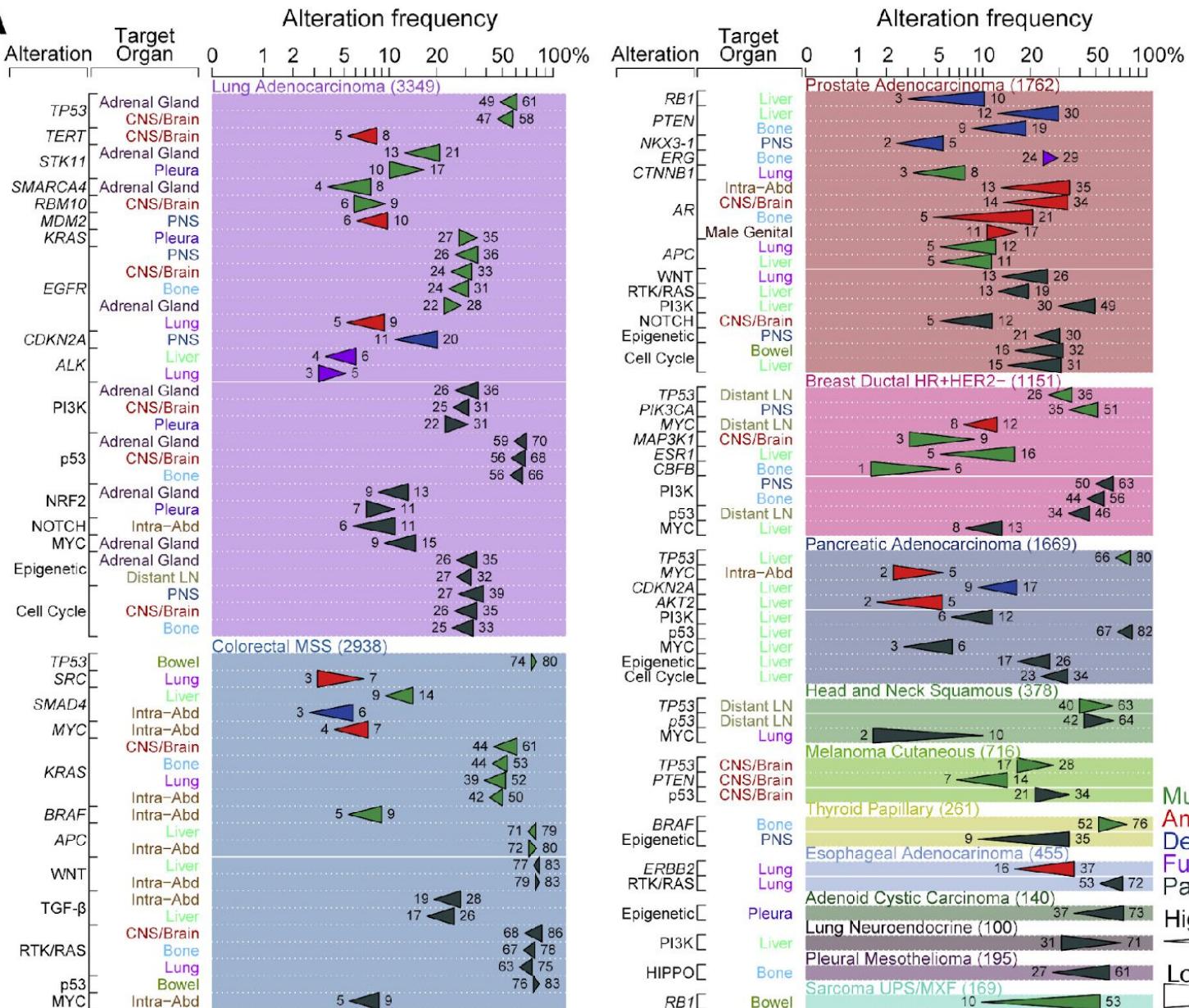
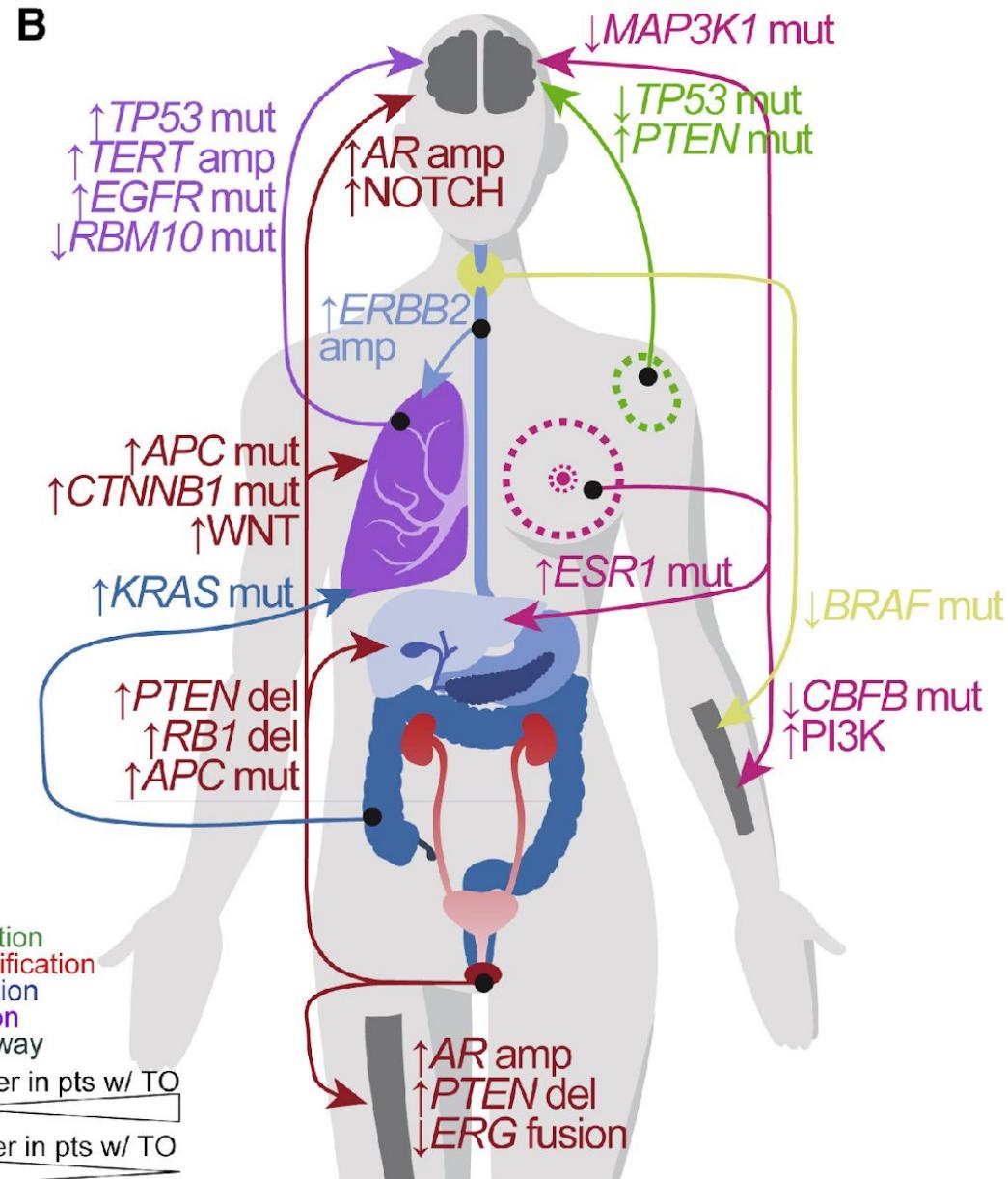
Bastien Nguyen, Christopher Fong,
Anisha Luthra, ..., Samuel F. Bakhoun,
Francisco Sanchez-Vega,
Nikolaus Schultz

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In brief

Clinico-genomic analysis of MSK-MET, a cohort of over 25,000 patients with metastasis across 50 cancer types, identifies somatic alterations associated with organ-specific metastasis and highlights that chromosomal instability correlates with metastatic burden in a cancer type-dependent manner.

A**B**

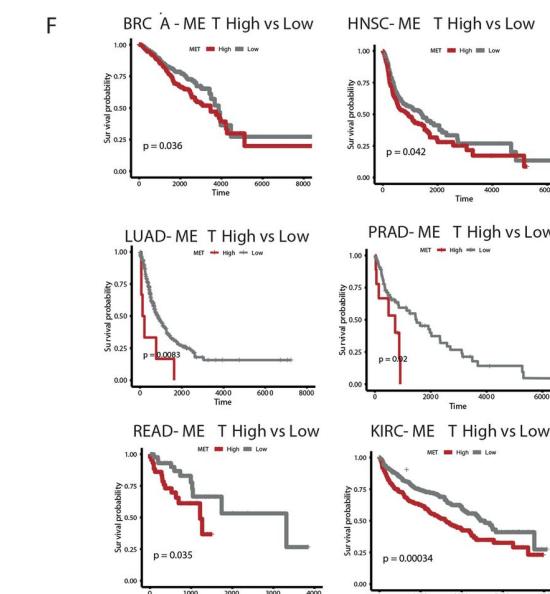
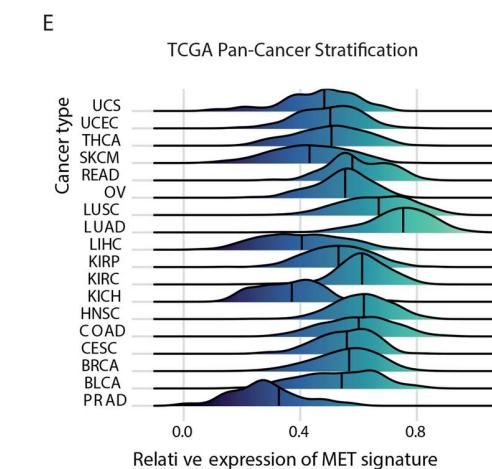
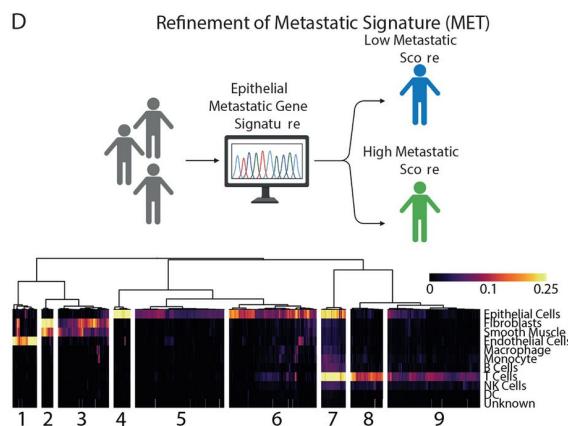
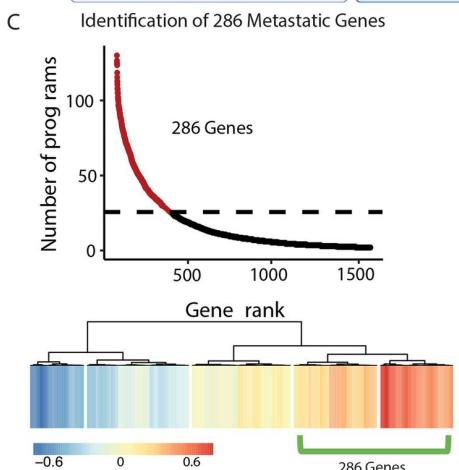
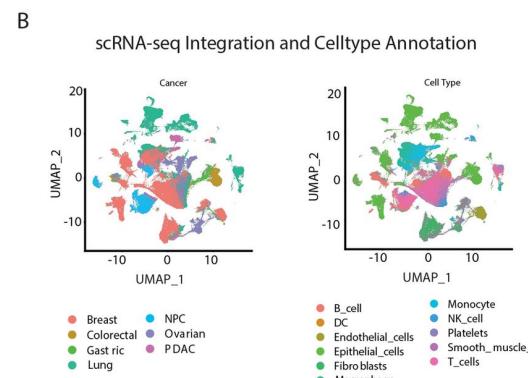
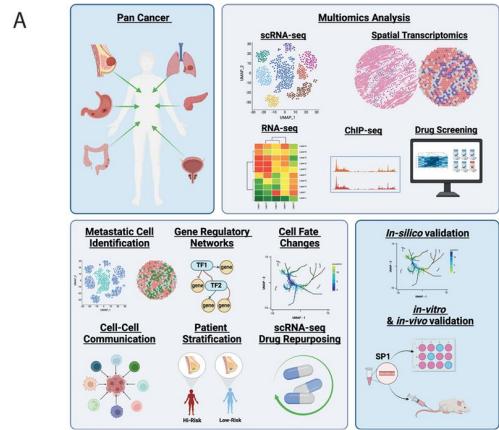
RESEARCH

Open Access



Pan-cancer drivers of metastasis

Ryan Lusby¹, Engin Demirdizen^{2†}, Mohammed Inayatullah^{2†}, Paramita Kundu^{3,4}, Oscar Maiques^{3,4}, Ziyi Zhang¹, Mikkel Green Terp², Victoria Sanz-Moreno^{3,4} and Vijay K. Tiwari^{1,2,5,6,7*}



Lusby, R., Demirdizen, E., Inayatullah, M. et al.
Pan-cancer drivers of metastasis. Mol Cancer 24, 2 (2025).
10.1186/s12943-024-02182-w

Genomic landscape of metastatic breast cancer identifies preferentially dysregulated pathways and targets

Matt R. Paul, ... , Angela DeMichele, Lewis A. Chodosh

