



IX SIMPOSIO · SYMPOSIUM | 2024

BIOPSIA LÍQUIDA · LIQUID BIOPSY

EL CAMINO A LA ONCOLOGÍA DE PRECISIÓN · THE WAY TO PRECISION MEDICINE

25, 26 Y 27 DE ENERO · JANUARY 25th, 26th and 27th

Unveiling the epigenomic program of CTCs in advanced colorectal cancer: Implications for precision medicine

Angel Díaz-Lagares, PhD

Epigenomics Unit
Translational Medical Oncology Group (ONCOMET)
Instituto de Investigación Sanitaria de Santiago (IDIS)
Hospital Clínico Universitario de Santiago (CHUS)
Santiago de Compostela, Spain

angel.diaz.lagares@sergas.es

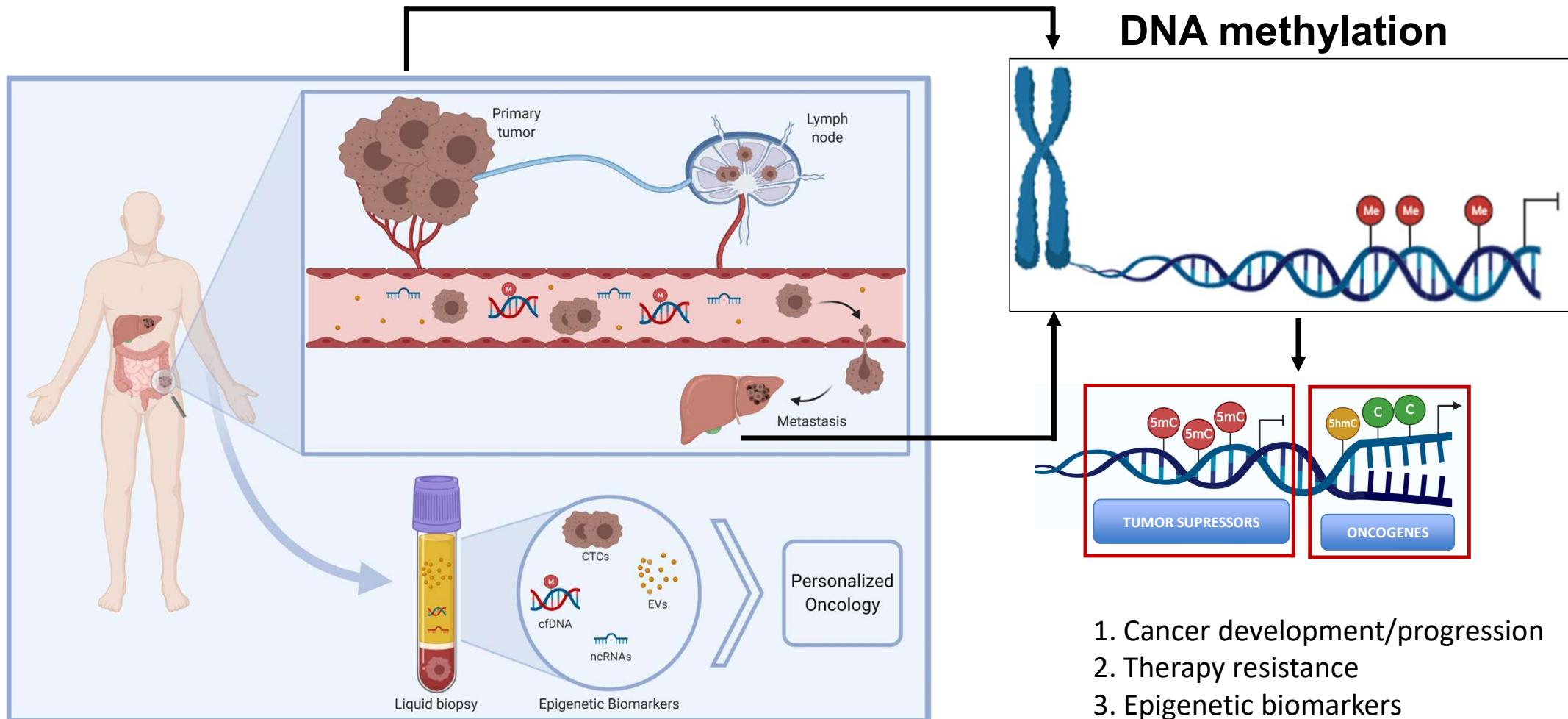
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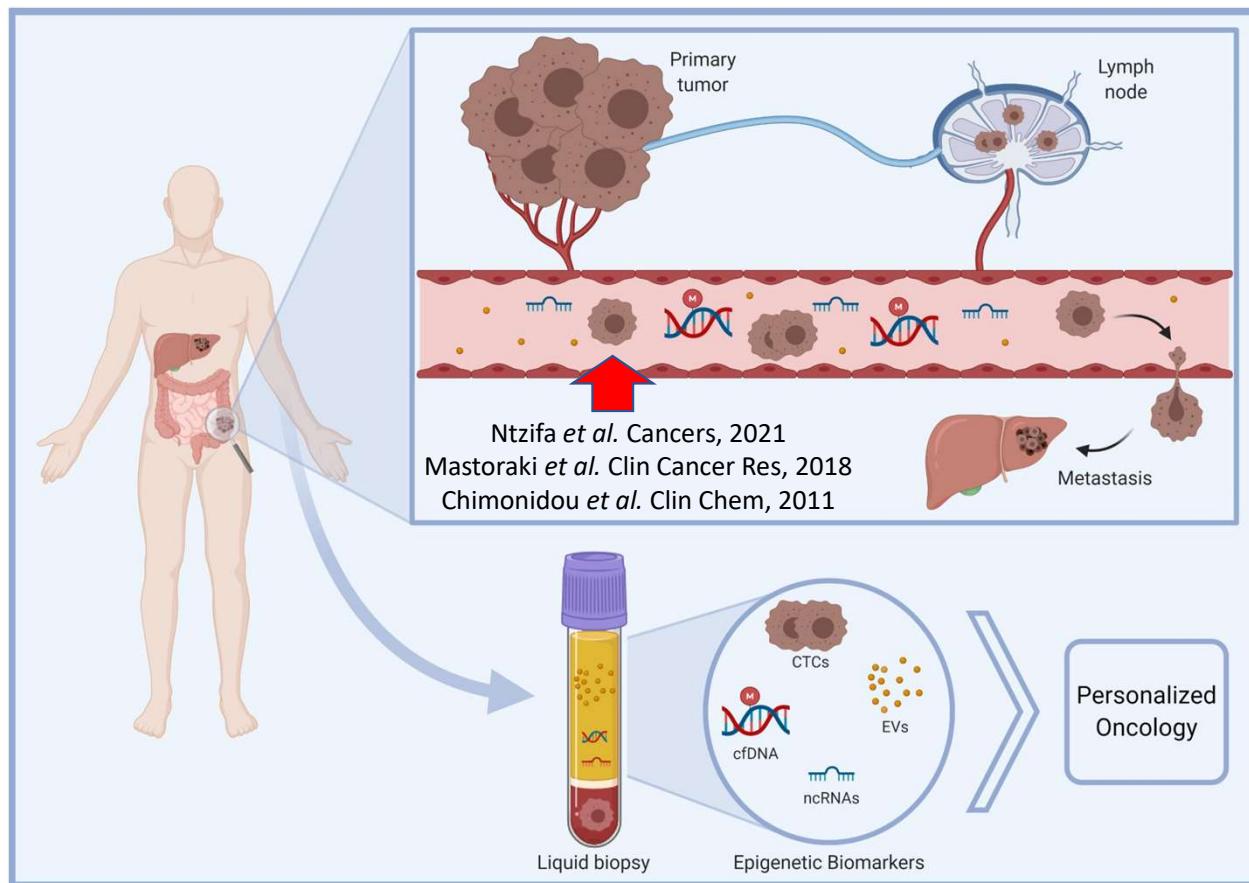


Introduction: CTCs and DNA methylation



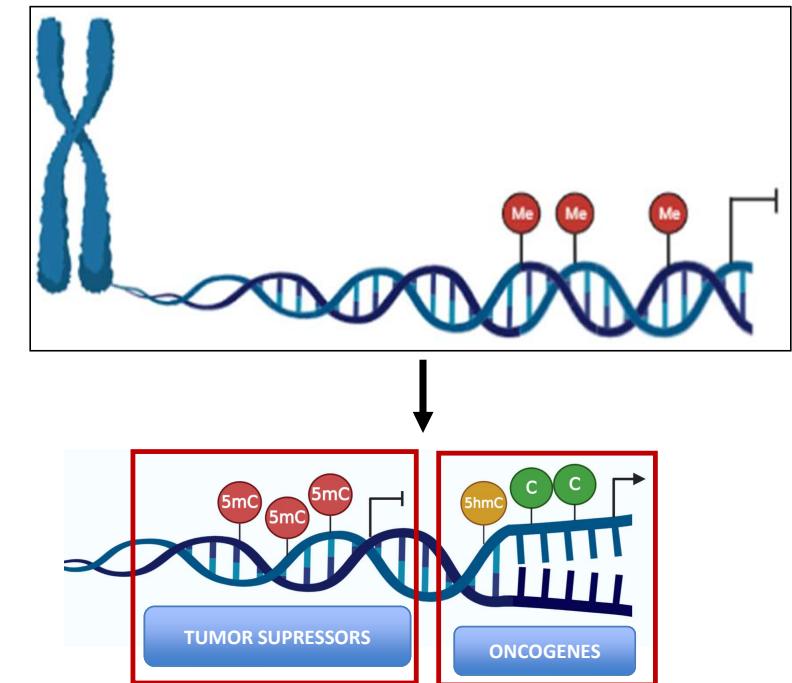
Rodriguez-Casanova A *et al.* Cancer Metastasis Through the Lymphovascular System, 2022 (adapted)

Introduction: CTCs and DNA methylation



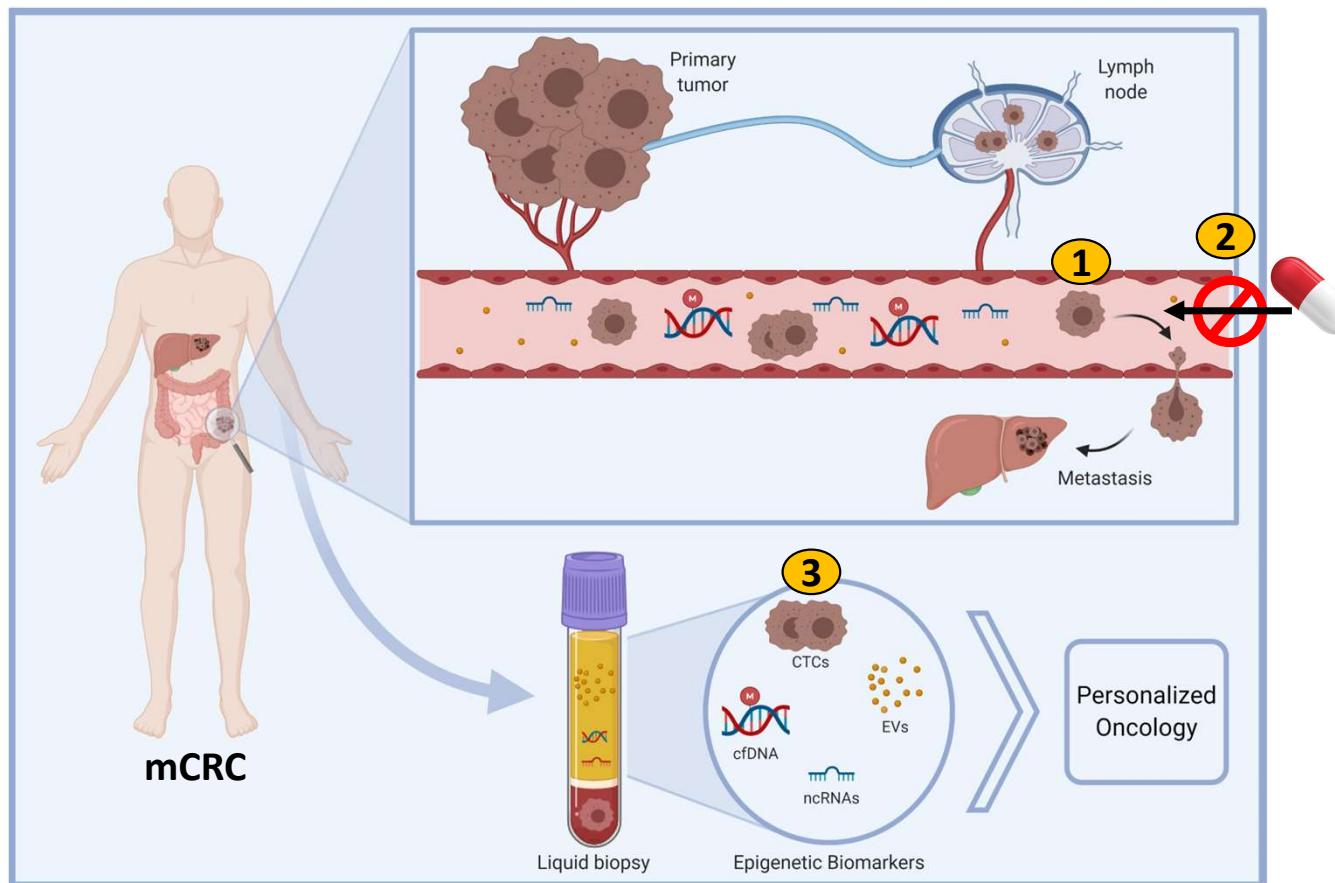
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DNA methylation

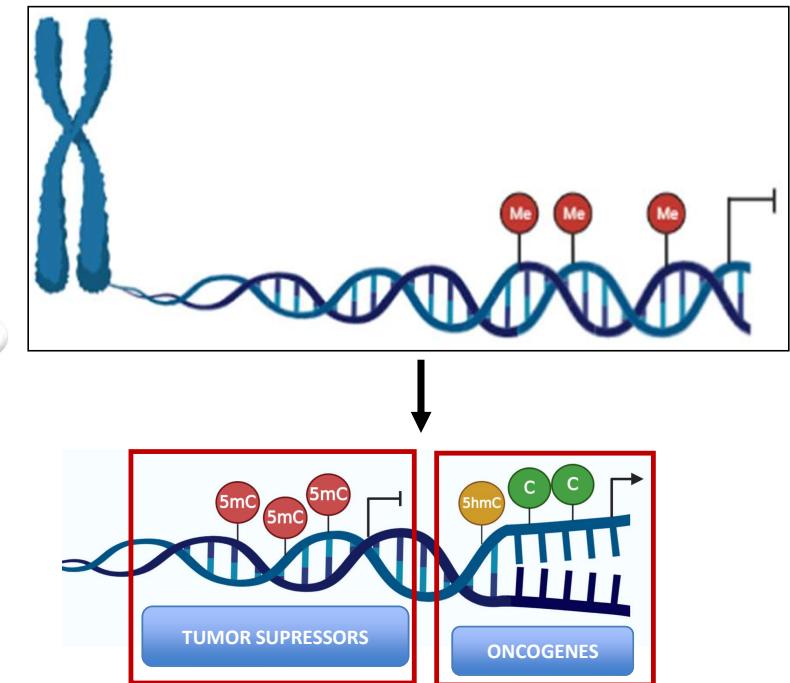


1. Cancer development/progression
2. Therapy resistance
3. Epigenetic biomarkers

Introduction: CTCs and DNA methylation



DNA methylation

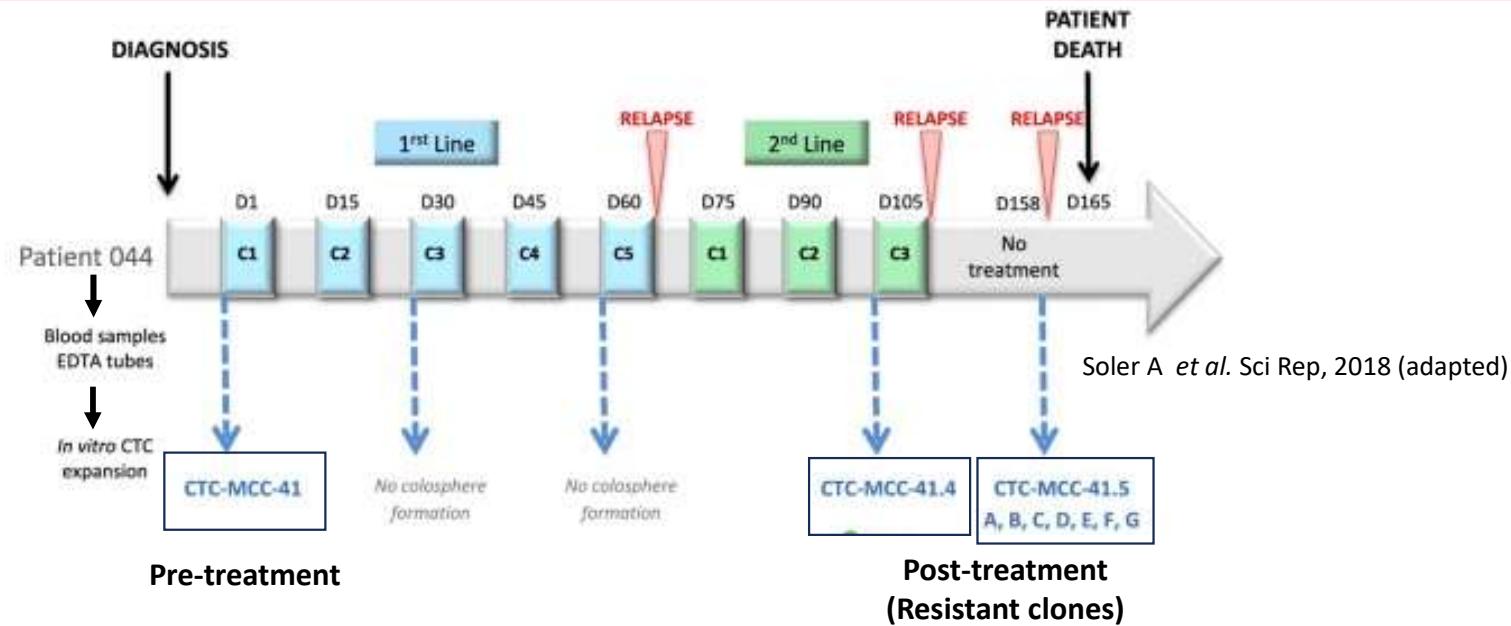
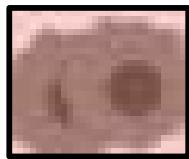


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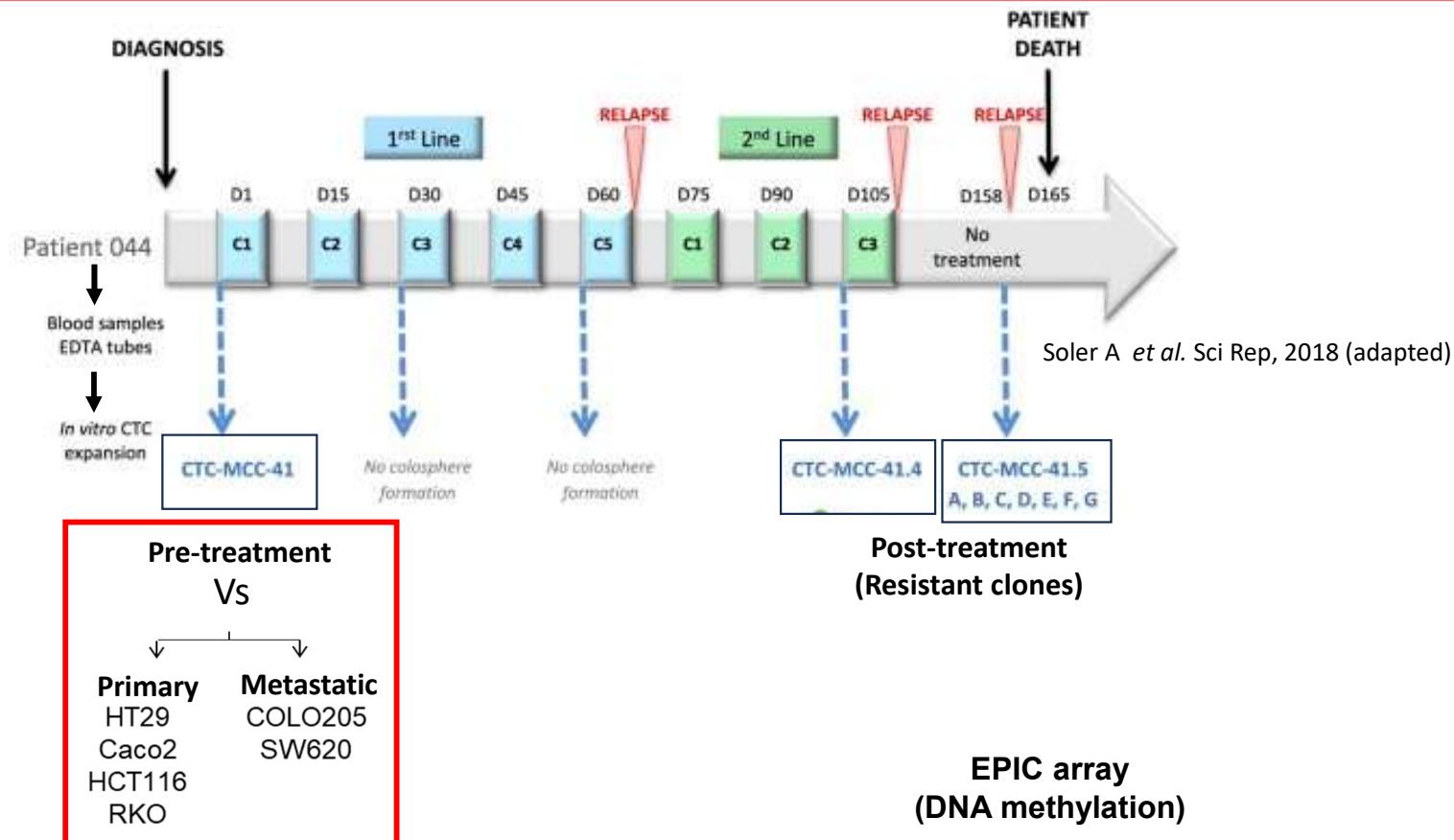
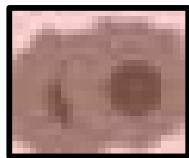
Metastasis-competent CTCs lines in colon cancer

Metastasis-competent CTC lines

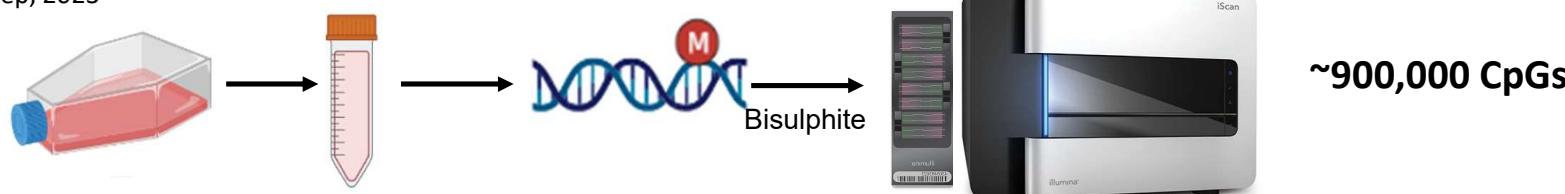


Metastasis-competent CTCs lines in colon cancer

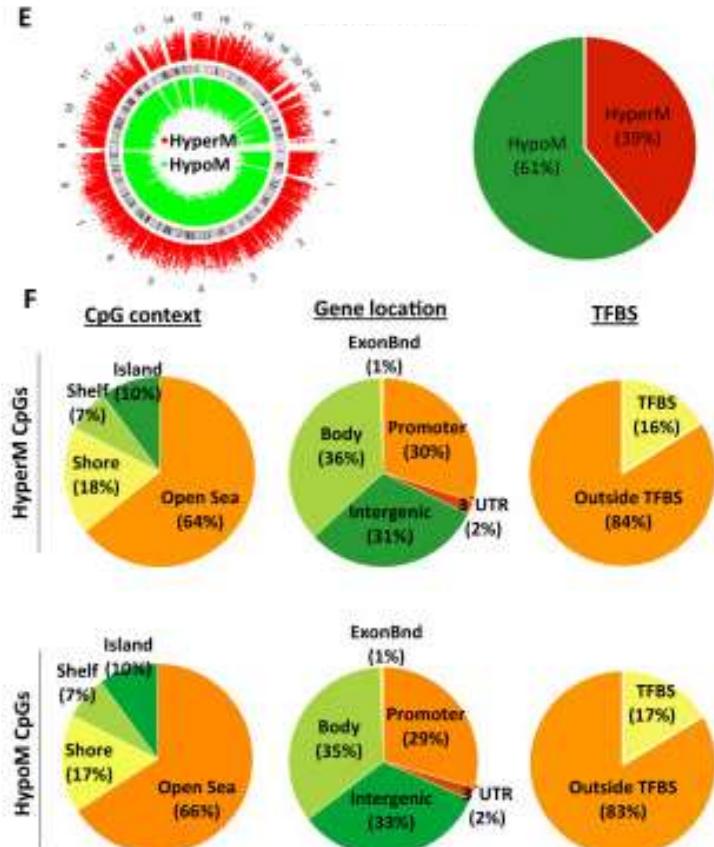
Metastasis-competent CTC lines



Bao-Caamano A et al. Sci Rep, 2023

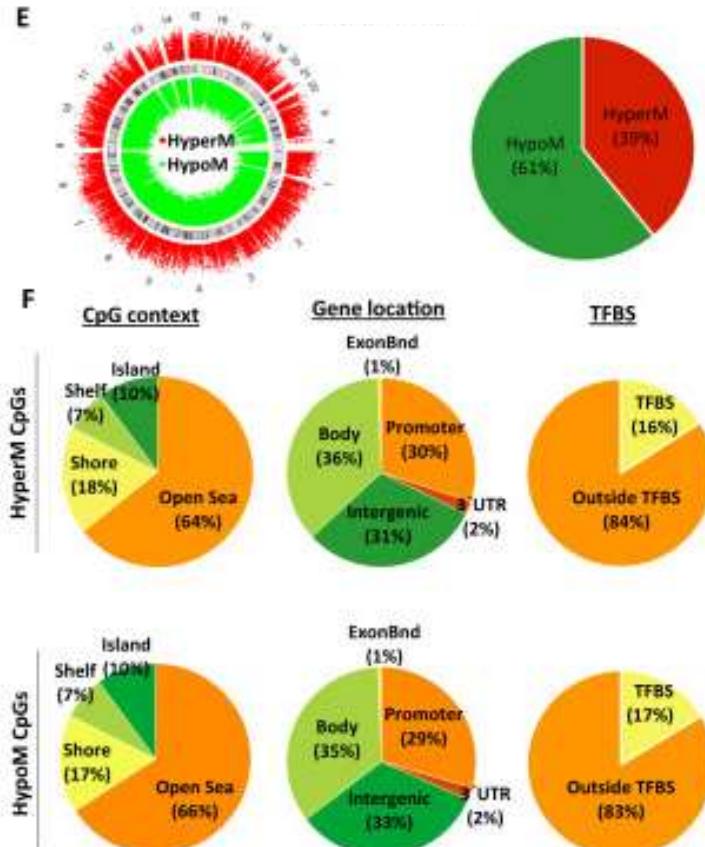


1. DNA methylation program of metastasis-competent CTCs



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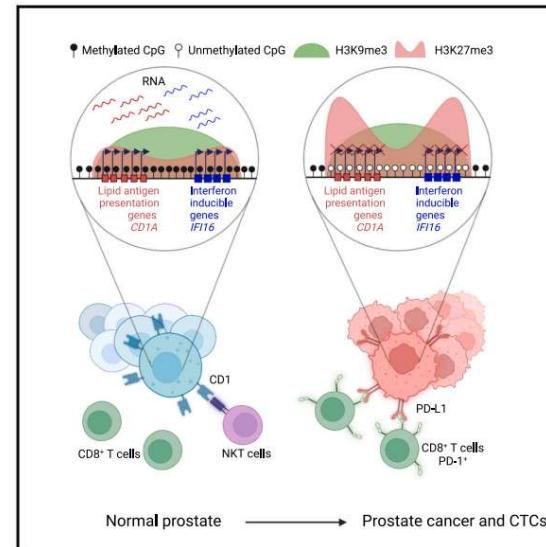
Bao-Caamano A *et al.* Sci Rep, 2023

Cell

Article

DNA hypomethylation silences anti-tumor immune genes in early prostate cancer and CTCs

Graphical abstract



Authors

Hongshan Guo, Joanna A. Vuille, Ben S. Wittner, ..., David T. Miyamoto, Shyamala Maheswaran, Daniel A. Haber

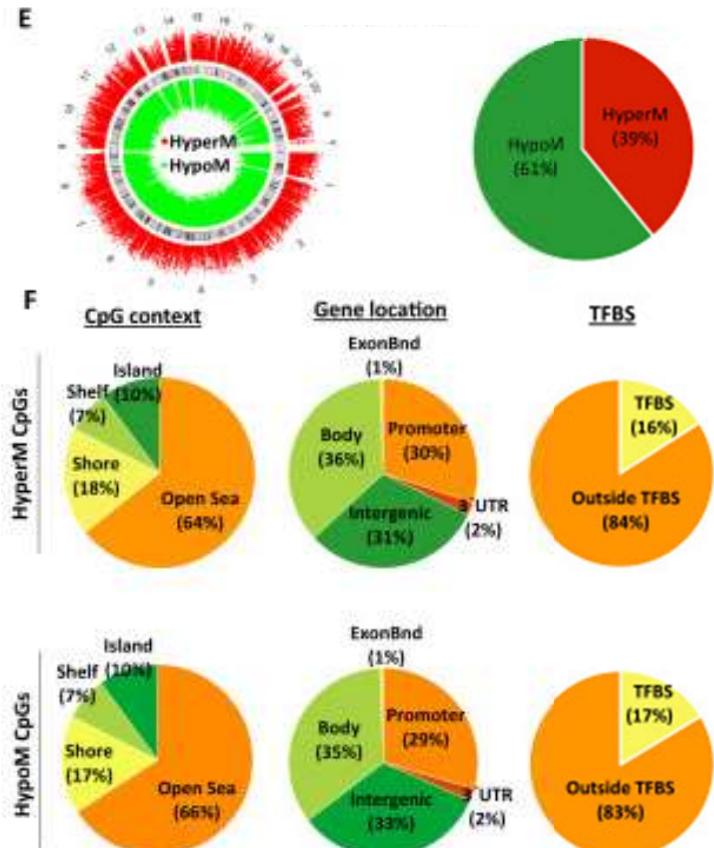
Correspondence

dmiyamoto@mgh.harvard.edu (D.T.M.), maheswaran@helix.mgh.harvard.edu (S.M.), dhaber@mgh.harvard.edu (D.A.H.)

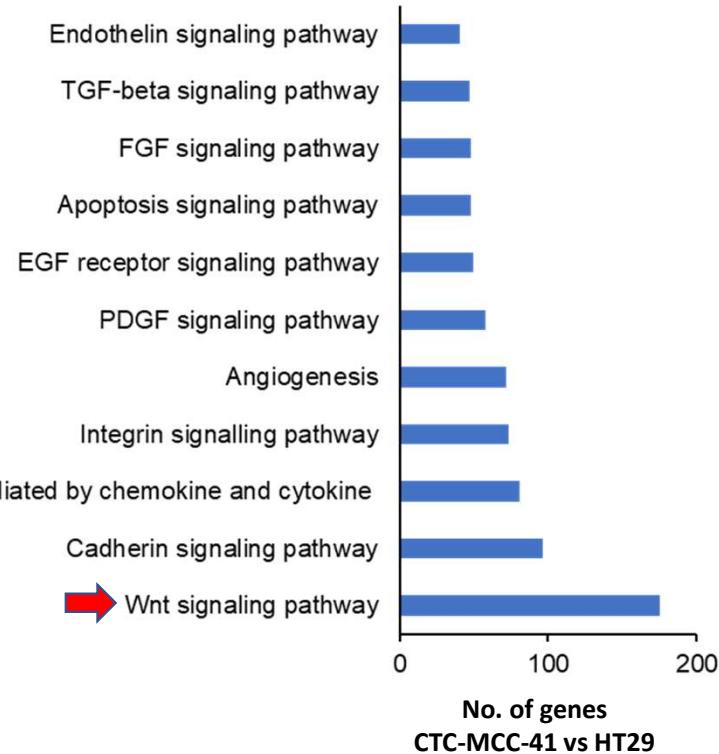
In brief

Analysis of primary prostate cancer and circulating tumor cells reveals how DNA hypomethylation during early prostate tumorigenesis silences immune surveillance genes while sparing proliferation-associated genes.

1. DNA methylation program of metastasis-competent CTCs



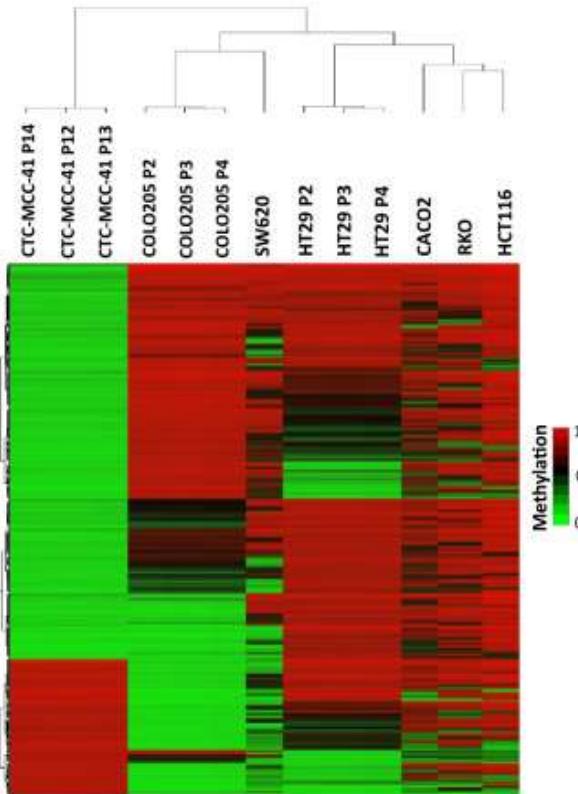
DNA methylation in CpG islands of promoters



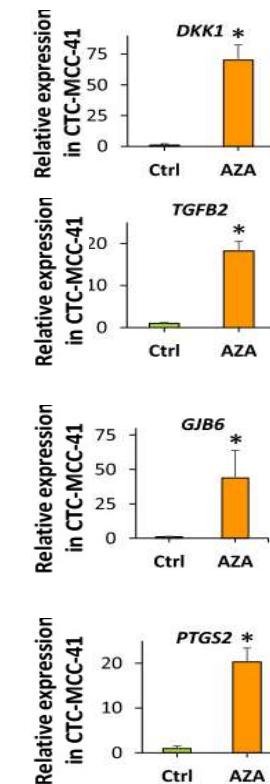
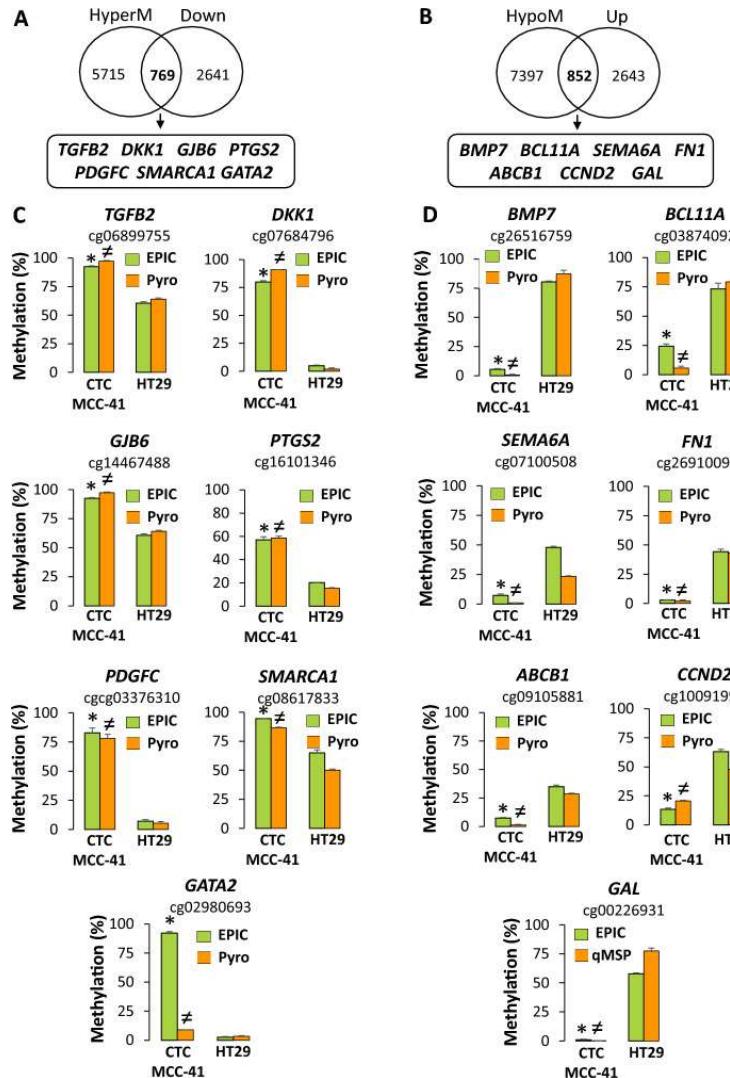
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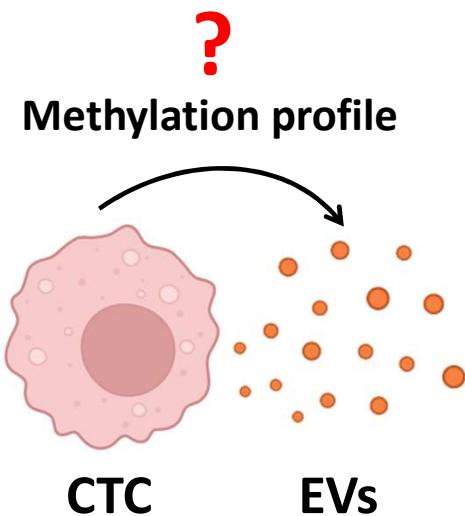
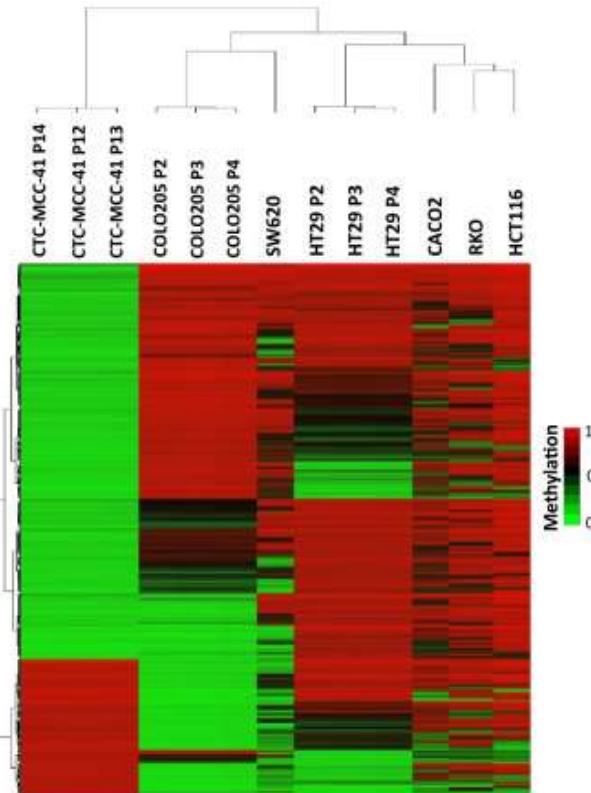


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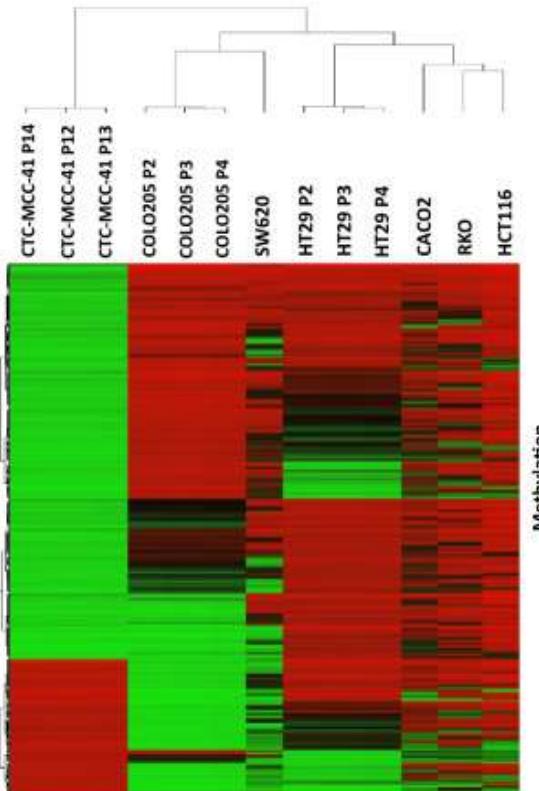
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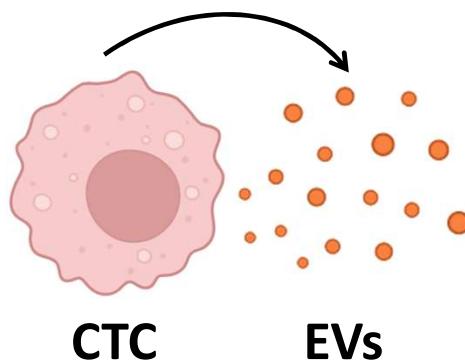


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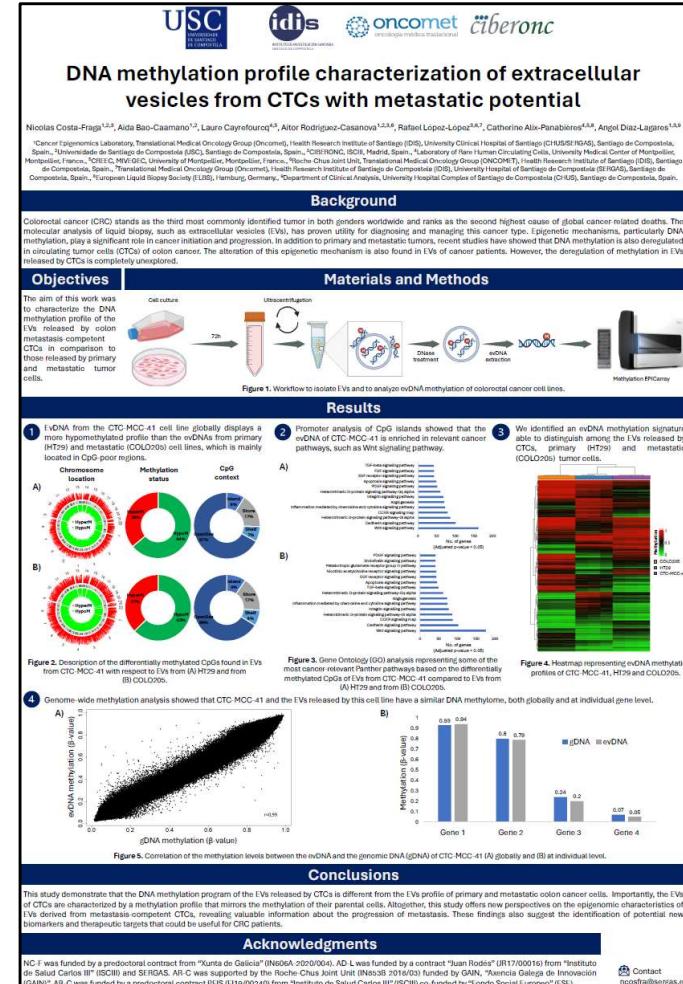


Methylation profile



Unpublished data
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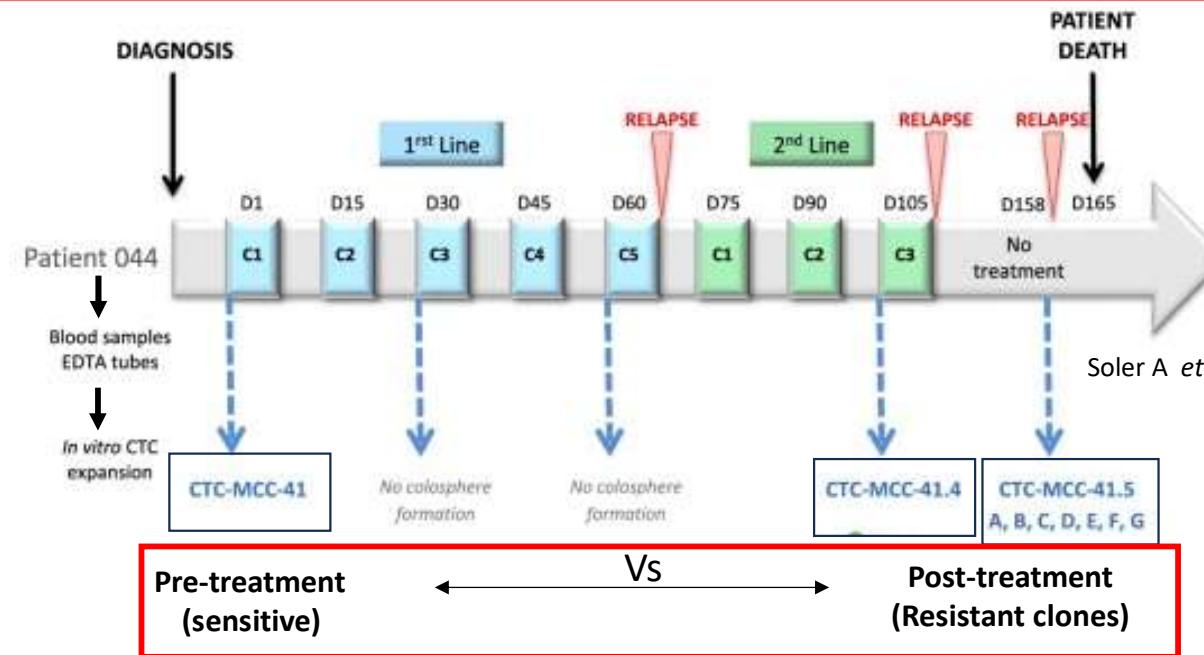
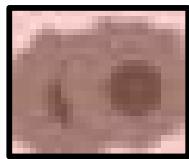
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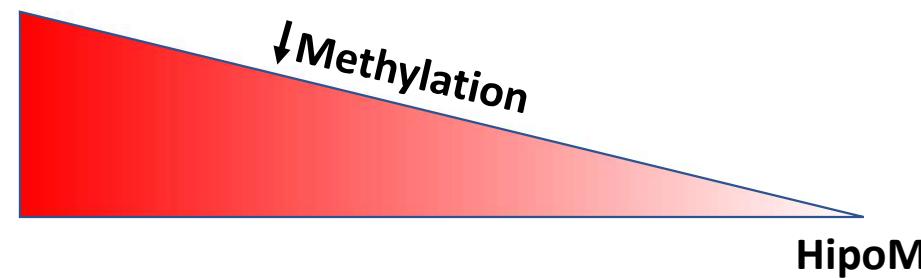
Nicolás
Costa-Fraga

2. DNA methylation program of therapy-resistant CTCs

Metastasis-competent CTC lines



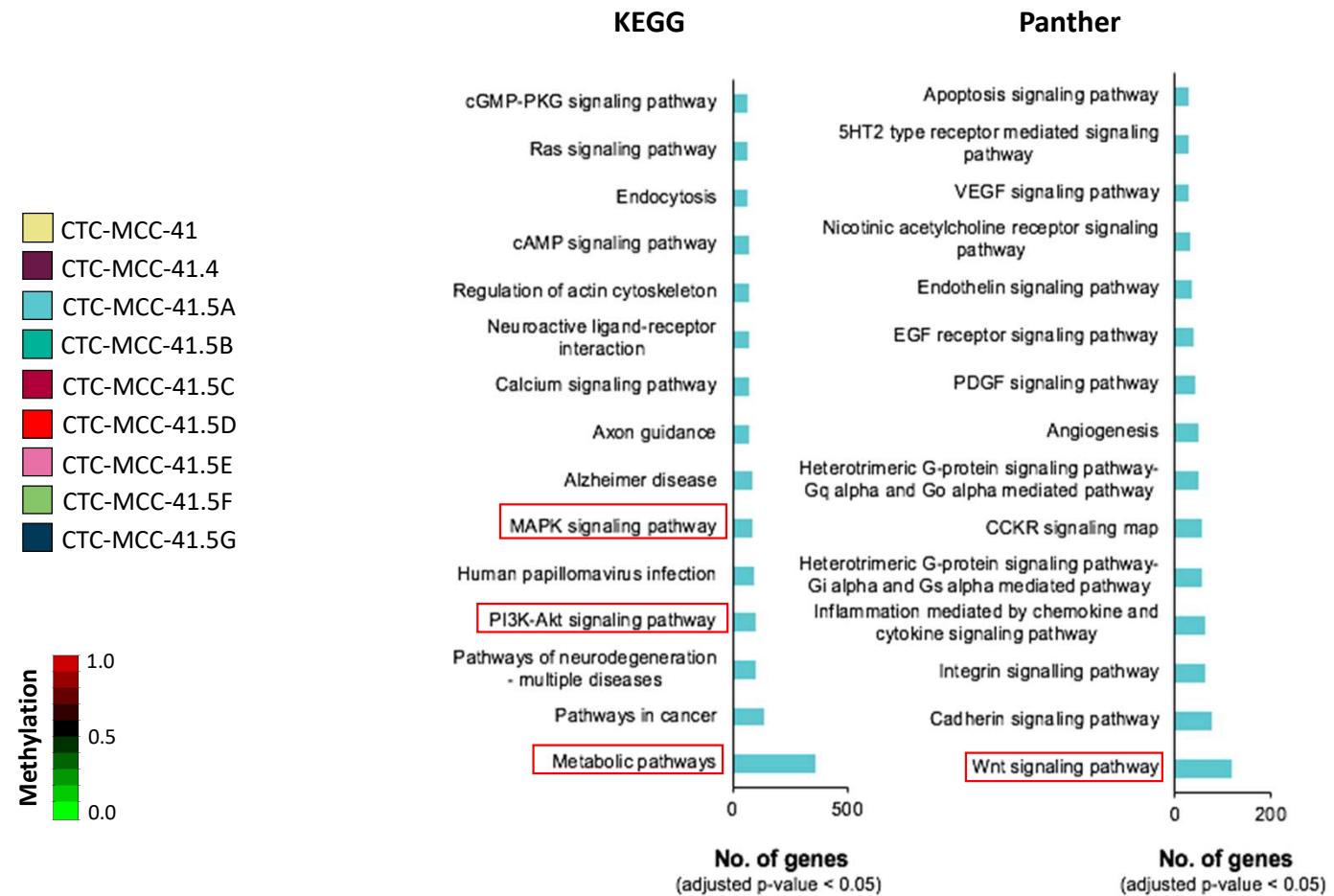
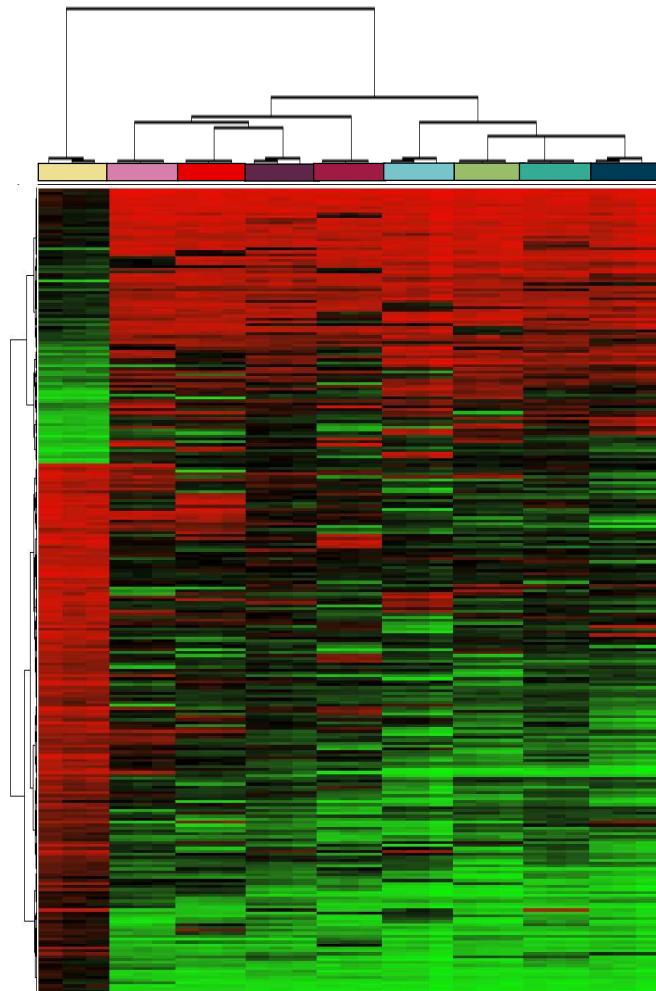
Bao-Caamano A et al. Front Cell Dev Biol, 2023



EPIC array (DNA methylation)

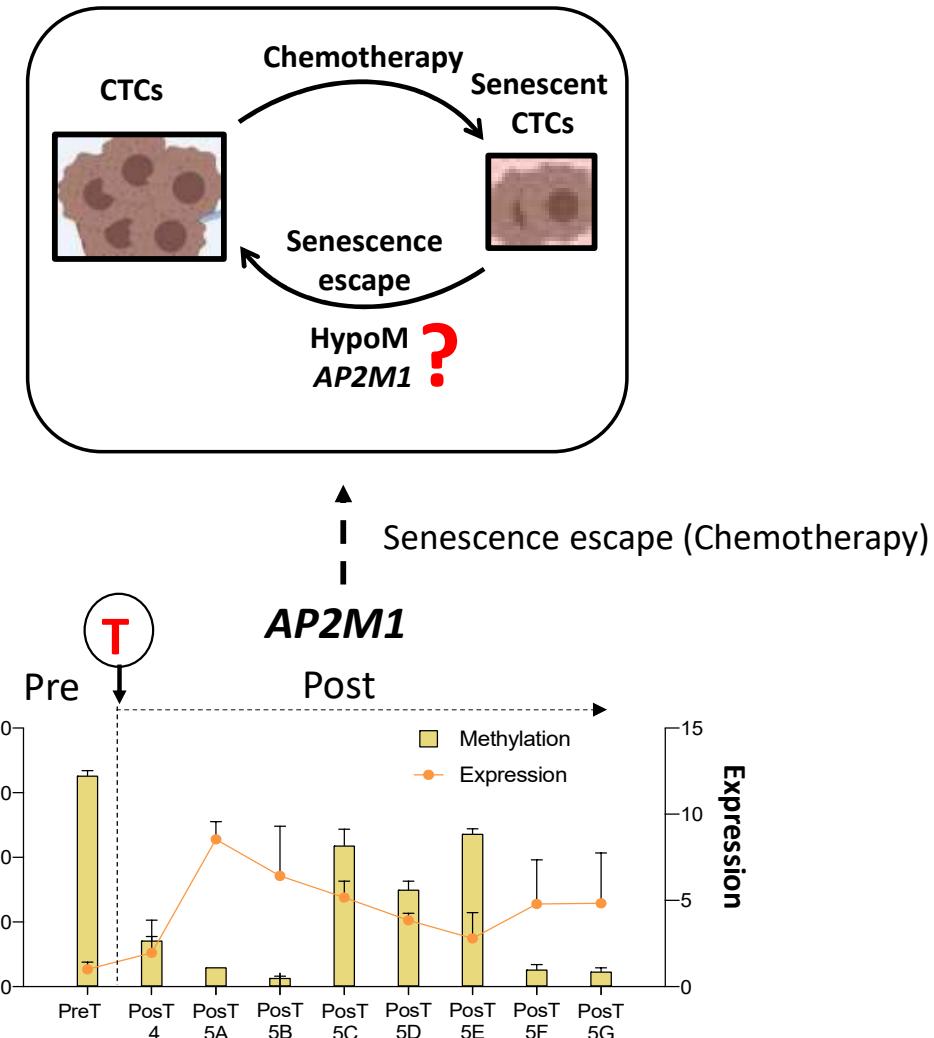
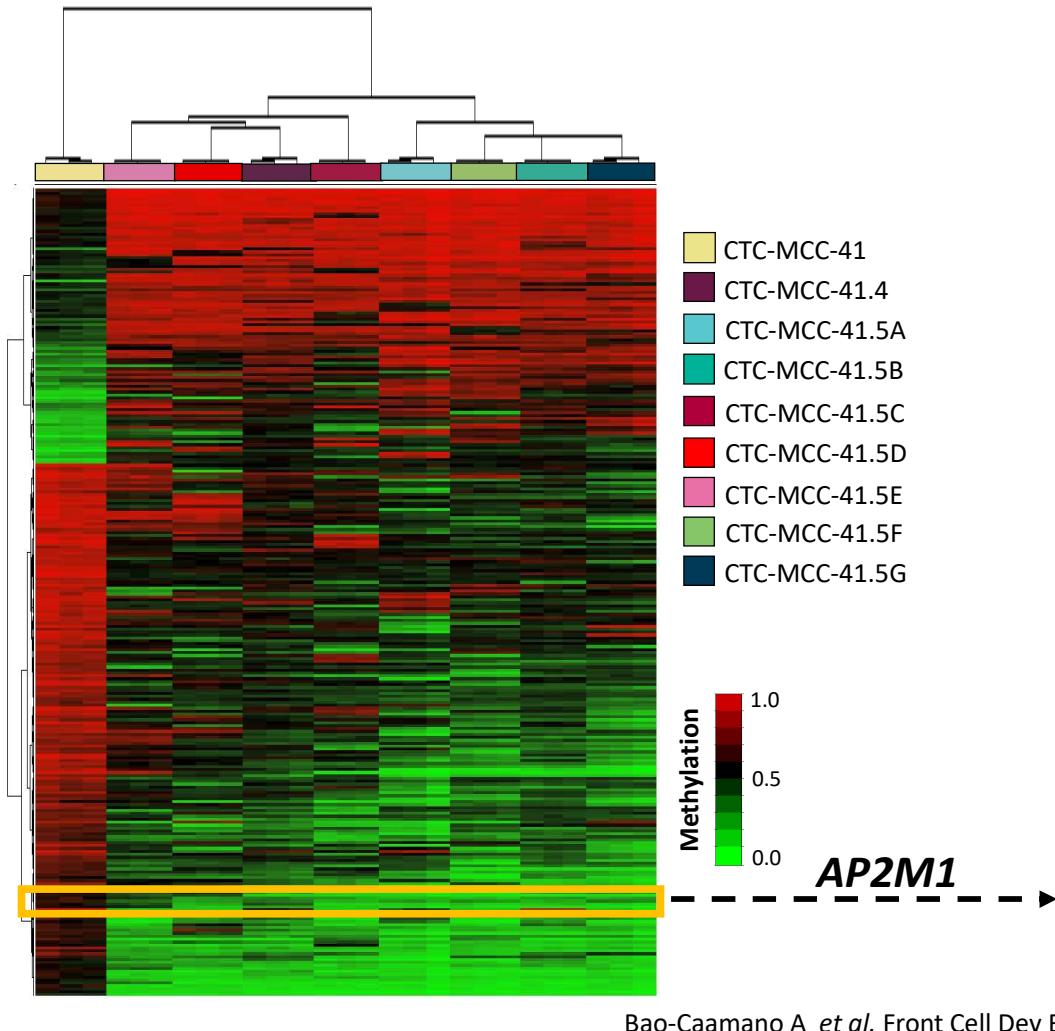


2. DNA methylation program of therapy-resistant CTCs

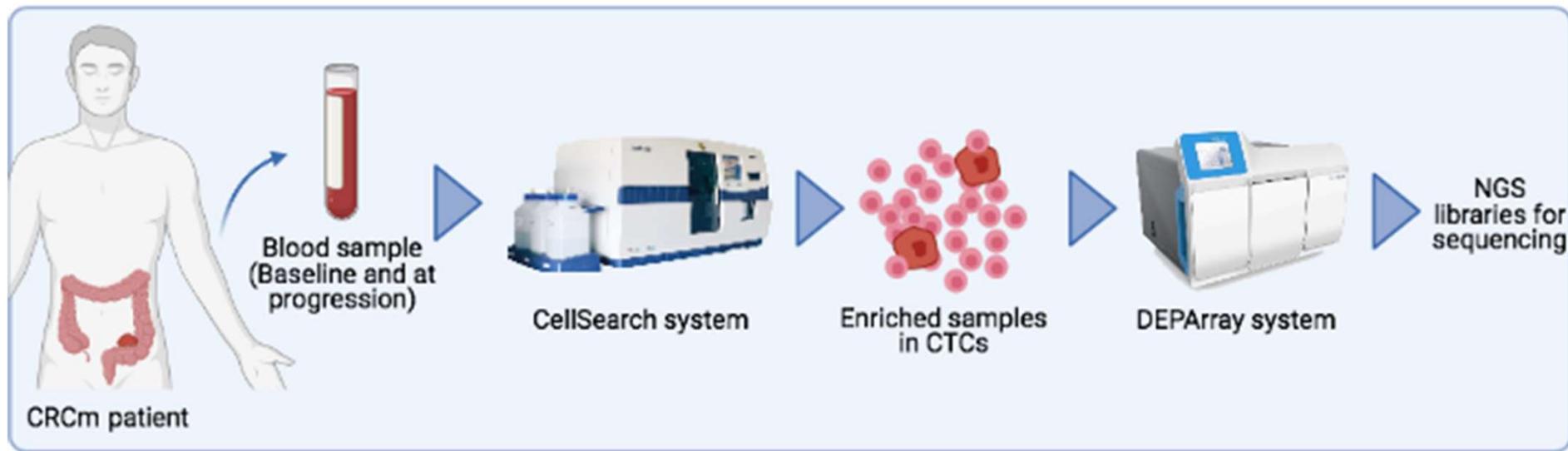


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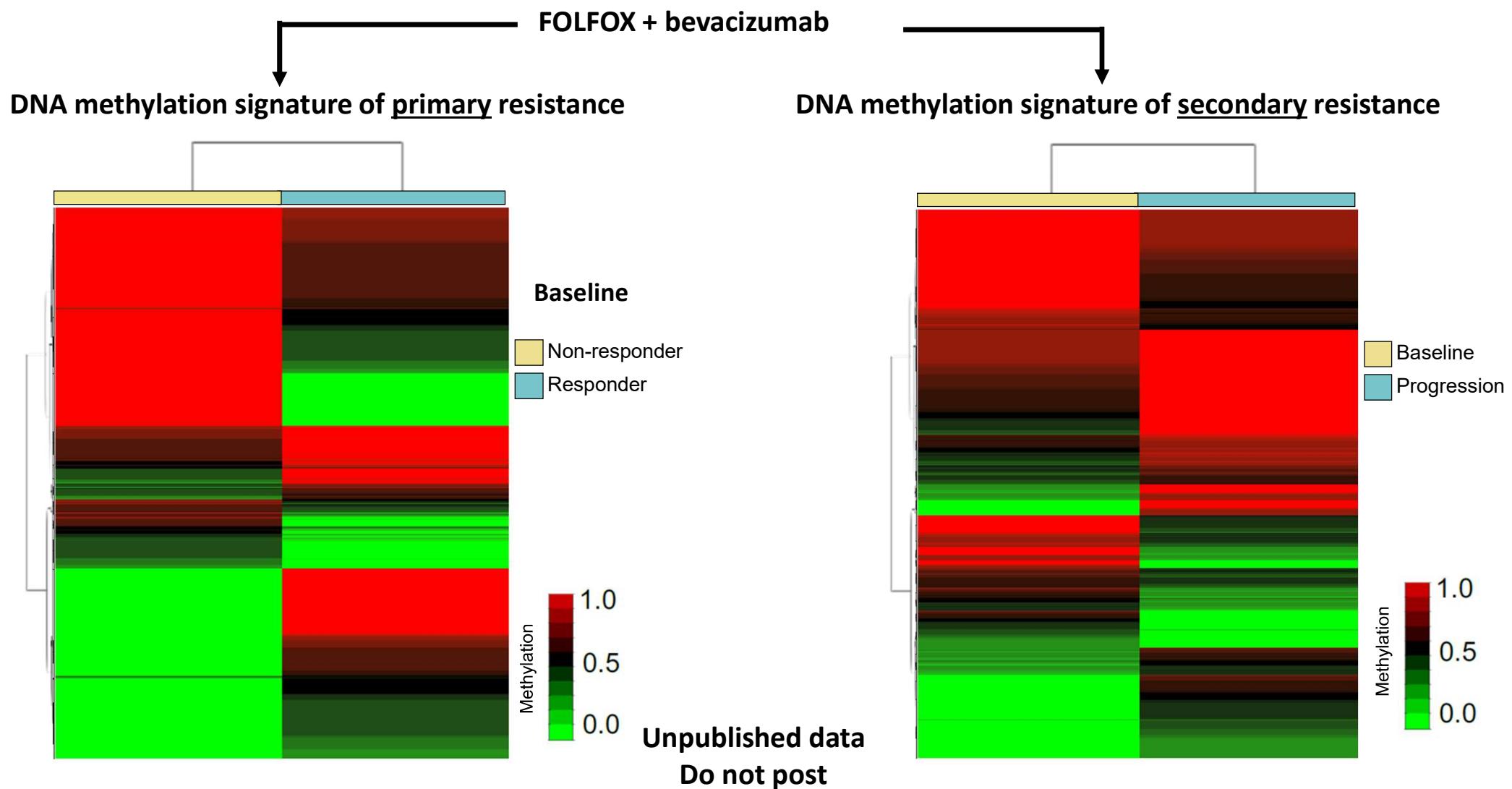
3. DNA methylation biomarkers of therapy resistance in CTCs



FOLFOX + Bevacizumab

Unpublished data
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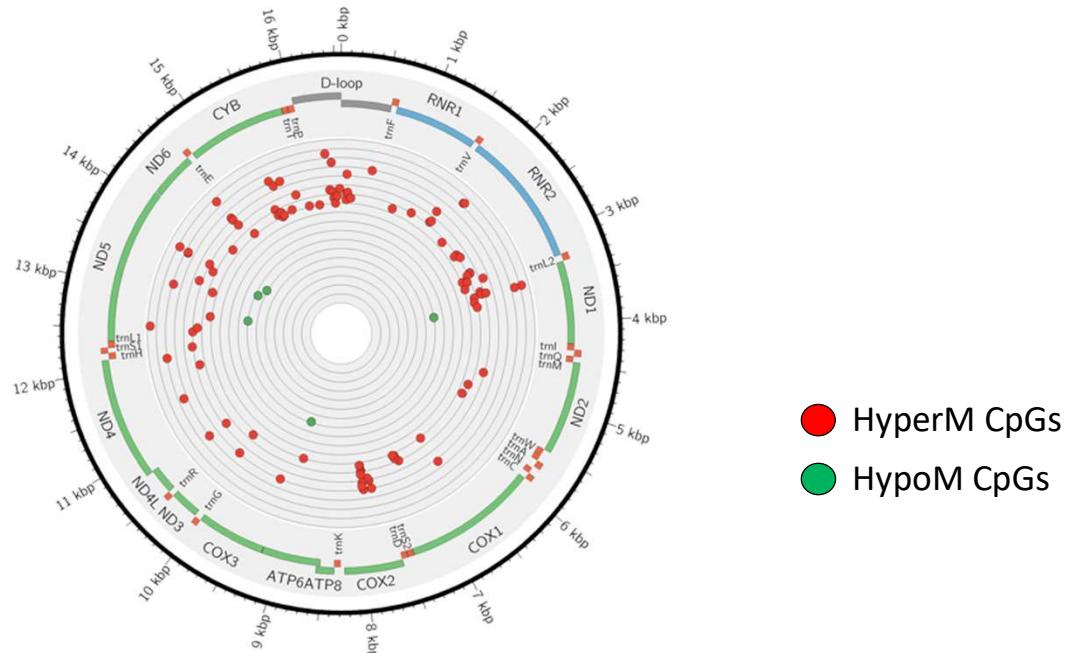
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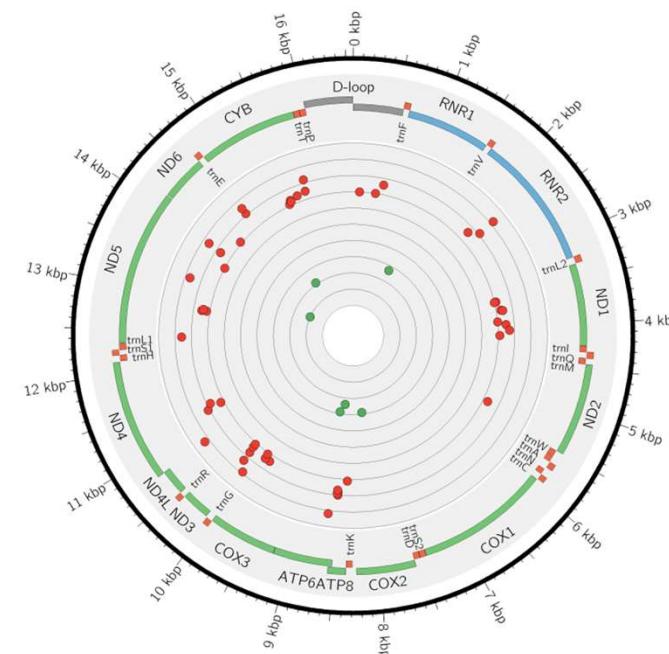
Methylation changes in mitochondrial DNA & primary resistance

Methylation changes in mitochondrial DNA & secondary resistance

Baseline: Responder vs Non-responder

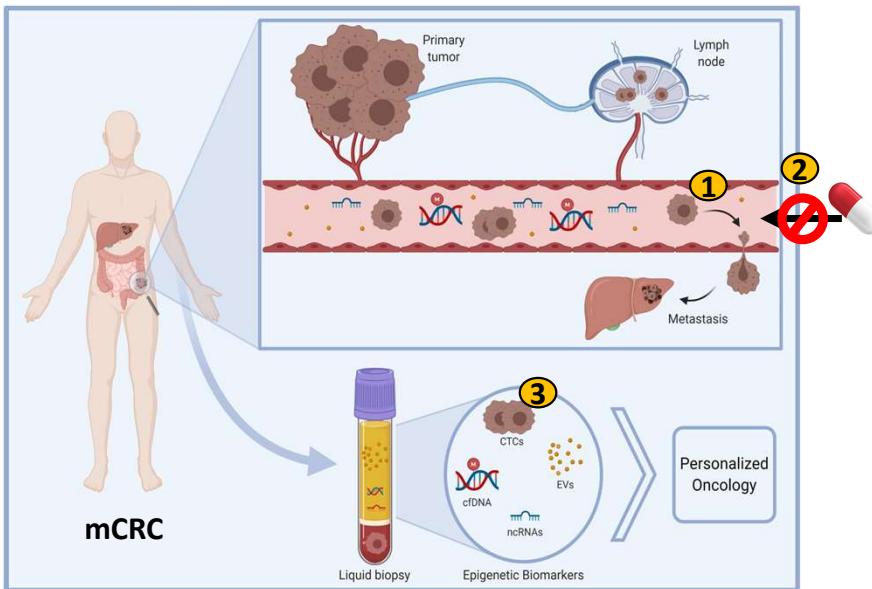


Baseline vs Progression



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Take home messages



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- ① Metastasis-competent CTCs have a unique DNA methylation program, that provides information of novel potential biomarkers and therapeutic targets.
- ② The DNA methylome of CTCs can be reprogrammed during therapy resistance leading to the hypomethylation of multiple genes, such as *AP2M1*, that are new potential biomarkers of chemotherapy resistance.
- ③ The DNA methylation profile of peripheral CTCs could be useful as a biomarker to predict chemotherapy resistance and to evaluate the development of secondary resistances and progression, leading to new noninvasive tools for precision oncology.

Acknowledgements



Cancer Epigenomics Unit
IDIS, Santiago de Compostela, Spain



INSTITUTO DE INVESTIGACIÓN SANITARIA
SANTIAGO DE COMPOSTELA



Angel Díaz-Lagares, PhD

angel.diaz.lagares@sergas.es

X @adiazlagares

The Laboratory of Rare Circulating
Human Cells (LCCRH).
Montpellier University Hospital



C. Alix-Panabières, PhD

Brozos-Vazquez E

Vidal-Insua Y

Vazquez-Rivera F

Candamio-Folgar S

Abalo A

Lago-Lestón RM

Muinelo-Romay L

López-López R

Cayrefourcq L

Earl J

Castillo M

Longo F