

VII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN

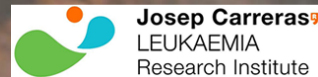
Vigo, 20 y 21 de febrero de 2025

Epigenetics and Cancer Precision Medicine: Recent Discoveries

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Epigenetic Setting: DNA Methylation and Histone Modifications

EPIGENETIC MODIFICATIONS

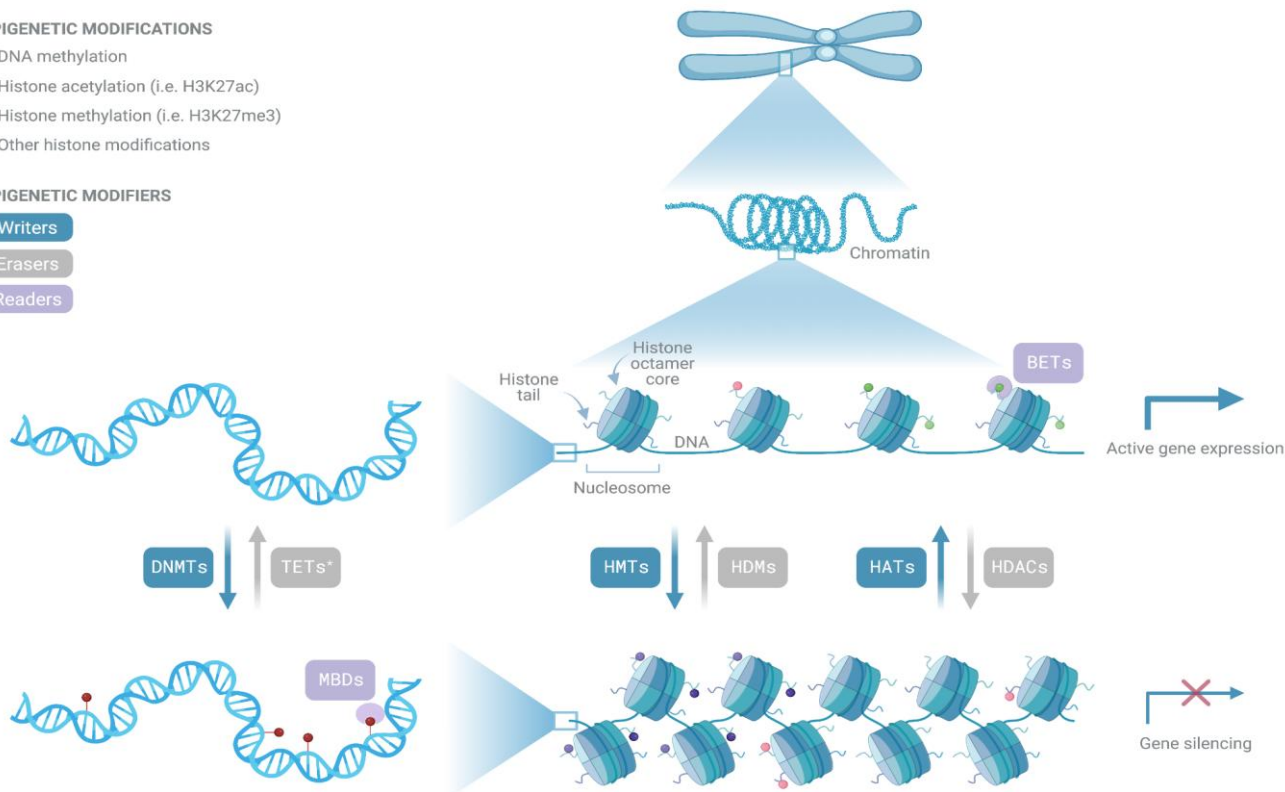
- DNA methylation
- Histone acetylation (i.e. H3K27ac)
- Histone methylation (i.e. H3K27me3)
- Other histone modifications

EPIGENETIC MODIFIERS

Writers

Erasers

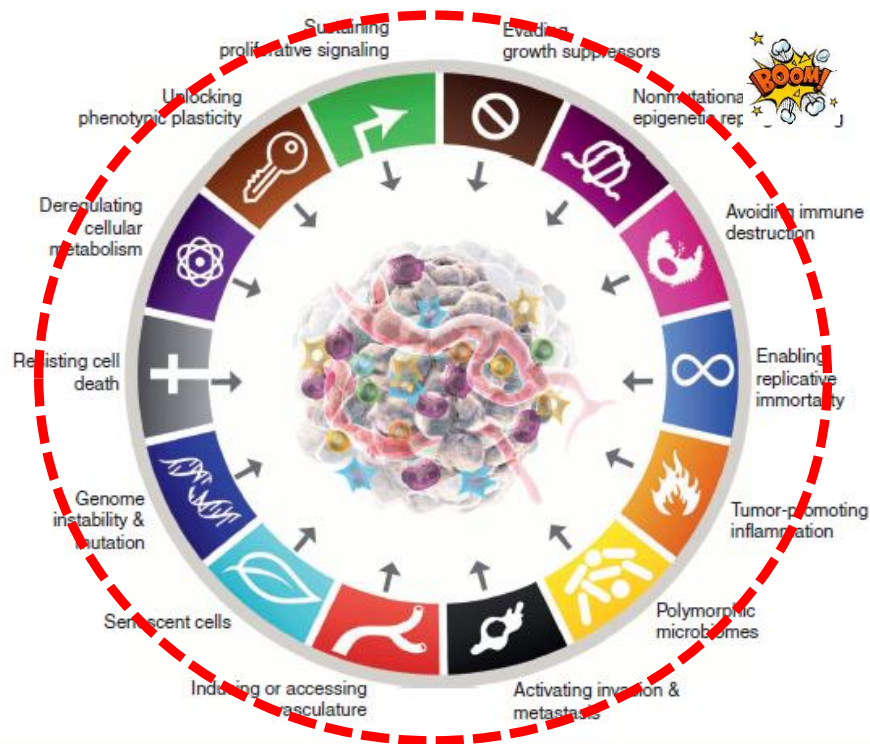
Readers



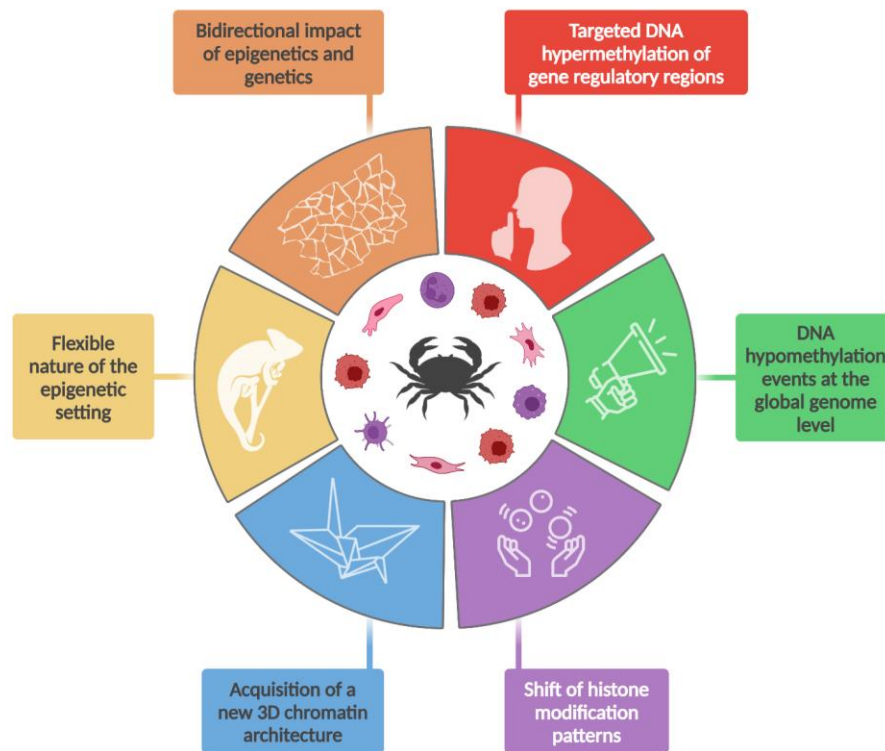
Epigenetics made it ! Hallmarks of Cancer

Hallmarks of Cancer: New Dimensions

REVIEW



The Epigenetic Hallmarks of Cancer



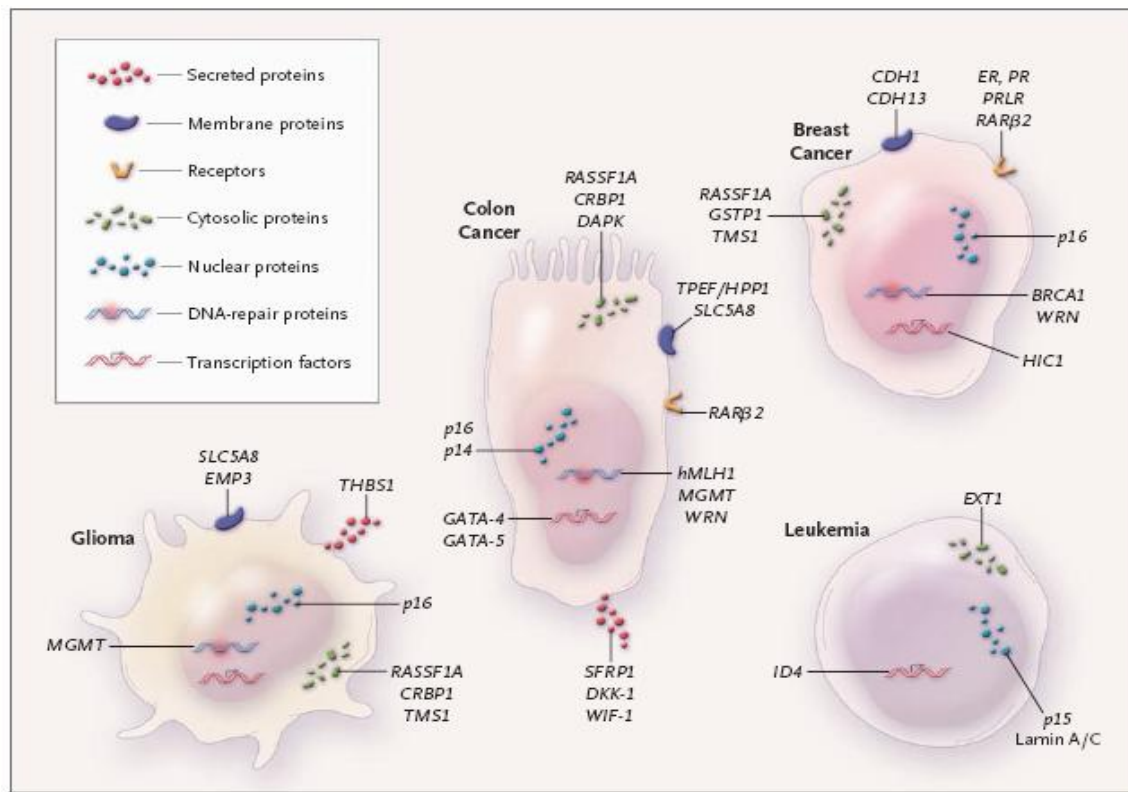


Table 3 | **Hypermethylated genes predict drug sensitivity**

Gene name	Gene function	Therapeutical consequences	Tumour type application	Example refs
ABCB1	Protein transport	Sensitivity to doxorubicin	Breast	120
APAF1	Apoptotic activator	Resistance to adriamycin	Melanoma	121
BRCA1	DNA damage response	Sensitivity to PARP inhibitors and alkylating agents	Breast, ovary	81
CDK10	Cell cycle control	Resistance to anti-oestrogens	Breast	122
CHFR	Ubiquitin protein ligase	Sensitivity to paclitaxel and docetaxel	Ovary, endometrium, stomach	123
ESR1	ER signalling	Resistance to anti-oestrogens	Breast	124
FANCF	DNA damage response	Sensitivity to cisplatin	Ovarian	125
GSTP1	Detoxification	Sensitivity to doxorubicin	Prostate, breast, kidney	126
IGFBP3	Signal transduction	Resistance to cisplatin	Lung	127
LINE1	Repetitive element	Resistance to fluoropyrimidines	Colon	22
MGMT	DNA repair	Sensitivity to temozolomide, BCNU, ACNU, procarbazine	Glioma, colon, lung, lymphoma	5
MLH1	DNA repair	Resistance to cisplatin	Colon, stomach, endometrium, ovary	128
MT1E	Antioxidant	Sensitivity to cisplatin	Melanoma	129
PITX2	Transcriptional regulator	Resistance to tamoxifen	Breast	130
PLK2	Cell division	Sensitivity to paclitaxel and carboplatin	Ovary	131
PRKCDBP	Signal transduction	Resistance to TNF α	Colon	132
SFN	Signal transduction	Sensitivity to cisplatin and gemcitabine	Lung	133
SLC19A1	Folate transporter	Resistance to methotrexate	Lymphomas	134
SULF2	Heparin signalling	Sensitivity to camptothecin	Lung	135
TFAP2E	Transcriptional regulator	Sensitivity to fluorouracil	Colon	136
TGM2	Apoptosis	Resistance to doxorubicin and cisplatin	Lung, breast, ovary	137
TP73	Stress response	Sensitivity to cisplatin	Renal, melanoma	138
WRN	DNA helicases	Sensitivity to irinotecan	Colon	139
ERCC5	DNA repair	Resistance to nemorubicin	Ovary	140

**Esteller et al.,
NEJM 2000**



#1

Global burden of primary liver cancer



905,700

people were **diagnosed**
with liver cancer in 2020



830,200

people **died** from liver
cancer in 2020



Liver cancer ranked among the
top 3 causes of cancer death in

46 countries
in 2020



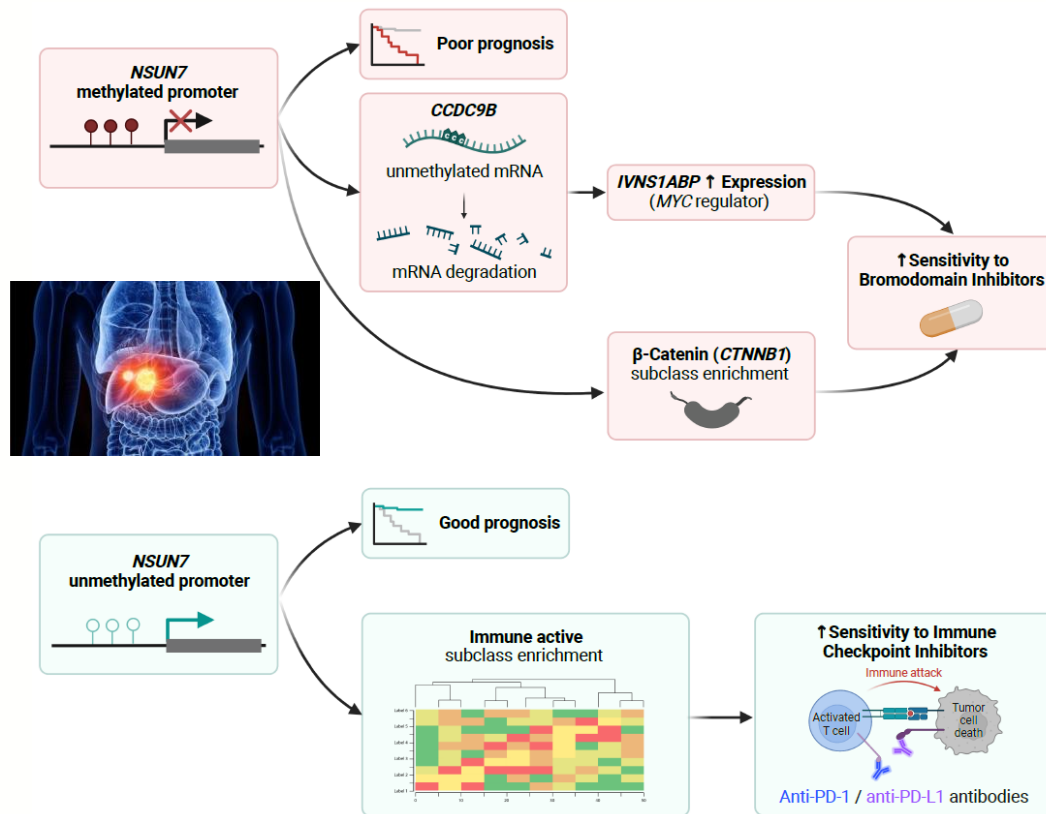
The number of people
diagnosed with or **dying** from
liver cancer globally could

increase by
more than 55%
between 2020 and 2040 if
current rates do not change



Liver cancer is a major cause of death in many countries. Efforts to reduce the incidence of preventable liver cancer should be prioritised to avoid the predicted rise in people diagnosed with liver cancer.

Epigenetic inactivation of the 5-methylcytosine RNA methyltransferase NSUN7 is associated with clinical outcome and therapeutic vulnerability in liver cancer



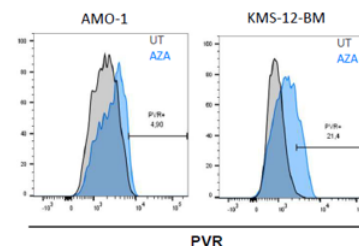
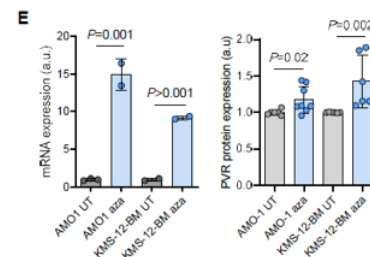
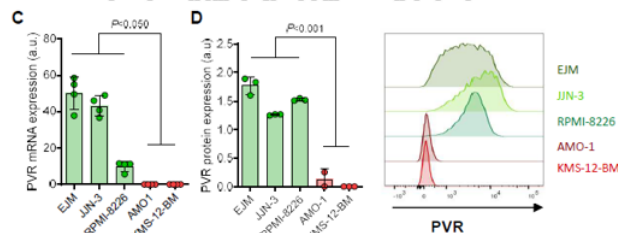
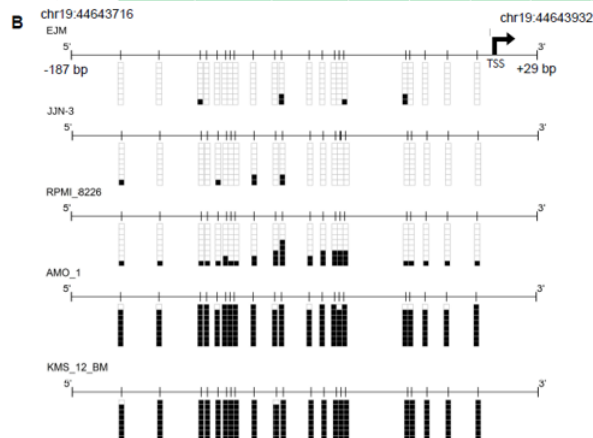


#2



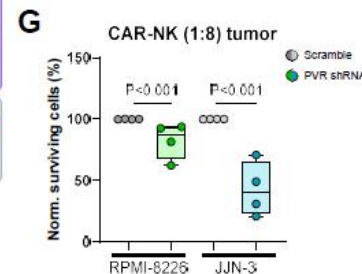
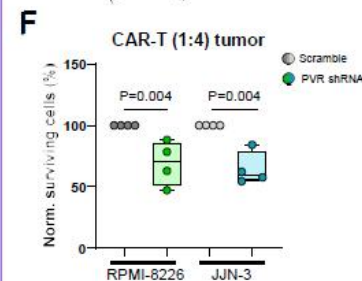
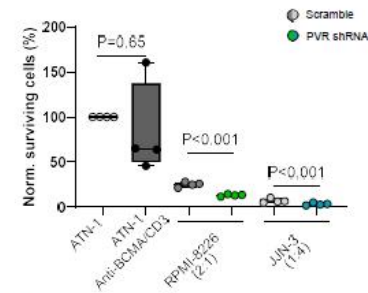
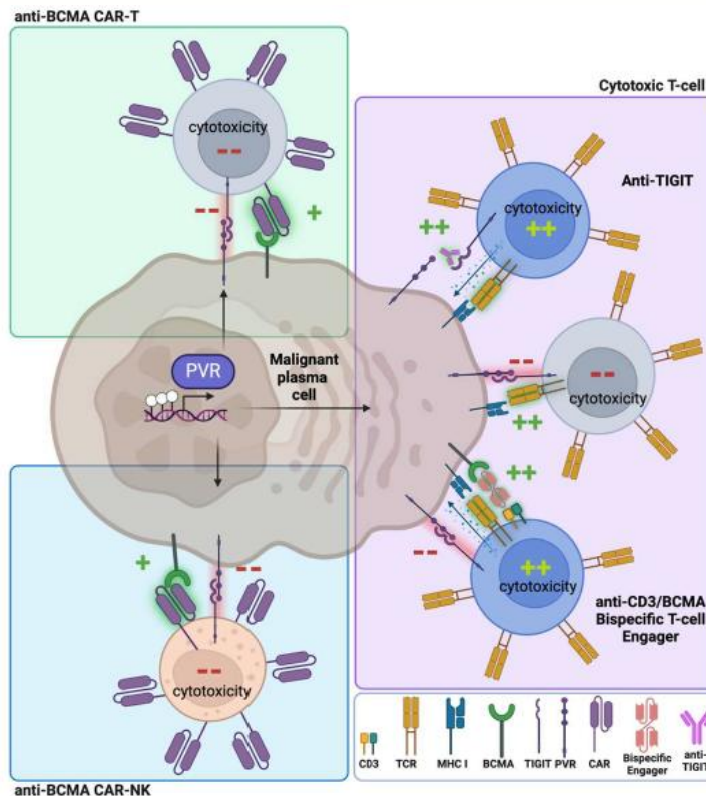
PVR (CD155) Epigenetic Status Mediates Immunotherapy Response in Multiple Myeloma

			Healthy B Plasm. Cells (CD138+)			Multiple myeloma cell lines												
ID	Map info	Location	HC1_CD138+	HC2_CD138+	HC3_CD138+	MM1.R	MM1.S	SK-MM-2	JIN-3	OPM-2	EJM	RPMI-8226	MM.1	L-363	ME-1	NCI-H929	AMO1	KMS-12-BM
cg04560018	4464367	TSS200	0.11	0.10	0.11	0.14	0.13	0.11	0.13	0.14	0.15	0.16	0.12	0.24	0.23	0.60	0.72	0.69
cg14538146	4464367	TSS200	0.02	0.01	0.02	0.01	0.02	0.02	0.02	0.03	0.02	0.03	0.03	0.26	0.07	0.67	0.92	0.95
cg07917289	44643756	TSS200	0.03	0.02	0.03	0.01	0.02	0.03	0.03	0.02	0.02	0.03	0.03	0.05	0.19	0.47	0.74	0.77
cg05012825	44643778	TSS200	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.02	0.03	0.06	0.16	0.43	0.80	0.98	0.98
cg13905416	44644140	TssExon	0.19	0.07	0.09	0.07	0.10	0.10	0.11	0.09	0.13	0.14	0.17	0.12	0.23	0.64	0.70	0.84



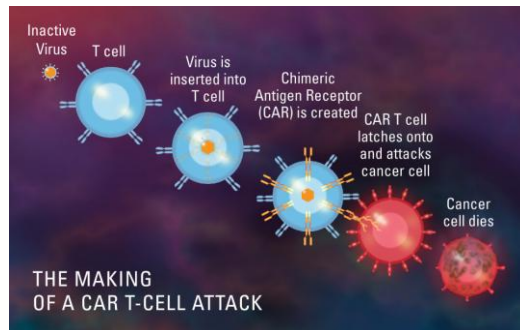
Laura Martinez-Verbo
Gerardo Ferrer
Leukemia 2024

PVR (CD155) Epigenetic Status Mediates Immunotherapy Response in Multiple Myeloma





#3



CAR T-Cell Therapy

Patient Zero: Emily Whitehead

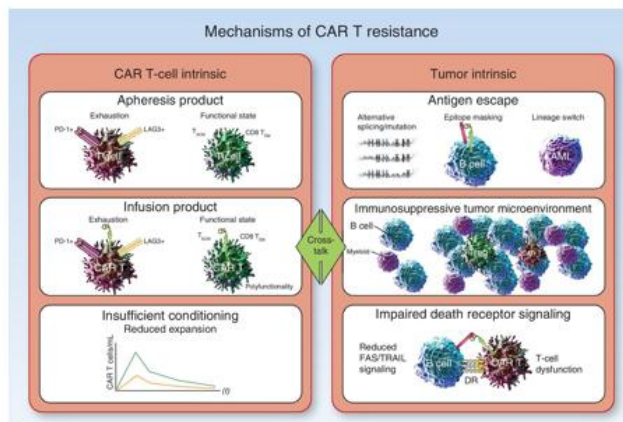
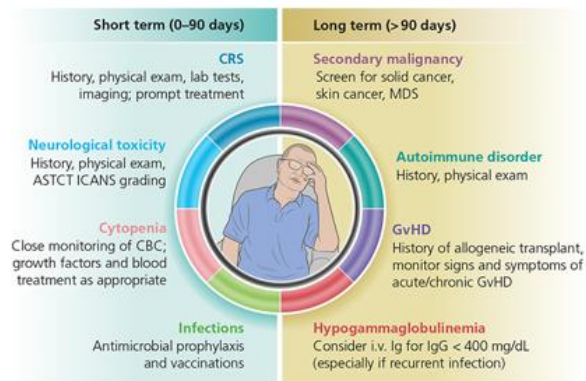


May 10, 2012

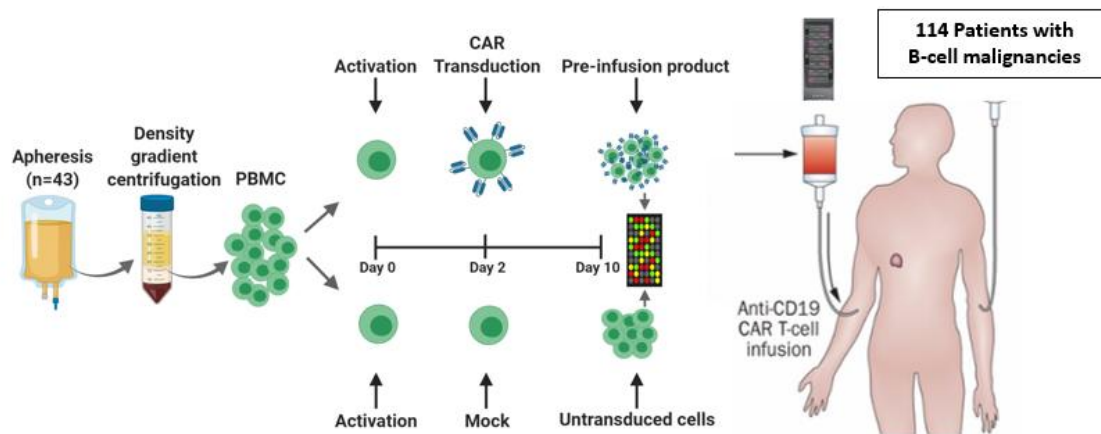


May 10, 2023

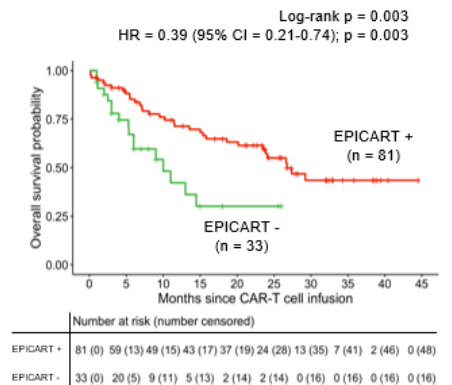
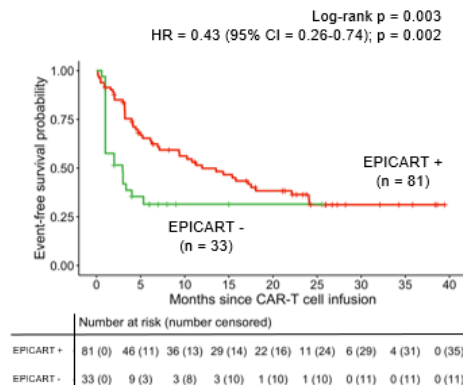
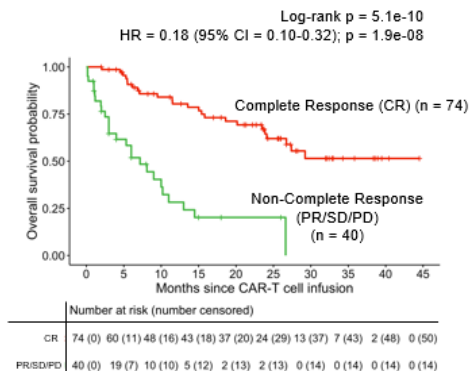
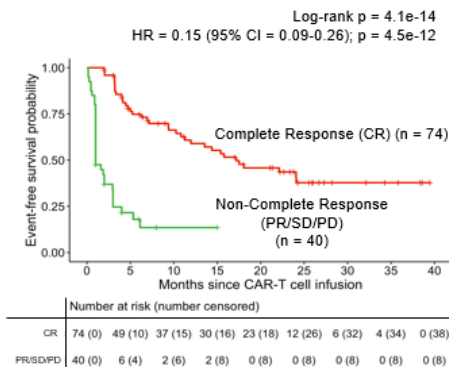
Issues with CAR T-Cell Therapy



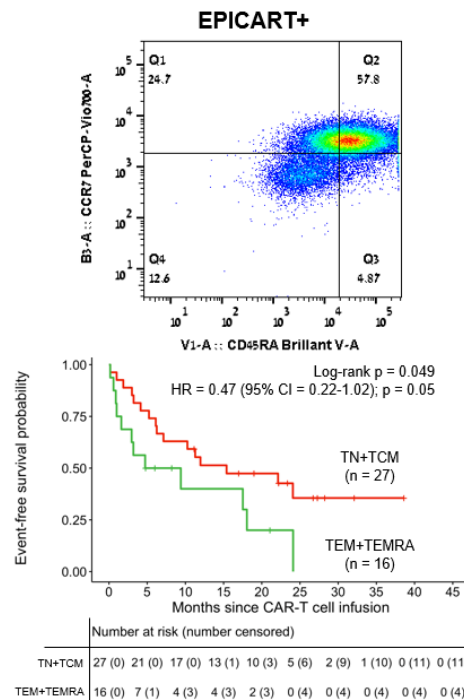
Epigenetic profiling and response to CD19 chimeric antigen receptor T-cell therapy in B-cell malignancies



The EPICART+ Signature: Impact on Clinical Outcome

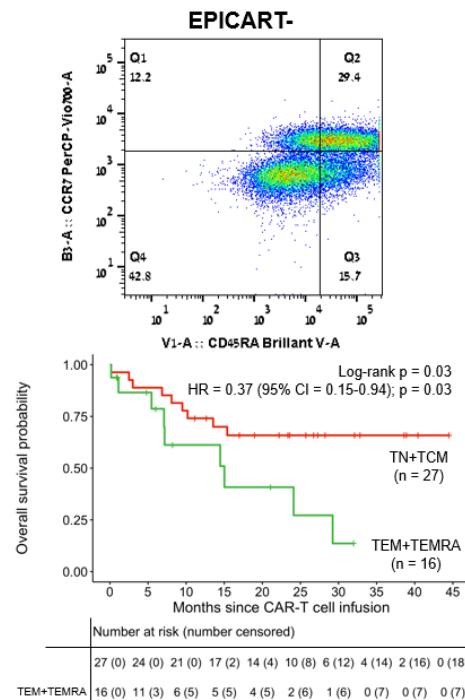


The EPICART+ Signature: Cell Populations



TN: Naïve T cells (Q2: CD45RA+CCR7+) and TCM: central memory T cells (Q1: CD45RA-CCR7+)

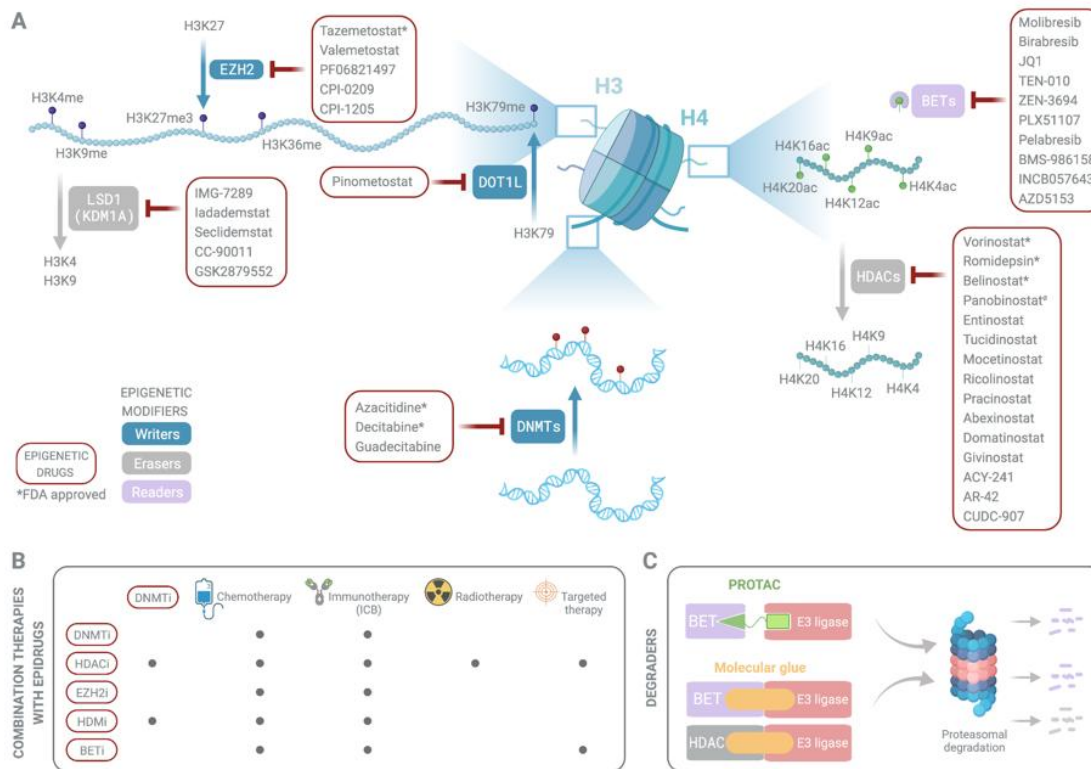
TEM: effector memory T cells (Q4: CD45RA-CCR7-) and TEMRA: effector T cells (Q3: CD45RA+CCR7-)



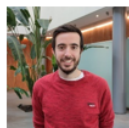


#4

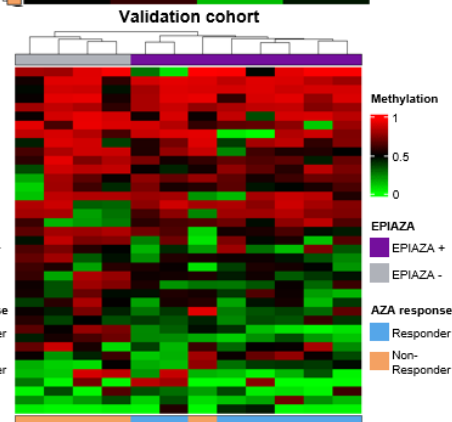
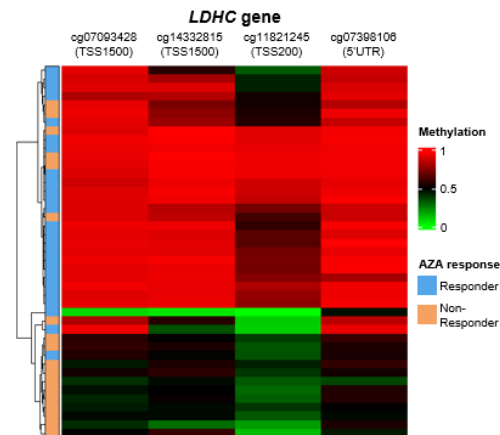
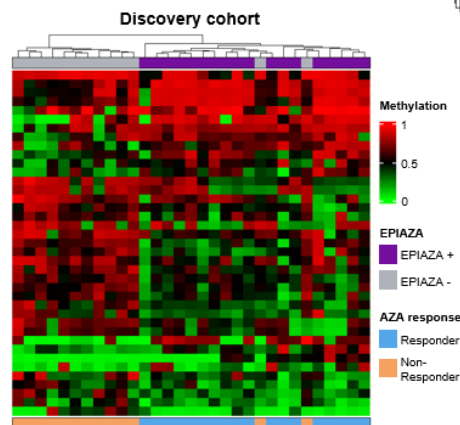
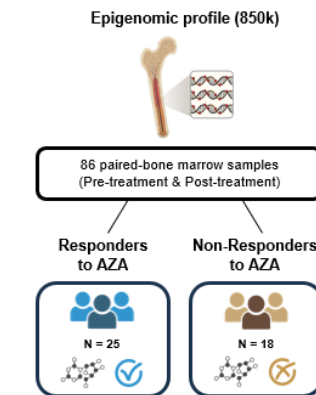
Epigenetic Drugs in Cancer



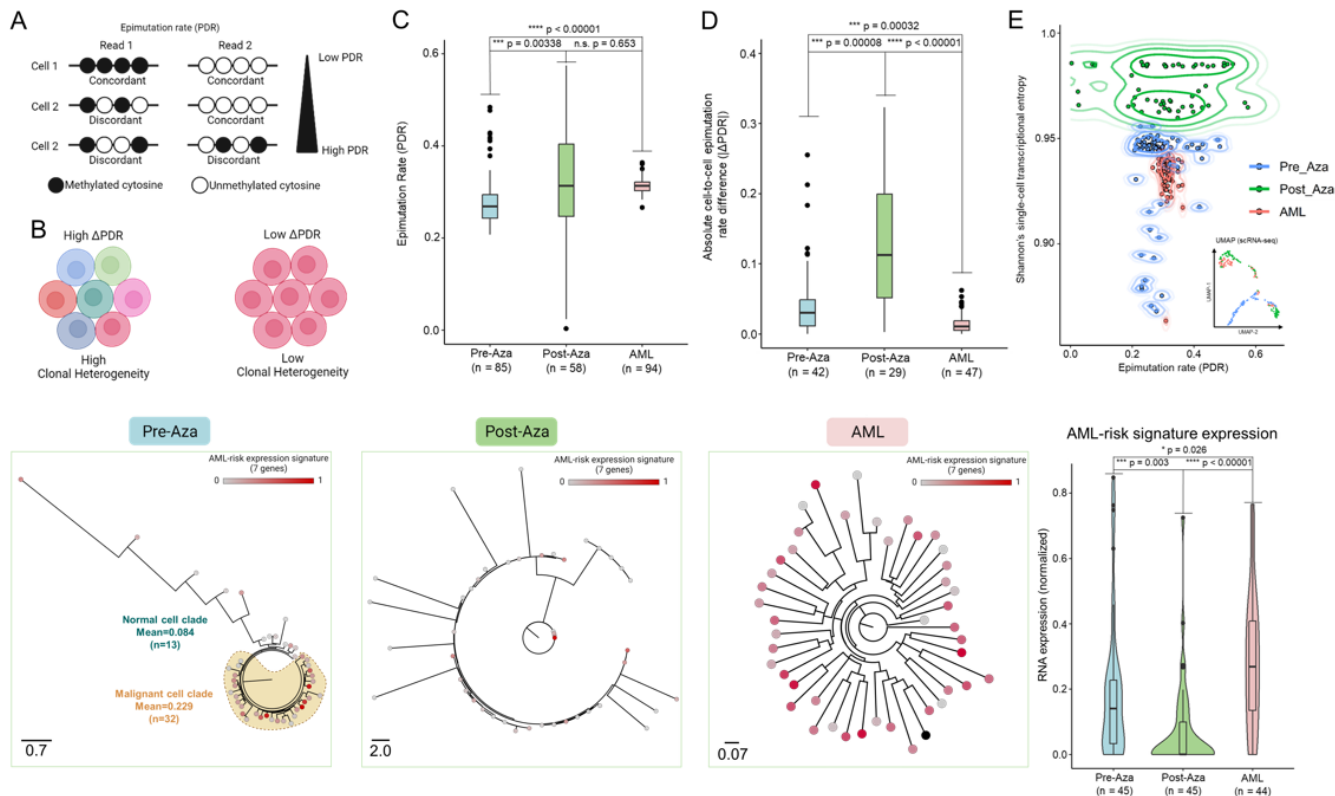
DNA Methylomes in MDS and 5-Azacitidine Treatment



Castells-Noguera A,
Campillo-Marcos I, et al.,
British Journal of
Haematology 2024



Single-Cell DNA Methylation Analysis





#5

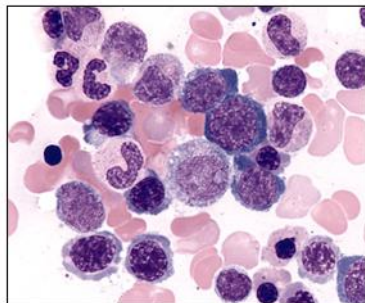
Unravelling the evolution of myelodysplastic syndromes upon 5-Azacytidine treatment through the use of single cell multi-omics approaches



Ignacio Campillo-Marcos

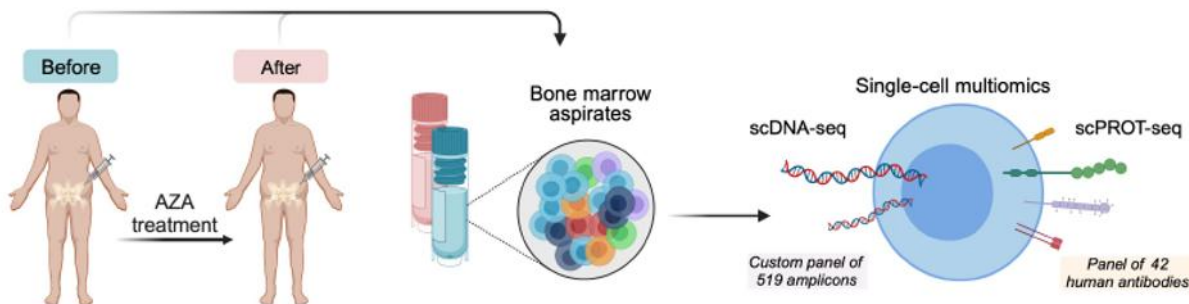


Marta Casado-Pelaez

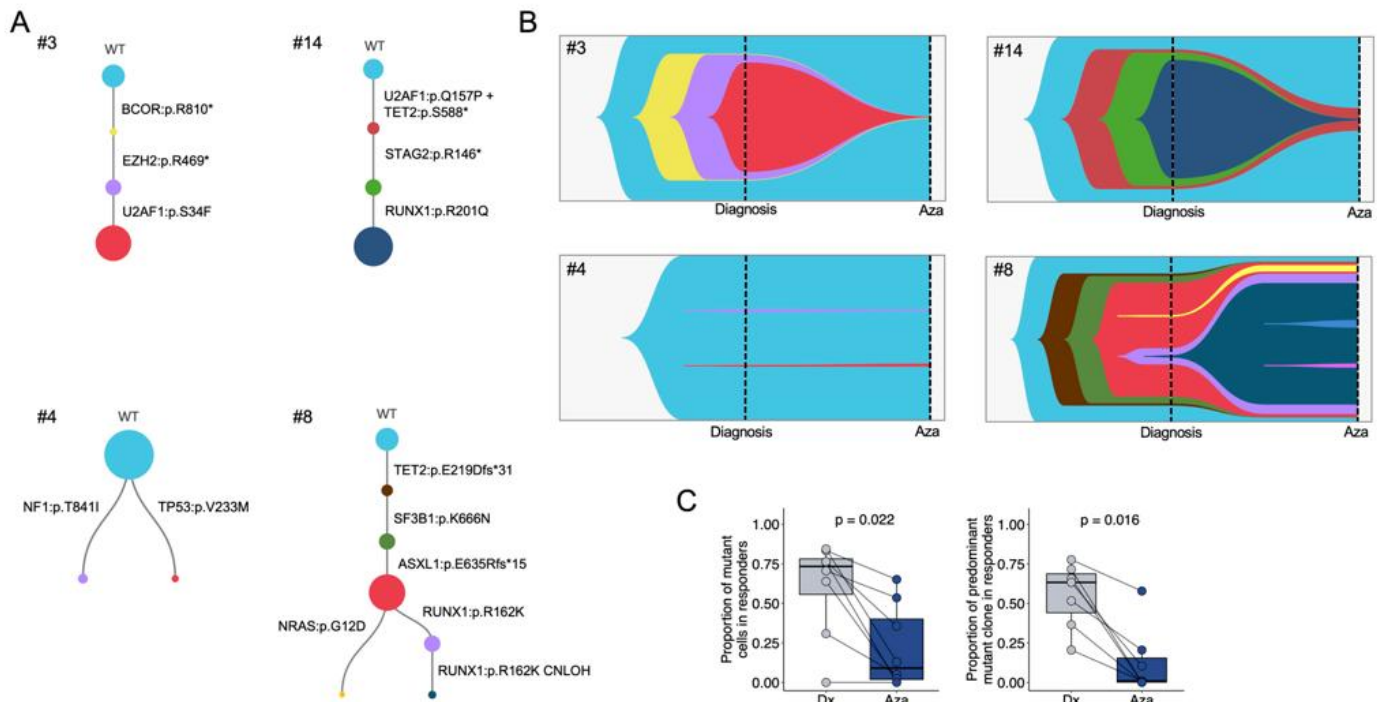


Myelodysplastic syndromes (MDS) are defined as a group of myeloid neoplasms characterized by inefficient haematopoiesis, morphologic dysplasia and peripheral cytopenia(s).

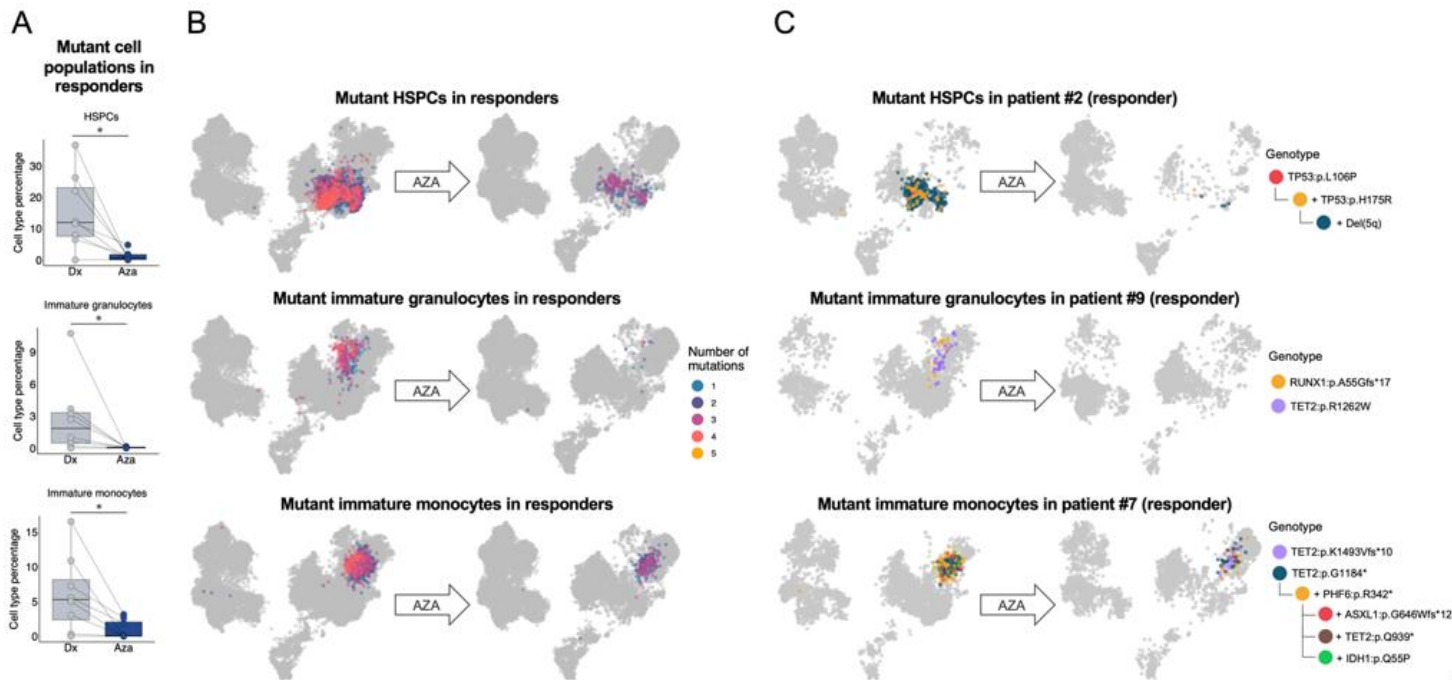
5-Azacytidine is a DNA hypomethylating agent frequently used to treat MDS.



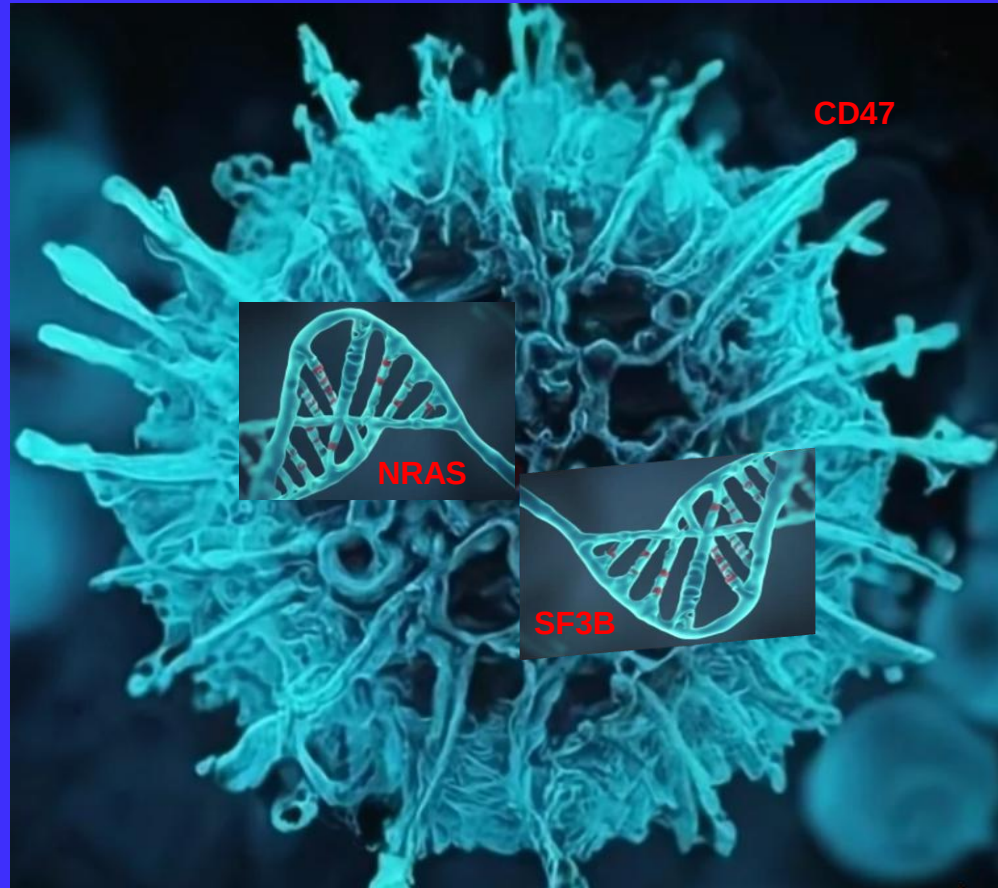
Single Cell Target Gene Sequencing in MDS Upon 5-Azacitidine Treatment



Single Cell Multiomics in MDS Upon 5-Azacitidine Treatment



For HMA Resistant MDS Patients: From Precision to Personalized Medicine



For HMA Resistant MDS Patients: From Precision to Personalized Medicine

