

GENETIC REPROGRAMMING OF TAMS BY ENGINEERED EXOSOMES RESULTS IN POTENT SINGLE AGENT ANTI-TUMOR ACTIVITY

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**AACR ANNUAL MEETING
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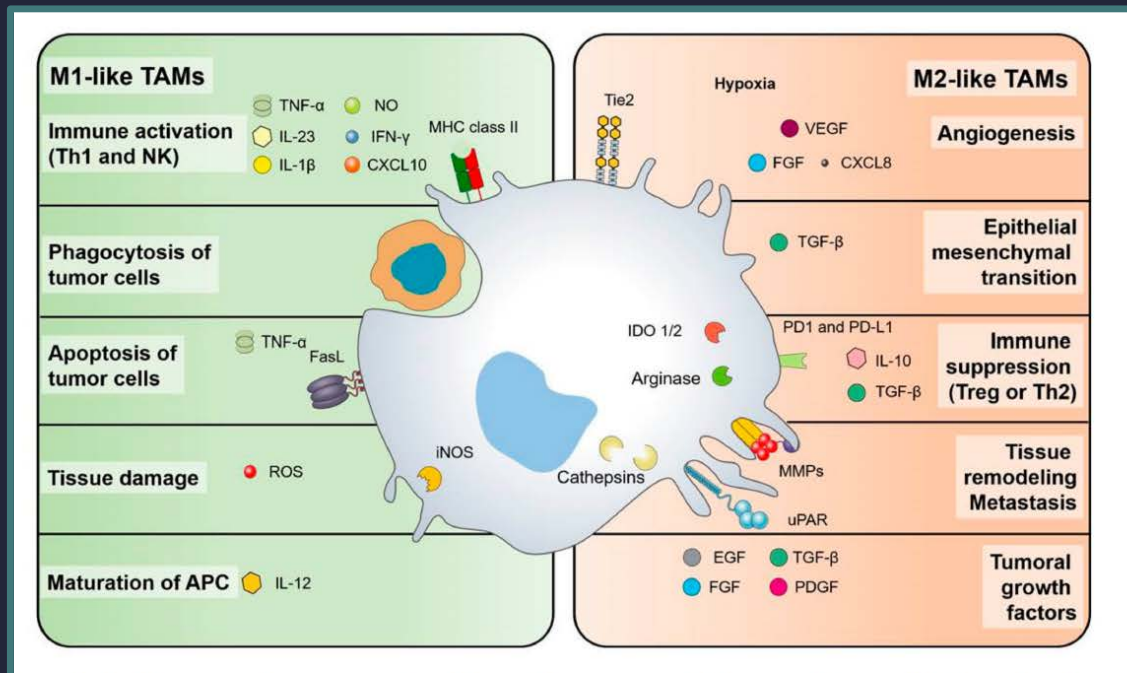
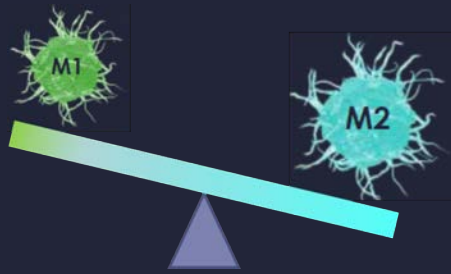
Disclosure Information

AACR Annual Meeting 2020

Dalia Burzyn

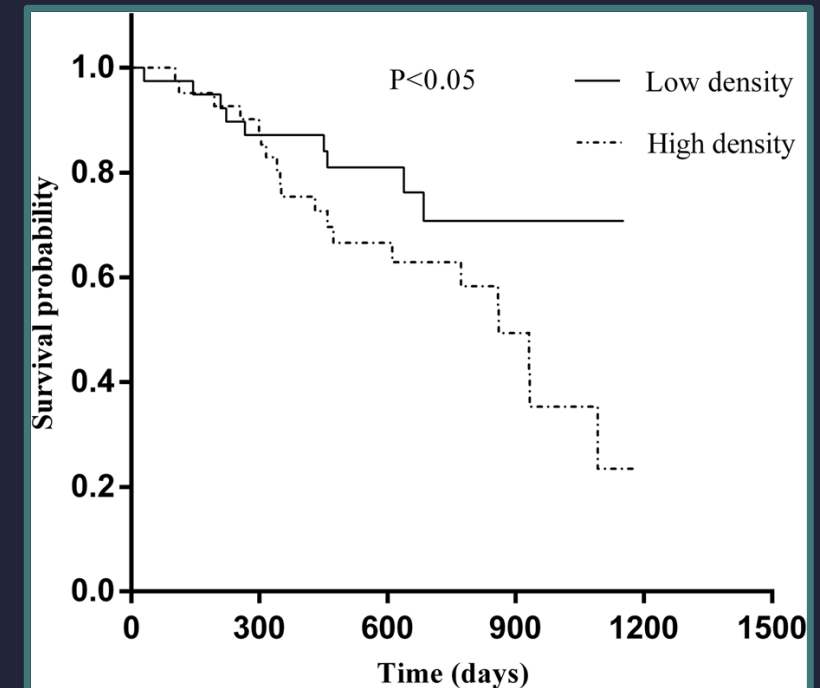
- I have the following financial relationships to disclose:
 - Employee of Codiak BioSciences
- I will not discuss off label use and/or investigational use in my presentation

M2-like tumor-associated macrophages (TAMs) promote cancer progression



Anfray et al. Cells, 9, 46, 2020

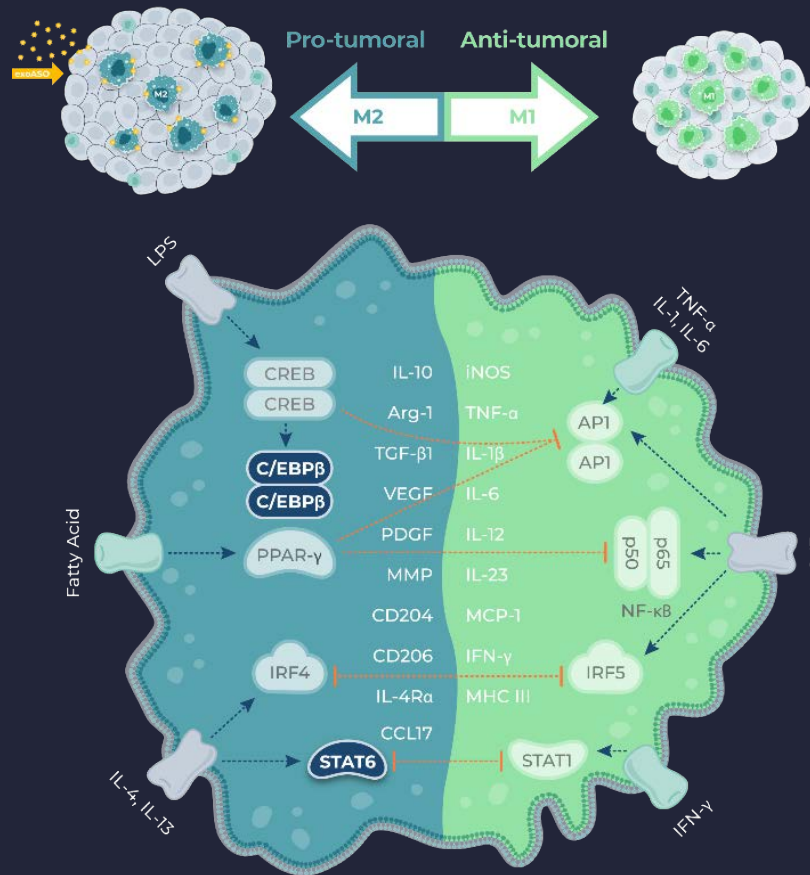
Total M2 macrophage density correlation to overall survival in lung cancer



Jackute et al. BMC Immunology 19:3, 2018

Reprogramming TAMs by targeting key “undruggable” pathways

TAM reprogramming



exoASO-STAT6 or C/EBPβ



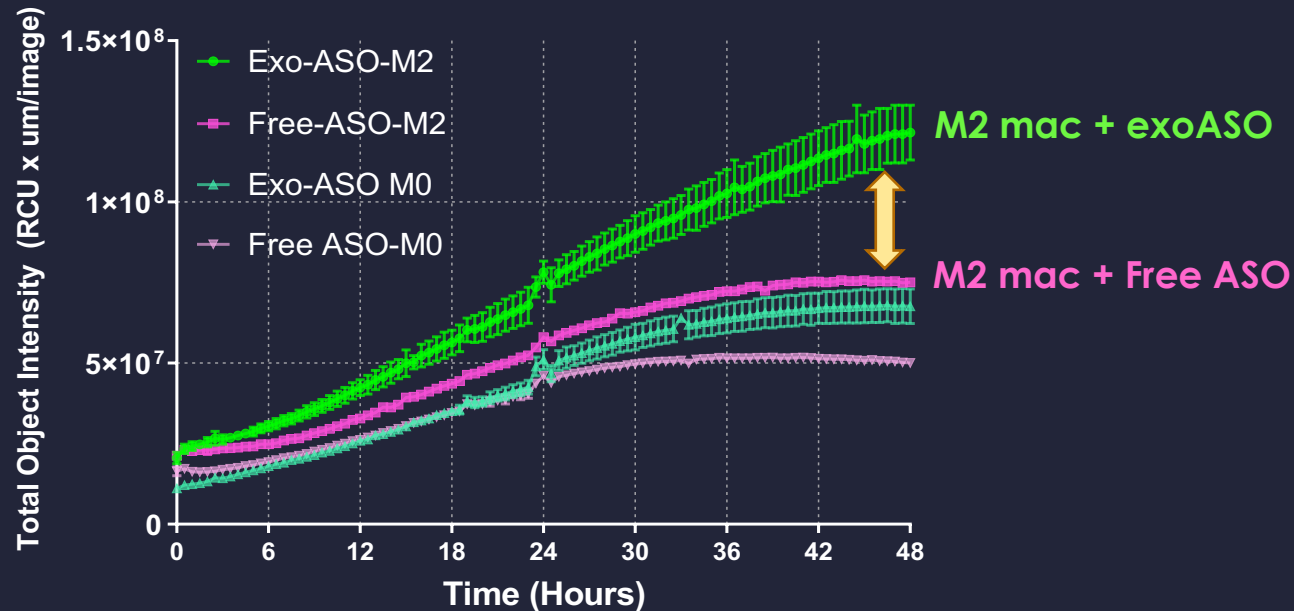
- Selective modulation of key M2 transcription factors by combining:
 - Preferential tropism of exosomes to myeloid cells
 - Codiak's exoASO™ platform to load exosomes with specific antisense oligonucleotides (ASOs)



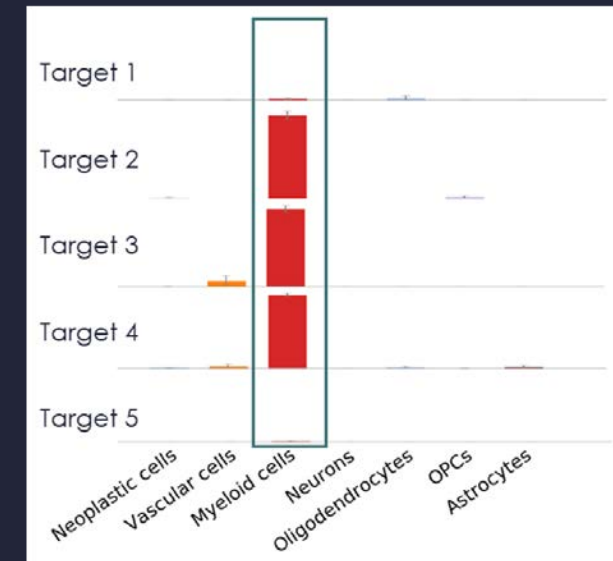
exoASO shows enhanced tropism to M2 macrophages *in vitro*

Exosome-mediated selective uptake
in human M2 macrophages

- Exosome surface protein PTGRFN may mediate selective delivery to macrophages and other myeloid cells via the cell type specific expression of its cognate receptors in these cells

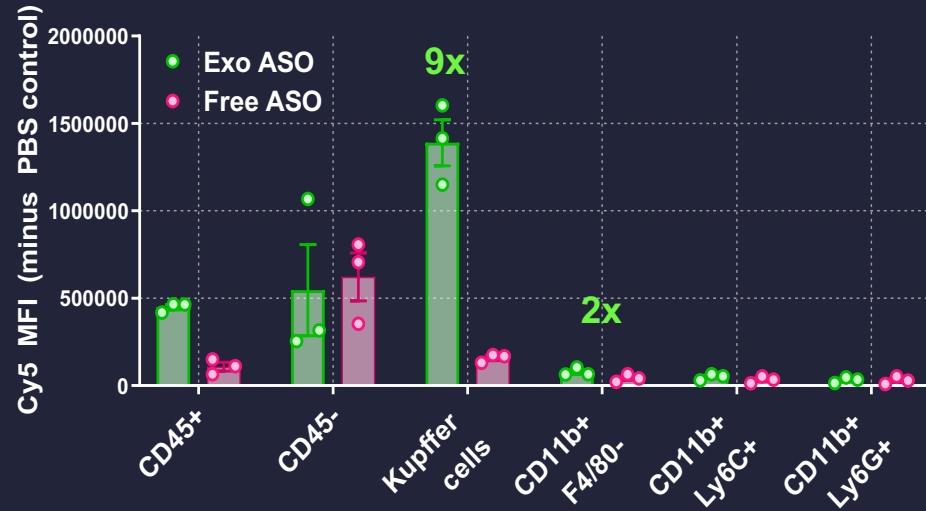


PTGRN cognate receptors in human GBM

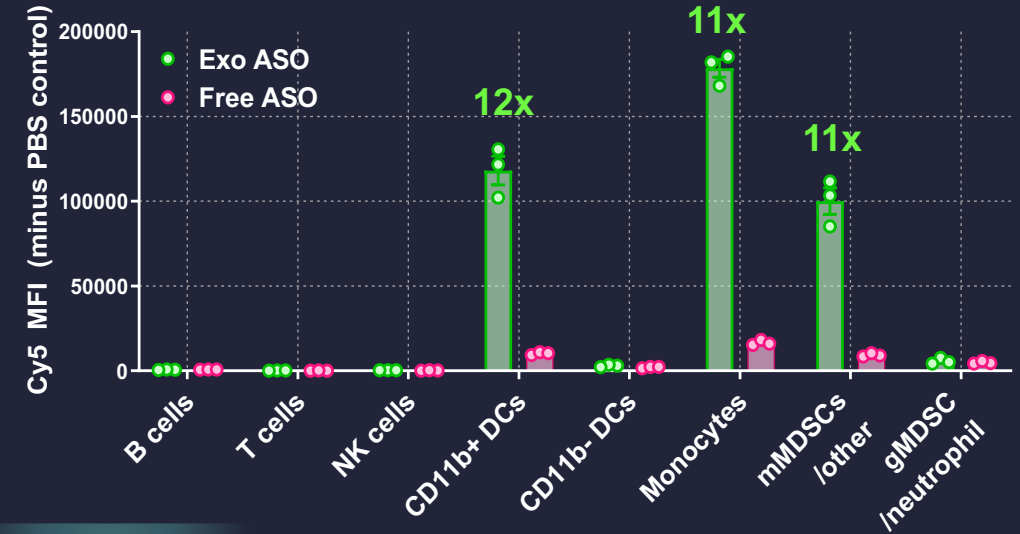


In vivo exosome-mediated selective delivery of ASOs to macrophages and MDSCs

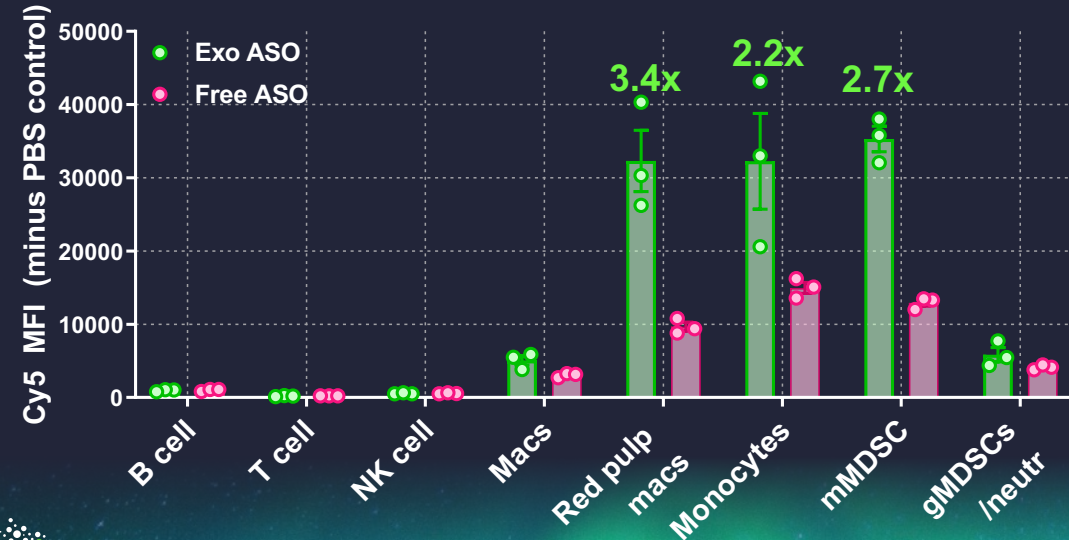
LIVER (IV)



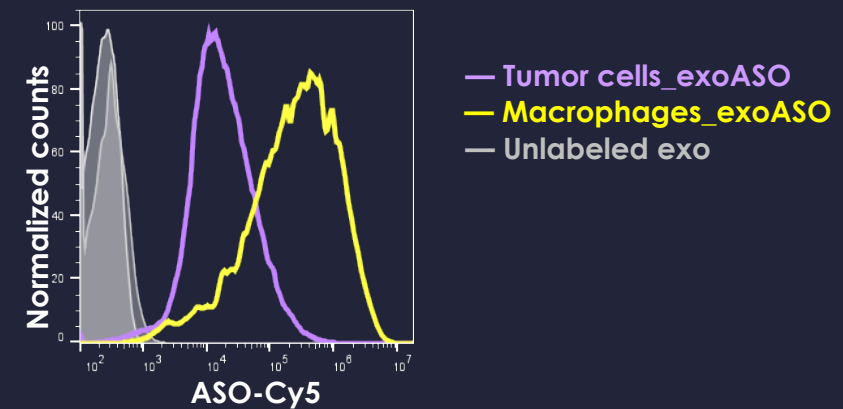
BLOOD (IV)



SPLEEN (IV)



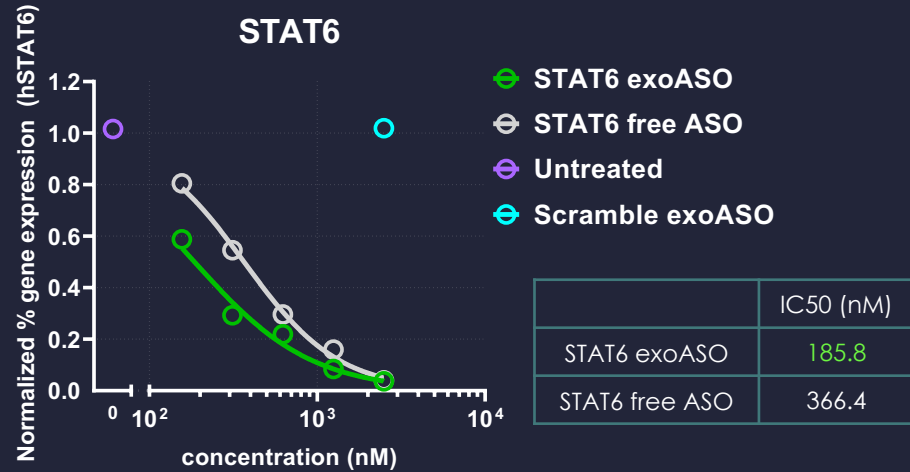
TUMOR (IT)



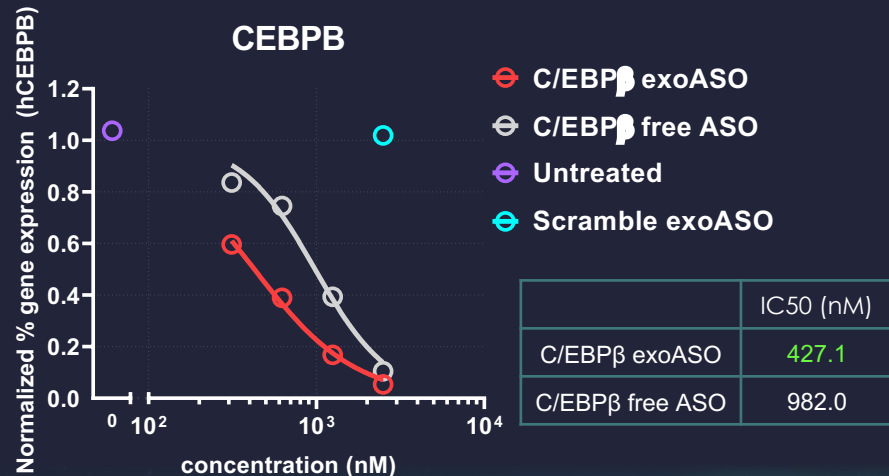
STAT6 and C/EBP β silencing by exoASO repolarizes primary human M2 macrophages *in vitro*

Target gene knockdown

STAT6

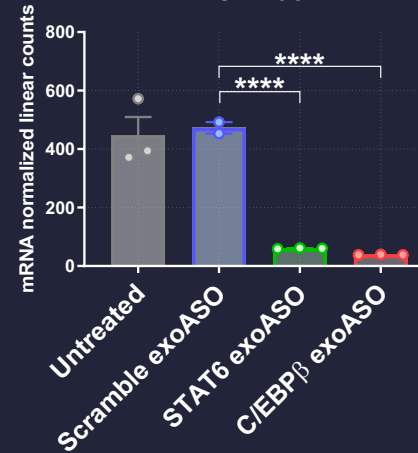


CEBPB



Effective macrophage reprogramming

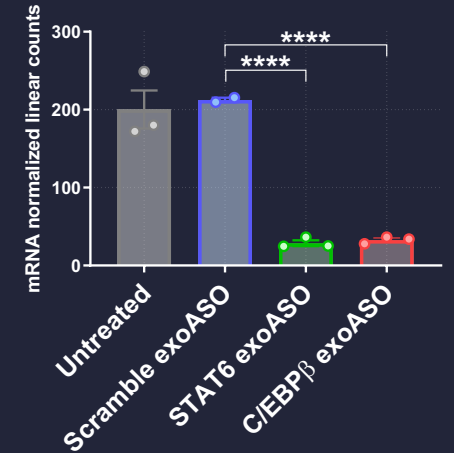
CD163



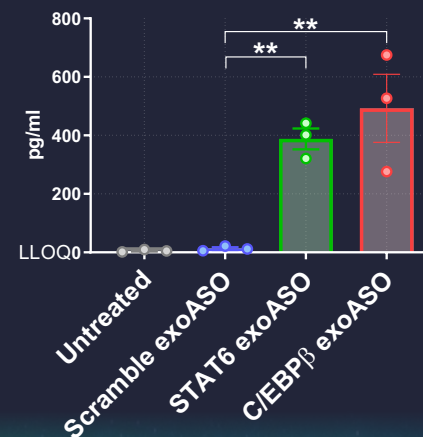
TGF β 1



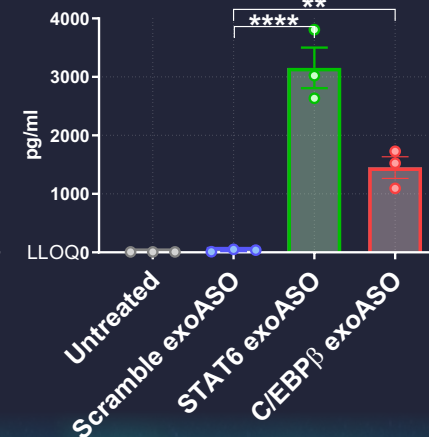
CD206



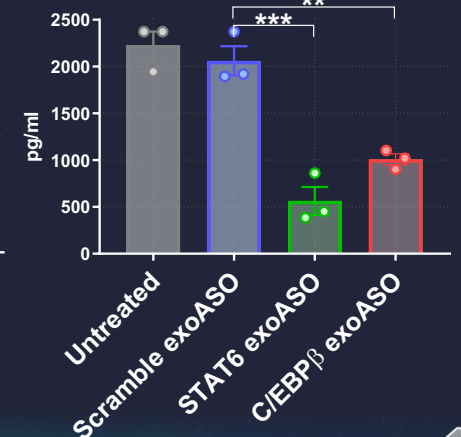
TNF α



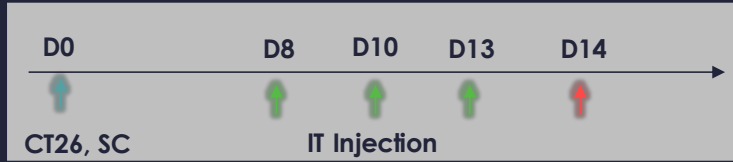
IL12p40



TARC/CCL17

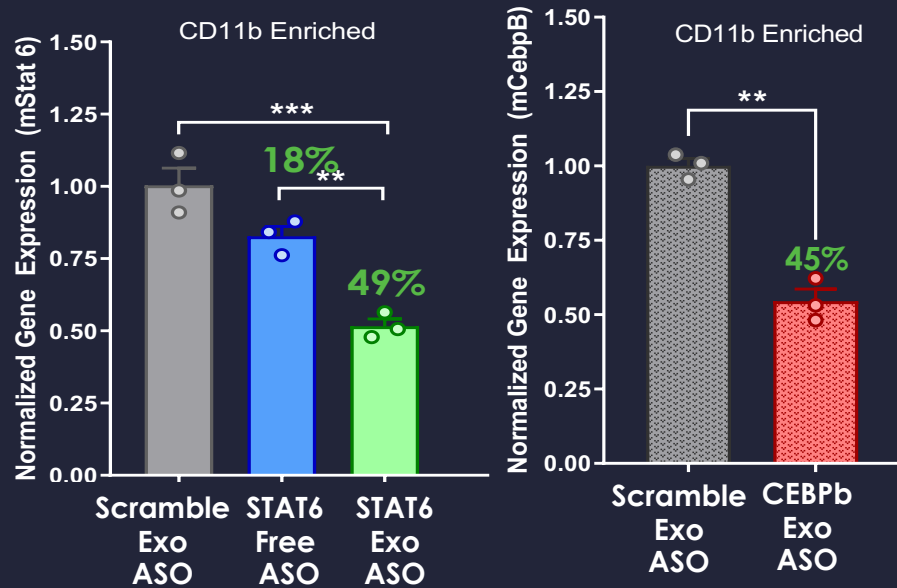


exoASO-STAT6 and C/EBP β induce *in vivo* knockdown and reprogramming of TAMs

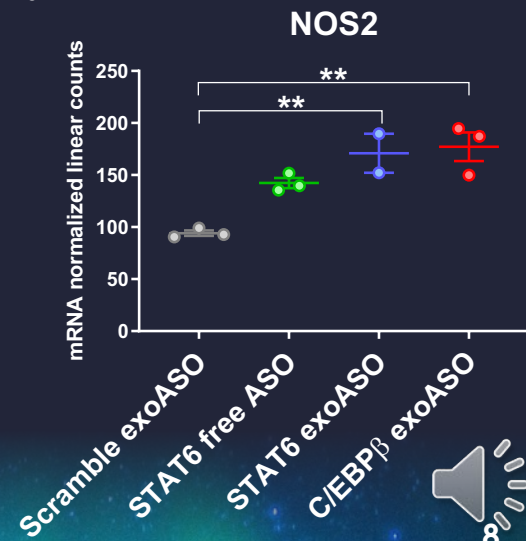
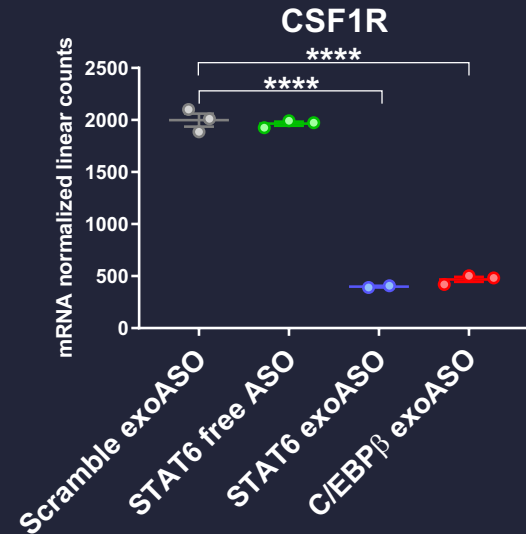
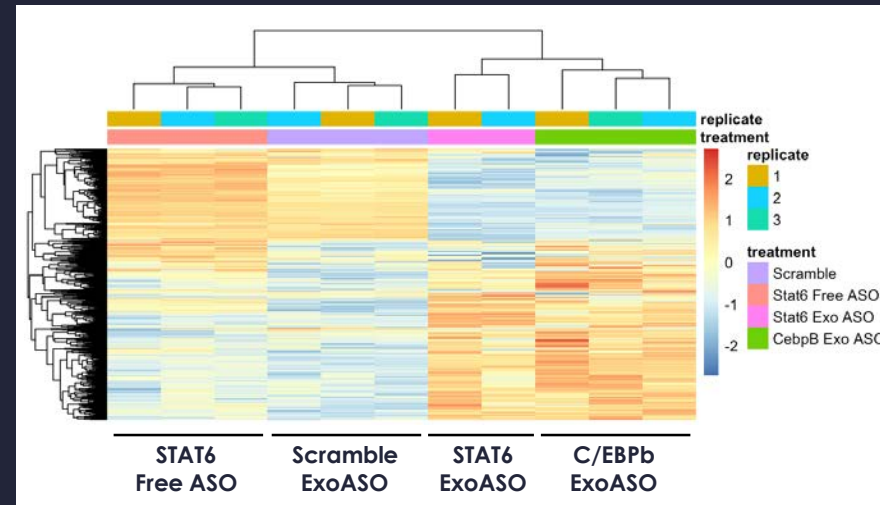


After intratumoral treatment, tumor-associated myeloid cells were isolated and gene expression was analyzed

Target gene knockdown



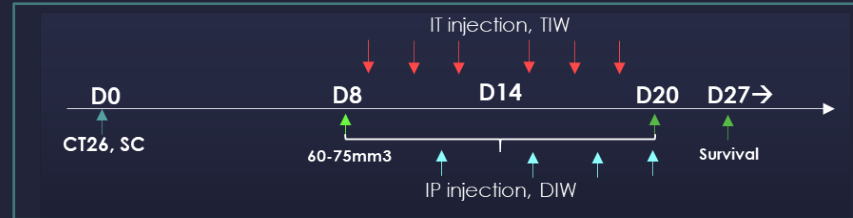
Reprogramming to anti-tumoral phenotype



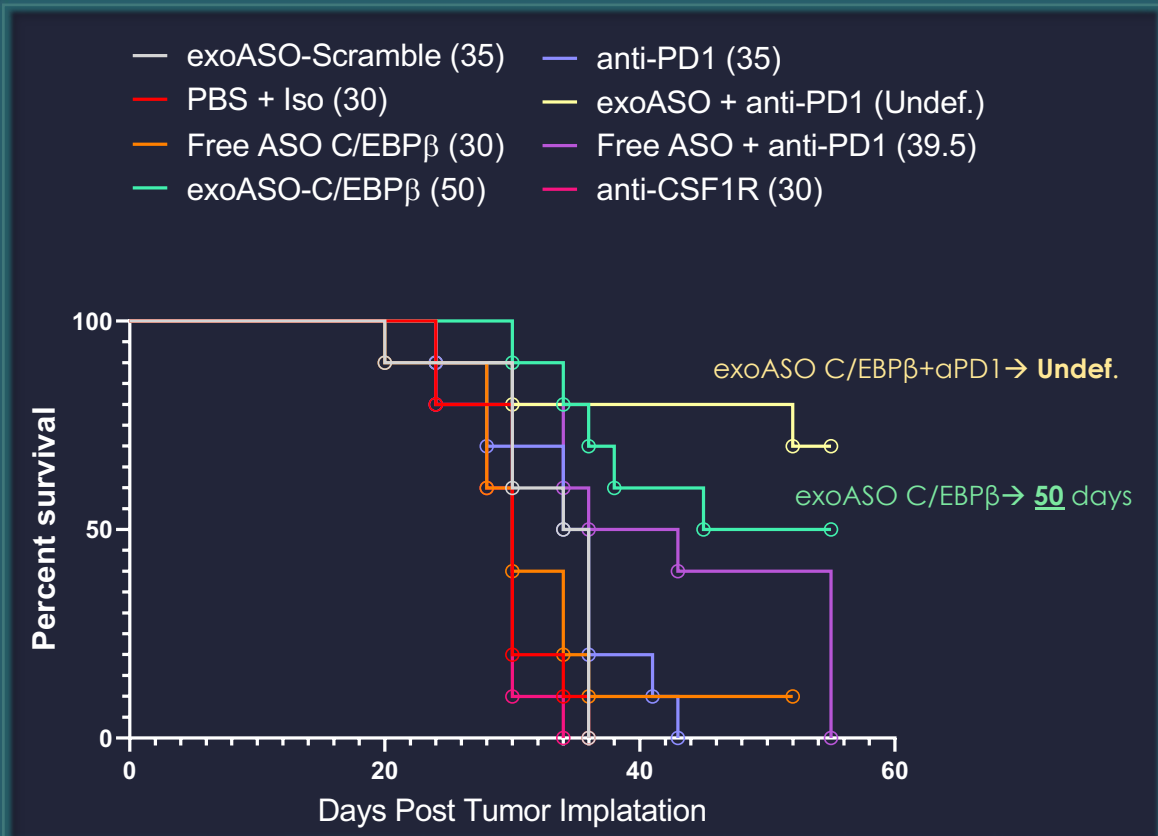
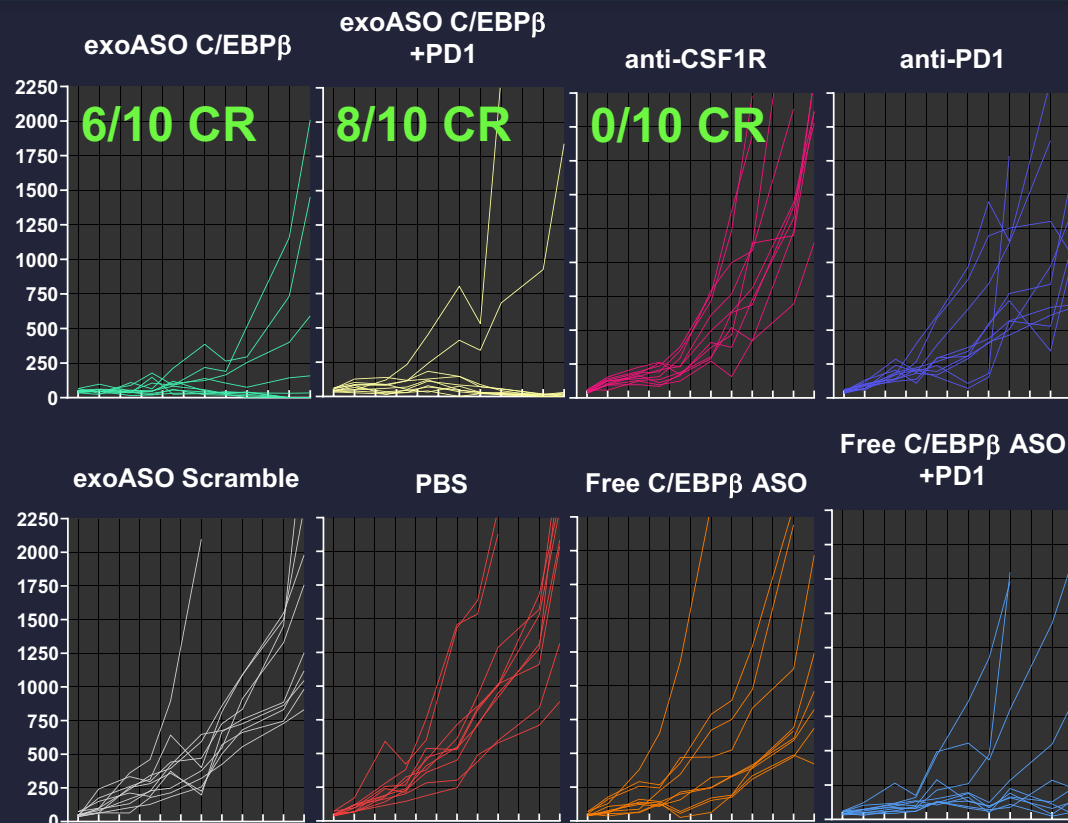
Potent monotherapy and combination antitumor activity with exoASO-C/EBP β and STAT6

* Similar anti-tumor activity with STAT6

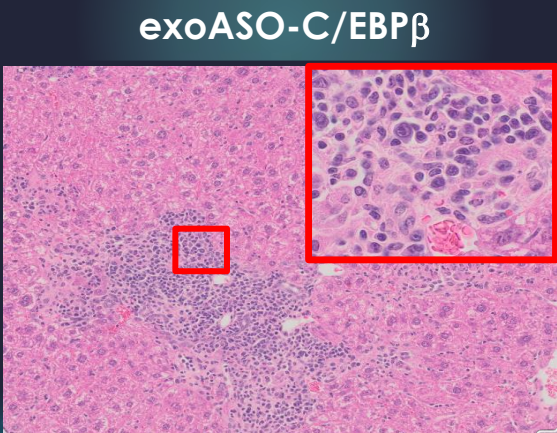
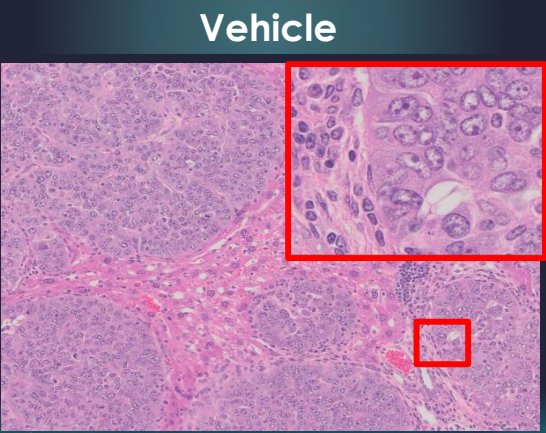
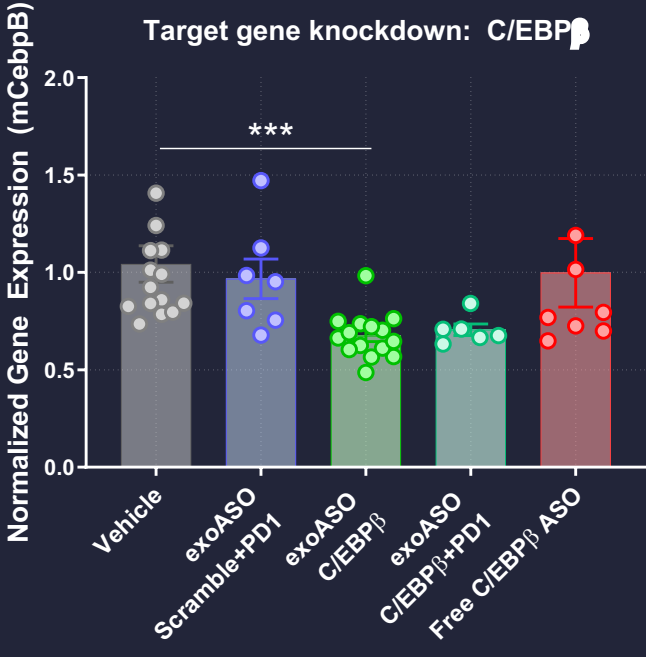
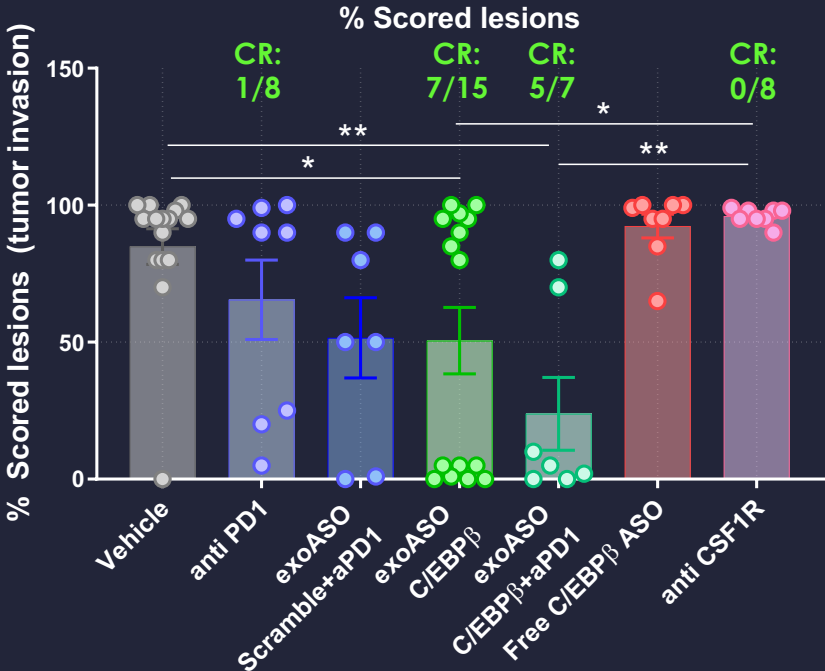
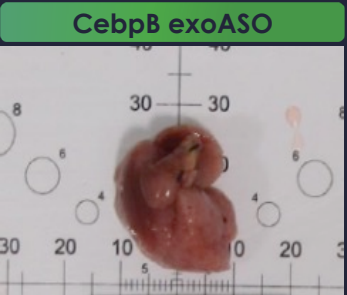
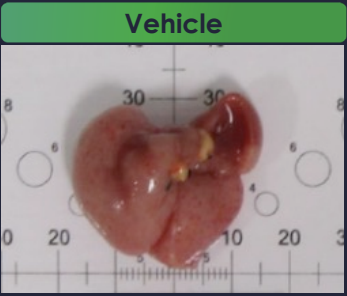
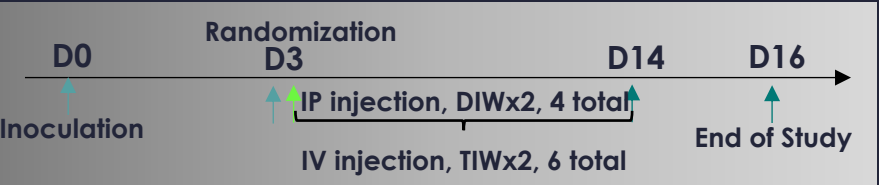
Antitumoral efficacy



Survival

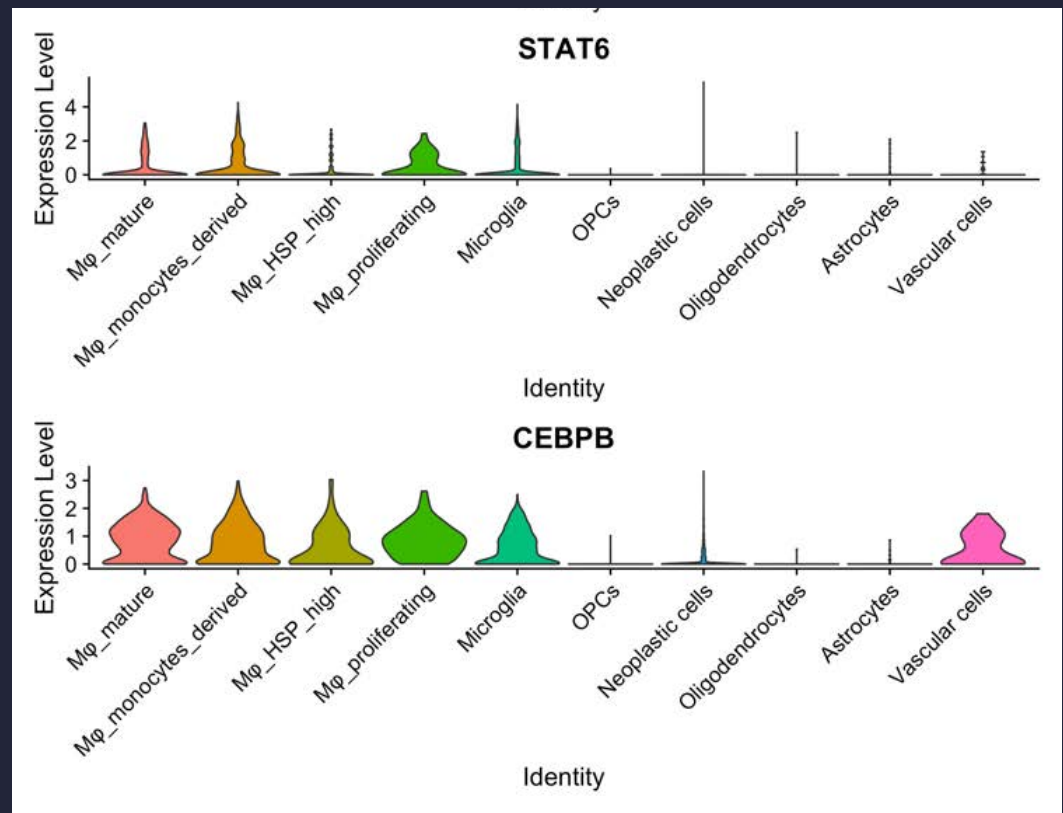


Systemic administration of exoASO-C/EBPβ results in potent anti-tumor response in an HCC model

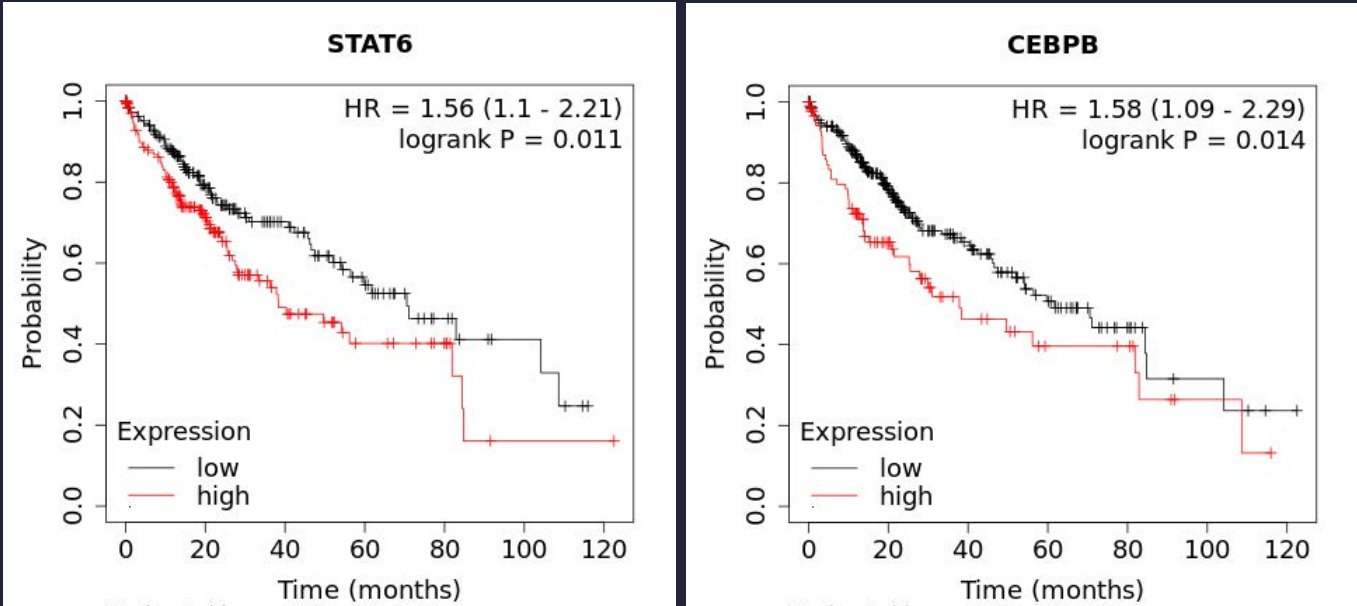


STAT6 and C/EBPβ are highly expressed in human tumor macrophages and correlate with poor prognosis

Expression in human GBM



Correlation with survival in human HCC



exoASO: a first-in-class strategy to target TAMs in a highly selective manner

exoASO-STAT6 or C/EBP β

- Developed a novel therapeutic to target and reprogram pathogenic M2 macrophages in cancer



DELIVERY TO TAMs

- Selective targeting of M2 macrophages in the tumor microenvironment (TME)

TARGETING STAT6 and C/EBP β

- Targeting STAT6 and C/EBP β induces higher target gene knockdown and superior macrophage reprogramming vs Free ASO, both in vitro and in vivo

ANTI-TUMORAL EFFICACY

- Treatment with exoASOs against STAT6 and C/EBP β results in potent anti-tumor efficacy via local and systemic administration

The logo graphic consists of a cluster of white circles of varying sizes, with one solid green circle positioned below the cluster, partially overlapping the letter 'I' in the word 'CODIAK'.

CODIAK
