



XIX CONGRESSO
NAZIONALE
SIES 2026

**TARGETING IDO1 AND ATP CATABOLISM
OVERCOMES THE TOLEROGENIC EFFECTS OF
CYTARABINE ON ACUTE MYELOID LEUKEMIA
IMMUNE MICROENVIRONMENT**

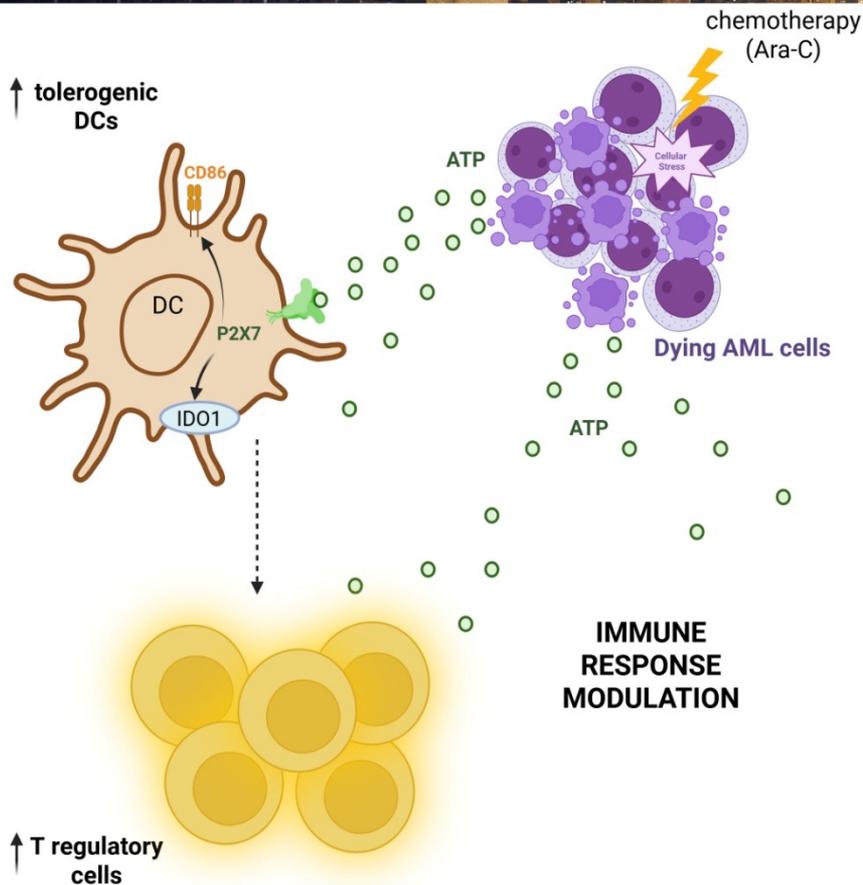
Darina Ocadlikova, *IRCCS Azienda Ospedaliero Universitaria di Bologna*

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Palazzo degli Affari



Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other



CHEMOTHERAPY

DIRECT CYTOTOXIC EFFECT

MODULATION OF IMMUNE RESPONSE THROUGH THE RELEASE OF ATP by chemotherapy-treated AML cells

SHAPING OF ANTI-TUMOR IMMUNITY BY DCs AND T REGULATORY CELLS

•Ocadlikova D et al. ATP Release from Chemotherapy-Treated Dying Leukemia Cells Elicits an Immune Suppressive Effect by Increasing Regulatory T Cells and Tolerogenic Dendritic Cells. *Front Immunol.* 2017 Dec 22;8:1918.

•Ocadlikova D et al. Noncanonical NF- κ B signaling in dendritic cells is required for ATP-driven indoleamine 2,3-dioxygenase 1 induction through P2Y11 receptor. *J Leukoc Biol.* 2025 Apr 23;117(4).



OBJECTIVE

Impact of ATP signaling and its catabolism on the leukemia immune microenvironment following chemotherapy in different murine AML models

METHODS

Murine AML cell lines

- WT and P2X7R KO BALB/c mice injected with WEHI-3B AML cells
- intra-bone injections of B/6-derived C1498 AML cell lines for combination therapy experiments

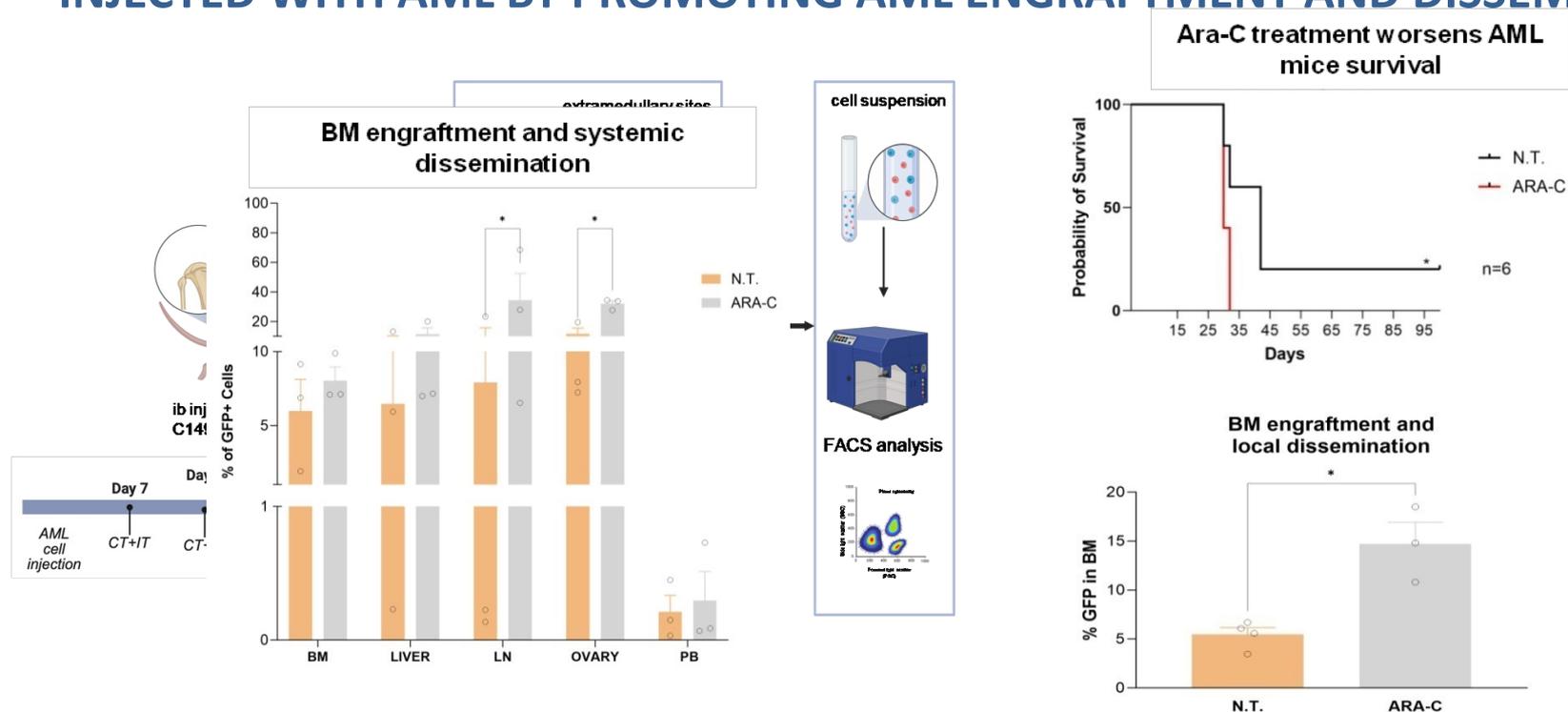
Treatment

Ara-C (day 9 and 11 post-AML cell injection)

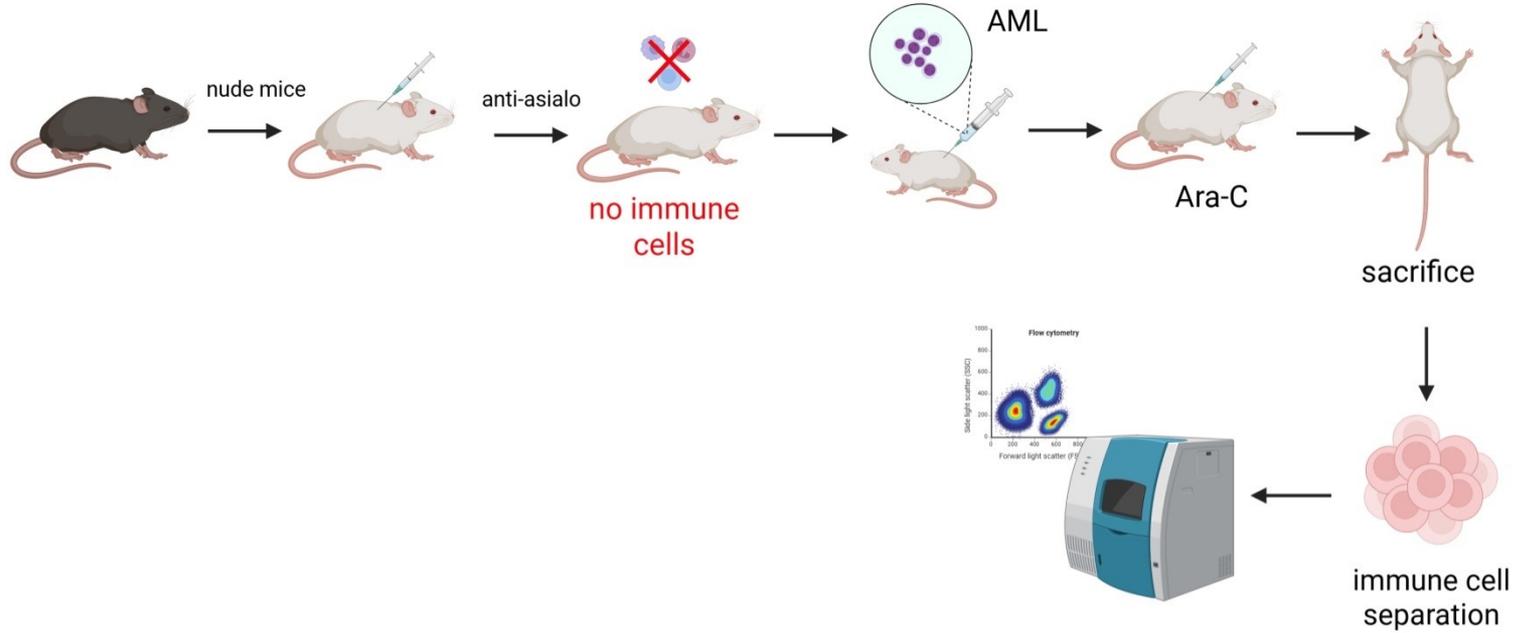
Analysis

analysis of infiltrating DCs and T cells by FACS

ARA-C TREATMENT PARADOXICALLY REDUCED SURVIVAL PROBABILITY OF MICE INJECTED WITH AML BY PROMOTING AML ENGRAFTMENT AND DISSEMINATION

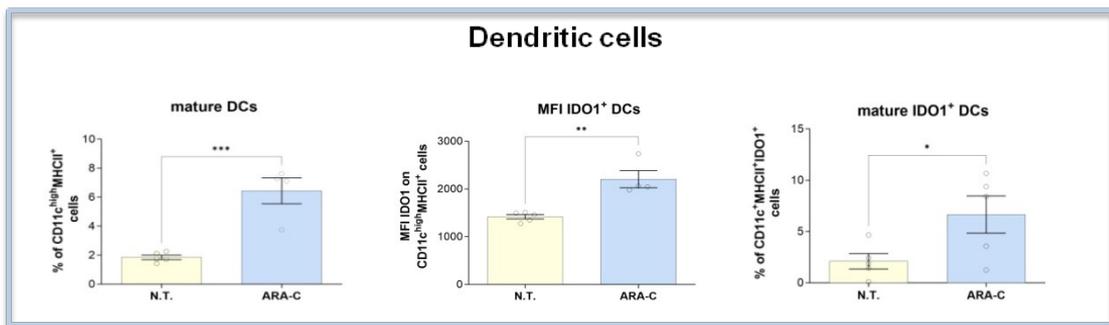
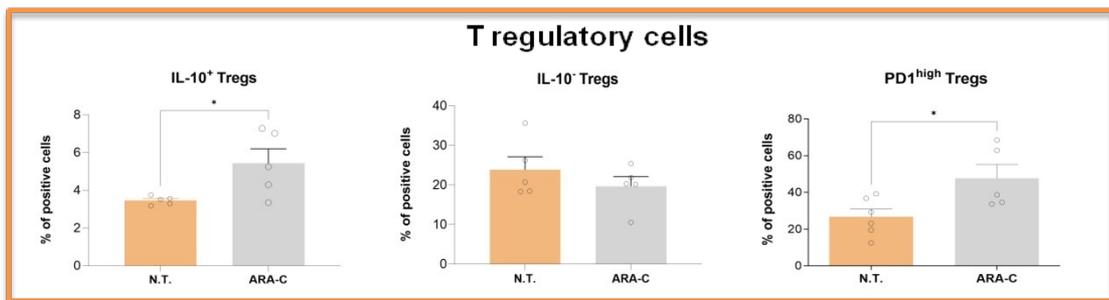
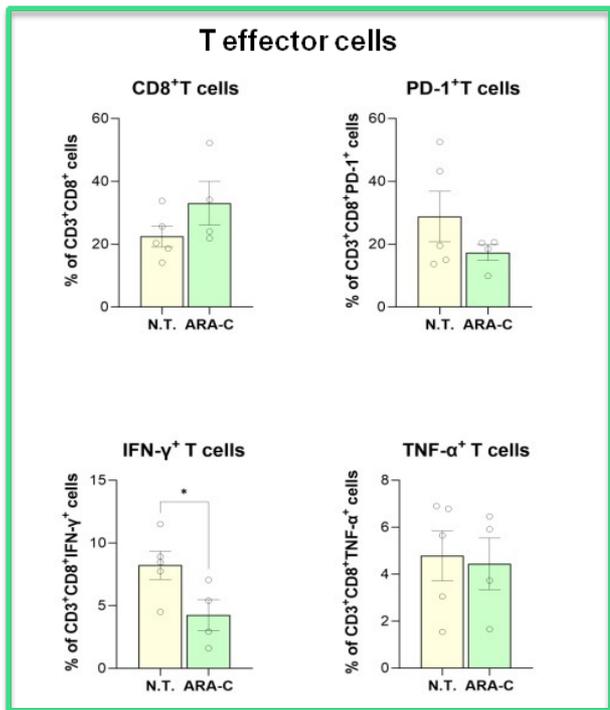


THIS EFFECT WAS TOTALLY ABROGATED IN IMMUNODEFICIENT MICE SUGGESTING THE INVOLVEMENT OF THE IMMUNE SYSTEM



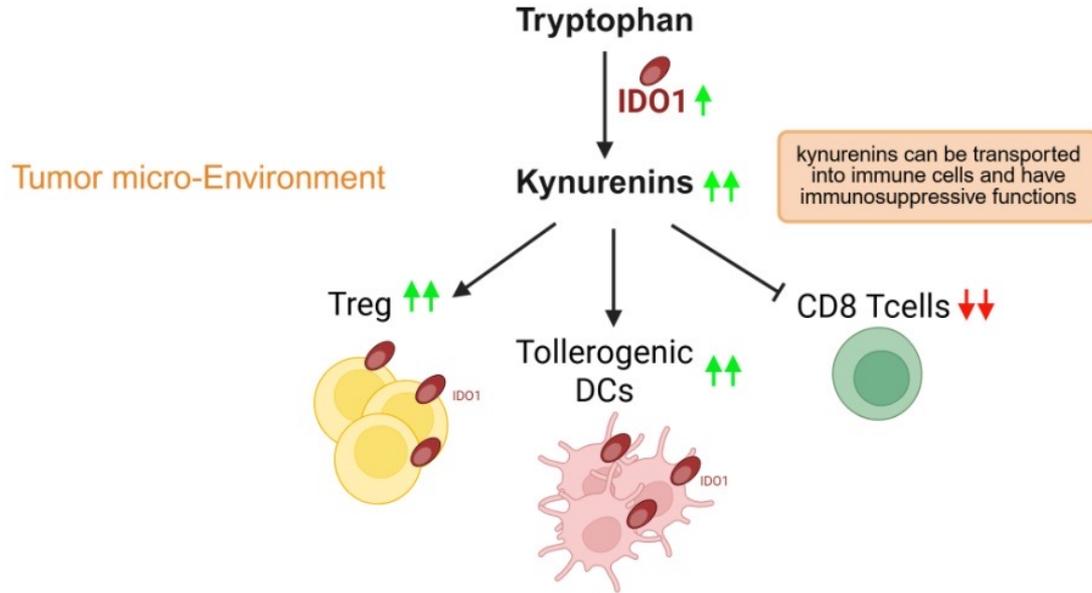
Nude mice experiments: immune system is implicated in Ara-C-mediated engraftment and dissemination

ARA-C TREATMENT: TOLLEROGENIC EFFECT ON IMMUNE MICROENVIRONMENT-FOCUS ON T CELLS AND DENDRITIC CELLS

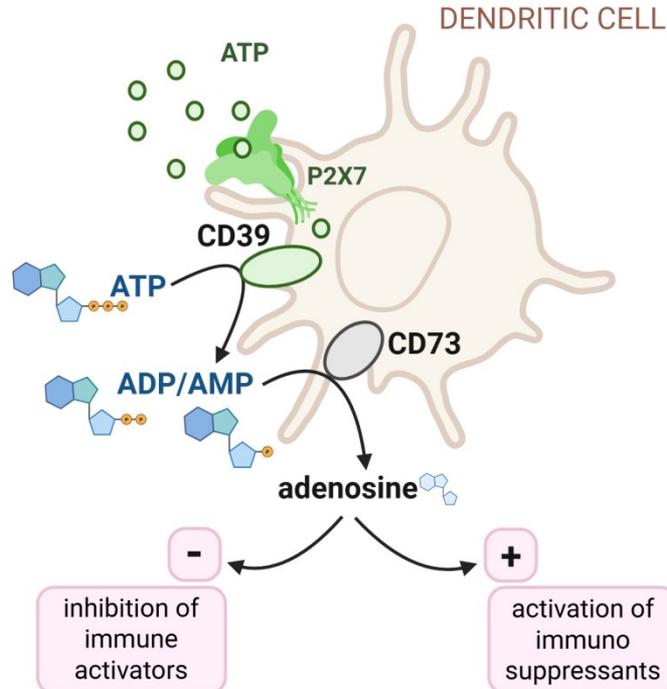


ROLE OF IDO1 IN TUMOR MICROENVIRONMENT: INHIBITION OF T-CELL RESPONSE THROUGH IDO1 EXPRESSION ON IMMUNE CELLS

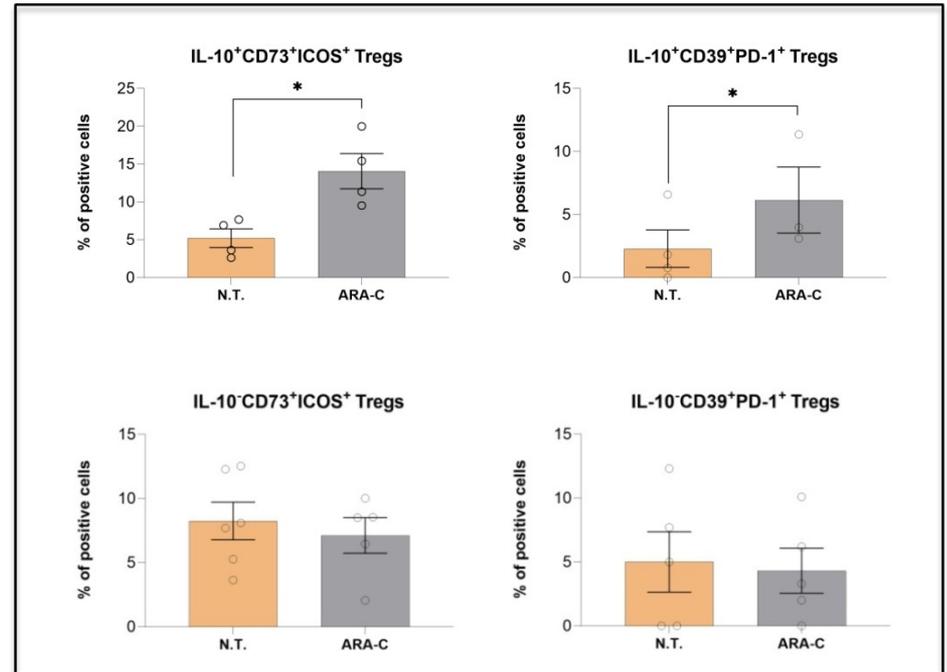
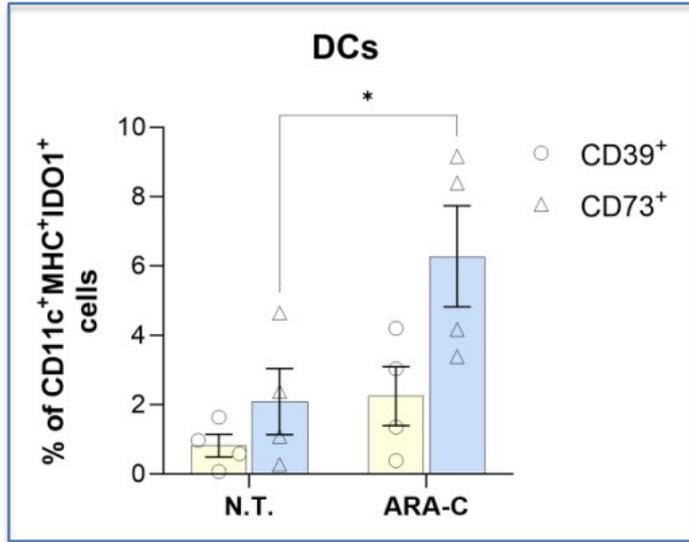
Immune regulation through tryptophan metabolism



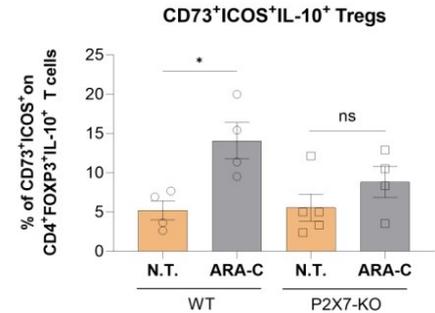
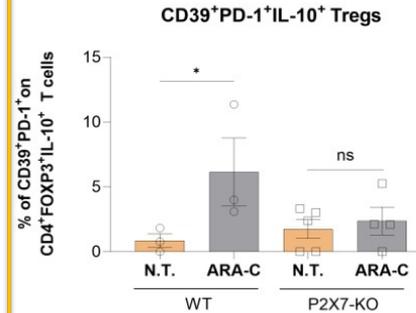
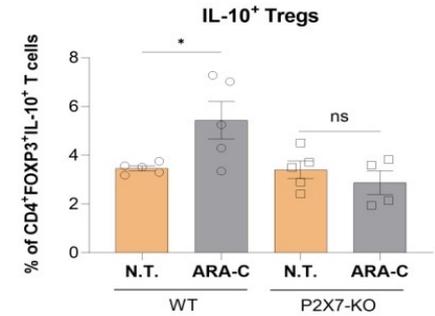
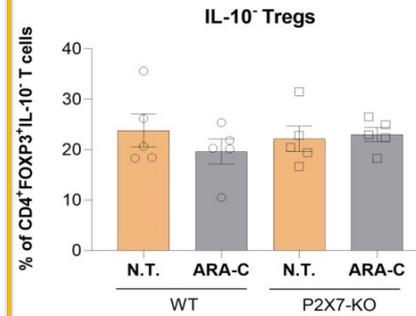
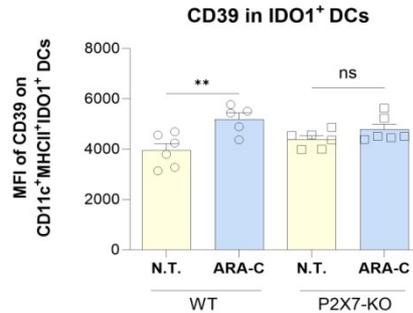
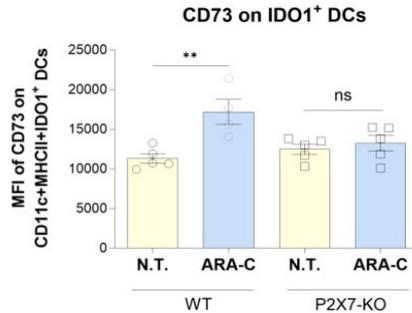
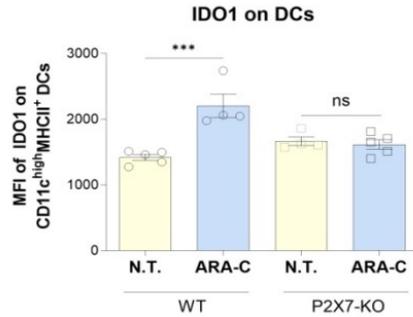
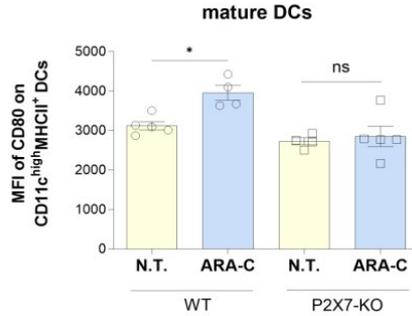
ROLE OF ATP CATABOLISM IN TUMOR MICROENVIRONMENT: MODULATION OF T-CELL RESPONSE THROUGH CD39 and CD73 EXPRESSION ON IMMUNE CELLS



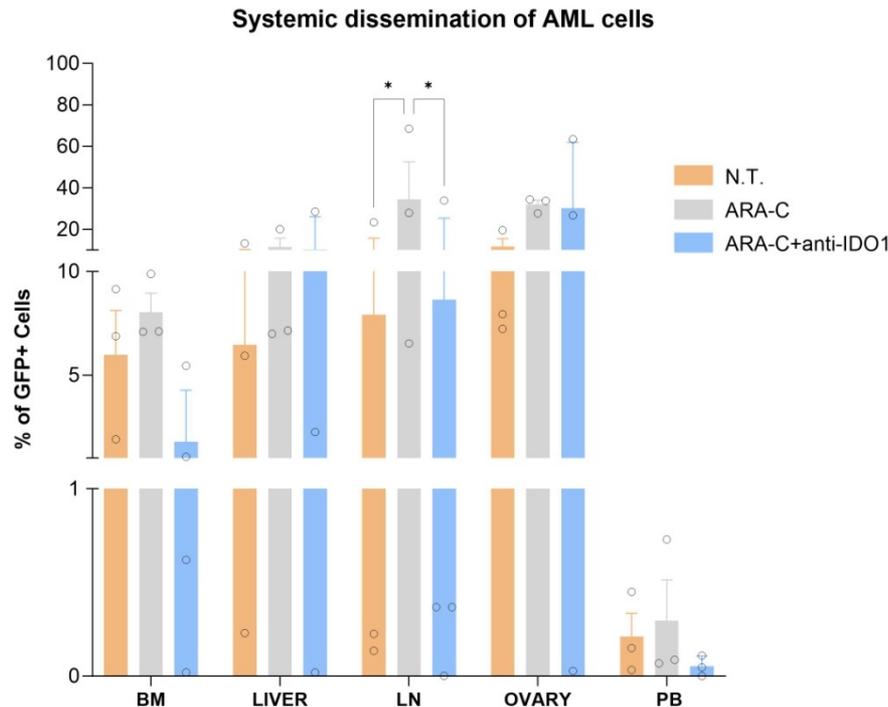
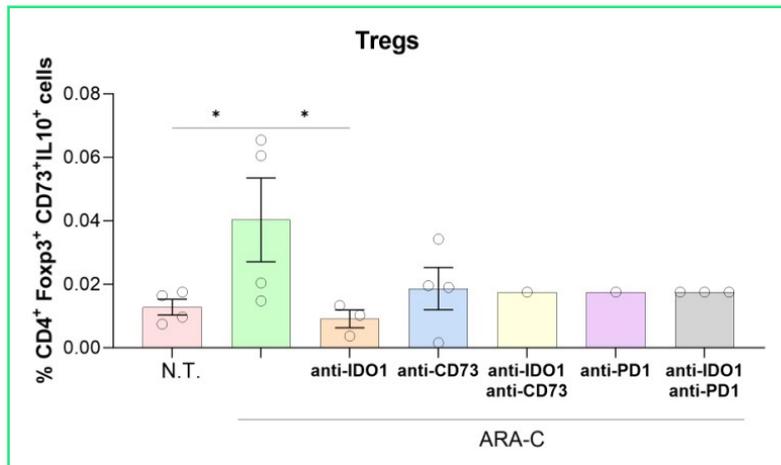
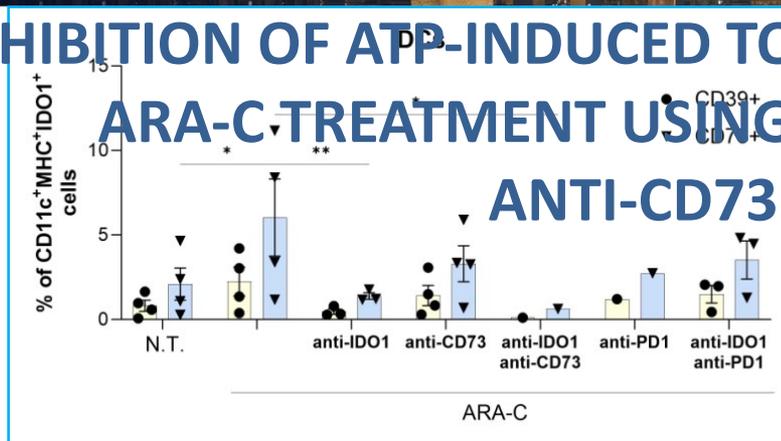
INCREASE OF CD39 AND CD73 ECTONUCLEOTIDASES EXPRESSION ON IDO1⁺ CD11c^{high} DCs AND IL-10⁺ TREGS AFTER ARA-C TREATMENT

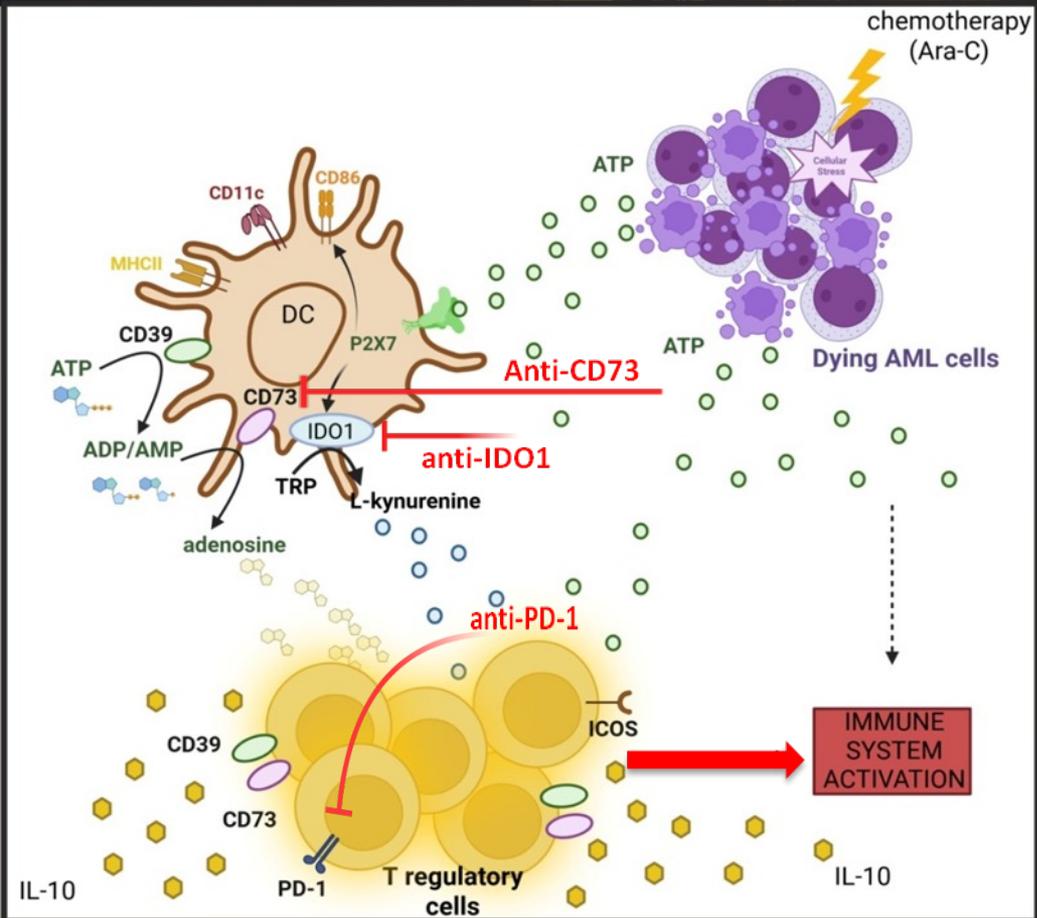


ATP INCREASES TOLEROGENTIC IMMUNE CELL POPULATIONS FOLLOWING ARA-C TREATMENT IN AML



INHIBITION OF ATP-INDUCED TOLLEROGENIC MECHANISMS DURING ARA-C TREATMENT USING IMMUNE INHIBITORS ANTI-IDO1, ANTI-CD73, ANTI-PD1





Ara-C may promote the induction of tolerogenic immune microenvironment through ATP–IDO1–dependent activation of regulatory DCs and Tregs in AML

Strong mechanistic rationale for combining immunotherapy such as anti-IDO1 and anti-CD73 with chemotherapy to counteract or disrupt such tolerogenic mechanisms, thereby restoring effective antitumor immune responses

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