Immunostimulatory nanofilaments turn cancer cells into neoantigen agnostic cancer vaccines

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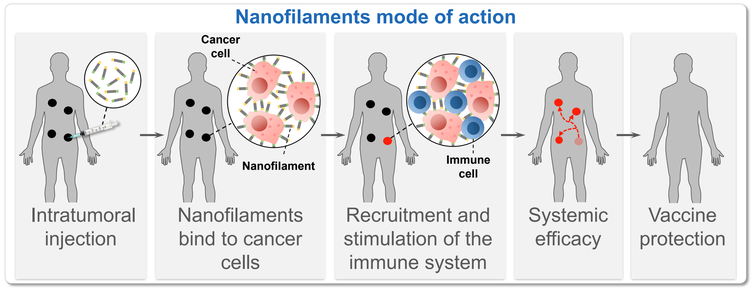
1-TATUM bioscience. 2-MISO chip.

Abstract # 1314

INTRODUCTION

- **Checkpoint inhibitor** treatment **require pre-existing anti-tumor T cells** for efficacy, which are **often inactive or lacking** in patients (Zheng *et al.* 2022).
- **Personalized cancer vaccines** can generate educated T cell populations, but demands **excessive investment in time and resources**, making it impractical to scale (Weber *et al.* 2024, O'Leary 2024)
- **TATUM bioscience** is developing **a new class of immunotherapy called nanofilament**, which **binds to cancer cells** and **transforms them into immunological targets**, leveraging cancer cells as the source of antigens for *in situ* vaccination.



RESULTS

IN VITRO DISPLAY VALIDATION

By engineering filamentous M13 bacteriophage to display therapeutic proteins iteratively, **we selected TAT003 as our lead candidate**:

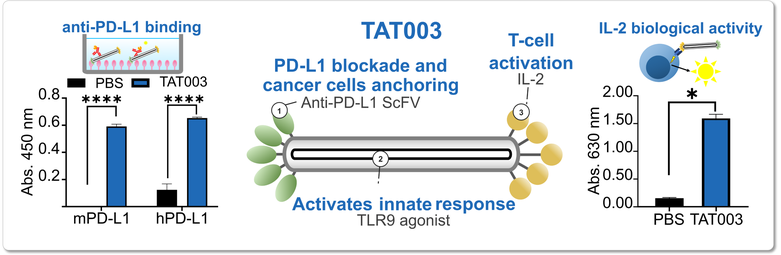
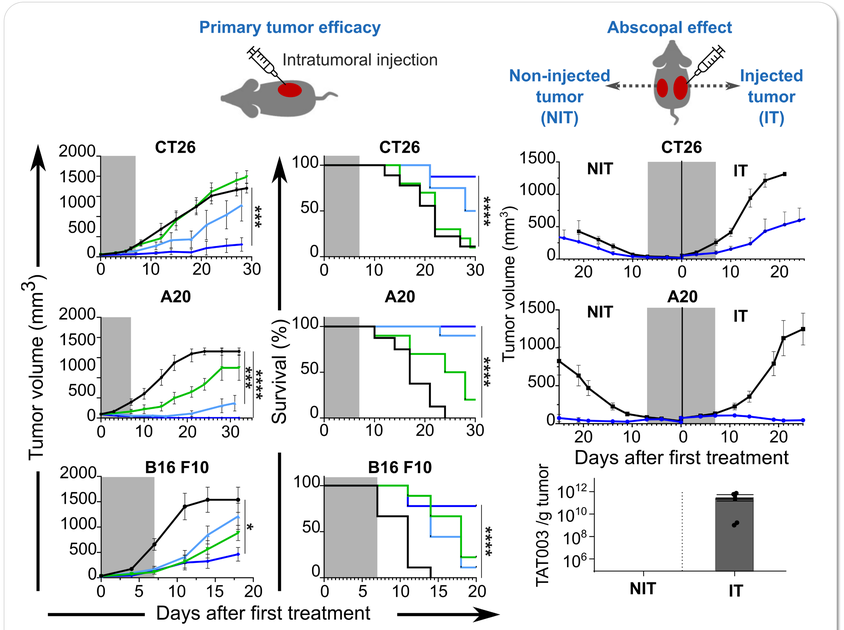


Figure 1: TAT003 displays biologically active anti-PD-L1 and IL-2 molecules. The biological activity of anti-PD-L1 and IL-2 molecules on TAT003 was confirmed by PD-L1 coated ELISA (n=3) and cell assay using HEK Blue IL-2 (n=3). Statistics One-way ANOVA *: P<0.05, ****: P<0.0001

RESULTS (CONTINUED)

EFFICACY MOUSE STUDY



Primary tumor C.R. rates

	CT26	A20	B16 F10
PBS	0/9	0/8	0/9
M13	0/10	2/10	1/9
TAT003ΔIL2	2/8	6/10	0/9
TAT003	3/7	8/8	1/9

Abscopal C.R. rates

		CT26	A20
PBS	IT	0/9	0/15
	NIT	0/9	0/15
TAT003	IT	3/9	16/18
	NIT	3/9	15/18

Figure 2. TAT003 efficacy in syngeneic mouse models. Efficacy of TAT003 treatment in the CT26, A20 and B16 F10 models. TAT003 was administered on day 0, 3 and 7 as highlighted by the gray shading. Efficacy was further evaluated in multi-tumor CT26 and A20 models by injecting TAT003 only in the tumor located on the right flank. The presence of TAT003 particles in injected and non-injected tumors was investigated by qPCR the day after the last treatment. C.R. = Complete remission, Statistics: One way ANOVA for Tumor growth, Mantel-Cox for survival, *: P<0.05, *** P<0.001, ****P<0.0001.

RESULTS (CONTINUED)

IMMUNE PROFILING

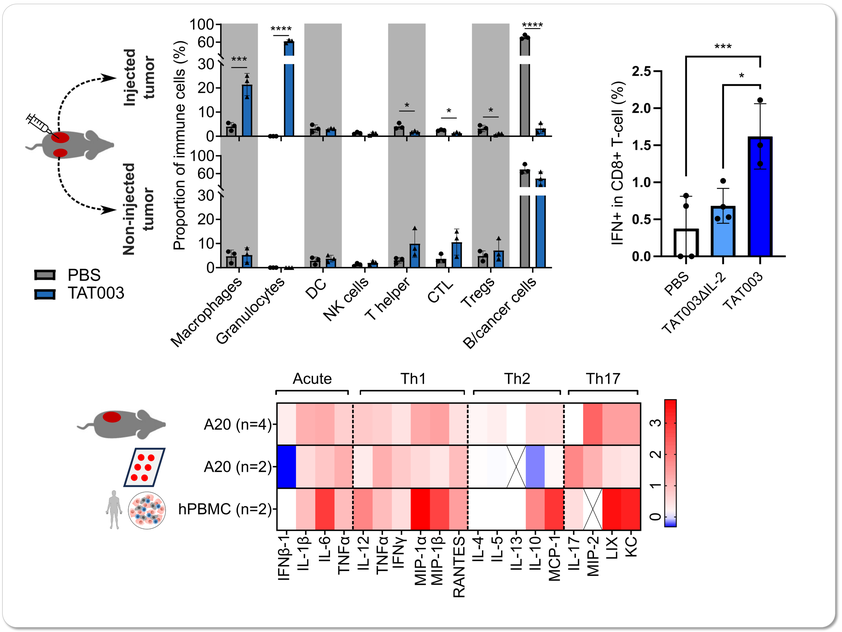


Figure 3. TAT003 remodels the tumor microenvironment and activates several key actors of anti-tumor immunity. Immune profiling experiment was performed by flow cytometry on tumor tissue homogenates on Day 8 (n=4) (Left panel). PBMC isolated from PBS, TAT003ΔIL2 or TAT003-treated mice were stimulated with cancer cells *in vitro* (right panel). Cancer-cell specific activation was mesured by intracellular IFNγ staining in CD8+ T cells (van Vloten *et al.* 2019). Cytokine profiling was performed on TAT003-treated A20 tumor homogenates on Day 8, on microdissected A20 tumors treated *ex vivo* MISO Chip's tissue culture chip and on TAT003 stimulated human Peripheral Mononuclear Cells (hPBMC). Statistics: Mutliple t-tests *:P<0.05, ***:P<0.001, ****:P<0.0001

CONCLUSIONS

- TAT003 combines **three complementary therapeutic activities** to spark an effective anti-tumor immune response.
- **Local treatment** with TAT003 induces **systemic** and **durable** tumor growth inhibition.
- TAT003 treatment **remodels the tumor micro-environment** by stimulating **myeloid cells** that ignite an intense **T-cell-driven** immune response against cancer cells.

References: Zheng C et al. Cancer Cell. 2022 Apr 11;40(4):410-423.e7 (PMID: 35413272), Weber JS *et al.* Lancet. 2024 Feb 17;403(10427):632-644 (PMID: 38246194), O'Leary K. Nat Med. 2024 Jan 25. (PMID: 38273121), van Vloten JP *et al.* Mol Ther Methods Clin Dev. 2019 Jan 29;13:154-166. (PMID: 30788384).