TONIX PHARMACEUTICALS

TNX-1700

Gastric and Colorectal Cancers

NASDAQ: TNXP

Version PO6102 Oct 2, 2025 (Doc 1619)

Cautionary Note on Forward-Looking Statements

Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate” and “intend,” among others. These forward-looking statements are based on Tonix’s current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, the risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; risks related to the timing and progress of clinical development of our product candidates; risks related to the failure to successfully launch and commercialize Tonmya and any of our approved products; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by Tonix on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the Securities and Exchange Commission (the “SEC”) on March 18, 2025, and periodic reports and current reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.

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[1]human trefoil family factor 2 – human serum albumin fusion protein
[2]myeloid-derived suppressor cells
[3]azoxymethane/dextran sodium sulfate
[4]murine TFF-2 – murine serum albumin fusion protein

TNX-1700: Targeting Gastric and Colorectal Cancer[1]

Gastric and colorectal cancer are leading cancers in the US. Colorectal cancer is the 2nd most common cause of cancer deaths for men and women combined.[2]

>1.4M **People living with colorectal cancer in the US[3]**

>140K **People living with gastric cancer in the US[4]**

Current standard of care:

- PD-1 blockade
  - Response rate in gastric cancer is 10-20%, however, tumors which exhibit high levels of microsatellite instability or deficient mismatch repair, response reaches 30-50%, but these patients are rare (10-15% of all gastric cancer)[5,6]

Large unmet need:

- Gastric and colorectal cancer have a relative 5-year survival rate of 37.9% and 65.4%, respectively[3,4]
  - Despite advances in the field, patients are still in need of life saving treatment

[1]TNX-1700 is in the pre-IND stage and has not been approved for any indication.
[2]American Cancer Society, accessed March 2025 - https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html
[3]NIH, accessed October 2025 - https://seer.cancer.gov/statfacts/html/colorect.html
[4]NIH, accessed October 2025 - https://seer.cancer.gov/statfacts/html/stomach.html
[5]Kono et al., *Gastric Cancer* 2020; 23:565-578
[6]Amonkar et al., J. Clin. Onc. 2019; 37; suppl

TNX-1700 (hTFF2-HSA): A Potential Treatment for Gastric and Colorectal Cancers

Pre-IND Candidate

Targeting a Condition with Significant Unmet Need

Targeted as a treatment for cancer

- Particularly for gastric and colorectal cancer
- Mechanism of Action (MOA) is different from checkpoint inhibitors
- Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies

Patents and patent applications directed to recombinant TFF2 (rTFF2)

- Issued patent licensed from Columbia University

Inventor: Dr. Timothy Wang, MD

- Chief, Division of Digestive and Liver Diseases at Columbia University and Cancer Research Center and Silberberg Professor of Medicine
- Investigated the molecular mechanisms of gastrointestinal carcinogenesis for decades
- Leadership roles in gastroenterology and cancer biology fields

Pre-clinical evidence for inhibiting growth of cancer cells

- Several studies have shown rTFF2 to be active in the treatment of cancer[1-2]

[1]Dubeykovskaya Z, et al. Nat Commun. 2016 7:1-11
[2]Dubeykovskaya ZA, et al, Cancer Gene Ther. 2019 26(1-2):48-57

IMMUNOLOGY PORTFOLIO

TNX-1700 (TFF2-HSA): Fighting Gastric (GC) and Colorectal Cancer (CRC) by Targeting the Tumor Microenvironment

Trefoil Factor-2 (TFF2) Targeted as an Immunotherapy Treatment for Cancer

❖Mechanism of Action

- Partial agonist for the chemokine receptor CXCR4
  - Distinct from prototypical agonist SDF-1α
- Activates anti-cancer CD8+ T cells by altering the tumor microenvironment (TME) via suppression of myeloid-derived suppressor cells (MDSCs)
- Redirects granulocyte differentiation towards anti-tumorigenic neutrophils and away from MDSCs
- Promotes differentiation of MDSCs to a non-immunosuppressive cell type
- Inhibits myelopoiesis/normalizes hematopoiesis
- Synergizes with anti-PD-1
- **Activity of TFF2 is distinct from CXCR4 antagonists**
  - Prototypical antagonist of CXCR4 is Mozobil® (plerixafor/AMD3100)
  - Hematopoietic Stem Cell (HPSC) mobilizing agent – FDA approved for stem cell transplantation
  - Blocks recruitment and migration

❖Target Validation

- Human Gastric Cancer
  - TFF2 epigenetically silenced in GC
  - CXCR4+ PMN-MDSC expanded and negatively correlated with serum TFF2 level and CD8+ T cell abundance
  - CXCR4+PMN-MDSCs highly expressed immunosuppressive genes
  - Low TFF2 expression in tumor tissue in patients with diffuse-type or intestinal type GC correlated with poor overall survival
- Mouse CRC Tumor Models:
  - TFF2 knock-out in mice leads to faster tumor growth
  - Transgenic overexpression of TFF2 suppresses tumor growth
  - Adenoviral delivery suppresses tumor growth

Dubeykovskaya Z, et al., Nat Commun. 2016 7:1-11
Dubeykovskaya Z, et al., Cancer Gene Ther. 2019 26(1-2):48-57
Qian, et al., *Cancer Cell*. 2025 Aug 11;43(8):1512-1529

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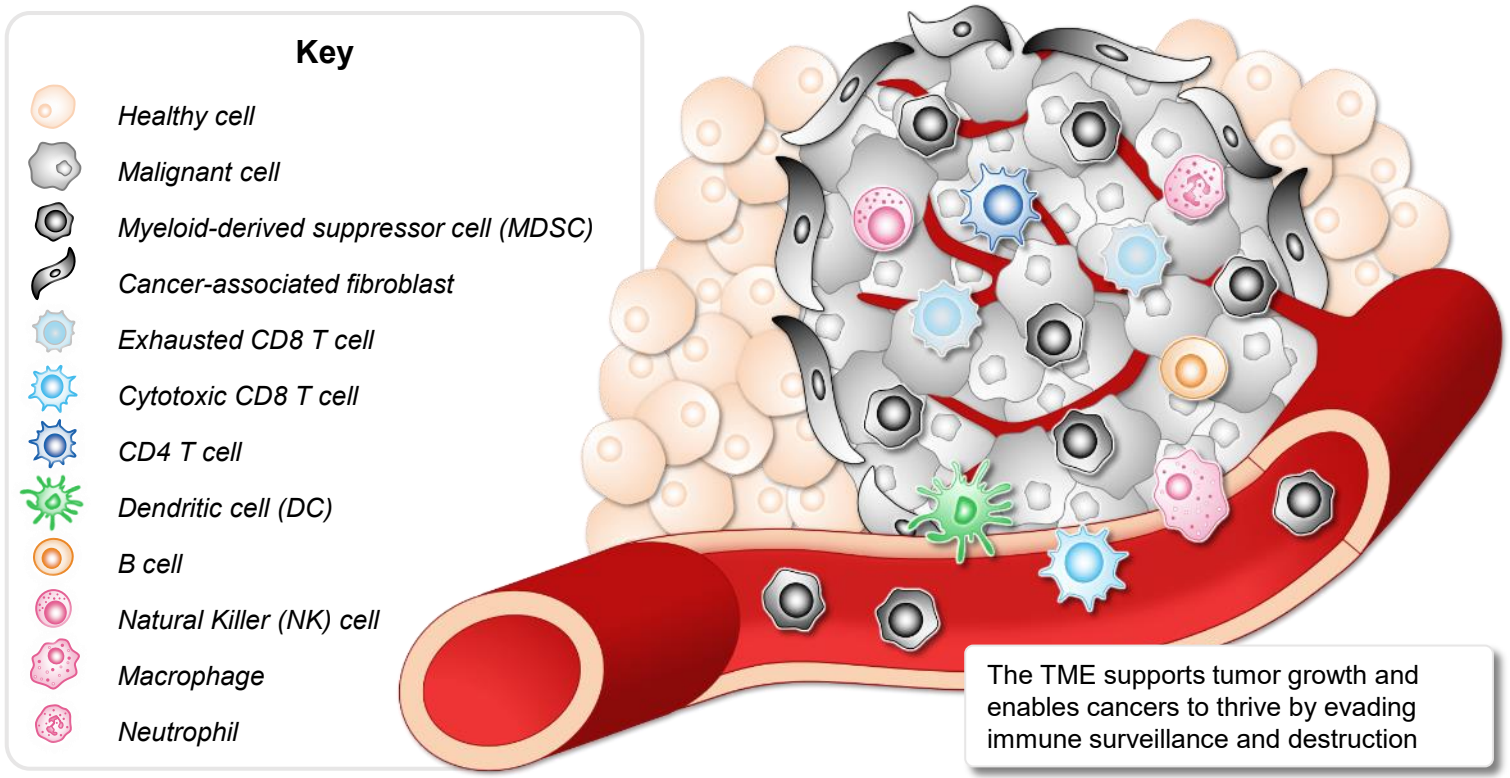
TNX-1700 (hTFF2-HSA) Fusion Protein

Tumor Microenvironment, MDSCs

Cancers Create Toxic, Immunosuppressive Tumor Microenvironments (TME)

- Tumors are surrounded by endothelial and stroma cells, and invading immune cells, both innate and adaptive[1,2]
- Complex regulatory network supports tumor growth, enabling cancers to thrive by evading immune surveillance and destruction[2-3]
- The TME sabotages tumor-killing cytotoxic CD8 T cells[1]
- Myeloid-derived suppressor cells (MDSCs) interfere with anticancer immunity[2,3]

Tumors Create a Toxic, Immunosuppressive Microenvironment[1-3]



[1]Belli C, et al. *Cancer Treat Rev.* 2018;65:22-32.
[2]Roma-Rodriguez C, et al. *Int J Mol Sci.* 2019;20(4):840.
[3]Tsai M, et al. *ISRN Biochem.* 2014:351959.

MDSCs Are a Major Treatment Target

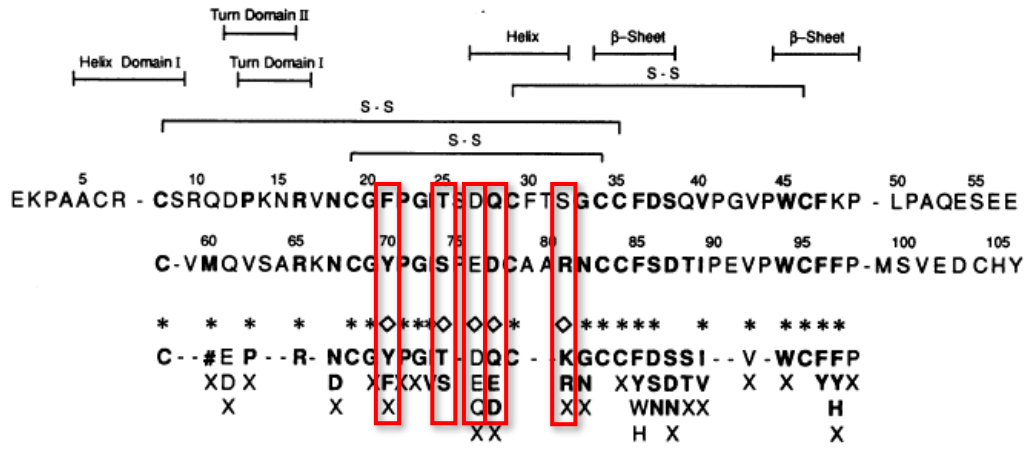
- Levels of MDSCs tend to correlate with tumor stage, patient survival, and metastatic burden and may predict poor response to certain cancer treatments[1]
- MDSCs represent a central mechanism of immunosuppression in cancer; targeting these cells could significantly improve our ability to fight cancer[2,3]
- Therapeutic strategies include[3]:
  - Promoting the differentiation of MDSCs to a non-immunosuppressive cell type
  - Blocking MDSC immunosuppressive functions
  - Inhibiting MDSC expansion
  - Eliminating MDSCs

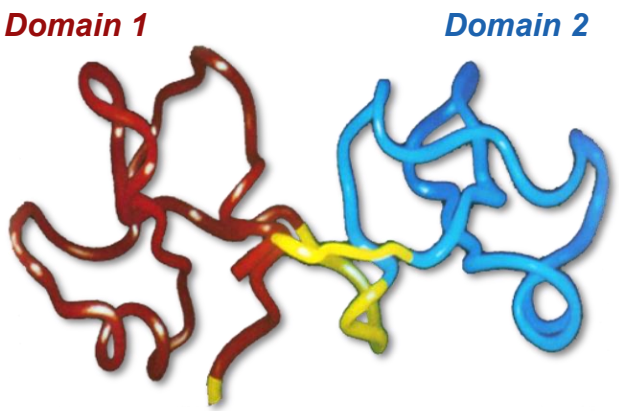
[1]Condamine T, et al. *Annu Rev Med.* 2015;66:97-110.
[2]Tuccito A, et al. *Virchows Arch.* 2019;474(4):407-420.
[3]Gabrilovitch DI, et al. *Nat Rev Immunol.* 2009;9(3):162-174.

TFF2 Structure

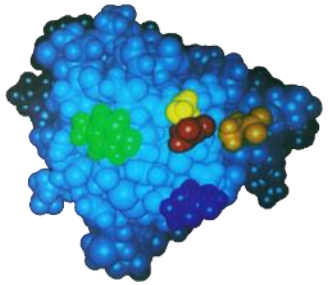
Domains, CXCR4 Interaction, Cell Migration

TFF2 Contains 2 Trefoil Domains, Each Containing 5 Conserved Residues

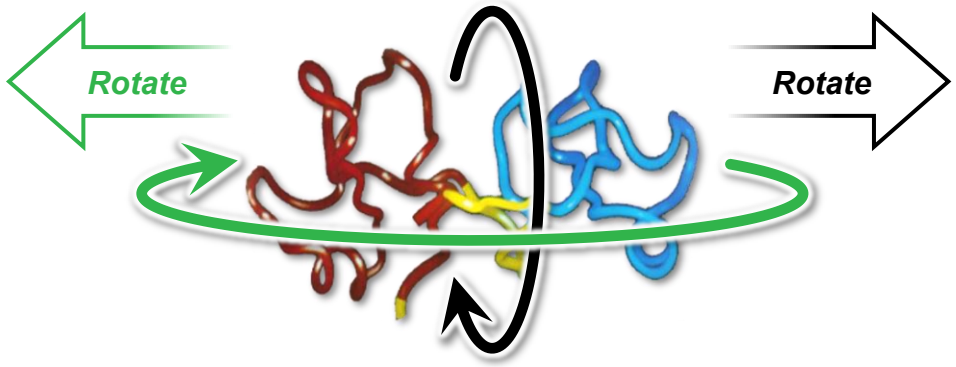


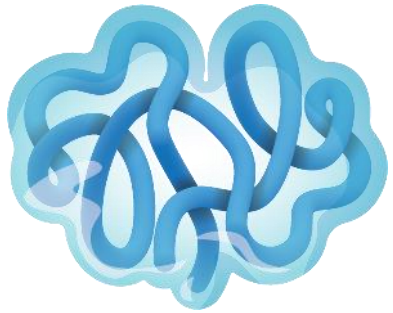


Crystal structure



Space-filling model (side)





Simplified view (top)

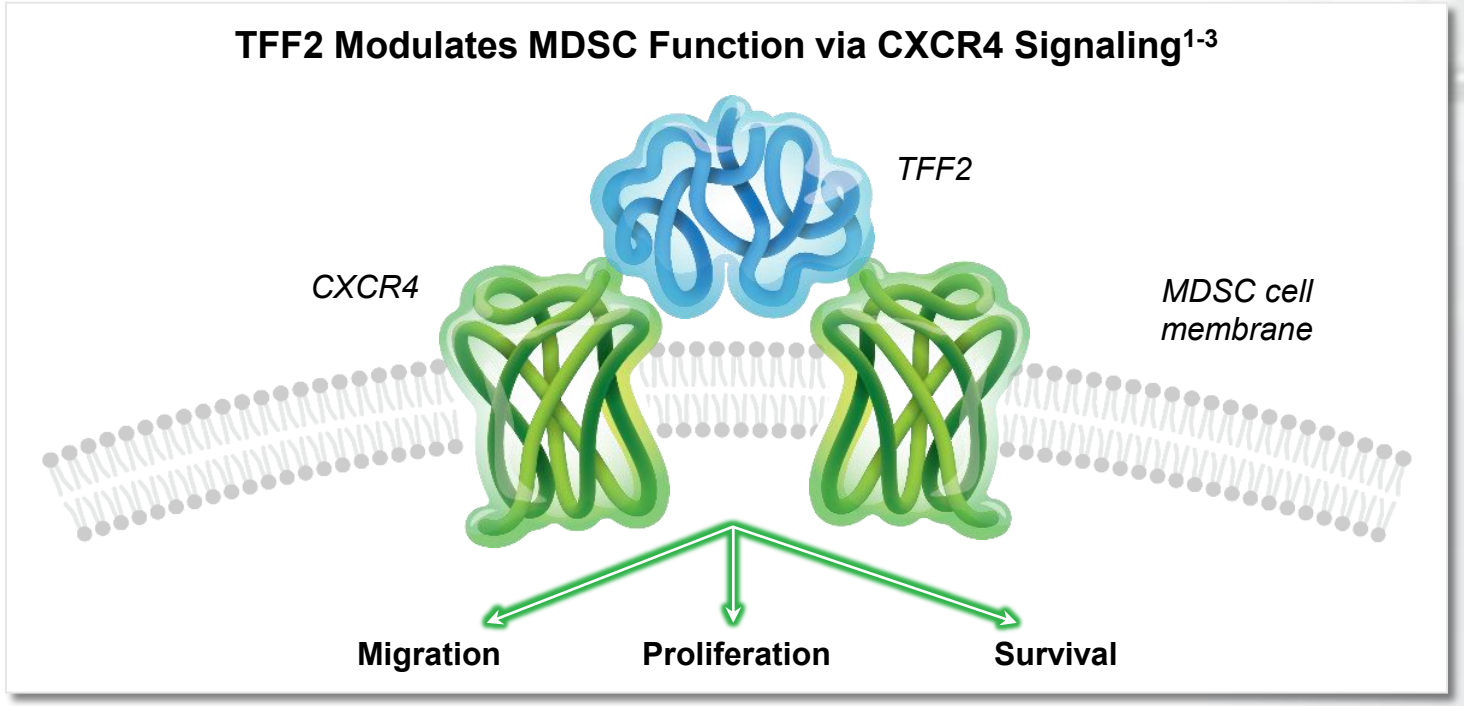
IMMUNOLOGY PORTFOLIO

Carr M, et al. *Biochemistry*, 1994 91:2206-2210

Carr et., PNAS (1994)

TFF2 Signals Through CXCR4

- Importantly, TFF2 activates CXCR4 and may therefore modulate immune and tumorigenic responses, specifically by reducing the expansion or migration of immunosuppressive MDSCs[1-3]
- TFF2 upregulates ApoE fifty-fold in myeloid progenitor cells; ApoE has been shown to suppress MDSCs[4]

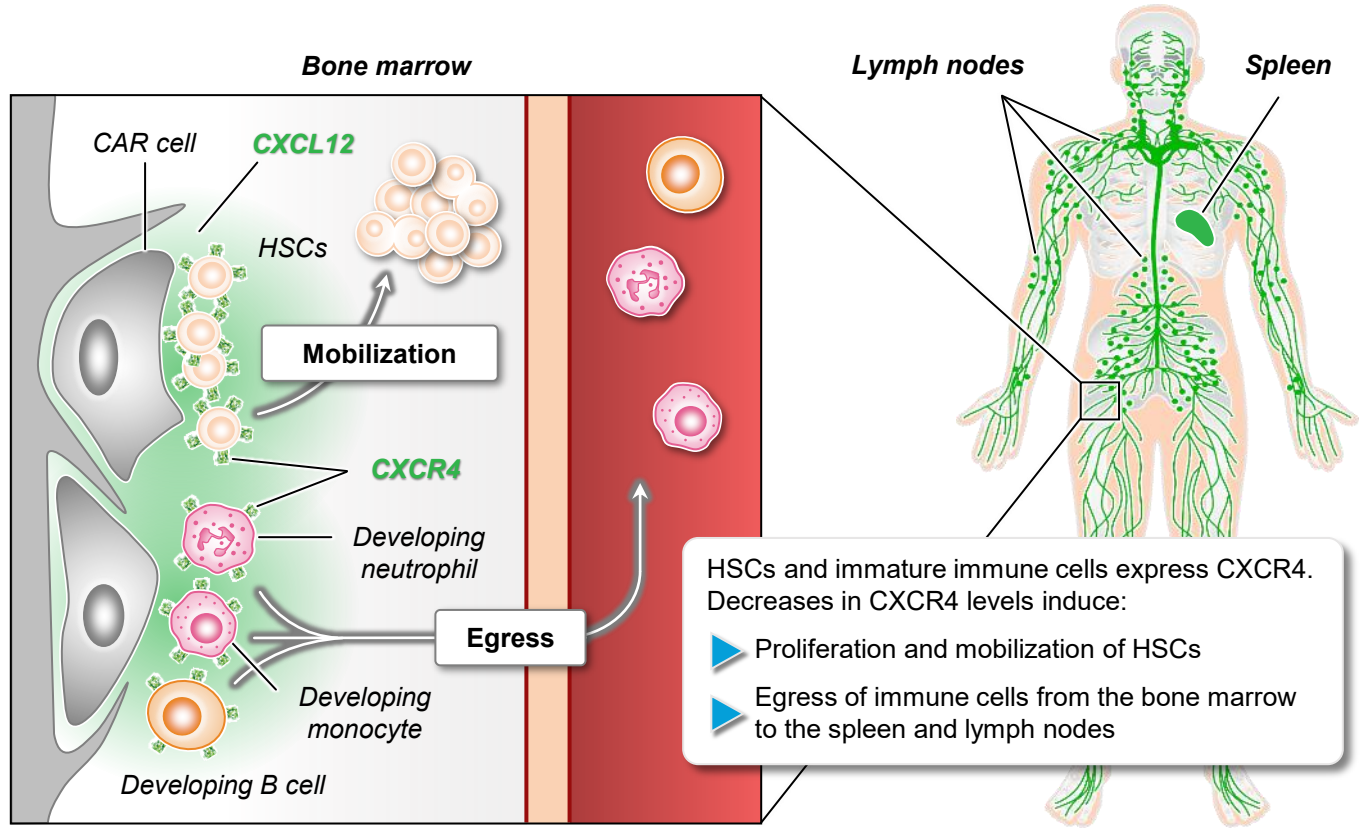


[1]Dubeykovskaya Z, et al. *J Biol Chem.* 2009;284(6):3650-3662.
[2]Balkwill F. *Semin Cancer Biol.* 2004;14(3):171-179.
[3]Teixidó J, et al. *Int J Biochem Cell Biol.* 2018;95:121-131.
[4]Tavazoie MF et al, *Cell* 2018; 172:825-840.

Chemokines Direct Immune Cell Production and Migration

- Immune cells constantly migrate from the blood into and out of lymphoid organs, processes known as homing and egress[1,2]
- Homing and egress are regulated by chemokines[1,2]
- CXCL12-CXCR4 is a crucial chemokine signaling axis that regulates[1-3]:
  - Proliferation and mobilization of hemopoietic stem cells (HSCs)
  - Retention of developing immune cells within the bone marrow

CXCR4 Signaling Directs Mobilization and Egress[1-3]



[1]Griffith JW, et al. Annu Rev Immunol. 2014;32:659-702.
[2]Schultz O, et al. Annu Rev Immunol. 2014;34:203-242.
[3]Balkwill F. Semin Cancer Biol. 2004;14(3):171-179.

TNX-1700 Protein Design

Albumin Fusion Proteins

Strategies for Half-Life Extension: Albumin Fusion

- **Albumin**
  - Most abundant plasma protein
  - Involved in transport of nutrients in the body
  - Interaction with cellular receptors Gp18, Gp30, and Gp60, which regulate transcytosis/endocytosis of albumin across the endothelial cell surface
  - High circulatory half-life of ~ 19 days mediated mainly due to neonatal Fc (FcRn)-mediated recycling
- **Marketed albumin fusions, conjugates and albumin binders**
  - Levemir
  - Tanzeum
  - Victoza
  - Abraxane
  - Idelvion
  - Tresiba
  - Ozempic
  - Mounjaro

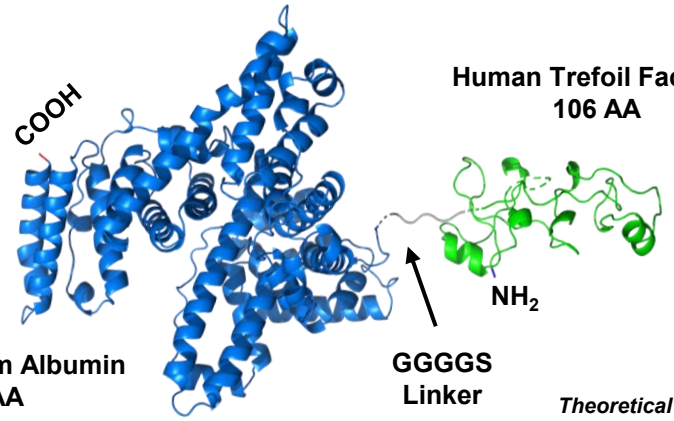
TNX-1700 (hTFF2-HSA) Fusion Protein

Structure, Preliminary Safety

TNX-1700 is a Fusion Protein of TFF2 and Human Serum Albumin (HSA)

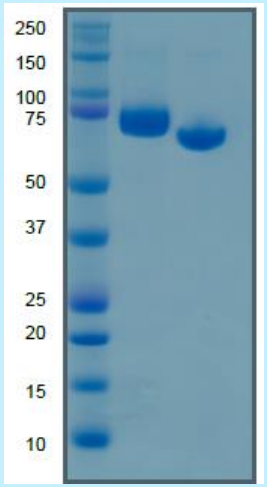
Fusion of TFF2 with HSA for half-life extension

Murine TNX-1700 generated for mouse studies

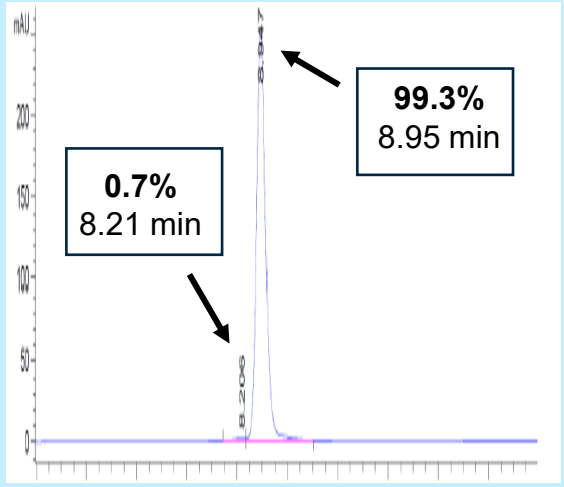


Theoretical MW = 78.1 kDa

SDS PAGE



Size Exclusion



Preliminary Safety of TNX-1700

Mouse Toxicity Study

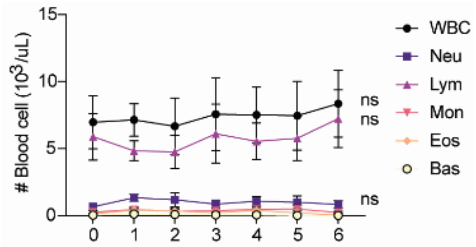
No observable toxicity at efficacious dose Mice: C57BL/6; n=3/group

Dose: murine TNX-1700; 22.5 mg/kg or vehicle IP

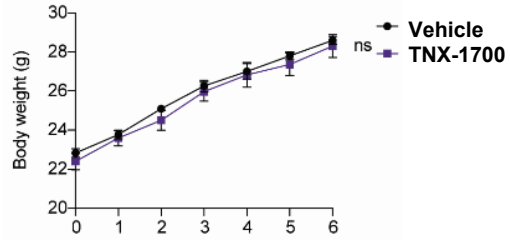
Frequency: 3x/week; 6 weeks

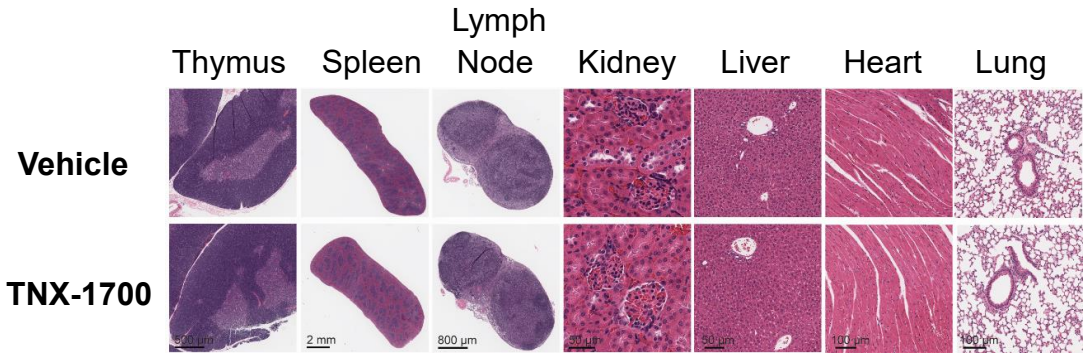
- No effect on WBC count and body weight
- No inflammation in lymphoid and non-lymphoid organs

WBC Count



Body Weight





Qian, et al., *Cancer Cell*. 2025 Aug 11;43(8):1512-1529

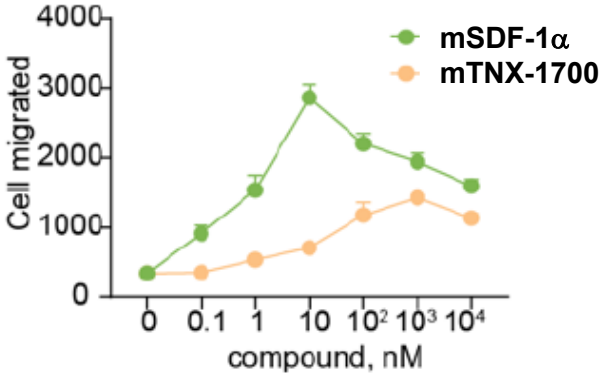
TNX-1700 (hTFF2-HSA) Fusion Protein

Target Validation, In Vitro

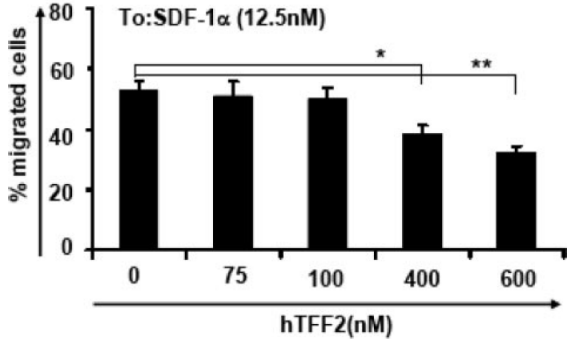
Target Validation

TFF2/TNX-1700 is a Partial CXCR4 Agonist (and an Antagonist to SDF-1α) *in vitro*

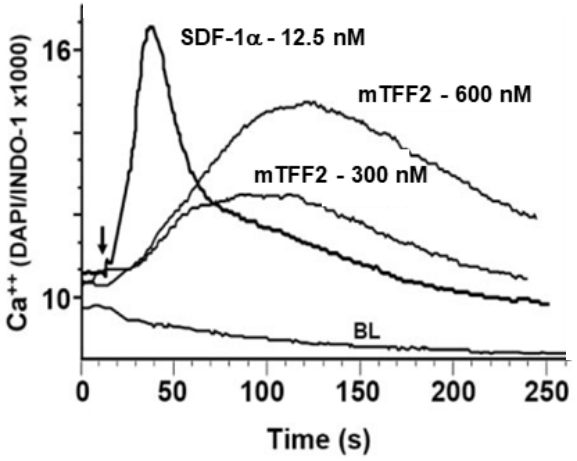
Chemotaxis



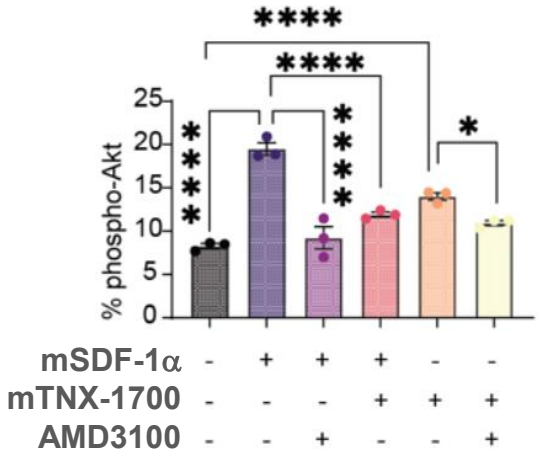
TFF2 blocks SDF-1α induced chemotaxis



Calcium flux

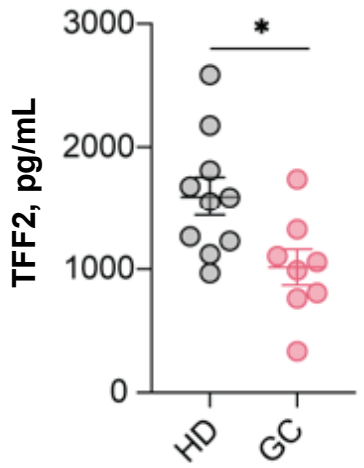


mTNX-1700 and AMD3100 block Akt phosphorylation

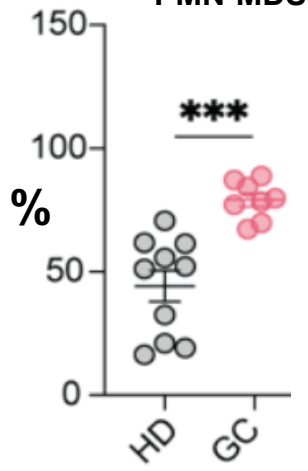


Reduced Level of TFF2 Correlates with Elevated CXCR4+ PMN-MDSCs in GC

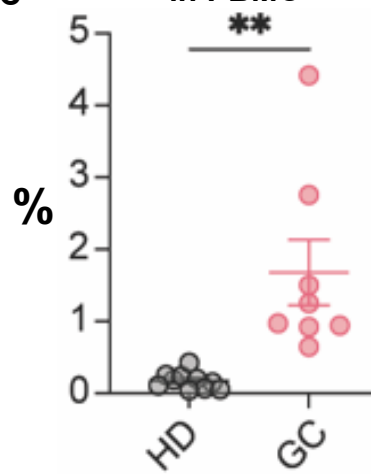
Plasma TFF2



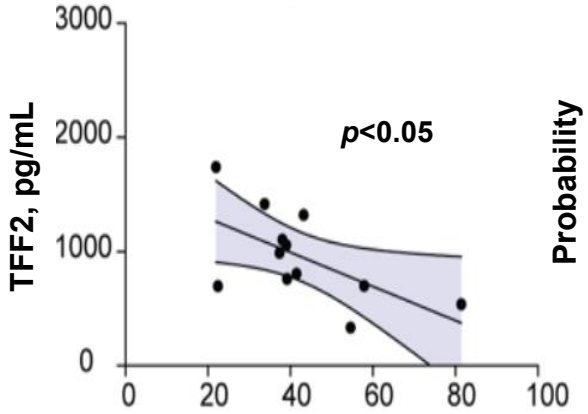
% CXCR4+ in PMN-MDSC



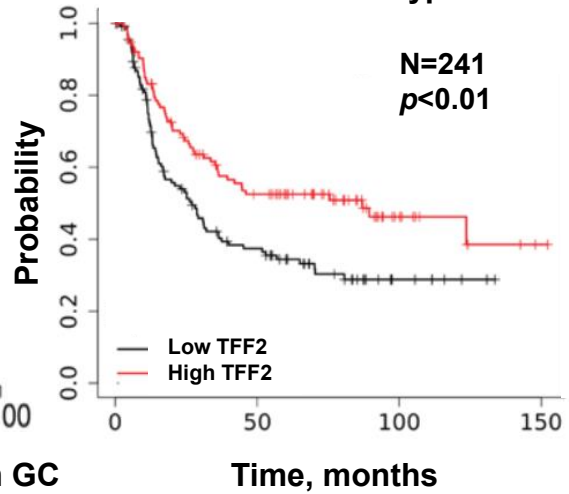
% PMN-MDSC in PBMC



Spearman correlation of TFF2 vs. CXCR4+ PMN-MDSC in GC



Kaplan-Meier TFF2 in diffuse-type GC



Qian, et al., Qian, et al., *Cancer Cell*. 2025 Aug 11;43(8):1512-1529
Dubeykovskaya Z. et al., JBC. 2009 284: 3650

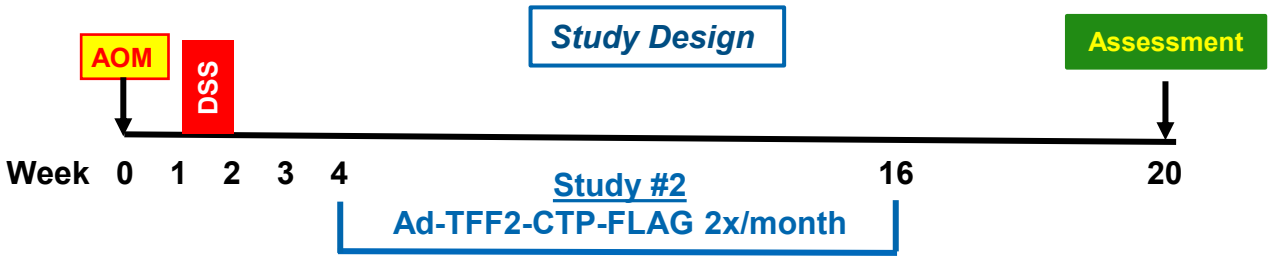
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

TNX-1700 (hTFF2-HSA) Fusion Protein

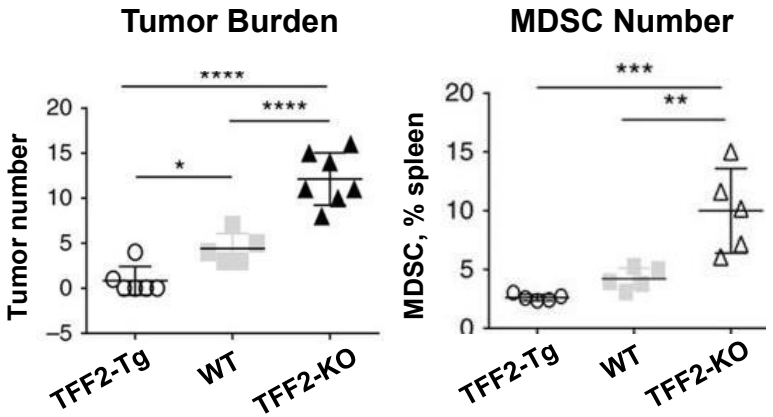
Chemoprevention Studies

Murine AOM/DSS Model, Target Validation, In Vivo

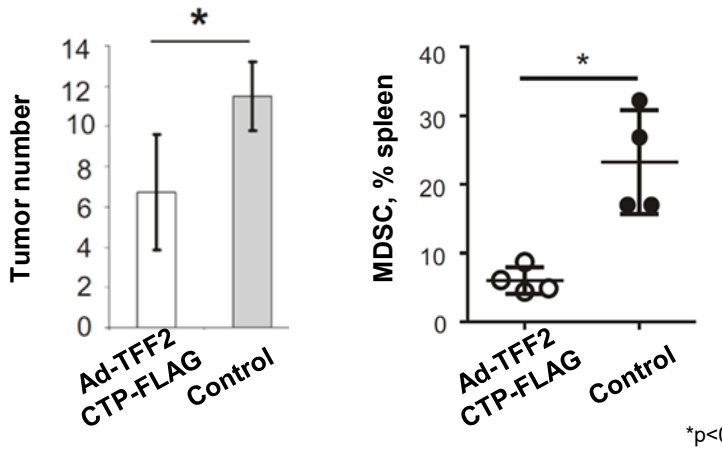
Target Validation *in vivo*:
Efficacy in the AOM/DSS CRC Induction Model in C57BL/6 Mice



Study #1
- TFF2-Transgenic (Tg)
- Wild-Type (WT)
- TFF2-KO
- N=6/group



Study #2
- Ad-TFF2-CTP-FLAG
- Control
- N=4/group



*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Dubeykovskaya Z, et al., Nat Commun. 2016 7:1-11
Dubeykovskaya Z, et al., Cancer Gene Ther. 2019 26(1-2):48-57

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Therapeutic Studies

Synergy with PD-1 Blockade

Gastric Cancer (GC)

ACKP, PC, Orthotopic Syngeneic Murine Models

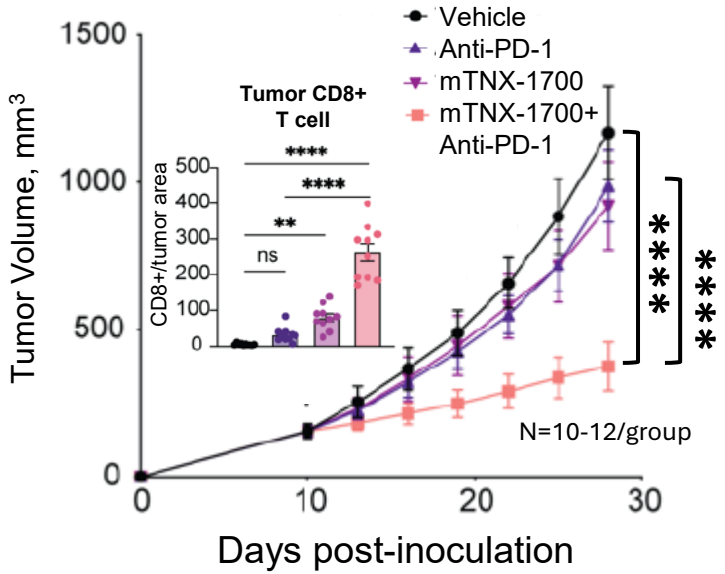
mTNX-1700 Exhibits Synergy with anti-PD-1 mAb in Decreasing Tumor Volume, Blocking Metastasis and Increasing Survival in a Syngeneic Mouse Model of GC

CXCR4 partial agonism + checkpoint blockade has superior efficacy in mouse model

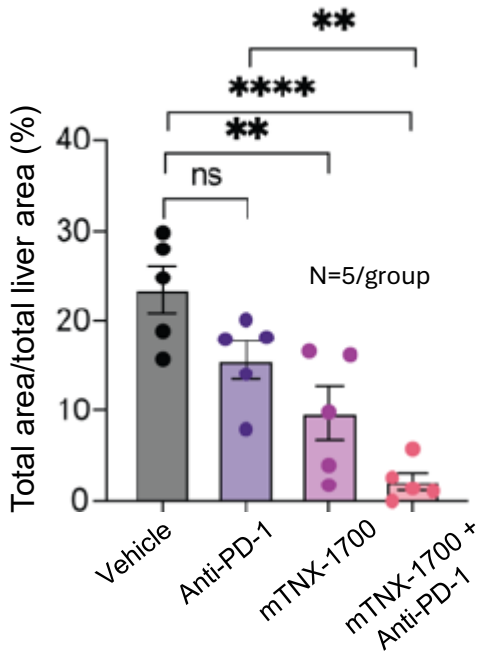
ACKP Model

mTNX-1700 + anti-PD-1

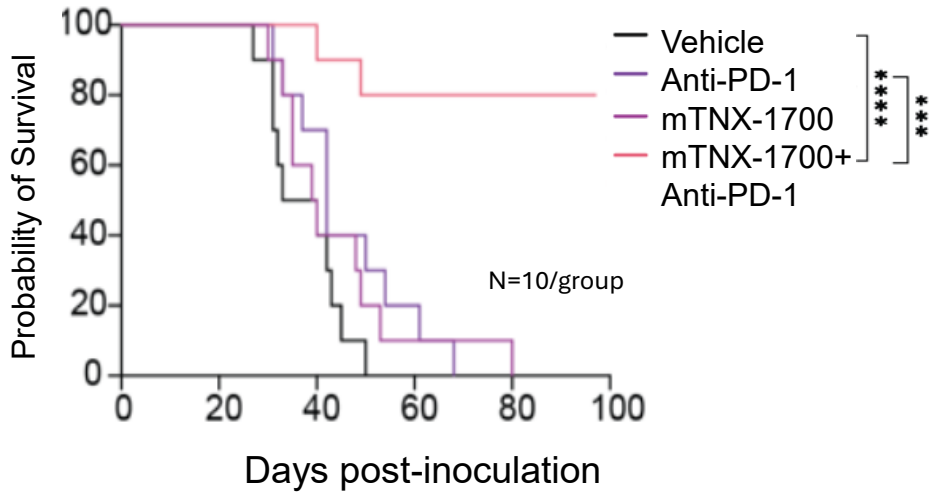
Tumor Inhibition



Blocking Liver Metastasis



Increasing Survival

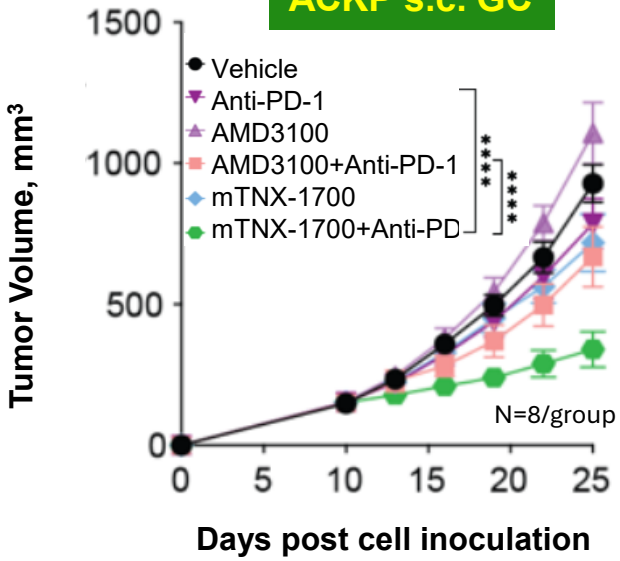


Qian, et al., *Cancer Cell*. 2025 Aug 11;43(8):1512-1529

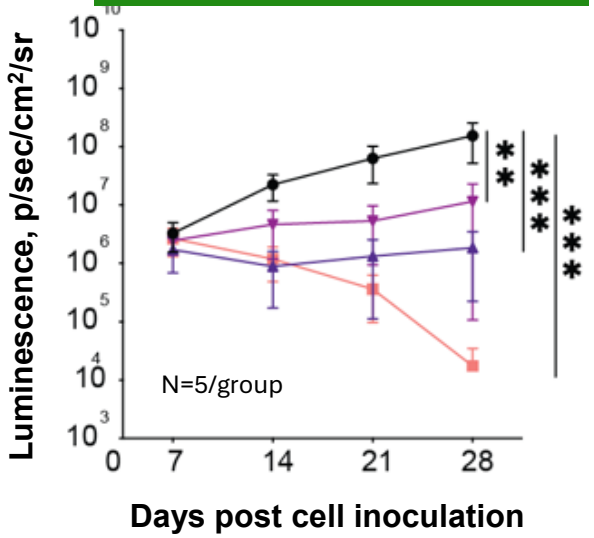
ns, non-significant, **p<0.01, ***p<0.001, ****p<0.0001

Efficacy of mTNX-1700 on Tumor Growth in Multiple Syngeneic Murine Models of Gastric Cancer (GC) and Colorectal Cancer (CRC)

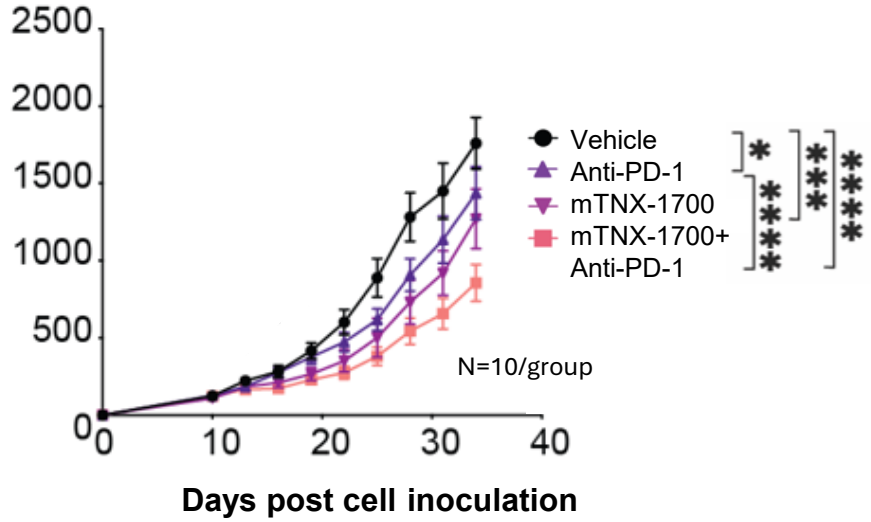
ACKP s.c. GC



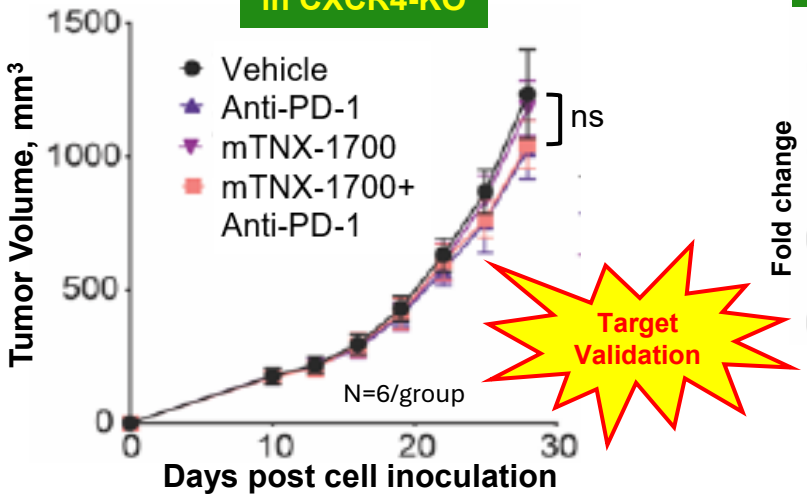
ACKP-Luc Orthotopic GC



PC s.c. GC

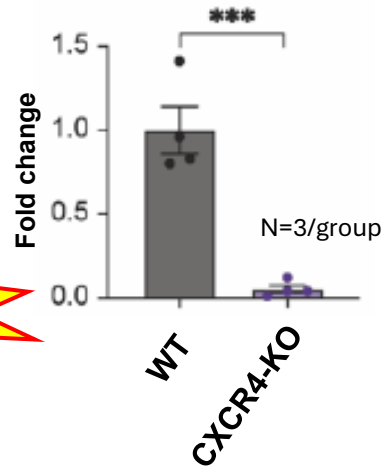


No Efficacy in CXCR4-KO



Target Validation

PMN, CXCR4 mRNA



❖TNX-1700 is Active in Multiple Models in Two Cancer Types:

- Autochthonous GC model
- ACKP lung metastasis model
- MC38 s.c. CRC model
- CT26.wt s.c. CRC model
- CT26-Luc orthotopic CRC model

ns, non-significant; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

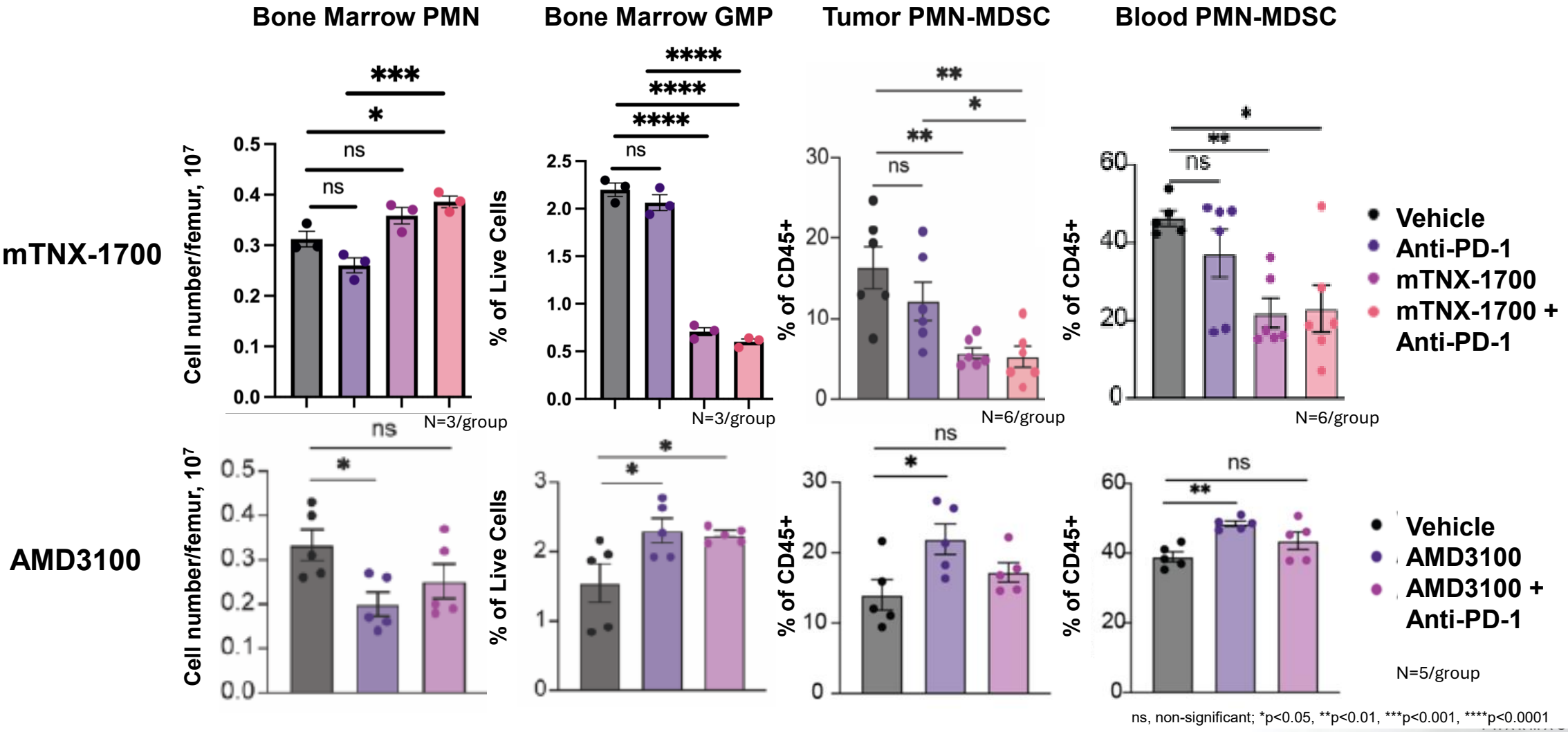
Qian, et al., *Cancer Cell*. 2025 Aug 11;43(8):1512-1529; Daugherty et al., AACR 2023; Daugherty et al., SITC 2023

IMMUNOLOGY PORTFOLIO

The CXCR4 Partial Agonist mTNX-1700 Reduces PMN-MDSCs in the TME, Blood and Biogenesis in the Bone Marrow

ACKP GC Model

The CXCR4 full antagonist AMD3100 has the opposite effect



Qian, et al., *Cancer Cell*. 2025 Aug 11;43(8):1512-1529

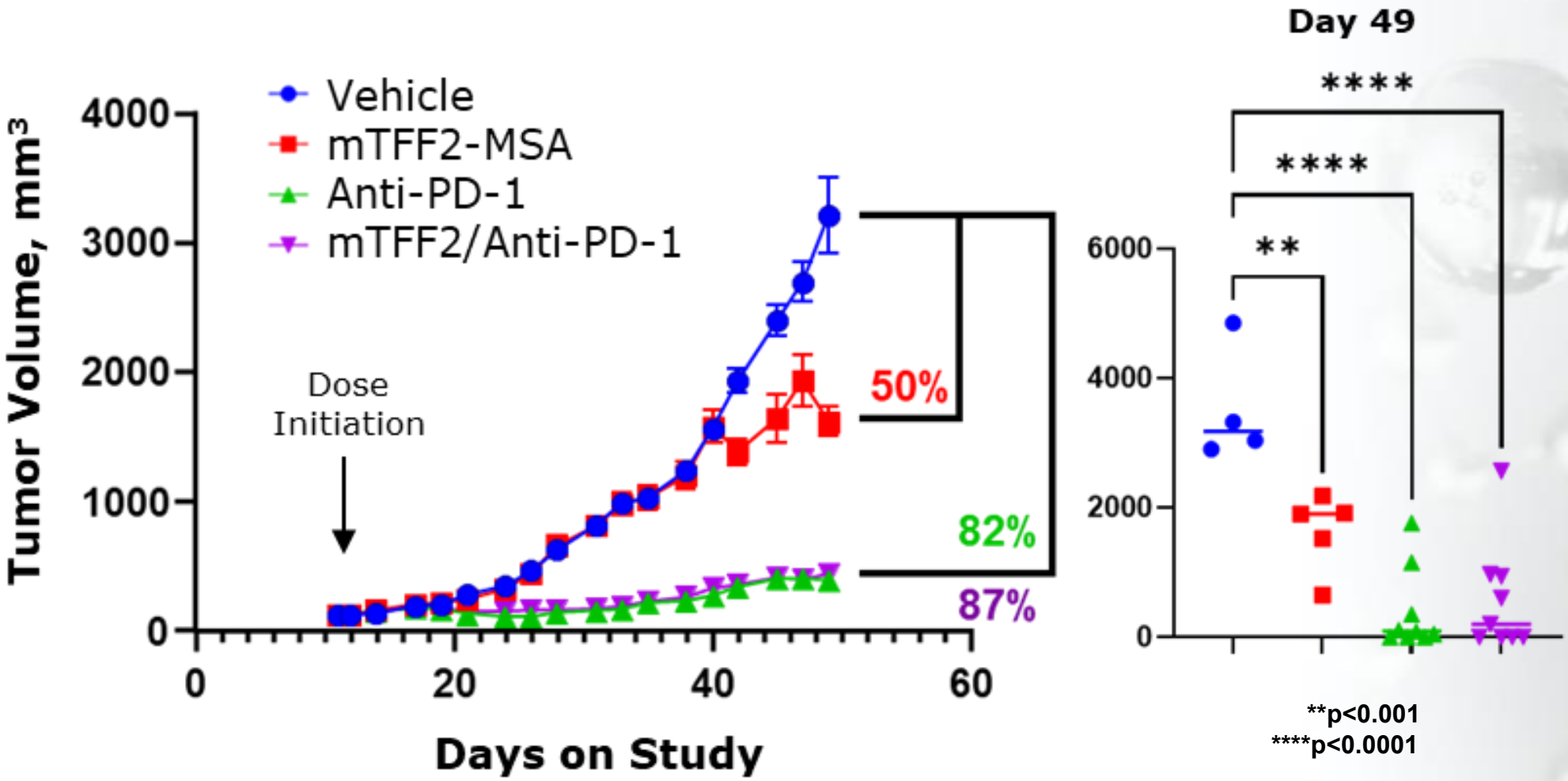
Therapeutic Studies

Synergy with PD-1 Blockade

Colorectal Cancer (CRC)

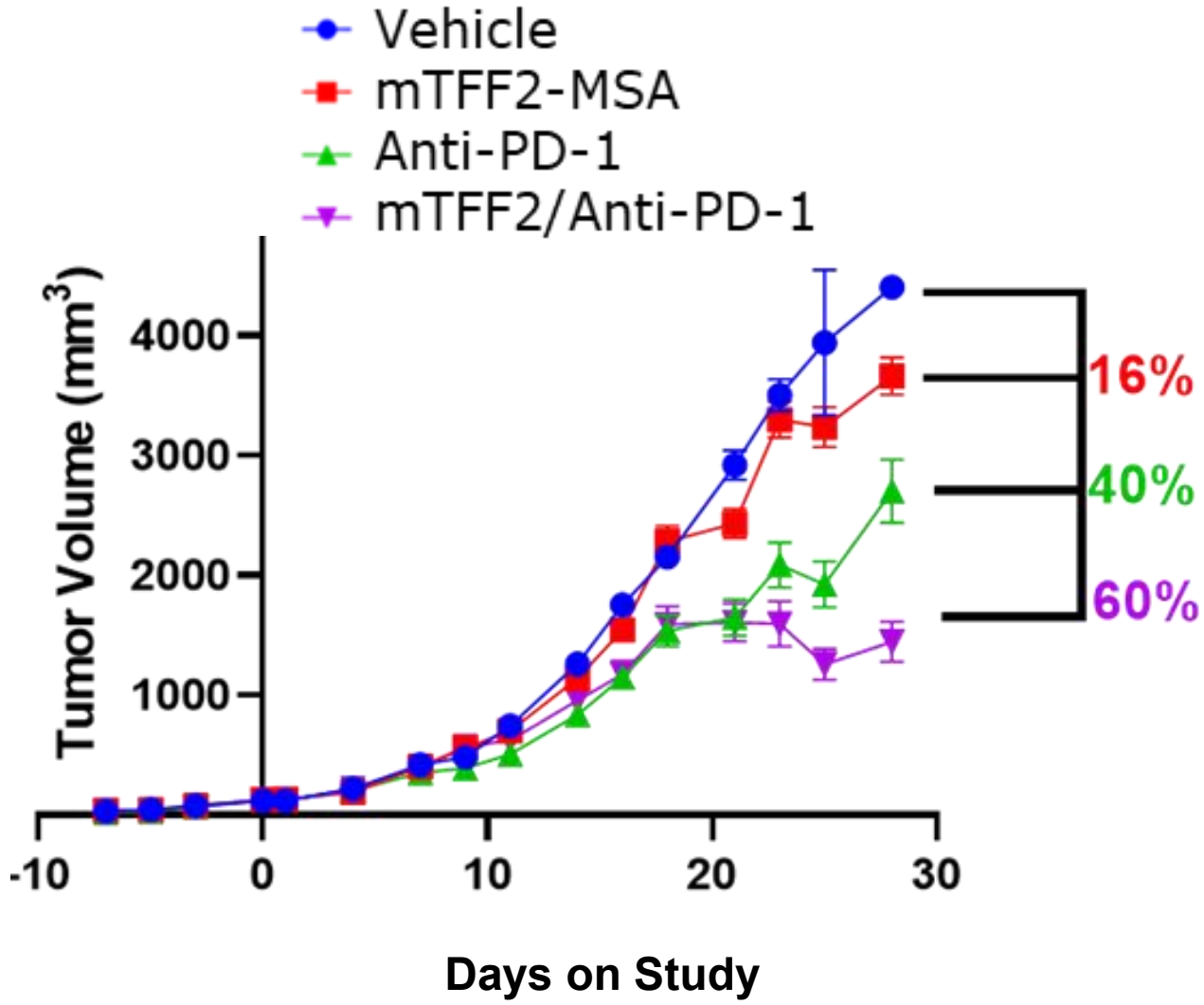
MC38 and CT26.wt Subcutaneous and CT26-Luc Orthotopic Syngeneic Murine Models

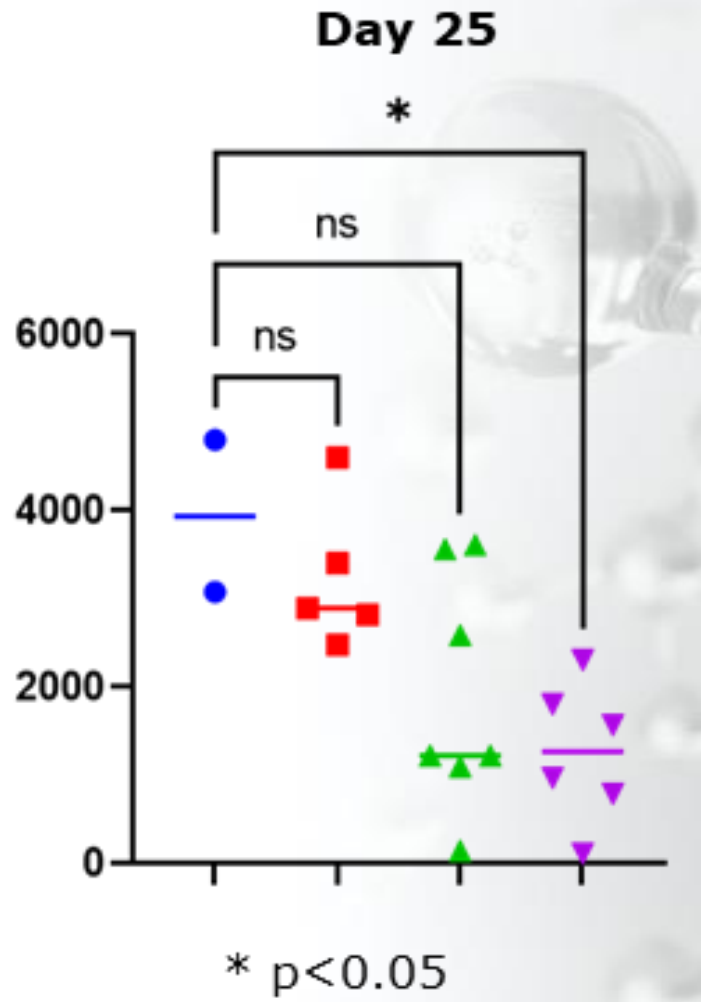
Inhibition of Tumor Growth in the MC38 CRC Model



Daugherty et al., AACR 2023

Inhibition of Tumor Growth in the CT26.wt CRC Model



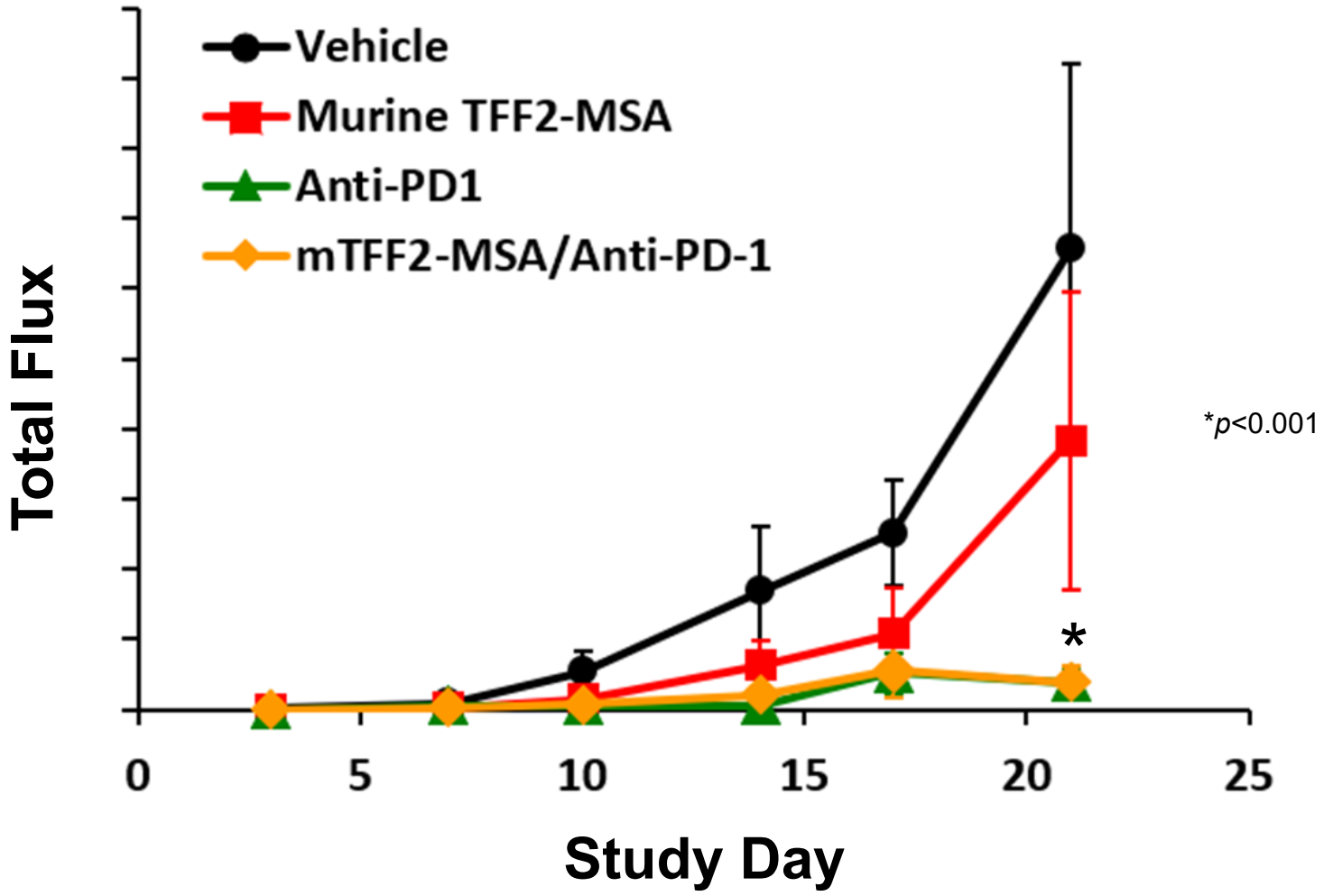


IMMUNOLOGY PORTFOLIO

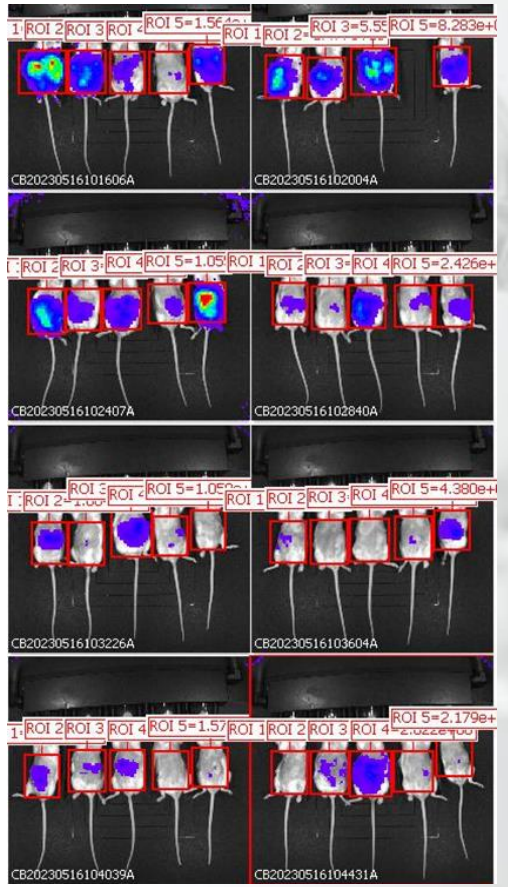
Daugherty et al., AACR 2023

TONIX PHARMACEUTICALS

Inhibition of Tumor Growth in the CT26-Luc Orthotopic Tumor Model



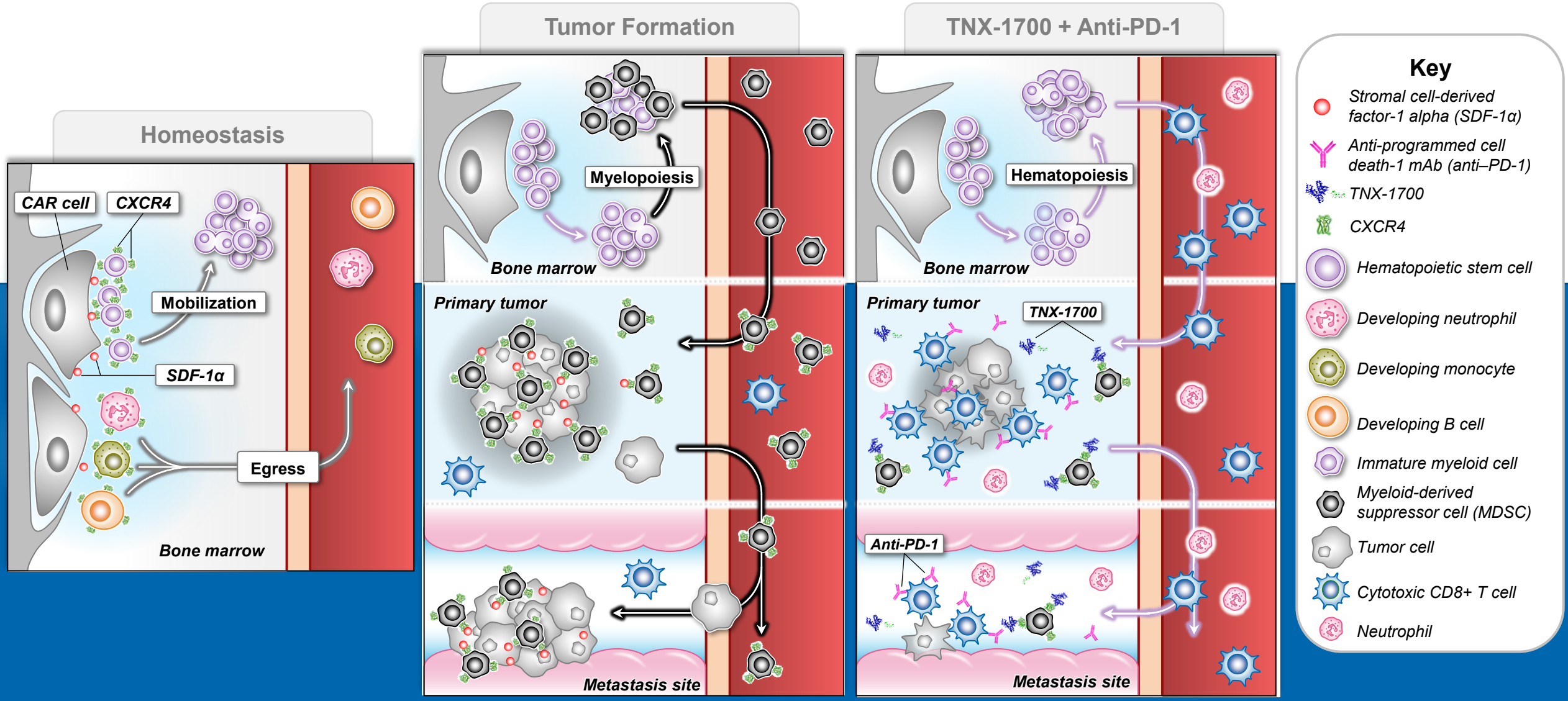
*p<0.001



Daugherty et al., SITC 2023

Summary

TNX-1700 Alters the TME by Activating Anti-Cancer CD8+ T Cells *via* Suppression of MDSCs Resulting in Reduction of Tumor Growth and Metastasis



Conclusions

- TFF2 is a naturally occurring anti-inflammatory peptide that is a key part of the inflammatory reflex.
- TFF2 is a partial agonist for CXCR4, suppresses the proliferation and expansion of myeloid progenitors, thus reducing MDSCs.
- Overexpression of TFF2, either through transgenic or adenoviral expression, reduces the development of colorectal cancer (CRC) following AOM/DSS treatment. mTNX-1700 synergizes with anti-PD-1 blockade to increase survival and eradicate gastric cancer (GC) in advanced orthotopic and metastatic models.
- mTFF2-MSA (mTNX-1700) peptide synergizes with PD1 blockade therapy to reduce tumor size and increase survival in CRC syngeneic subcutaneous and orthotopic mouse models.
- mTNX-1700 reduces the production of MDSC and promotes a T-cell rich microenvironment, inducing a 50-fold increase in intratumor CD8+ T cells.

THANK YOU

APPENDIX

AACR Presentations

Presentation #1

Title: MDSC-targeted TFF2-MSA suppresses tumor growth and increases survival in anti-PD-1 treated MC38 and CT26.wt murine colorectal cancer models

Authors: Bruce L. Daugherty[1], Rebecca J. Boohaker[2], Rebecca Johnstone[2], Karr Stinson[2], Jin Qian[3], Timothy C. Wang[3], Seth Lederman[1]
Tonix Pharmaceuticals, Inc., 26 Main Street, Suite 101, Chatham, NJ 07928
Southern Research, 2000 9th Ave S, Birmingham, AL 35205
Division of Digestive and Liver Diseases, Irving Cancer Research Center, Columbia University Medical Center, New York, NY 10032, USA

Topic: Oncolytic Viruses, Anticancer Vaccines, and Other Immunomodulatory Therapies
Location: Orange County Convention Center, Orlando, Fla.
Section: 24, #704
Date: Sunday, April 16, 2023
Time: 1:30 p.m. – 5:00 p.m. ET
Abstract: Click here

Presentation #2

Title: MDSC-targeted TFF2-MSA synergizes with PD-1 blockade therapy in diffuse-type gastric cancer

Authors: Jin Qian[1], Sandra Ryeom[1], Bruce Daugherty[2], Seth Lederman[2], Timothy C. Wang[2].
Division of Digestive and Liver Diseases, Irving Cancer Research Center, Columbia University Medical Center, New York, NY 10032, USA
Tonix Pharmaceuticals, Inc., 26 Main Street, Suite 101, Chatham, NJ 07928

Title: Combination Immunotherapies 1
Location: Orange County Convention Center, Orlando, Fla.
Section: 21, #5088
Date: Tuesday, April 18, 2023
Time: 1:30 p.m. – 5:00 p.m. ET
Abstract: Click here

AACR Presentations

Presentation #3

Title: A CXCR4 partial agonist TFF2-MSA improves anti-PD-1 immunotherapy in advanced gastric cancer by selectively targeting PMN-MDSC

Authors: Jin Qian[1], Chenkai Ma[2], Quin T. Waterbury[1], Christine S. Moon[1], Xiaofei Zhi[1], Feijing Wu[1], Ruhong Tu[1], Biyun Zheng[1], Hiroki Kobayashi[1], Leah B. Zamechek[1], Ryan H. Moy[1], Arnold Han[1], Bruce Daugherty[3], Seth Lederman[3], Timothy C. Wang[1]

[1]Irving Cancer Research Center, Columbia University Irving Medical Center, New York, NY,[2]Integrated Diagnostic, Human Health, Health and Biosecurity, CSIRO, Westmead, Australia,[3]Tonix Pharmaceuticals, Inc., Chatham, NJ

Topic: Immune Targets and Therapies

Location: San Diego Convention Center, San Diego, CA.

Session: MS.IM01.02

Date: Monday, April 8, 2024

Time: 3:20 p.m. – 3:35 p.m. PT

Abstract: Click Here

Appendix

Qian et al., AACR 2023_Abstract #5088

Daugherty et al., AACR 2023 Abstract #704

Qian J, Ma C, Waterbury QT, Zhi X, Moon CS, Tu R, Kobayashi H, Wu F, Zheng B, Zeng Y, Zheng H, Ochiai Y, White RA, Harle DW, LaBella JS, Zamechek LB, ZhongMing Hu L, Moy RH, Han AS, Daugherty BL, Lederman S, Wang TC. A CXCR4 partial agonist improves immunotherapy by targeting immunosuppressive neutrophils and cancer-driven granulopoiesis. *Cancer Cell*. 2025 Aug 11;43(8):1512-1529.e11. doi: 10.1016/j.ccell.2025.06.006. Epub 2025 Jun 26. PMID: 40578360; PMCID: PMC12233206. A CXCR4 partial agonist improves immunotherapy by targeting immunosuppressive neutrophils and cancer-driven granulopoiesis - PubMed