#1079 Development of a biologically aligned ex vivo TumorGraft3D platform to evaluate STC-1010-mediated immune priming and colorectal tumor killing

I. Melero[1,2], M. Frot[3], F.-J. Chou[4], S. Suwunnakorn[4], M. Vallier[5], Y. Pijoff[3], V. Jagannathan[4], M. Mancini[4], B. Pinteur[3], G. Alzeeb[3], F. Ghiringhelli[5]

[1]Clínica Universidad de Navarra, CIBERONC, Pamplona, Spain; [2]Nuffield Department of Medicine, University of Oxford, Oxford, UK; [3]Brenus Pharma, Lyon, France; [4]Champions Oncology, Rockville, MD, USA; [5]Department of Medical Oncology, Centre Georges-François Leclerc, University of Burgundy–Franche-Comté, INSERM U1231, Dijon, France

SITC 2026
Poster #1079

01. Background

- **Colorectal cancer** (CRC) is the 2nd leading cause of cancer-related deaths globally[1], with most metastatic cases (mCRC) being microsatellite stable (MSS) and **poorly responsive to immune checkpoint blockade**[2,3].
- We developed STC-1010, an **in vivo antigen-based immunotherapy** using the proprietary off-the-shelf **"Stimulated Ghost Cells" (SGC) platform.**
- STC-1010 combines 3 human CRC lines, conditioned by controlled stress to reveal tumor plasticity and resistance antigens, then haptenated for enhanced immunogenicity[4]. STC-1010 is designed to activate T and B cells and trigger anti-tumor immunity in cold tumors.
  It is being evaluated in the first-in-human **Phase I/II BreAK CRC-001 trial (NCT06934538) in first-line MSS mCRC with standard of care.**
- **Innovation:** Patient-derived 3D tumor models are widely used for drug testing but **remain underexplored for active immunotherapies**.
  We developed an **ex vivo workflow reproducing the STC-1010 priming-to-killing** cascade in a **clinically aligned 3D CRC model.**

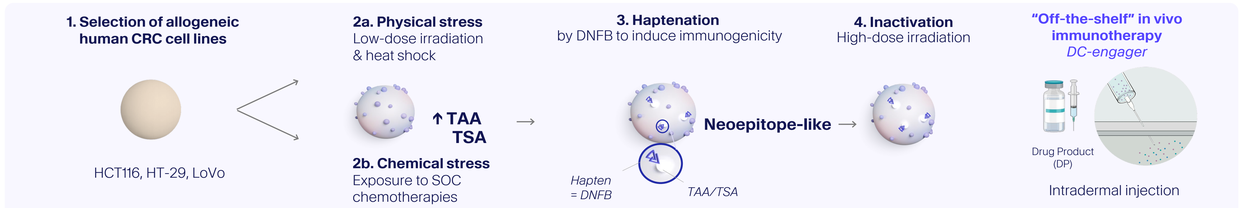
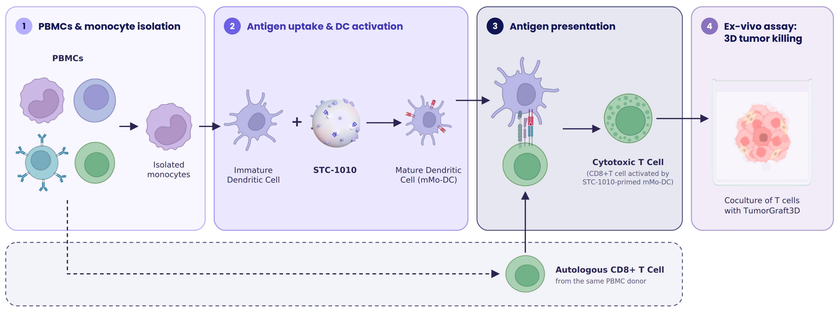


Figure 1: The Stimulated Ghost Cells (SGC) platform. CRC: colorectal cancer; DNFB: dinitrofluorobenzene; SOC: standard of care; TAA: tumor-associated antigens; TSA: tumor-specific antigens.

02. Ex vivo workflow Reflects the STC-1010 mechanism of action from DCs to primed CD8+ T cells



- **Monocytes and CD8+ T cells** from healthy-donor PBMCs were used to generate an **autologous DC–T-cell priming system**.
- **mMo-DCs were exposed to STC-1010** or vehicle, **and antigen uptake and DC activation** were assessed by flow cytometry and RNA-seq.
- Primed CD8+ T cells were then tested for **tumor killing in patient-derived TumorGraft3D cultures** (CTG3D).

03. DC priming STC-1010 is captured by DCs and switches on antigen processing

Results: STC-1010 is captured by mature DCs and activates antigen-processing pathways

- Our workflow enables the differentiation of monocytes into HLA-DR+ CD80+ **mature mMo-DCs** (A).
- Haptenated material was strongly detected in STC-1010-treated mMo-DCs (71% TNP+ vs <5% with vehicle), confirming **STC-1010 uptake** (B).
- Transcriptomic analysis of DCs identified enrichment of **antigen processing & presentation and phagosome pathways** (C).

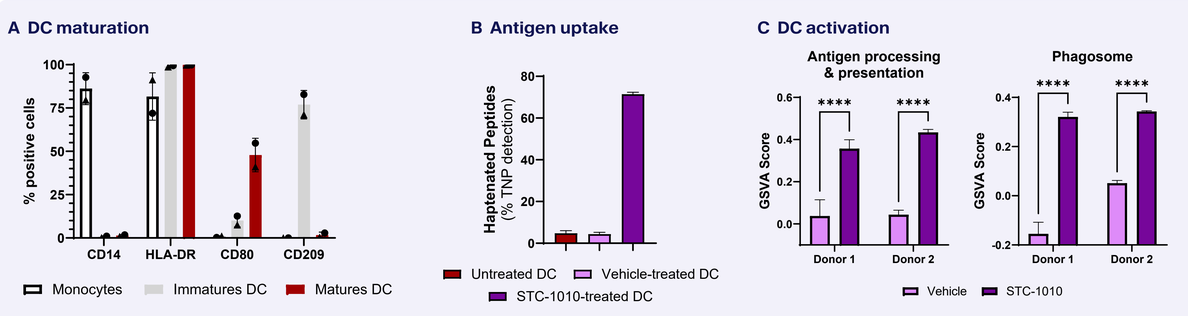


Figure 2: STC-1010 is captured by mature dendritic cells and activates antigen-processing pathways
A. Differentiation of monocytes into mMo-DCs, illustrated by loss of CD14 and acquisition of HLA-DR, CD80 and CD209. **B.** Detection of haptenated material in STC-1010-treated mMo-DCs by anti-TNP flow cytometry. **C.** RNA-seq/GSVA analysis of immune pathways activated after STC-1010 exposure. Data are mean ± SD of three replicates. Two-way ANOVA with Tukey's multiple-comparisons test; ****P<0.0001.

04. TumorGraft3D model establishment Selected to reflect the BreAK CRC-001 patient population

1 · Model generation TumorGraft3D™ (PDXO) platform, Champions Oncology: patient-derived xenograft 3D organoids

Patient (tumor sample) → PDX (in mice) → Tumor (harvested) → Fragment (separation) → CTG3D (establishment & expansion) → Aliquoting (& freezing) → Cryo (inventory)

2 · Ex vivo co-culture assay from thawed fragments to readout

Day −7 · Seeding | Day 0 · Add T cells | Day ~3 · Readout

7 days | ~3 days

Seeding
Cryopreserved CTG3D fragments are seeded with no added matrix, in indication-specific media

PDXO formation (7 days)
Fragments re-aggregate into multiclonal 3D tumors

Add STC-1010-primed T cells
STC-1010-primed T cells are added to the PDXOs

Tumor killing
Assessment of tumor cell viability (FVS780-TumorDump+) and tumor cell apoptosis (FVS780+AnnexinV+) by flow cytometry

Champions CRC models — RNA-seq & molecular profiling → **BreAK CRC-001 profile** — MSS · KRAS-mut · BRAF-WT · liver mets → **CTG-0359** — selected model

Characteristic	BreAK CRC-001 (N=9)	CTG-0359
Disease characteristics (mCRC)		
Synchronous metastatic disease	9 (100)	
Liver metastases	8 (88.9)	✓ Liver metastasis
Lymph node metastases	5 (55.6)	
Peritoneal metastases	3 (33.3)	
Lung metastases	3 (33.3)	
Molecular profile		
MSS	9 (100)	✓ MSS
KRAS-mutated	8 (88.9)	✓ KRAS-mutant
BRAF-mutated	0 (0)	✓ BRAF-WT

Results: CTG-0359 reflects key features of the BreAK CRC-001 population

- CTG-0359 was selected from **molecularly profiled CRC models** for its clinically relevant MSS, KRAS-mutant, BRAF-WT and liver-metastasis profile.

05. TumorGraft3D killing after STC-1010 treatment

Results: STC-1010-primed T cells induce tumor killing in CTG-0359

- STC-1010-primed T cells **reduced viable TumorGraft3D cells and increased tumor apoptosis** in both donors at E:T 5:1 and 10:1.
- The strongest response showed **~50% lower tumor viability** and **~2-fold higher apoptosis** versus vehicle-primed T cells.
- Tumor killing was donor- and E:T ratio-dependent, with the strongest effect at E:T 10:1.

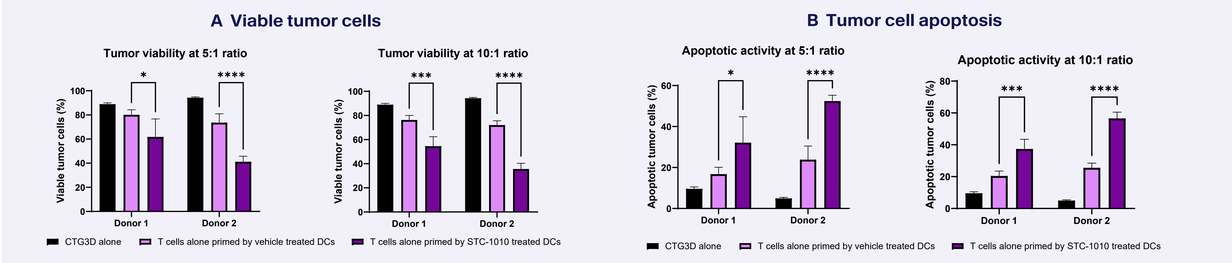


Figure 3: STC-1010-primed T cells reduce TumorGraft3D viability and increase apoptosis. A. Viable tumor cells (FVS780-TumorDump+). **B.** Apoptotic tumor cells (FVS780+AnnexinV+). Two PBMC donors were tested at E:T ratios of 5:1 and 10:1. Data are mean ± SD of four replicates. Two-way ANOVA with Tukey's multiple-comparisons test; *P<0.05, ***P<0.001, ****P<0.0001; ns, not significant.

06. Conclusion

- **STC-1010 is efficiently captured by mMo-DCs and activates antigen-processing and immune pathways.**
- **In a clinically aligned MSS TumorGraft3D model, STC-1010-primed CD8+ T cells reduced tumor viability by up to 50% and increased apoptosis by ~2-fold versus vehicle-primed T cells.**
- **This ex vivo platform links STC-1010 immune priming to tumor killing and can now be expanded across donors and molecularly annotated TumorGraft3D models to explore determinants of response and drive biomarker researches.**

(1) Cancer Today Data version: Globocan 2022 (version 1.1), 2025. (2) Cervantes A, et al. Ann Oncol. 2023;34(1):10–32. (3) Biller LH, Schrag D. Diagnosis and treatment of metastatic colorectal cancer: a review. JAMA. 2021;325(7):669–685. (4) Ghiringhelli F, Front. Oncol. 2024;14:1427428.

Contact: George Alzeeb · galzeeb@brenus-pharma.com