The menace of Cancer Metastasis:

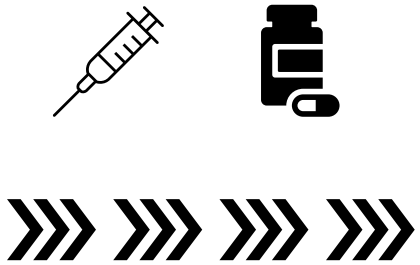
How do we fight it?

Arnab Roy Chowdhury, PhD,
Founder / Director

December, 2022

Bengaluru, India / Marlton, USA

Effect of new cancer drugs 2003-2021



124 FDA-approved drugs

255 solid cancer indications

Overall Survival

1.97-4.60 months

2.8 months

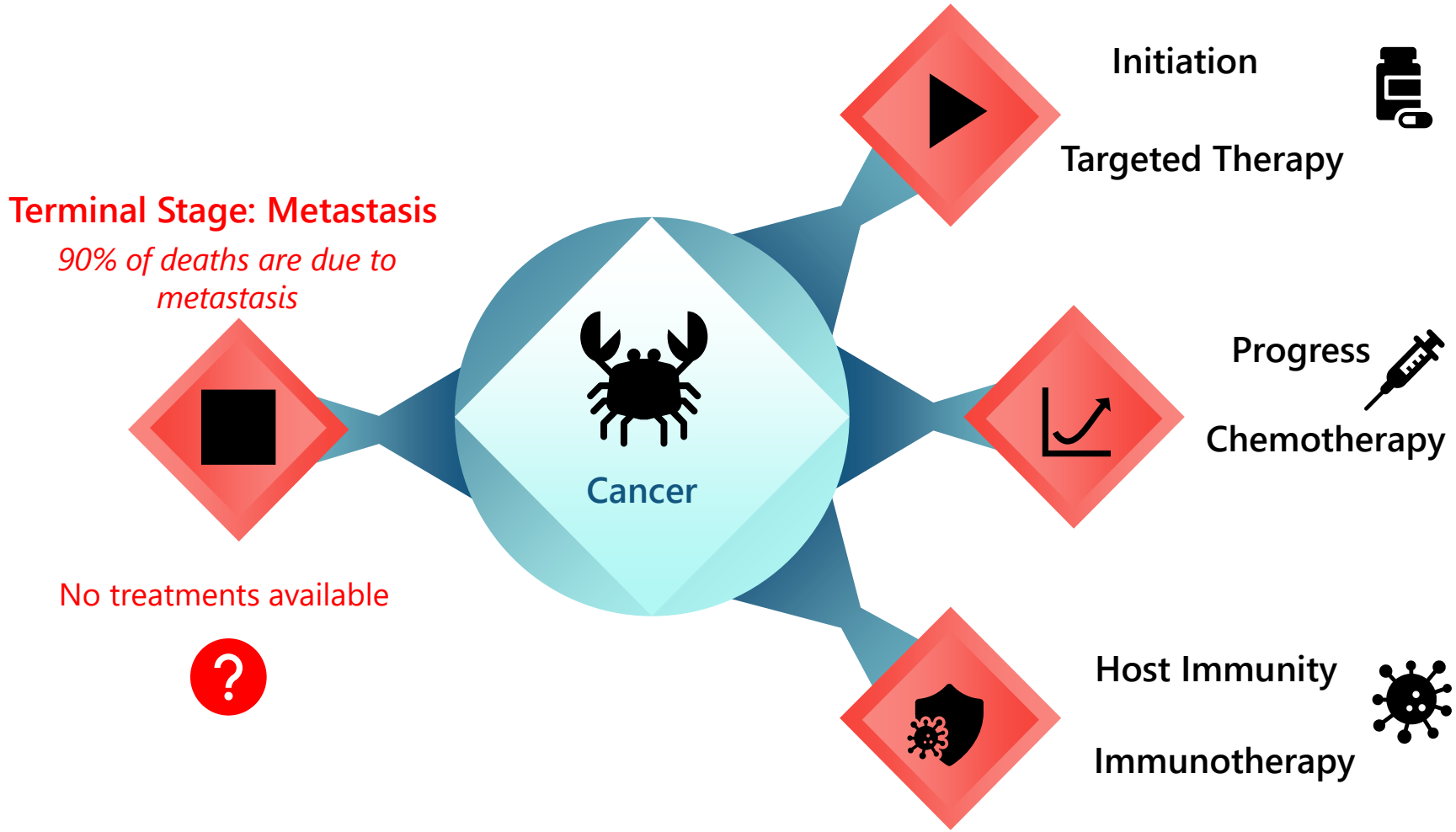
Progression Free Survival

1.50-5.58 months

3.3 months

J Clin Oncol. 2022 Dec 10; 40(35):4095-4106.

Numbers do not lie – cancer treatment is skewed



MESTASTOP™ SOLUTIONS
Giving Life a Second Chance...

Approved drugs for metastatic conditions treat the secondary tumour – NOT the process of metastasis

94 5-yr. survival of localized cancer (breast-colon-prostate-melanoma)	**21** 5-yr. survival of metastatic cancer (breast-colon-prostate-melanoma)
46 5-yr. survival of localized cancer (pancreas-lung-liver-esophageal)	**4.5** 5-yr. survival of metastatic cancer (pancreas-lung-liver-esophageal)
1 Approved drug for metastasis in last 10 years (Denosumab)	**0** Blockbuster cancer drugs treat metastasis

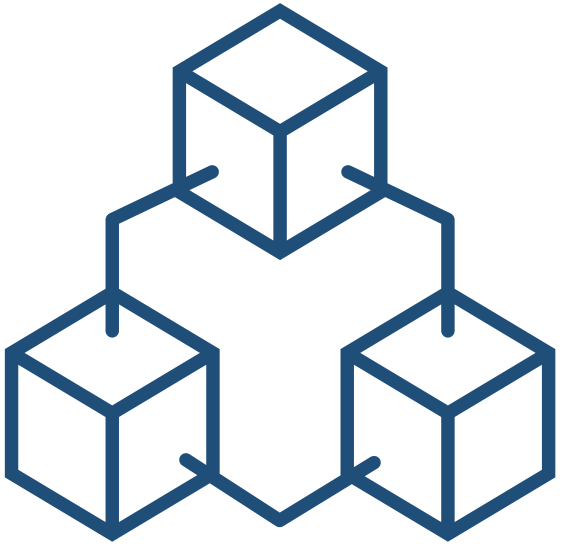
3-key challenges Impeding drug discovery

1. What is the IDEAL target that would translate into patients?
2. How to TRIAGE from 1000 to 1 molecule?
3. How to SELECT patients for clinical trials?

3 platforms to solve the puzzle

METASTOP™ SOLUTIONS
Giving Life a Second Chance...

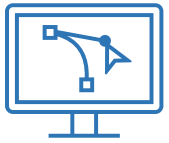
METAssay™



METSCAN™

METVivo™

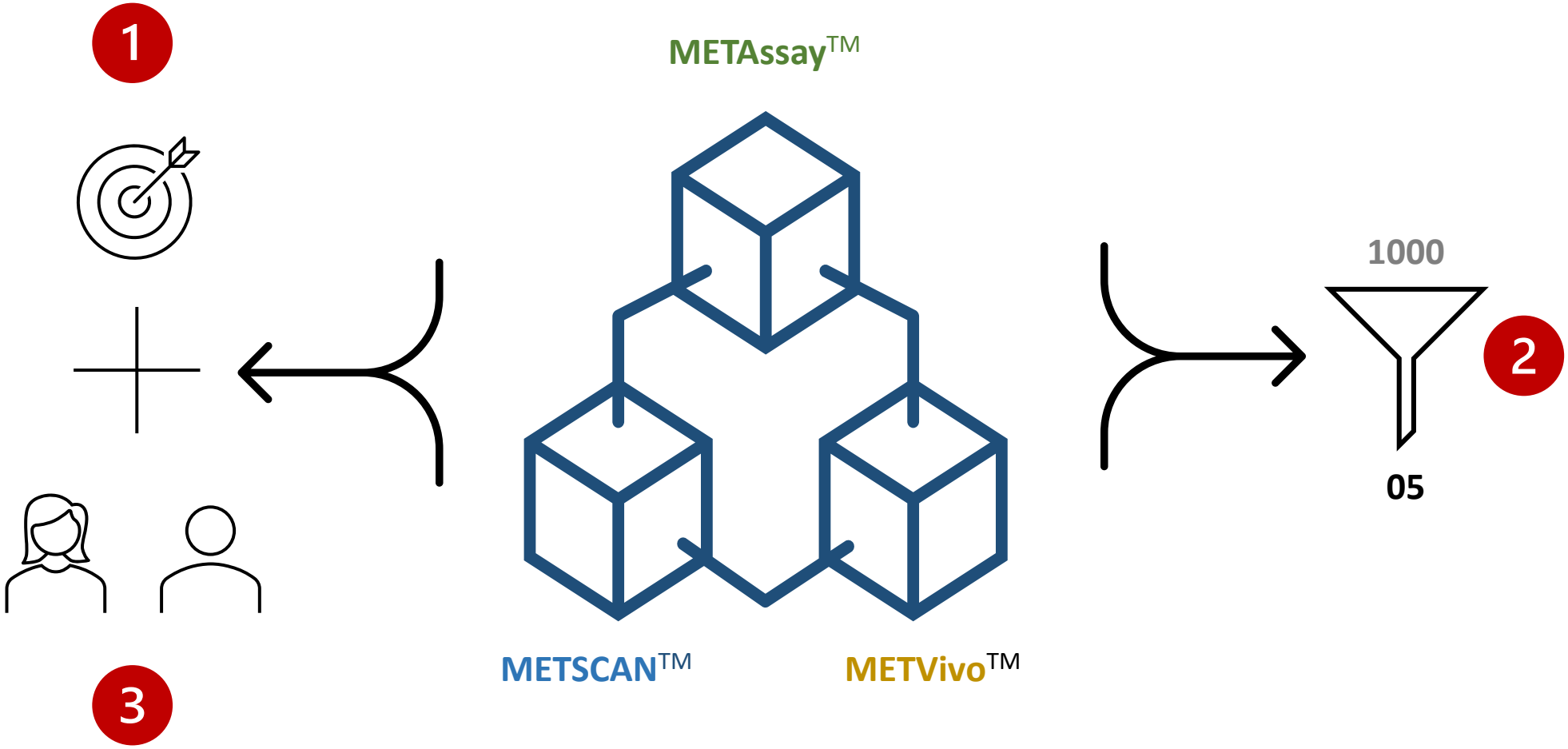
- 30 cellular assays dissecting metastasis
- How moving cells are different from growing cells



- Patient sample translation
- Which steps are most critical
- Which patients are at the highest risk

- Time-sensitive animal model
- Faster turnaround
- Robust, 100% met
- Kinetic and end-point

Our Solution



Our Capabilities

MESTASTOP™ SOLUTIONS
Giving Life a Second Chance...

- Give us an anti-cancer lead/candidate – we will help position for metastasis
- Give us a library of compounds, and we will pick the best 5 with anti-metastasis activity
- Give us approved drugs, and we will repurpose the best compound for metastasis AND/OR profile them for safety
- Interested in any tissue-specific cancer or metastasis? We can help understand biology by customizing our platform.

Publications, Patents & Awards

8 international posters to date

A cell-based phenotypic assay platform for cancer metastasis drug discovery and diagnostics

Dissecting tumorigenesis and metastatic properties of cell lines by phenotypic functional assays and plasticity ratio (PR)

EACR 2021

The role of plasticity ratio (PR) in differentiating between metastatic and tumorigenic properties in cell lines and patient tumor samples

MRS METASTASIS RESEARCH SOCIETY

Tumor cell induced platelet aggregation is independent of tumor invasiveness as observed from both cell lines and primary tumors - 2021

METSCAN, a novel and proprietory algorithm to predict the metastatic potential of primary tumour patients - Nov 2022

COLLABORATORS

IMMUNO BIOME | peptris | ECTICA TECHNOLOGIES

Rajiv Gandhi Cancer Institute and Research Centre | birac ignite innovate incubate

AWARDS

- Top 20 Biotech – India, 2021
- Top 10 R&D Startup – India, 2021
- Startup of the year in Biotech – India, 2021
- Top 20 Leading Healthcare Service Providers, India, 2022
- Winner - NITB Startup Expo, 2022
- Best Metastasis R&D specialists - GHP Global, 2022
- 3rd - IIT BHU Shark Tank, 2022
- Top 10 Healthcare, India, 2022
- Top 10 Biotech, India, 2022
- Next Generation presentation, Bio Eur 2022

PATENTS

PCT application published "Systems and methods for predicting cancer metastasis and screening of drugs"
#WO 2022/059026 A1

PCT filed "Methods for producing a spontaneous metastasis model"
#PCT/IN2022/050928

A novel, orthotopic spontaneous metastasis animal model for drug discovery that works in only six weeks

Survival and colonisation axis of metastasised cells in the secondary tissue: to target or not to target?

THE BRITISH ASSOCIATION FOR CANCER RESEARCH bacr

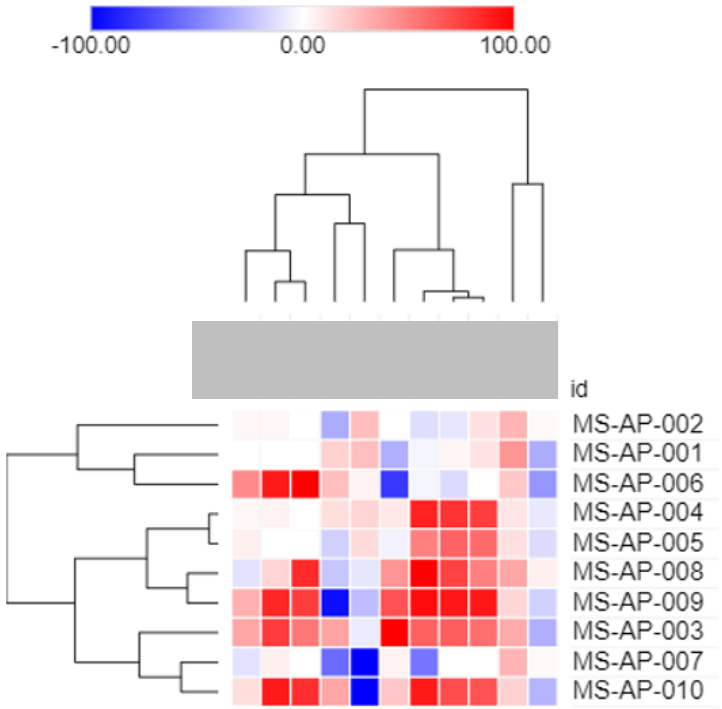
Exploiting the differential cellular biomecha
between metastatic and non-metastatic cell
tool for predictive diagnostics

2 PCT filed

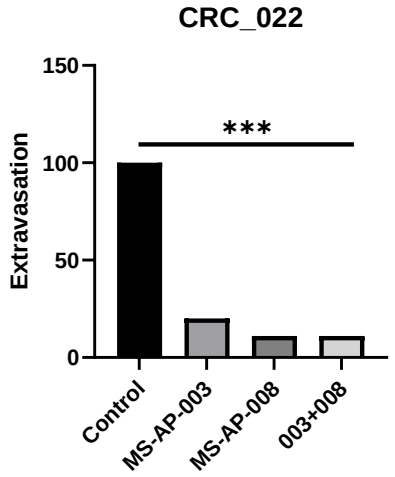
MESTASTOP™ SOLUTIONS
Giving Life a Second Chance...

Case Study I: Triaging and Repurposing

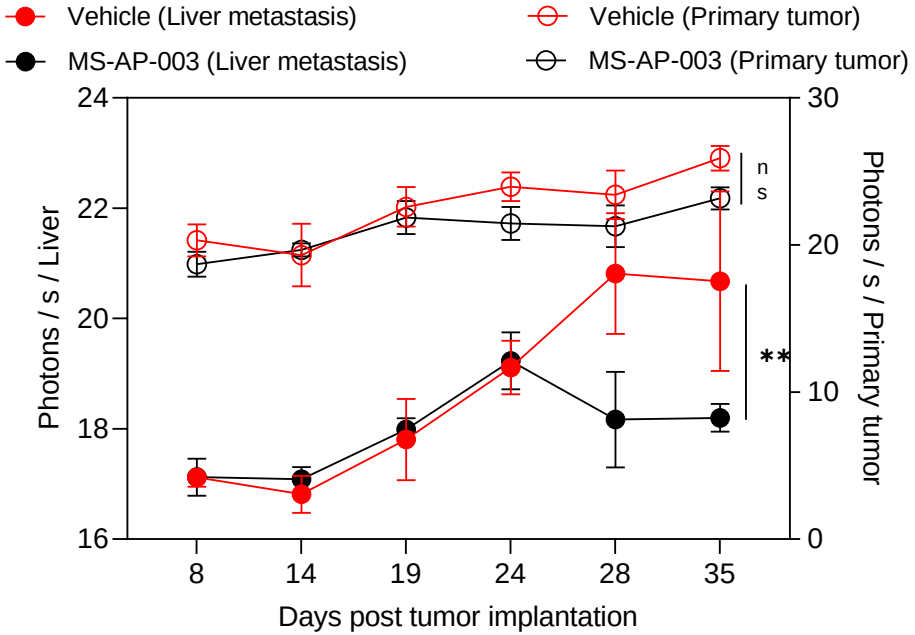
Case Study 1: Does the platforms work?



10 approved drugs with no reported anti-metastasis effect screened across the weighted platform

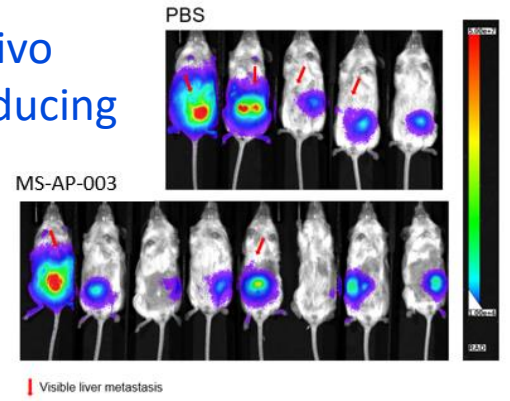


2 hits were progressed for multiple patient sample translational analysis

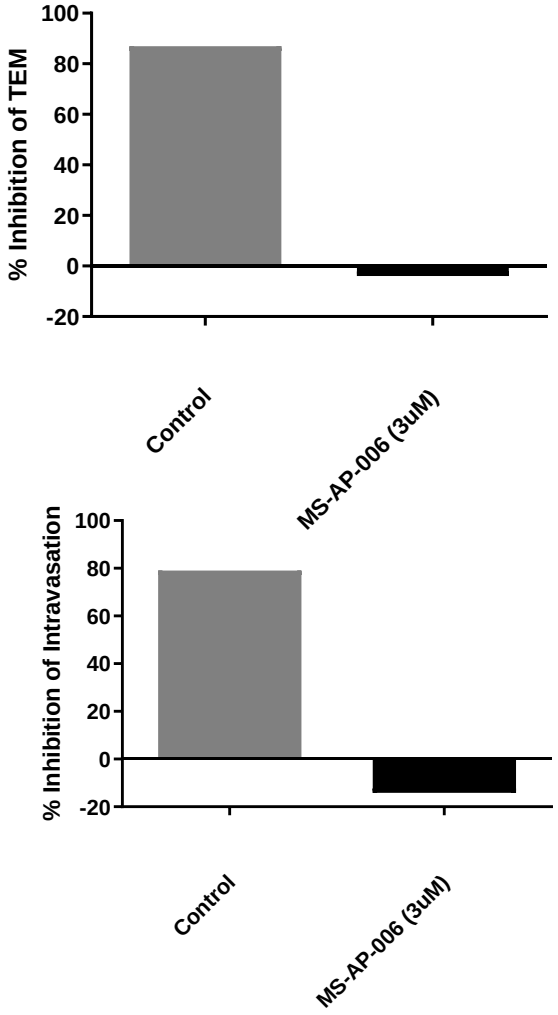


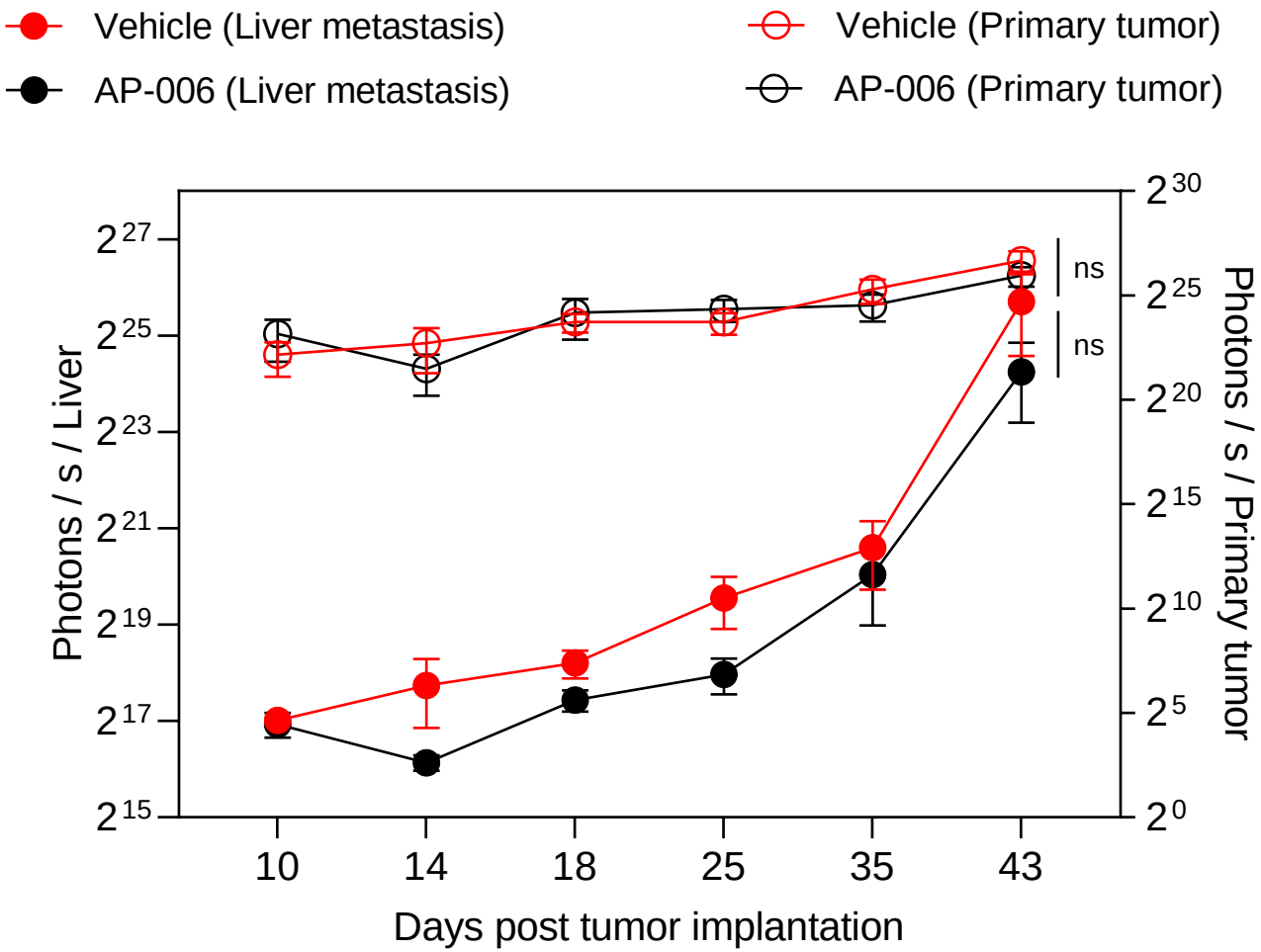
Excellent in vivo efficacy in reducing metastasis

No effect on tumour size



Negative Control establishes that platform is translational

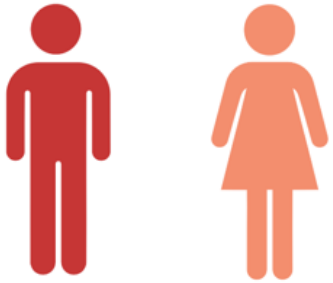




Clinical relevance of repurposing - Retrospective Study PoC

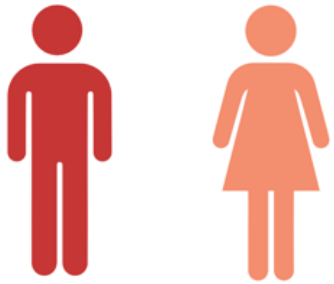
MESTASTOP SOLUTIONS
Giving Life a Second Chance...

Colorectal tumors isolated from treatment naive primary tumor patients with no clinical metastasis*



Sep 2011 - Sep 2016

Follow - up on patients*



Sep 2022

Survival Staus

Treatment & Medications

Clinical Annnotation

Machine Learning

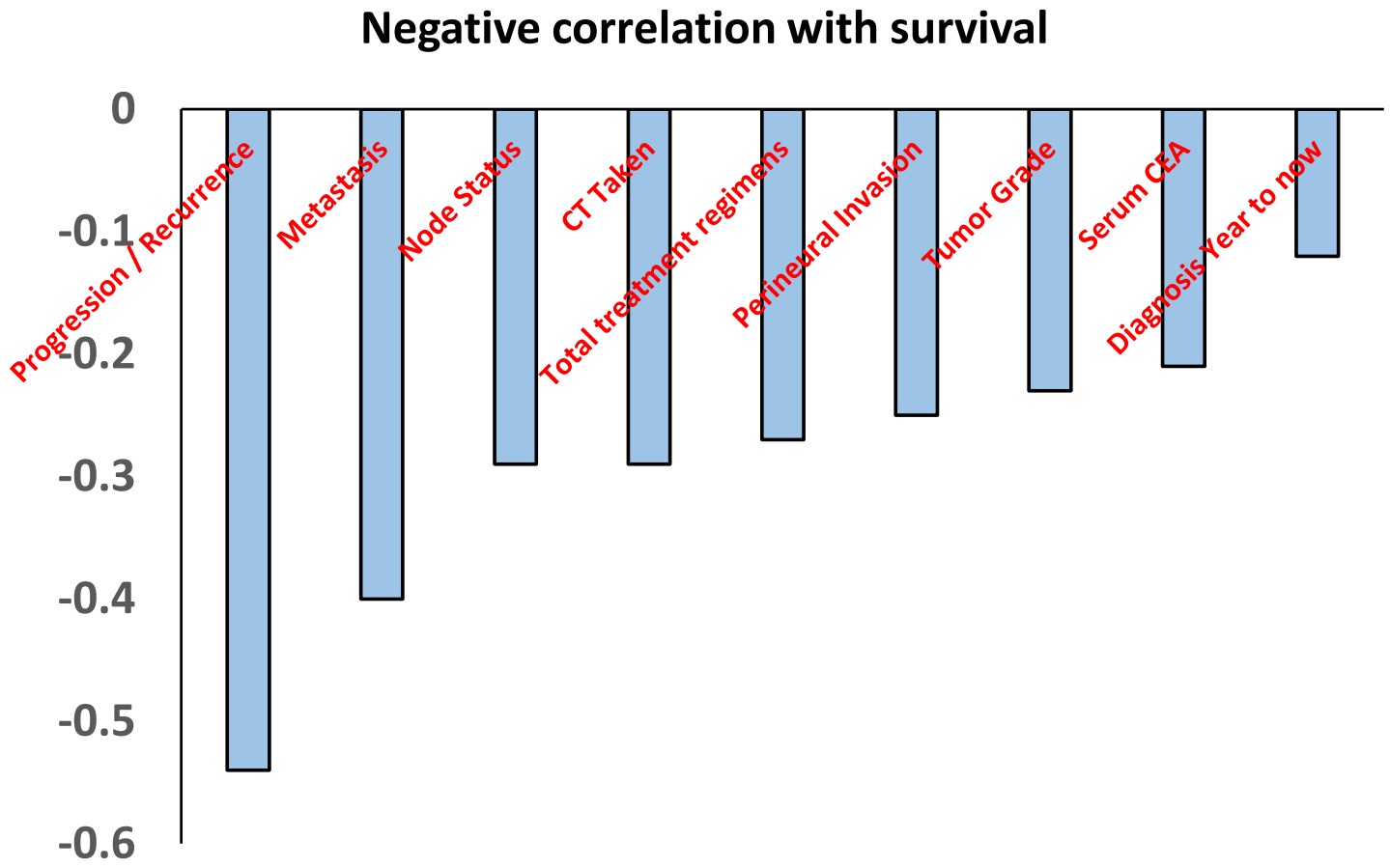
Identify most **weighted factors** contributing towards **survival** and **death**

+

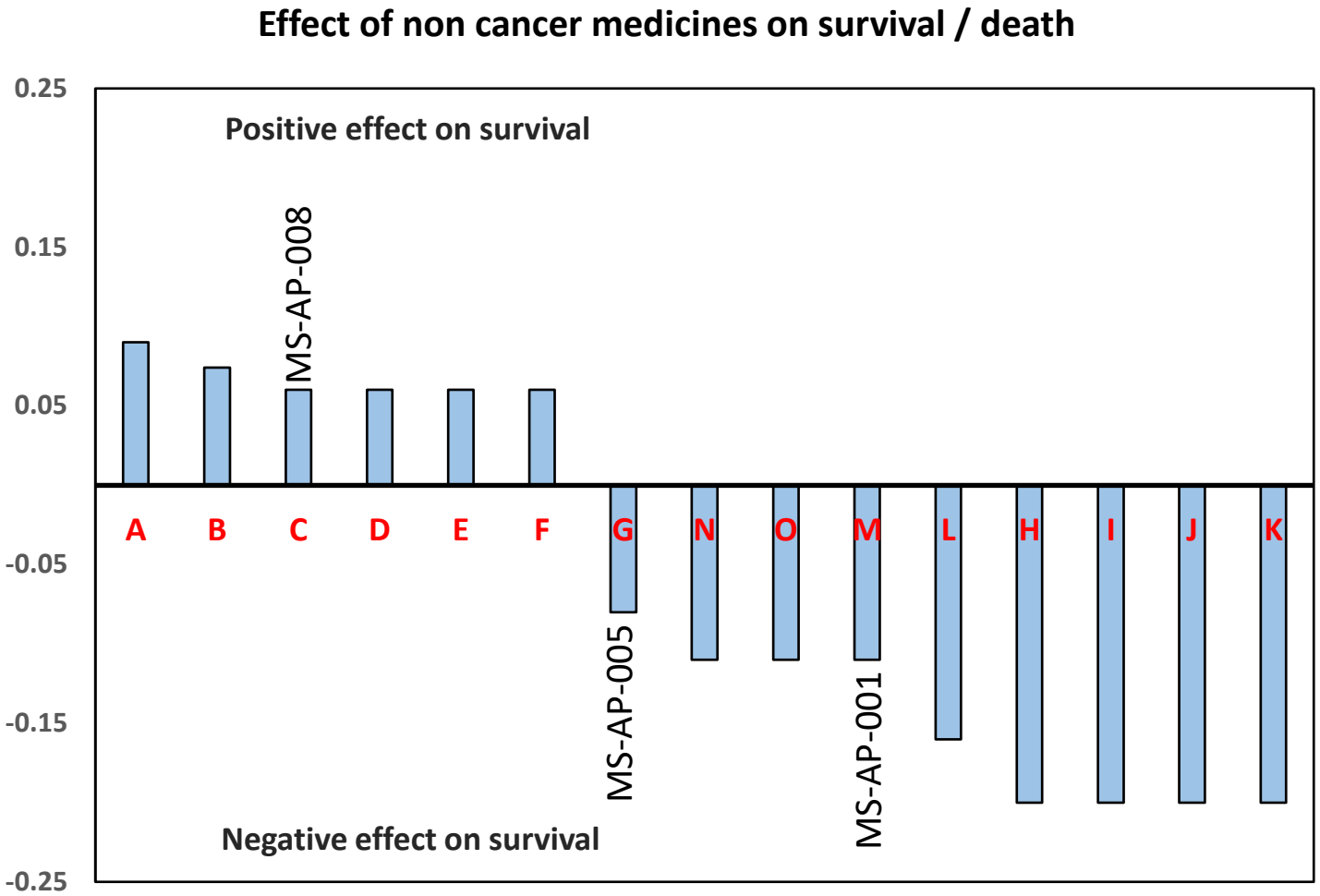
Effect of **medications**, treating **chronic diseases**, on **survival**

**In collaboration with Rajiv Gandhi Cancer Institute, Delhi*

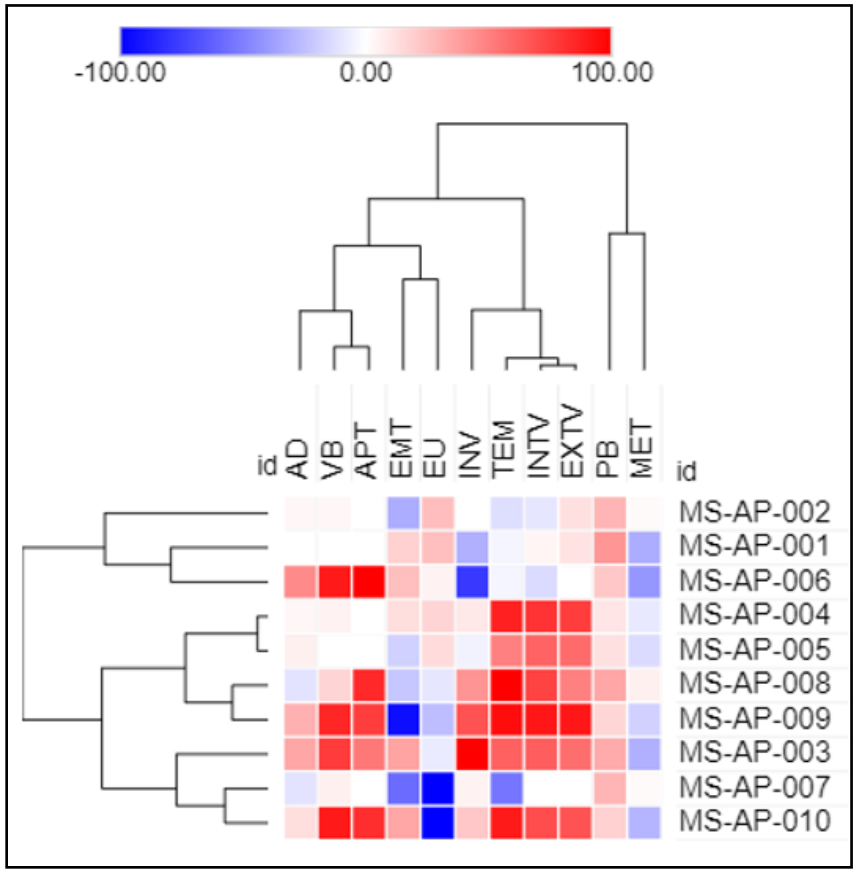
Most weighted steps, inversely affecting survival



Non-cancer medications that has effect on survival



Clinical data based weightage



METAssay data

Summary

- Machine learning algorithm, defining weightages, passed QC as it identified the correct parameters responsible for survival/death and rank-ordered them.
- Using the same program, other drugs were identified for their effect on survival (both positive and negative correlation)
- MS-AP-008 seems relevant in clinical settings in positively correlating with survival.
- MS-AP-008 clinical data matches with METAssay and METVivo data.
- Weaker compounds from the METAssay heat map are shown to correlate negatively with survival in the clinical setting, e.g MS-AP-001 and 005.
- Rank order of MS-AP-001 and MS-AP-005 from the METAssay panel also matches in the clinical setting.

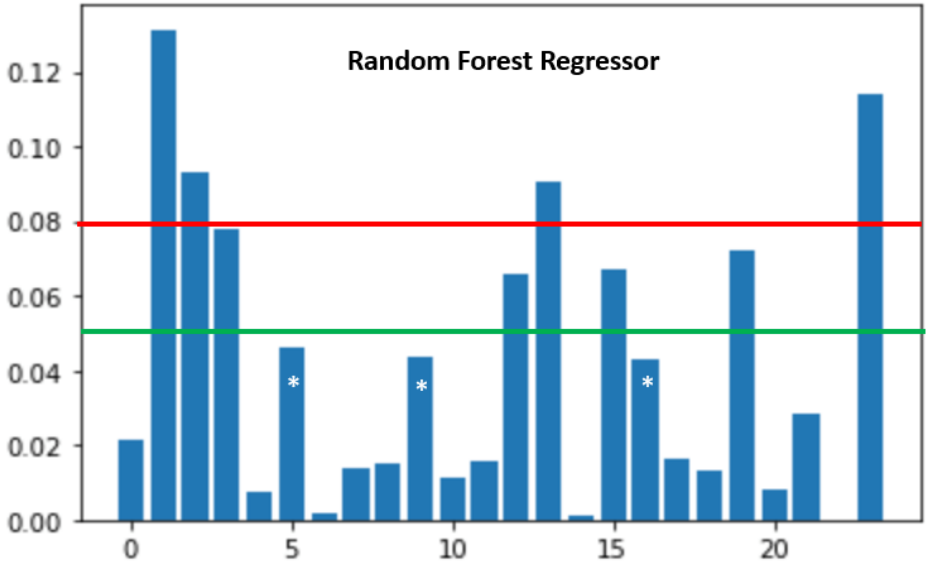
METAssay™ & METVivo™ can triage compounds that are clinically relevant

CASE STUDY II – Identification & Validation of Novel target

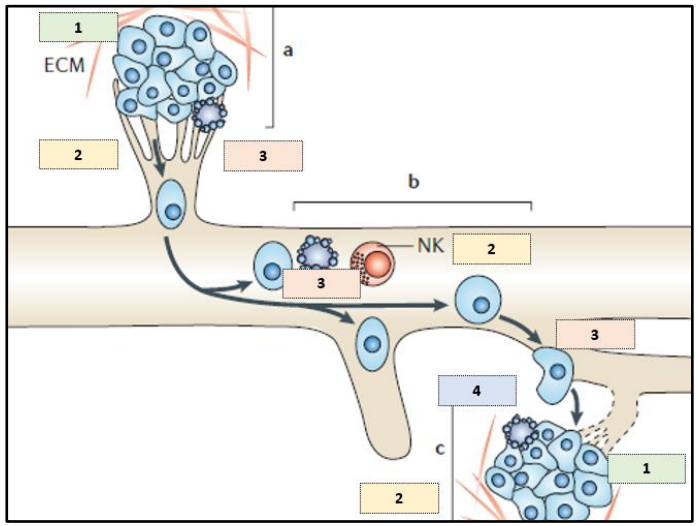
METAssay™ to METSCAN™: Identifying targets

METAssay™ wet lab data from cell lines and patient samples

Identification of 4 novel targets, all first-in-class for metastasis



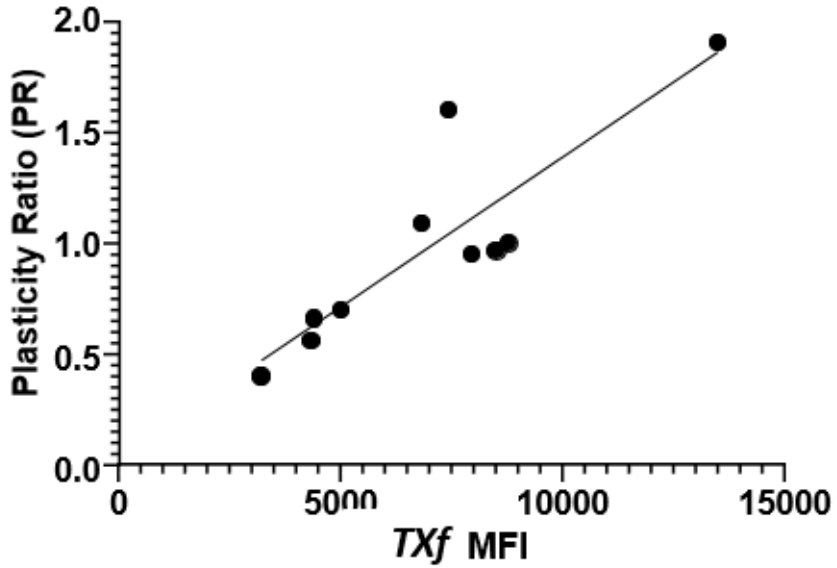
METSCAN™ Identifies weighted rate-limiting steps



Identification of four novel first-in-class targets for metastasis

Case Study: Targeted Discovery PoC established

1. *TXf* OE and CRISPR in colorectal cancer
2. *TXf* OE and CRISPR in triple-negative cancer
3. Pharmacological intervention of weighted steps both in 2D & 3D
4. Pharmacological intervention in patient tumour samples
5. Biochemical assay standardized

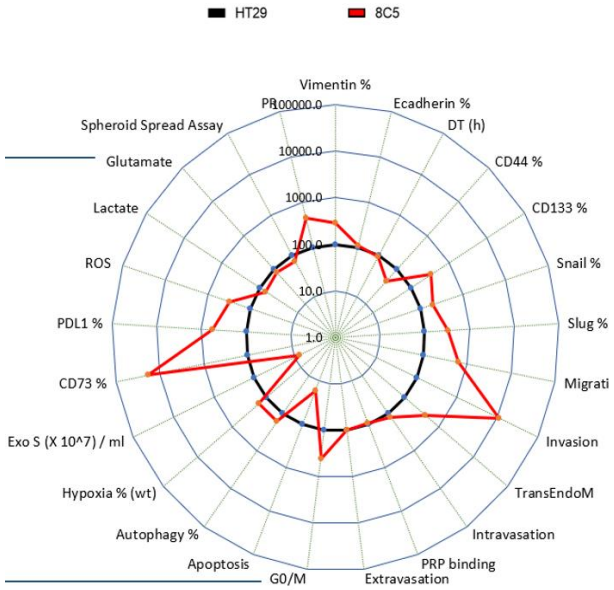


Positioned to start the first drug discovery programme

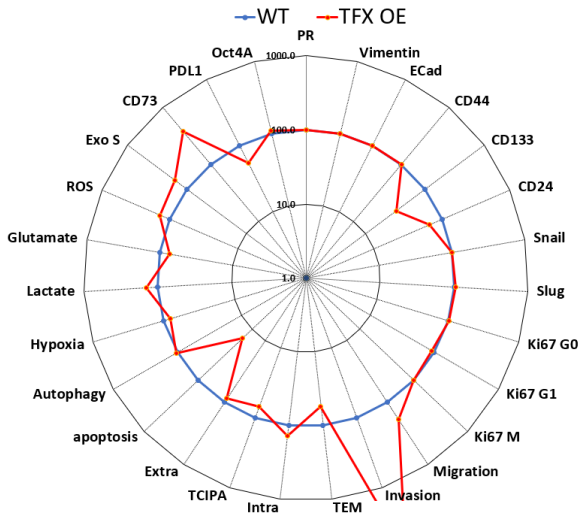
Discovery: genetic validation of first-in-class target

MESTASTOP SOLUTIONS
Giving Life a Second Chance...

Overexpression

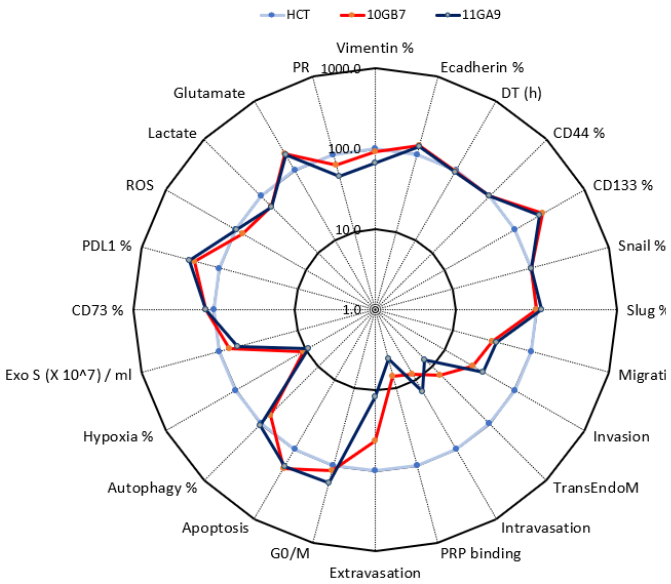


Colon

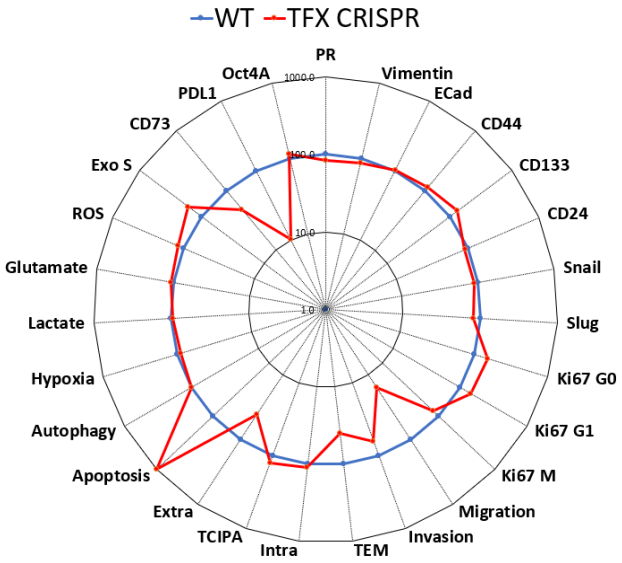


TNBC

CRISPR CAS

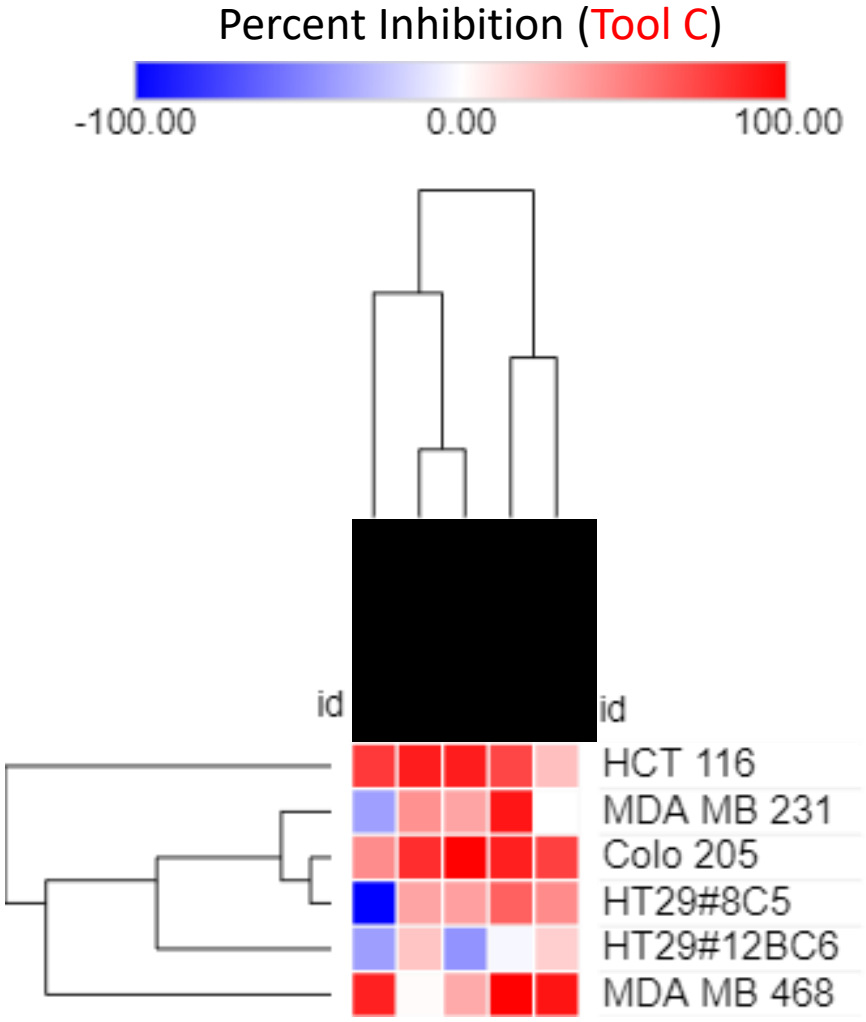


Colon

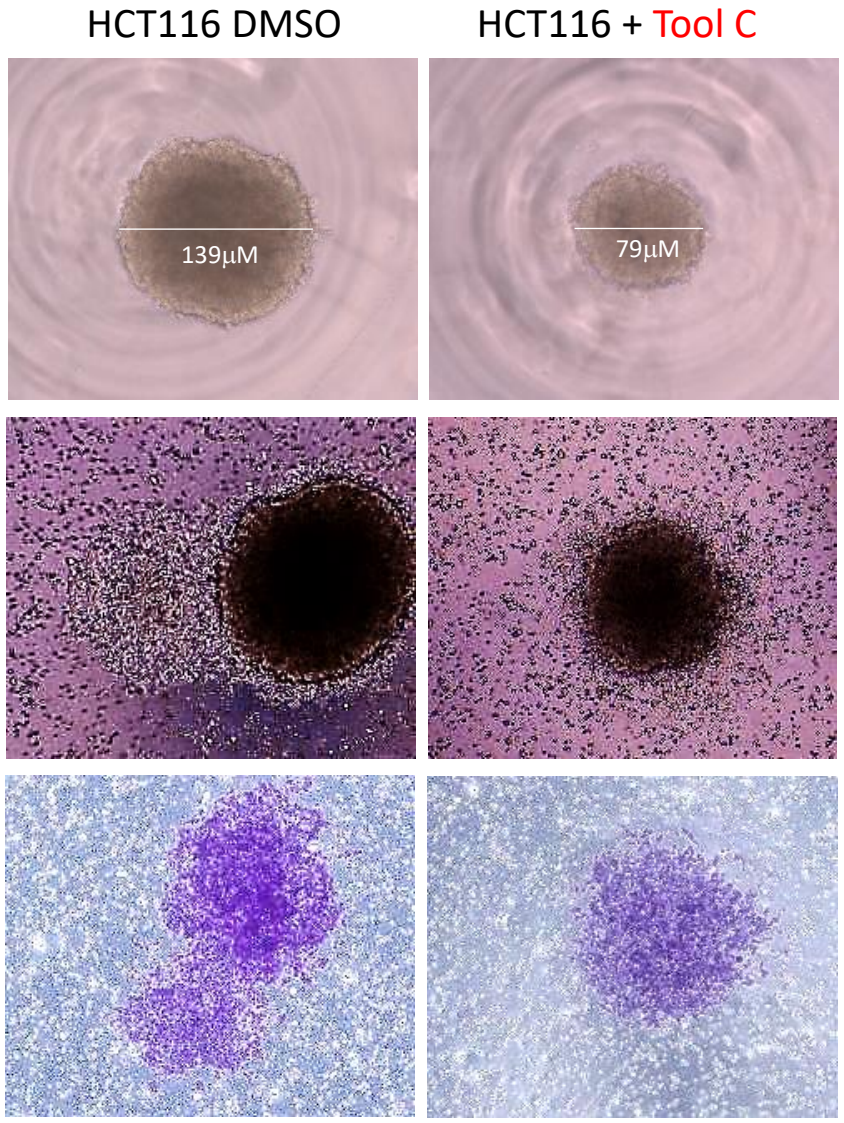


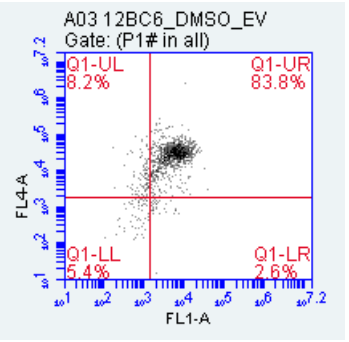
TNBC

Target Validation: Pan tumor effect * – both in 2D & 3D

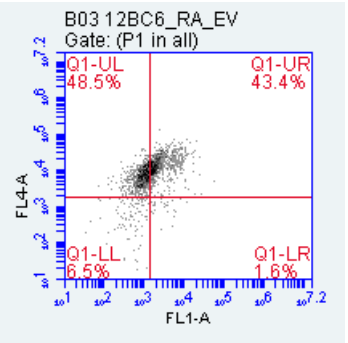


*Independent of p53

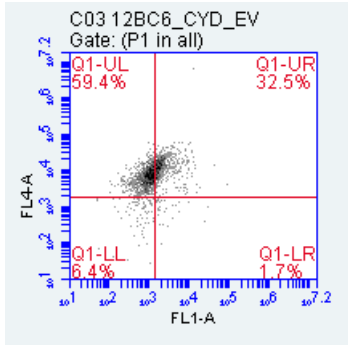




Control
PR = 0.97



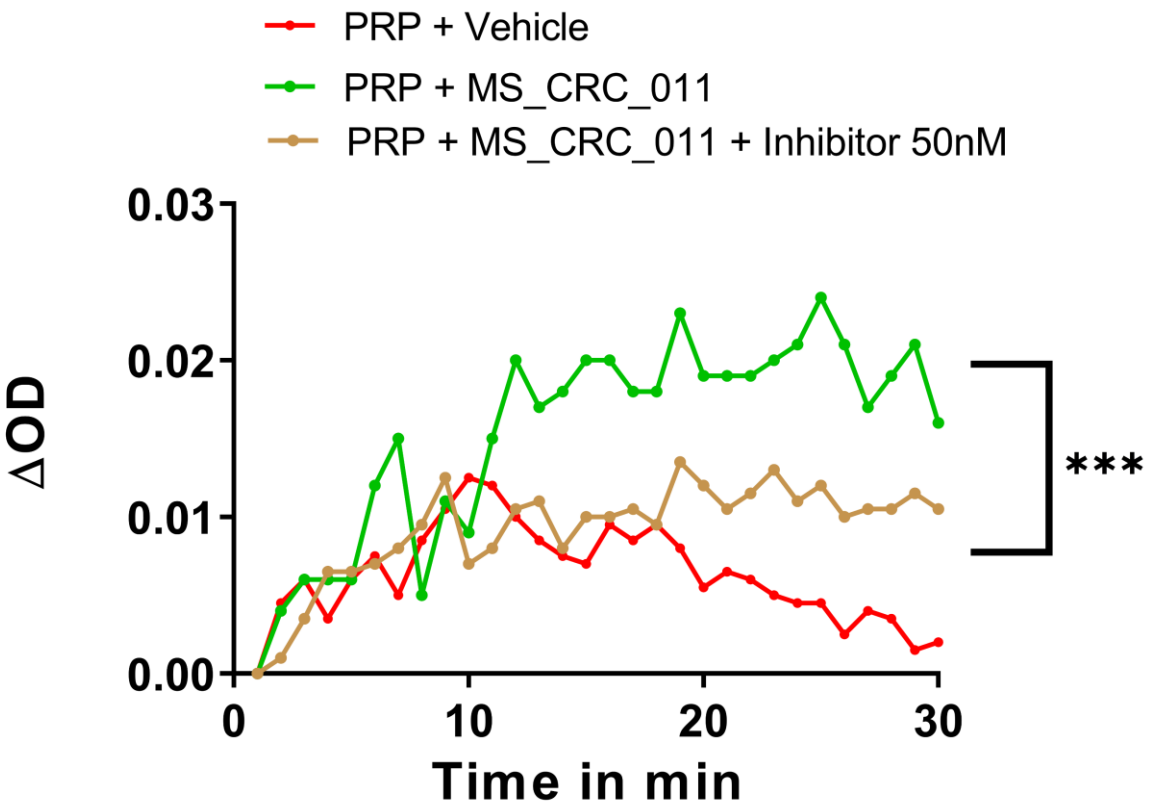
+ ve Control
PR = 0.54

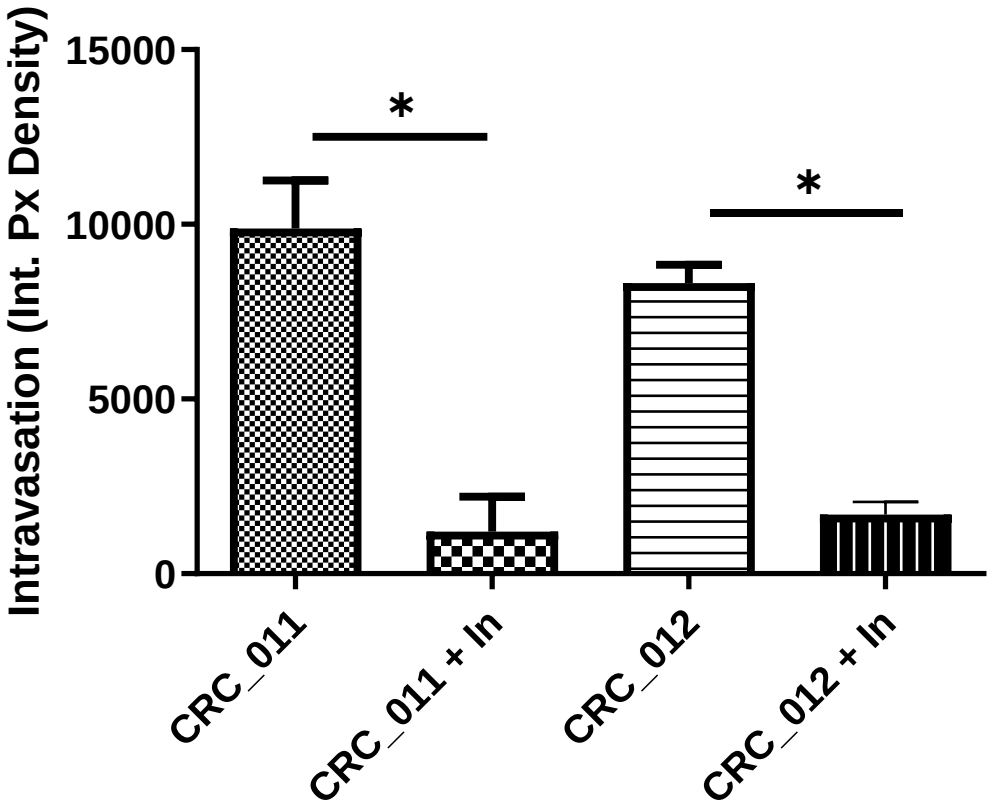


Tool C
PR = 0.42

Cell line confirmation

Target Validation: In Patient Samples

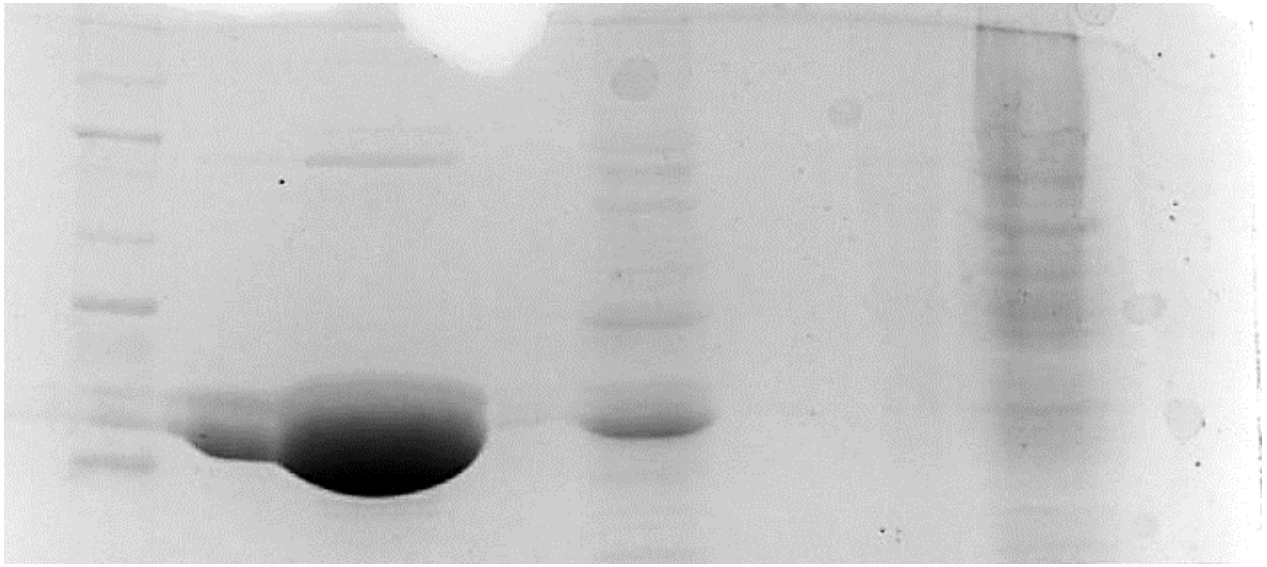




Patient confirmation

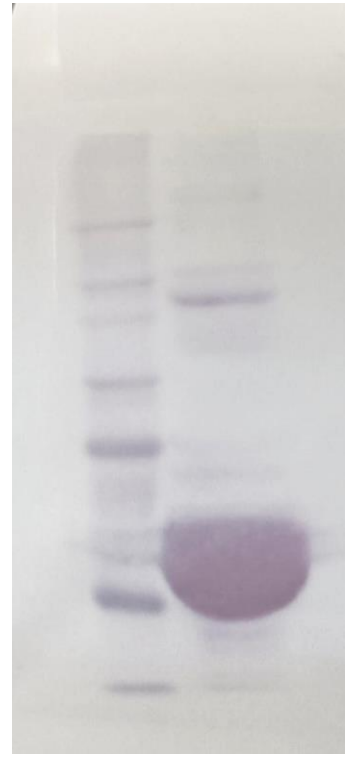
Expression & purification of *TXf*

Marker Elute Flow Through Load



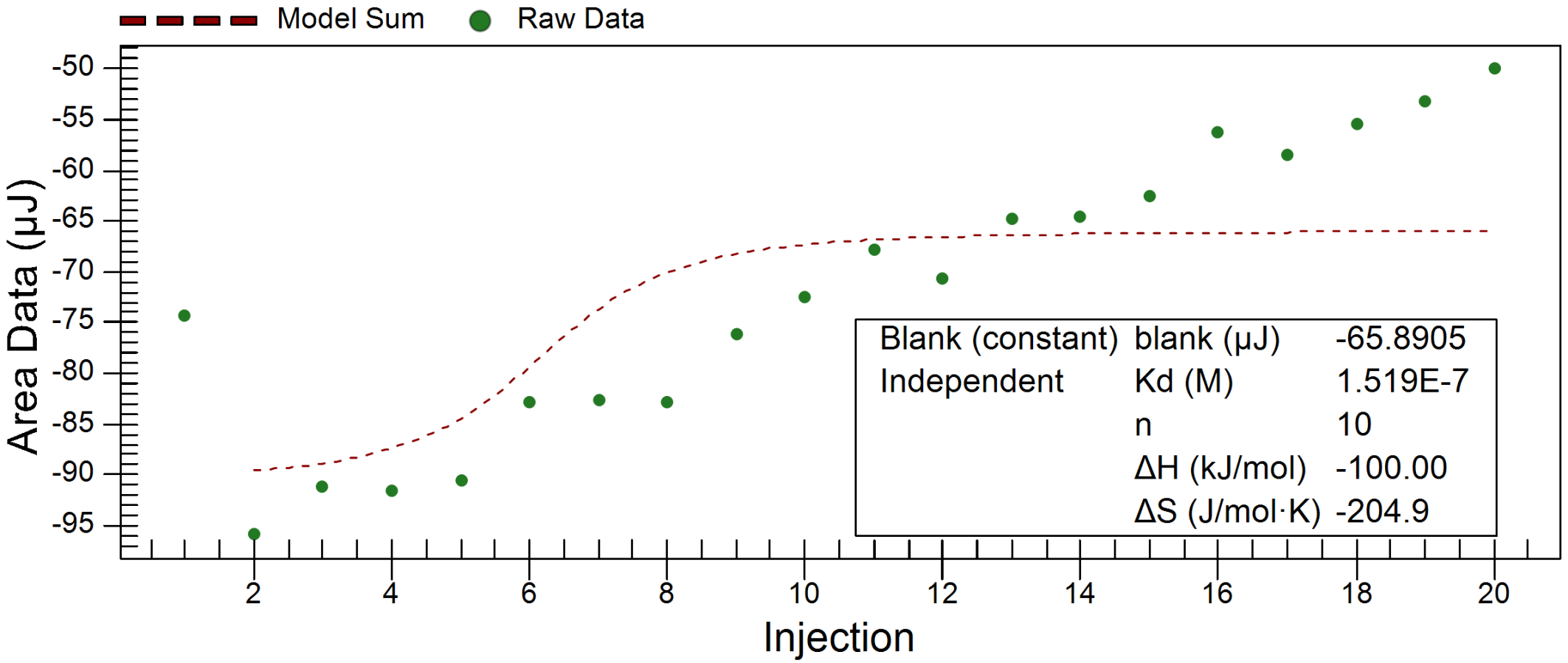
Gel Electrophoresis

Marker Elute



Western Blot

Biochemical assay optimization - ITC



Summary

- Algorithm identified eight critical steps
- Four first-in-class targets identified that play a critical role in these steps, especially in the latter part of the metastasis biology
- One target was the same TX*f* that was used for genetic engineering
- TX*f* purified and biochemical assay standardised

METSCAN™ can identify clinically relevant rate-limiting steps of metastasis

CASE STUDY III – Companion Diagnostics

METSCAN™ :Prediction of metastasis probability

Machine learning, prediction of metastatic probability

Goal: Predict the metastatic probability of treatment-naive primary tumours,

M0 (no metastasis), Any tumour grade or node status (blinded)

Support Vector
Machine
(92.3% Accuracy)

The first trial completed in CRC (13 patients)– no false negatives, three matches to date

A second trial ongoing for both CRC & H&N

International
Patent filed