

**DEVELOPMENT AND VALIDATION OF PERSONALIZED EX VIVO PLATFORM  
MIMICKING PATIENT HETEROGENEOUS TUMOR MICROENVIRONMENT TO  
ENABLE PERSONALIZED TREATMENT FOR BREAST CANCER'**



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# One Size Fits All

At present, most of the medicines for cancer patients are still representing empirical approach for therapy

## Journal of Medicine

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Volume 332

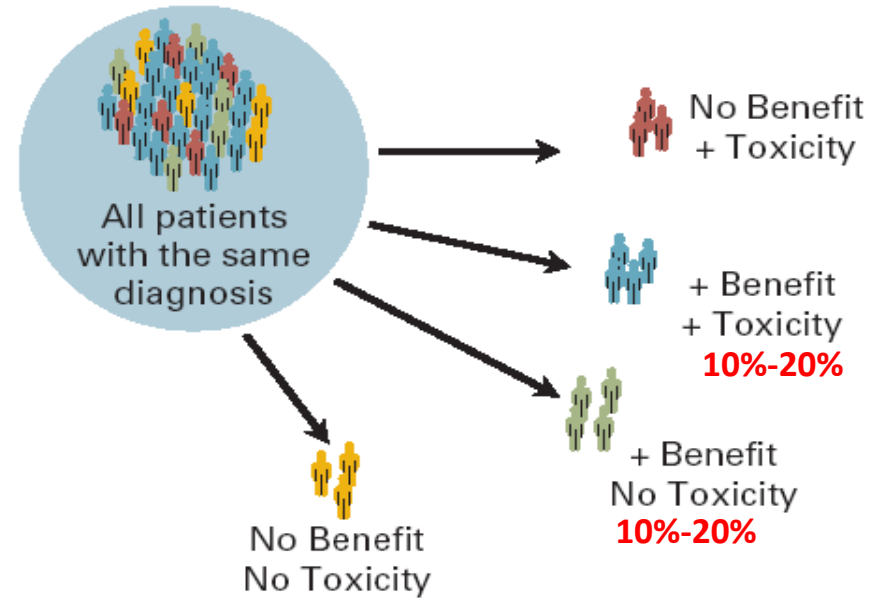
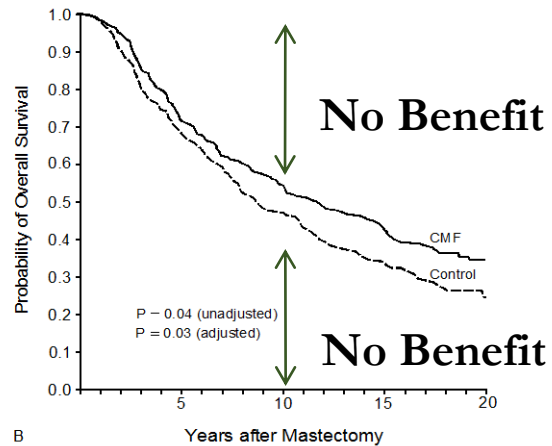
APRIL 6, 1995

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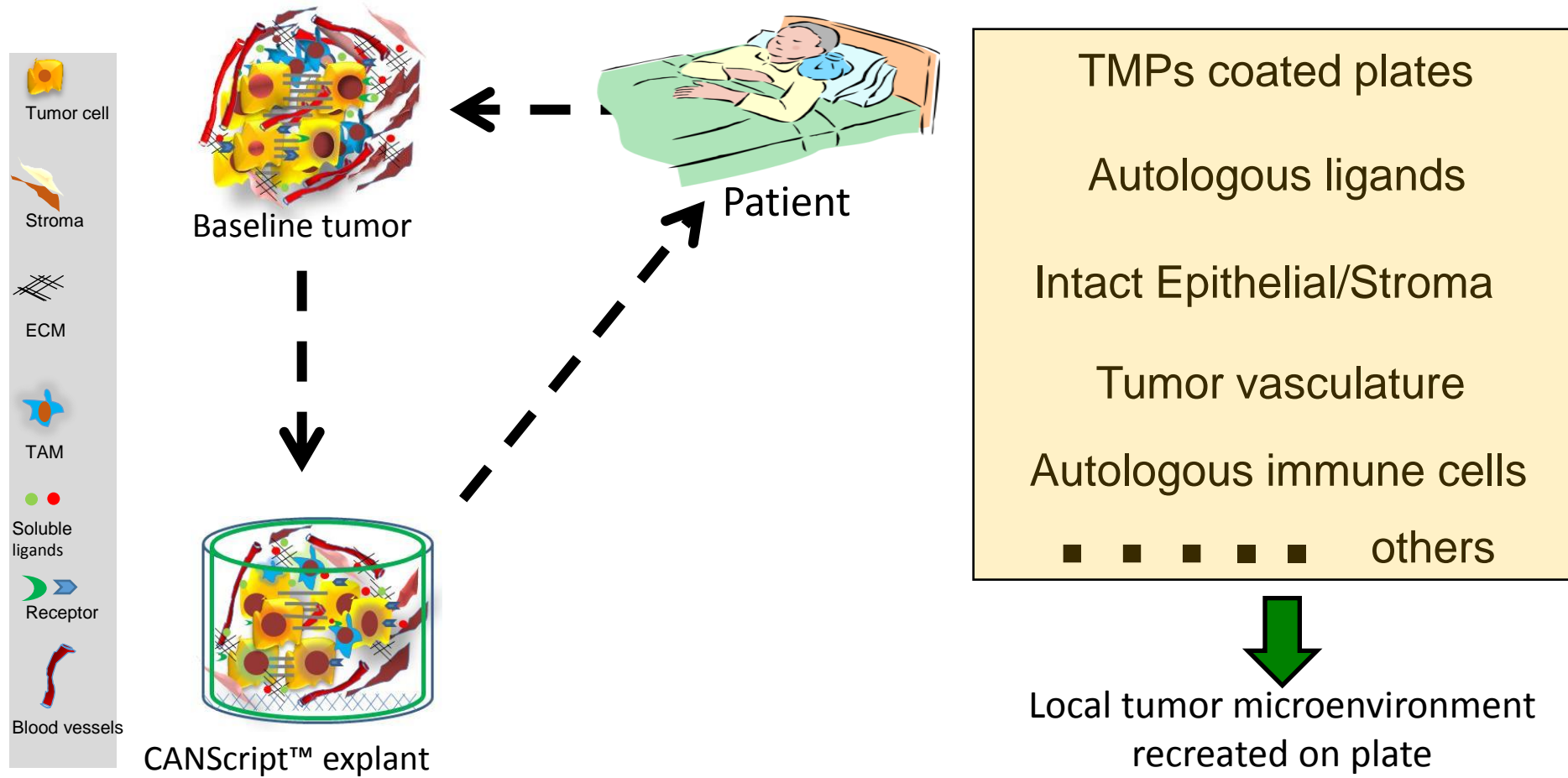
### ADJUVANT CYCLOPHOSPHAMIDE, METHOTREXATE, AND FLUOROURACIL IN NODE-POSITIVE BREAST CANCER

#### The Results of 20 Years of Follow-up

GIANNI BONADONNA, M.D., PINUCCIA VALAGUSSA, B.S., ANGELA MOLITERNI, M.D., MILVIA ZAMBETTI, M.D., AND CRISTINA BRAMBILLA, M.D.



# Creation of patient tumor microenvironment : CANScript™

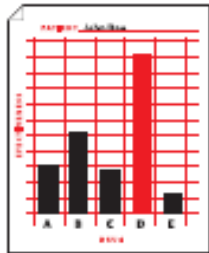


# CANScript™: A novel platform technology measures functional outcome of drug response

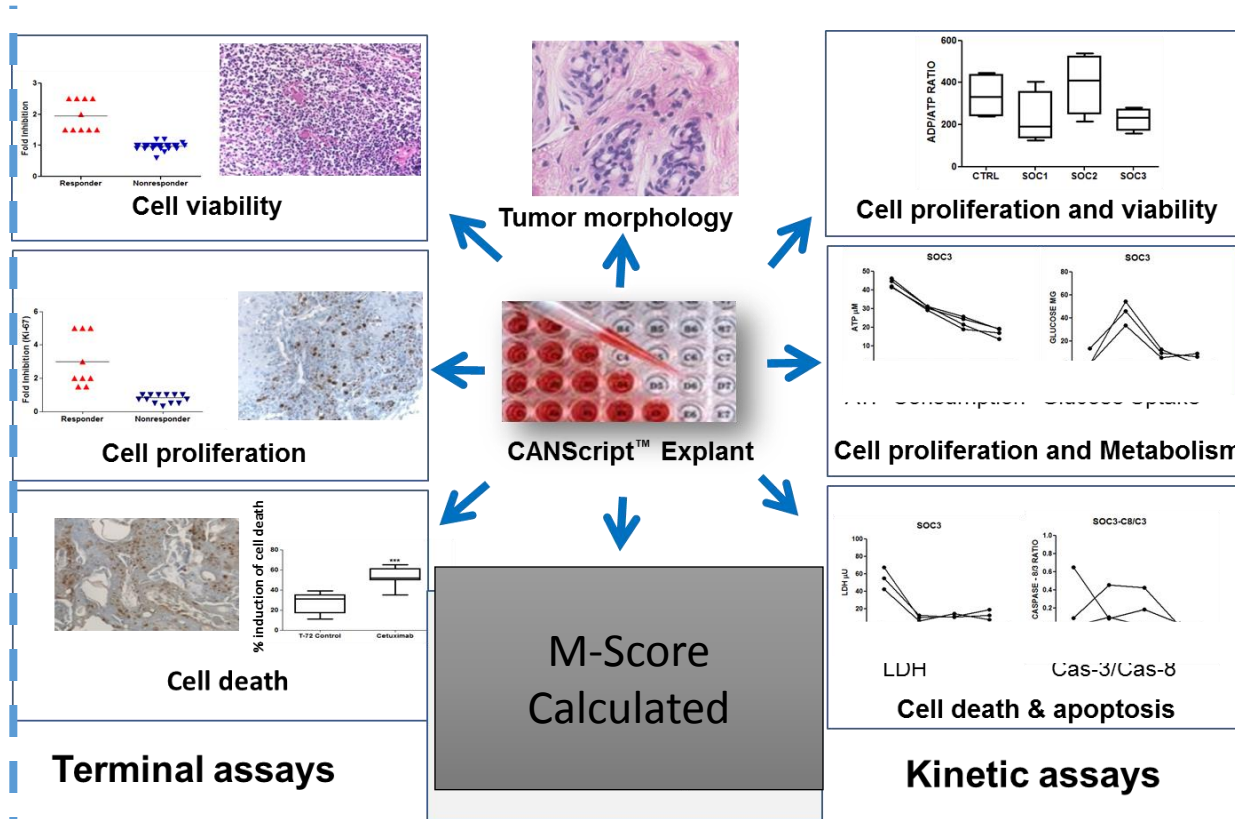
1. Patient's tumor tissue taken through biopsy/surgery is incubated with customized proteins and serum in a culture plate.



2. Various drug combinations are introduced to check tumor activity through a multidimensional assay platform over 4-5 days.

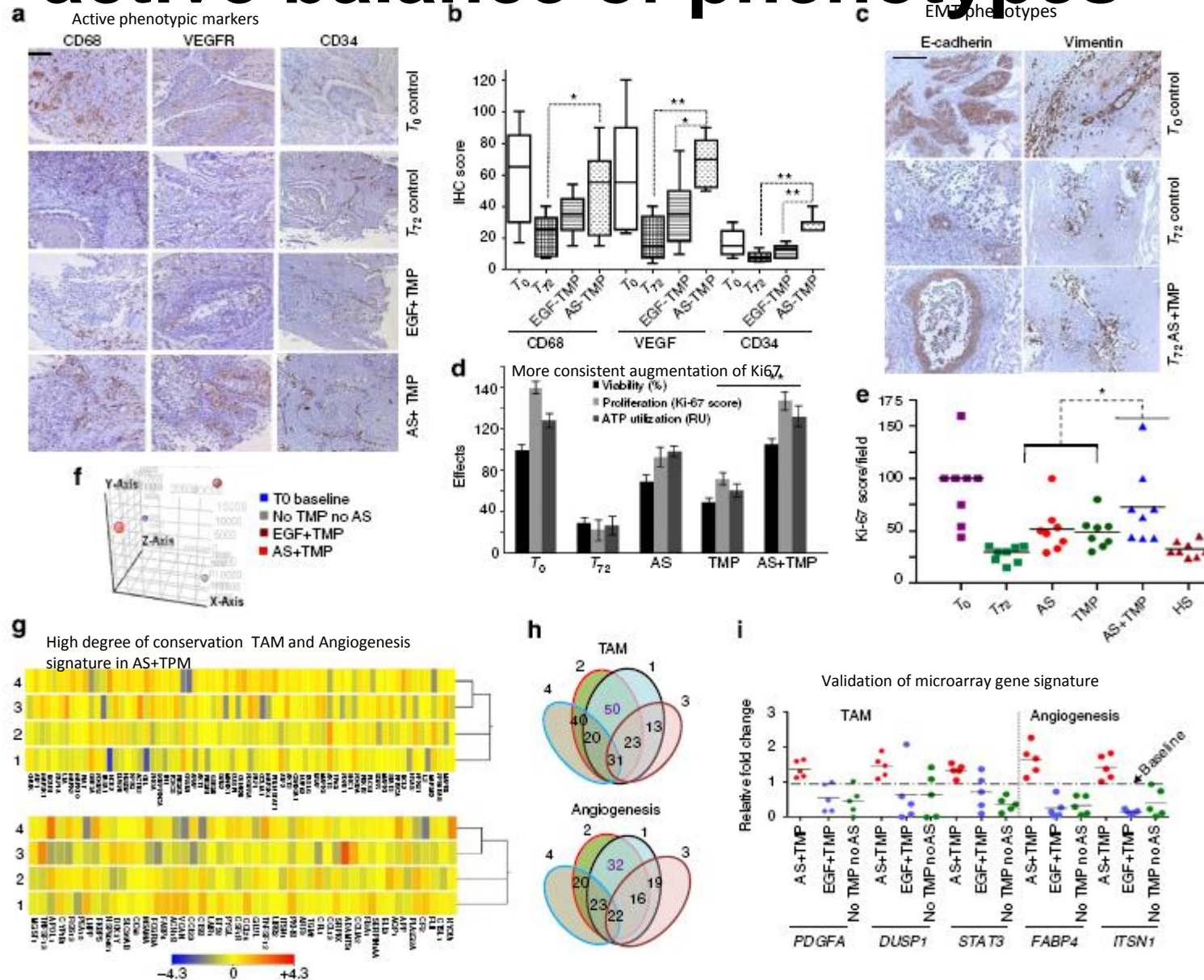


3. An algorithm combines the results into single predictive score "M-Score" for each drug combination.



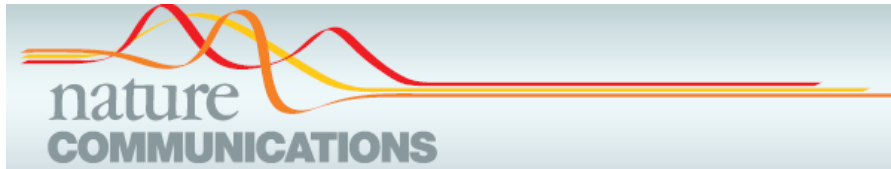
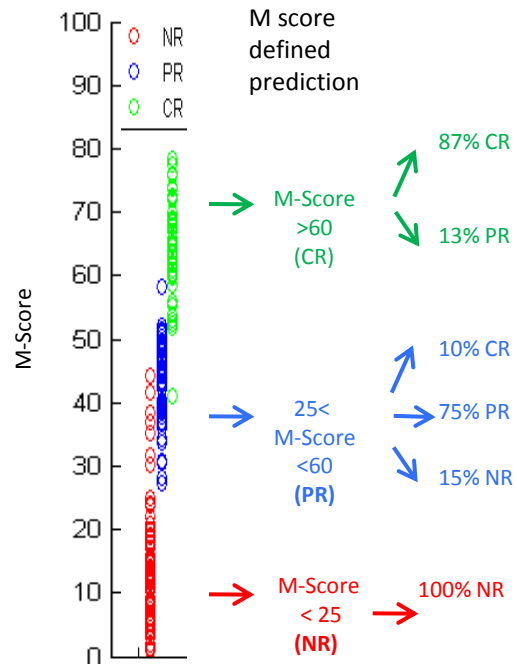
All assays are approved by FDA

# Integration of TMP and patient specific ligands for active balance of phenotypes



# Clinical Correlation of CANScript™

No. of Patients	>2000
Type of Cancer	Solid & Hematological
Cancer indications	8



## ARTICLE

Received 3 Oct 2014 | Accepted 22 Dec 2014 | Published 27 Feb 2015

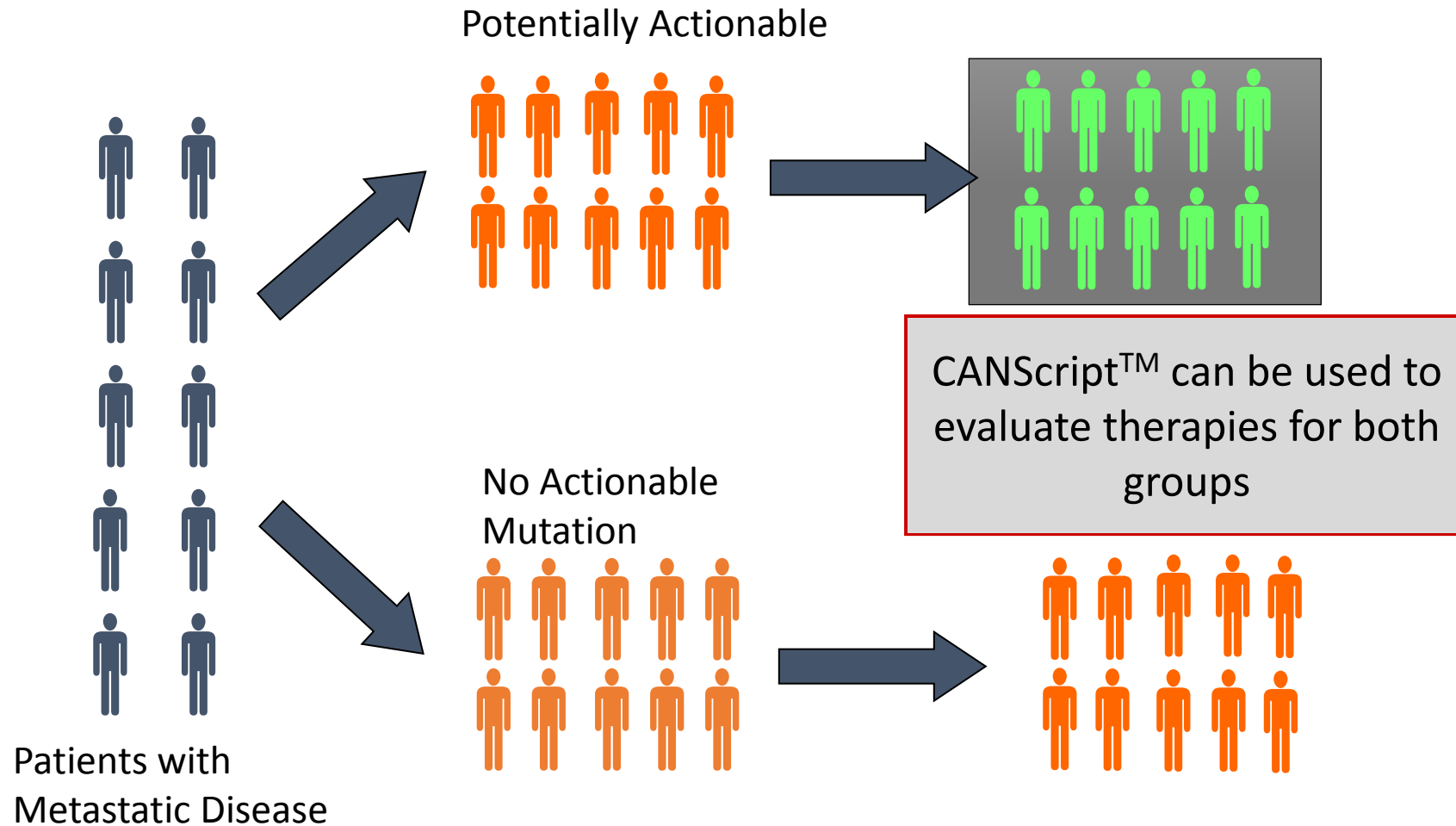
DOI: 10.1038/ncomms7169

OPEN

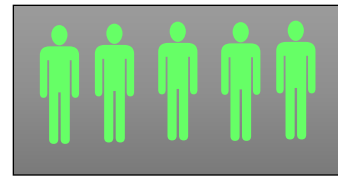
# Predicting clinical response to anticancer drugs using an *ex vivo* platform that captures tumour heterogeneity

Biswanath Majumder<sup>1</sup>, Ulaganathan Baraneedharan<sup>1,\*</sup>, Saravanan Thiyagarajan<sup>1,\*</sup>, Padhma Radhakrishnan<sup>1</sup>, Harikrishna Narasimhan<sup>2</sup>, Muthu Dhandapani<sup>1</sup>, Nilesh Brijwani<sup>1</sup>, Dency D. Pinto<sup>1</sup>, Arun Prasath<sup>1</sup>, Basavaraja U. Shanthappa<sup>1</sup>, Allen Thayakumar<sup>1</sup>, Rajagopalan Surendran<sup>3</sup>, Govind K. Babu<sup>4</sup>, Ashok M. Shenoy<sup>4</sup>, Moni A. Kuriakose<sup>5</sup>, Guillaume Bergthold<sup>6</sup>, Peleg Horowitz<sup>6,7,8</sup>, Massimo Loda<sup>6,7</sup>, Rameen Beroukhim<sup>7,8</sup>, Shivani Agarwal<sup>2</sup>, Shiladitya Sengupta<sup>7,9,10,\*</sup>, Mallikarjun Sundaram<sup>1,\*</sup> & Pradip K. Majumder<sup>1,9,\*</sup>

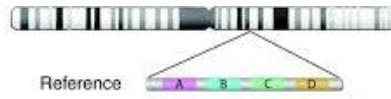
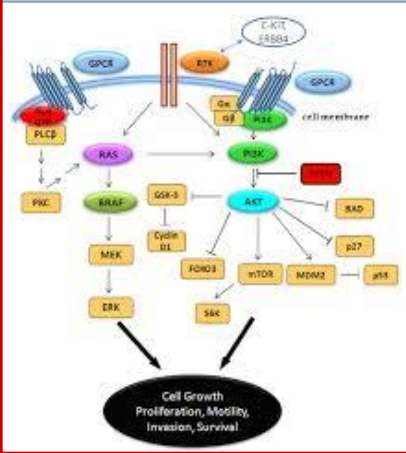
# CANScript™ Makes Genomics Actionable



# 'Potentially Actionable' Leaves Many Unanswered Questions



## 'Candidate' Identified



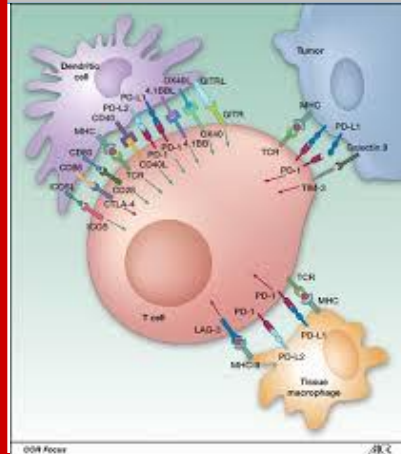
## "Targeting" Isn't Perfect



Nature: 2010

"We identified nearly 40 different kinase targets of sunitinib."

## Response Not Genetically Defined



## Tissue Type

The NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Vemurafenib in Multiple Nonmelanoma Cancers with BRAF V600 Mutations

"BRAF V600 appears to be a targetable oncogene in some, but not all, nonmelanoma"

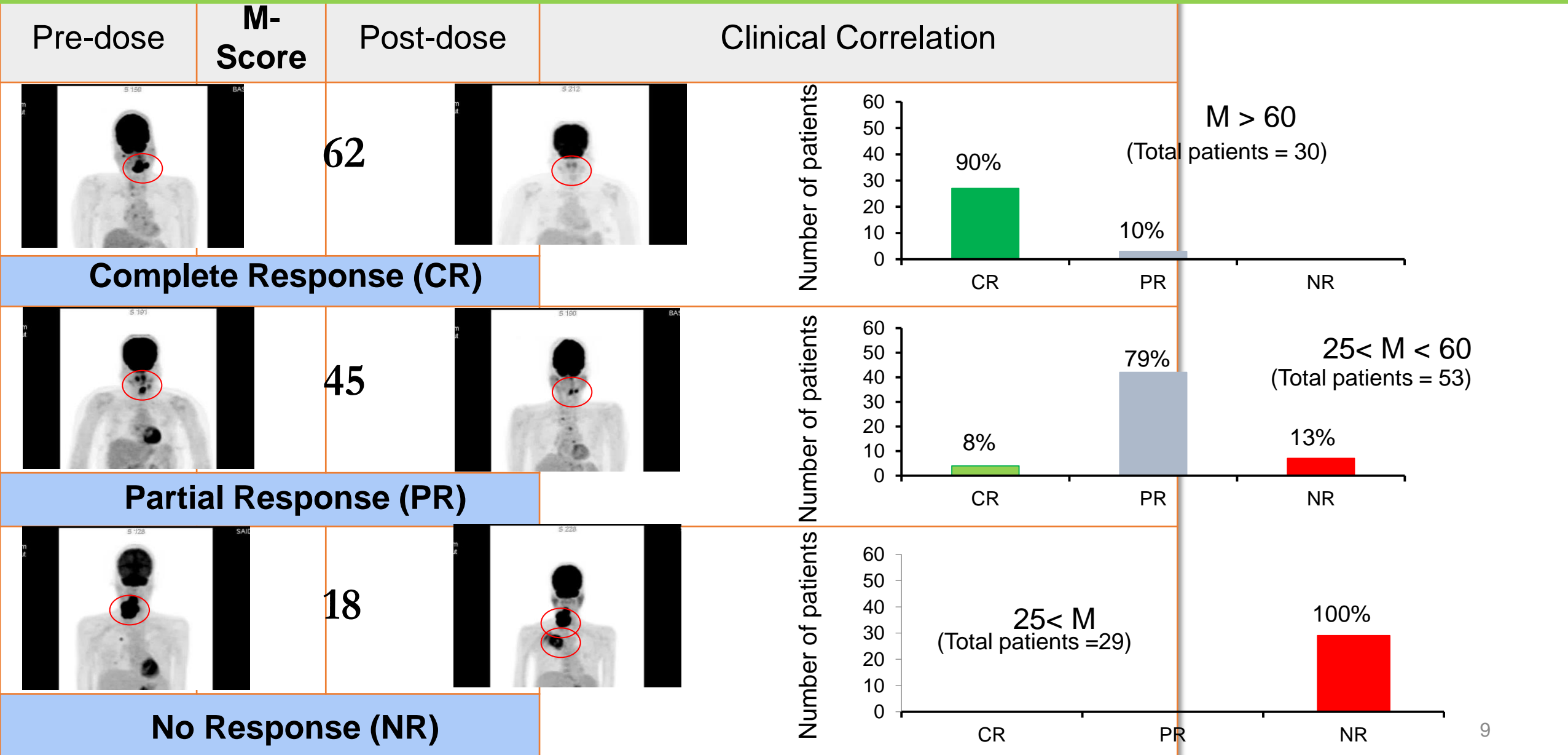
Note: 42% RR, all PR

## ≠ Same Effect



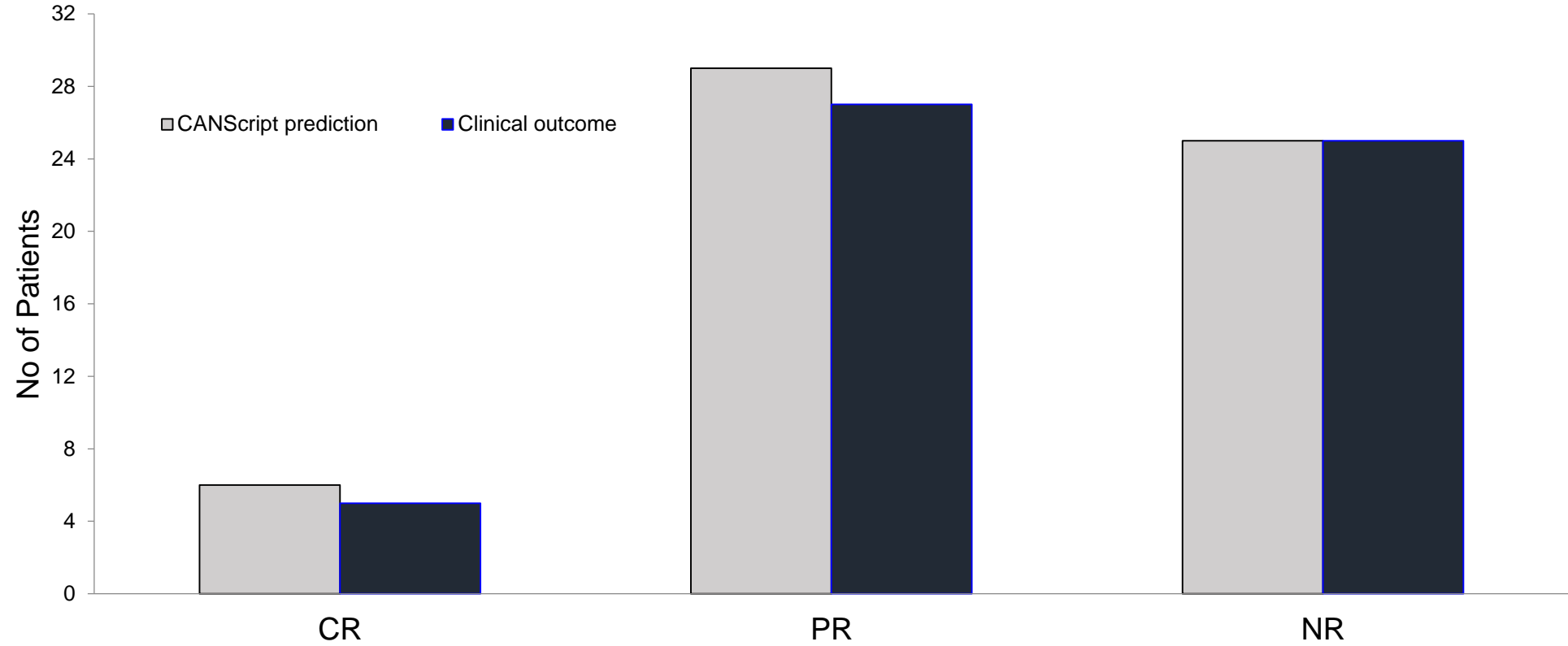


# CANScript™ Clinical Validation: HNSCC



# Overall CaBR tumors

*n=60*

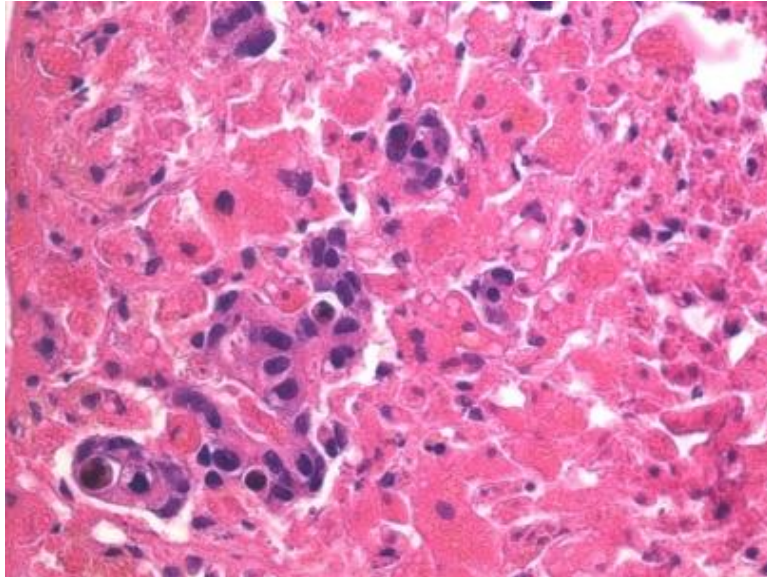


# Case study: A patient with Breast Cancer

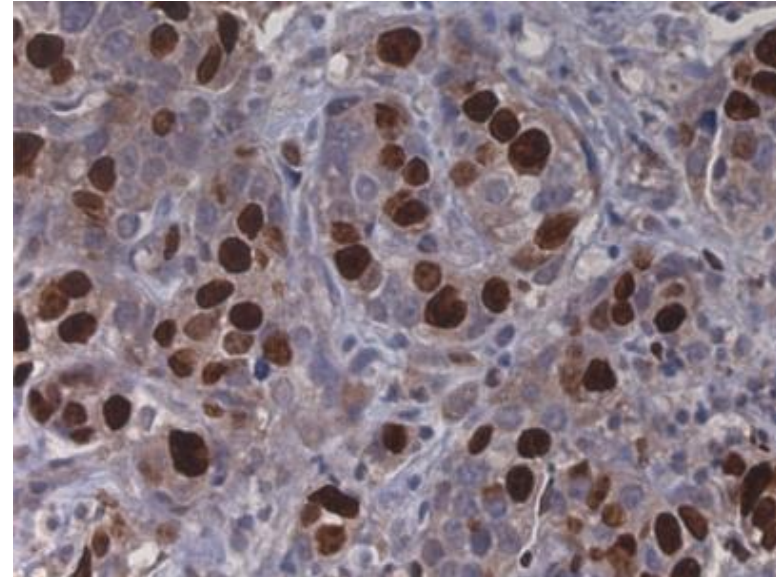
Patient: A lady doctor 54 years old

Presented with CaBR Stage III and Liver Mets

Prior treatment history: Chemo (Docetaxol+Dox) and radiation and did not show any response



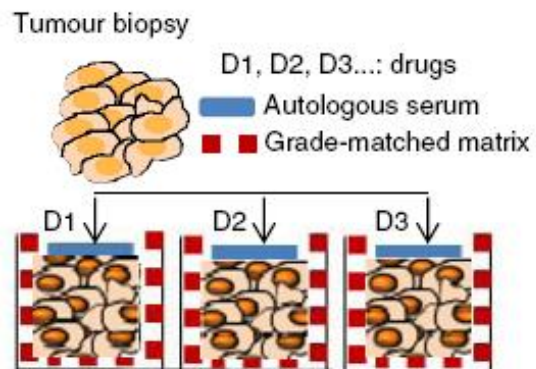
H&E



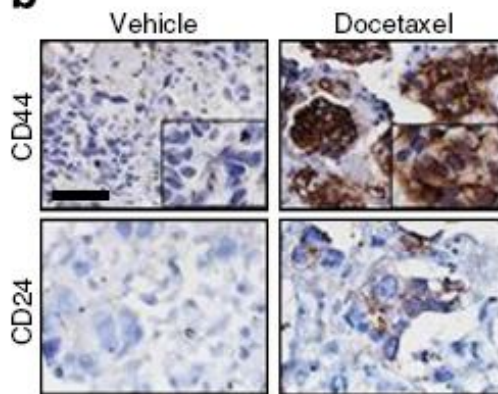
Ki-67

# Transient cell state phenotypes (CD44 hi CD24 hi) in breast cancer cell - DTC

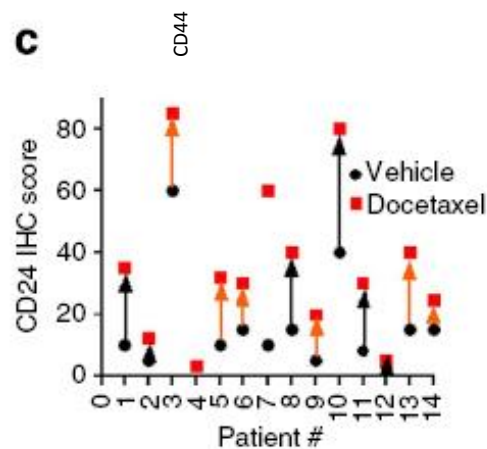
**a**



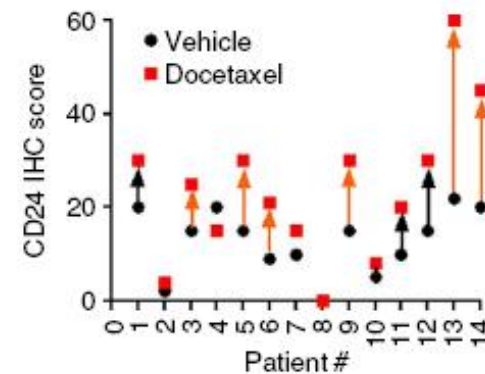
**b**



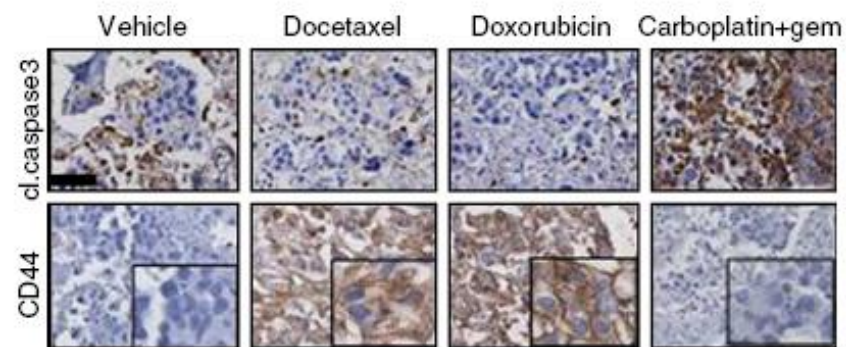
**c**



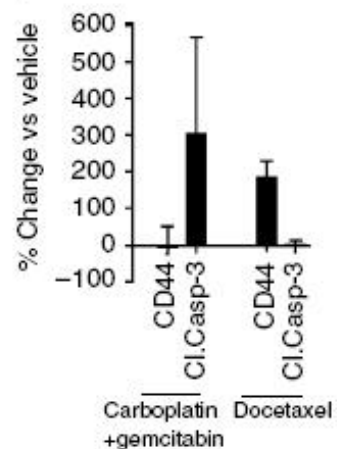
**d**



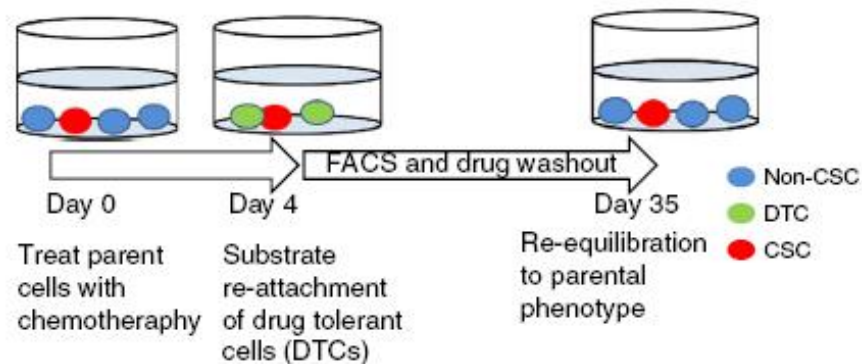
**e**



**f**



**g**

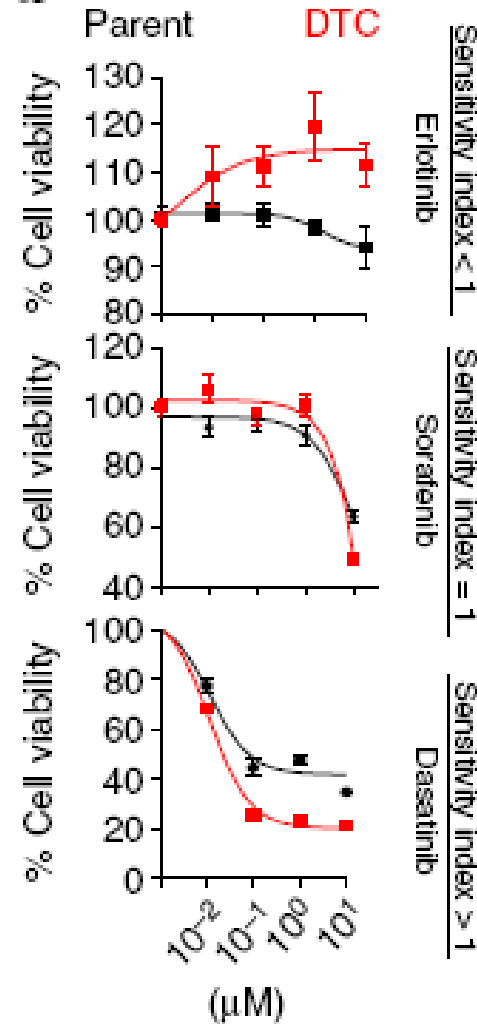


# Src and Hck pathways are deregulated in these DTC

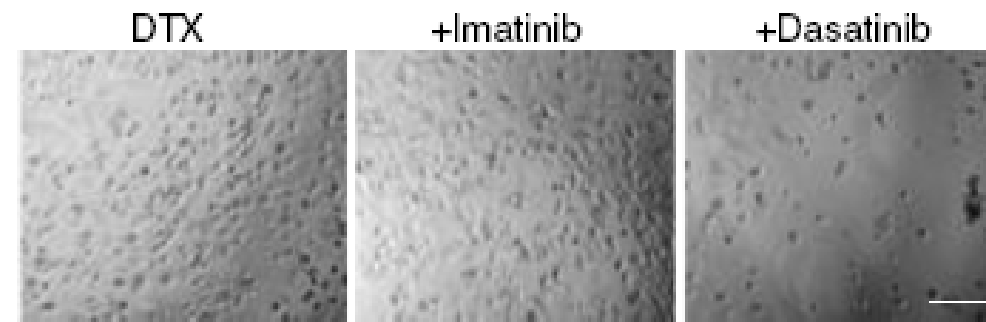
**a**

Inhibitor	Major target (s)
PI103	PI3K/AKT, mTOR
Sorafenib	VEGFR, PDGFR, Raf kinases
Vatalanib	VEGFR, PDGFR
Erlotinib	EGFR (HER-1)
SB-431542	TGF $\beta$ -1R
SGX-523	C-Met receptor
Dasatinib	BCR-Abl, Src family kinases
RK20449	HCK
Imatinib	BCR-Abl, PDGFR

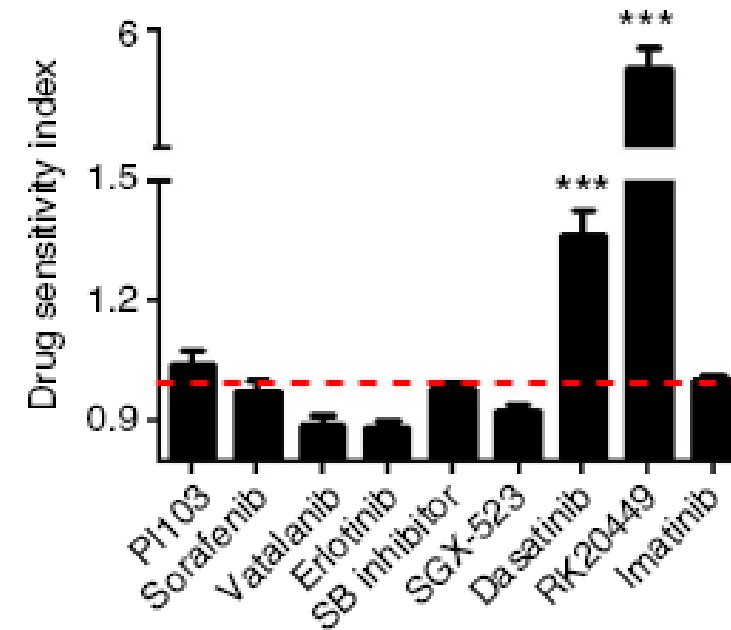
**b**



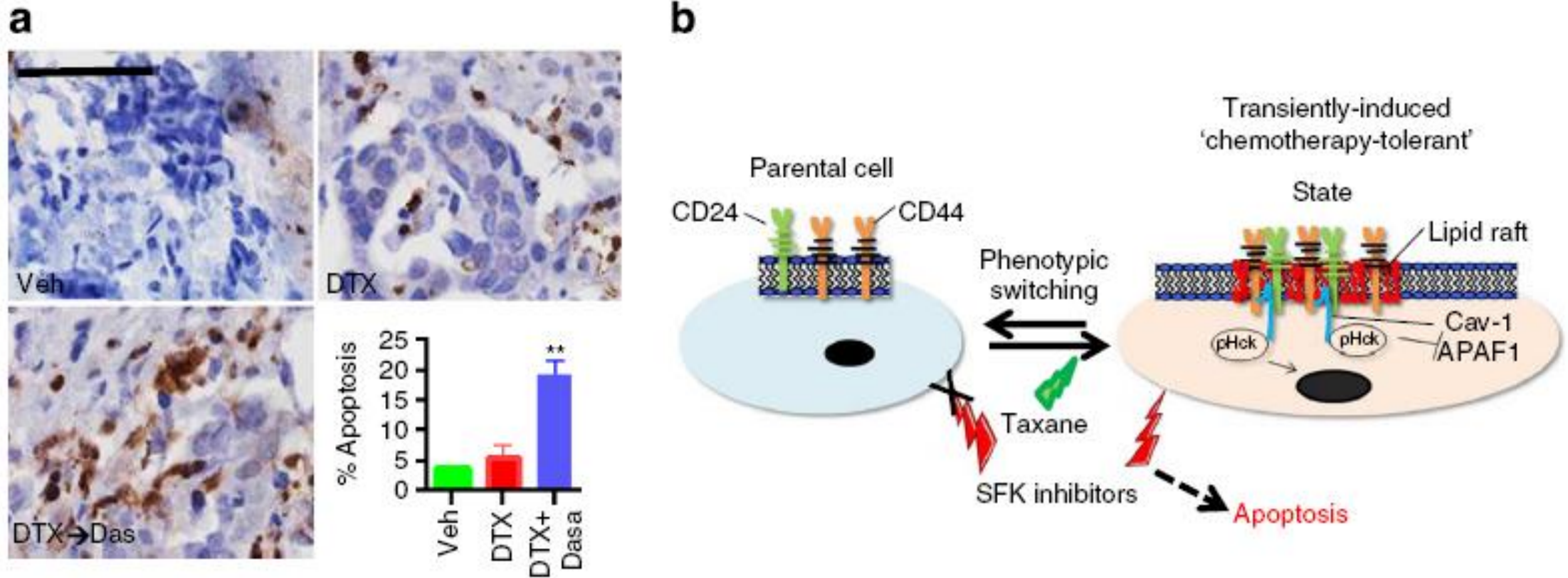
**c**



**d**

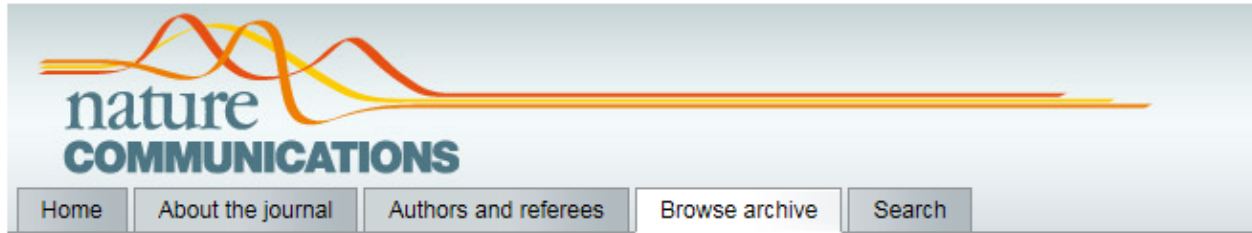


# CANScript™ finds DTX followed by Dasatinib is the drug of choice



Patient shows PFS with DTX followed by Src inhibitor (Dasatinib) for last three years

# Mitra-Harvard Collaboration



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NATURE COMMUNICATIONS | ARTICLE **OPEN**



## Temporally sequenced anticancer drugs overcome adaptive resistance by targeting a vulnerable chemotherapy-induced phenotypic transition

[Aaron Goldman](#), [Biswanath Majumder](#), [Andrew Dhawan](#), [Sudharshan Ravi](#), [David Goldman](#), [Mohammad Kohandel](#), [Pradip K. Majumder](#) & [Shiladitya Sengupta](#)

[Affiliations](#) | [Contributions](#) | [Corresponding authors](#)

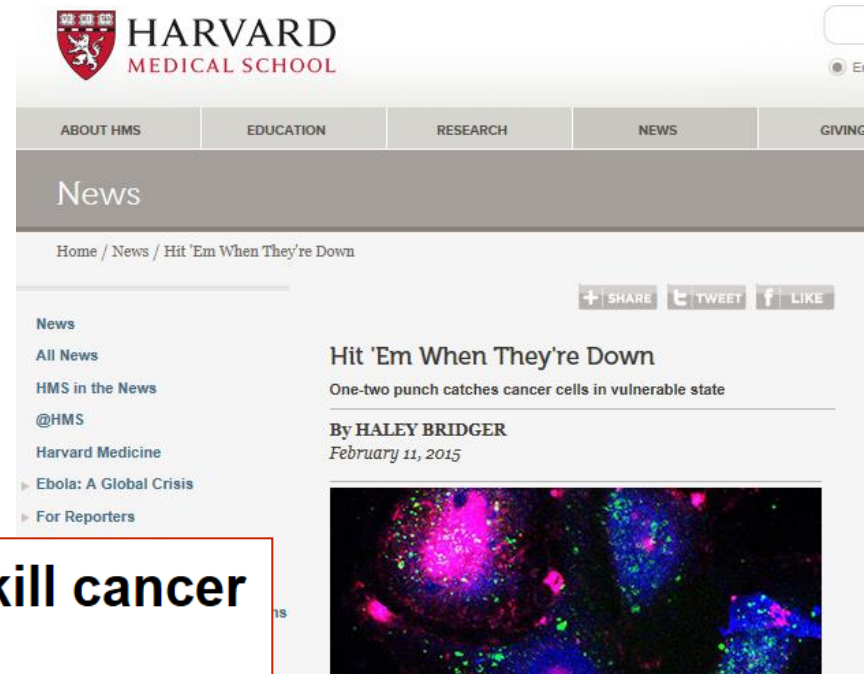
*Nature Communications* **6**, Article number: 6139 | doi:10.1038/ncomms7139

Received 18 July 2014 | Accepted 17 December 2014 | Published 11 February 2015

### Mitra Biotech, Harvard unravels how to kill cancer cells that avoid chemotherapy

*The method was to give another common drug just when the cancer cells begin to morph into a stem-cell like type that can avoid the chemo drugs.*

Hari Pulakkat | 13 February 2015, 6:38 AM IST



**Thank You**