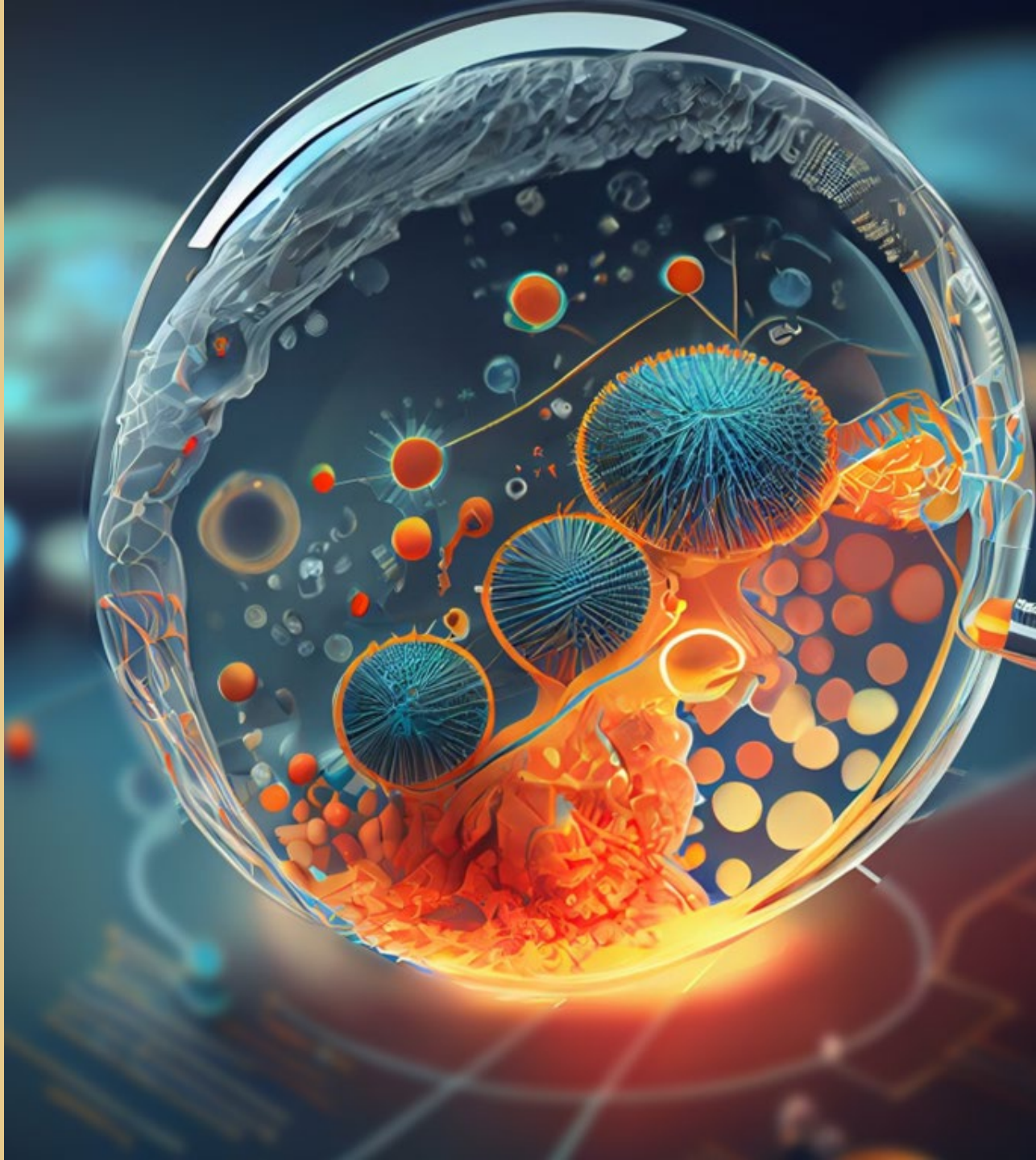
eha Sf(PM)

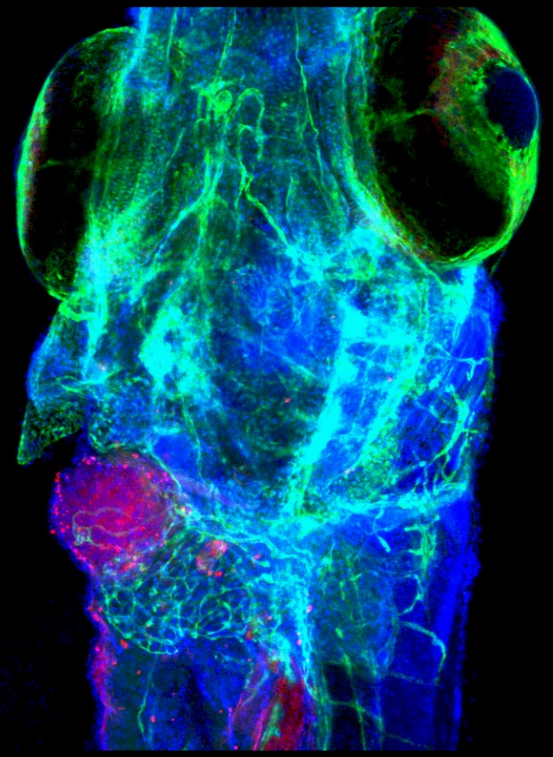
Zebrafish Avatars achieve over 90% accuracy in predicting patient response to therapy across CRC, breast, and ovarian cancer

RITA FIOR



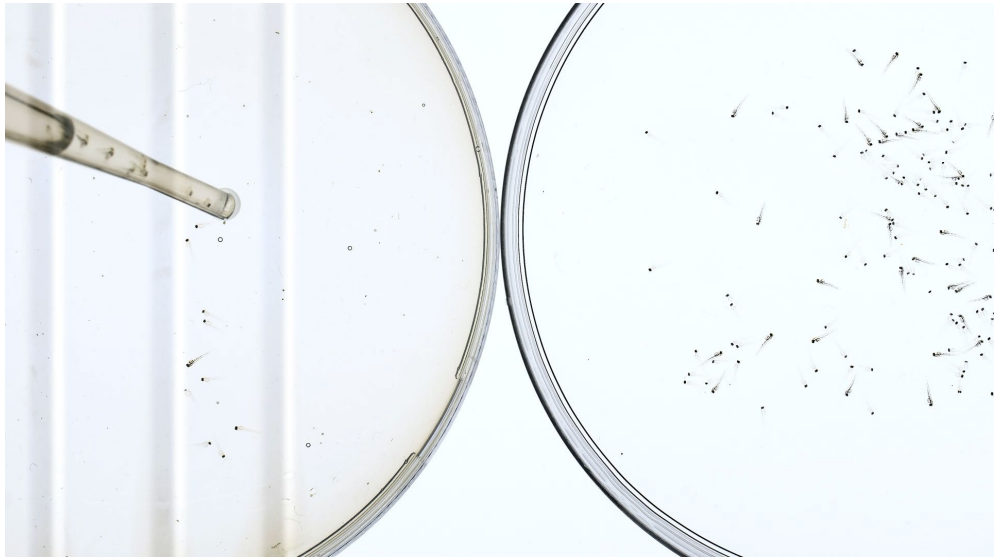
eha Sf(PM)

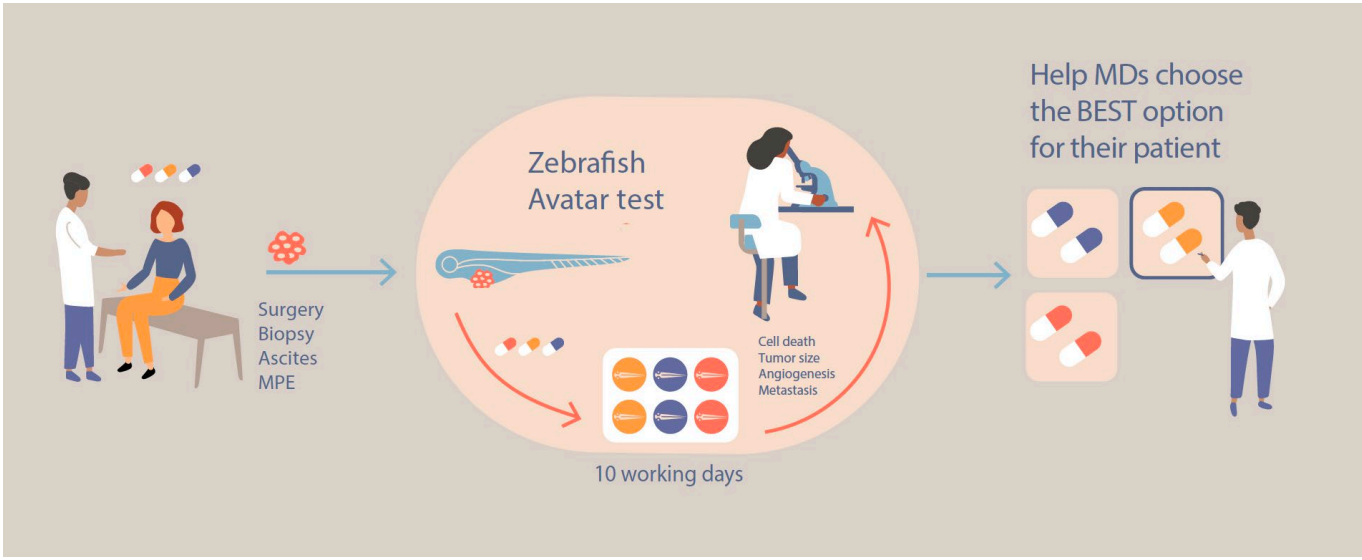
DISCLOSURE / AFFILIATION



Fundação Champalimaud

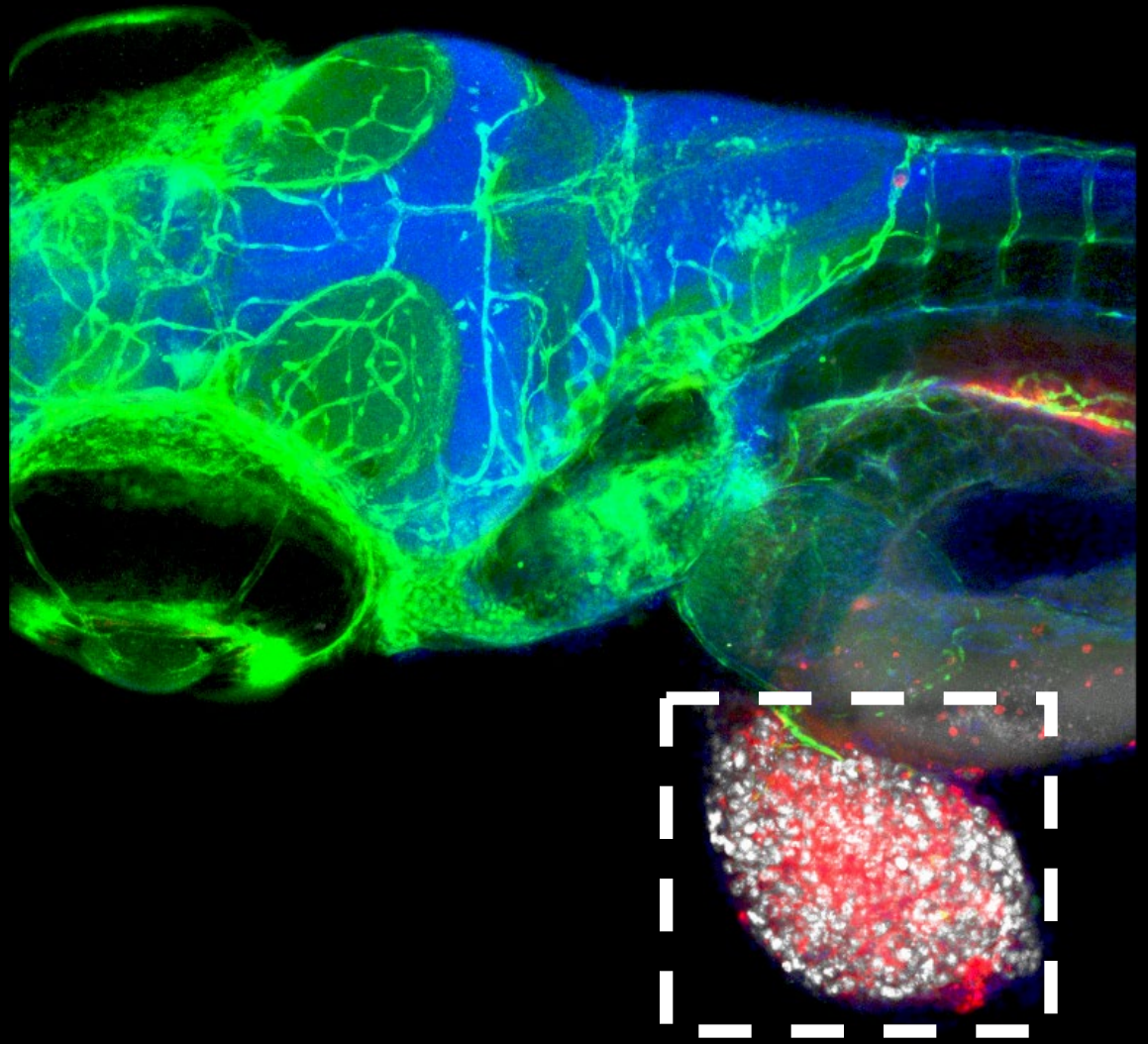
Zebrafish Avatars for personalized medicine



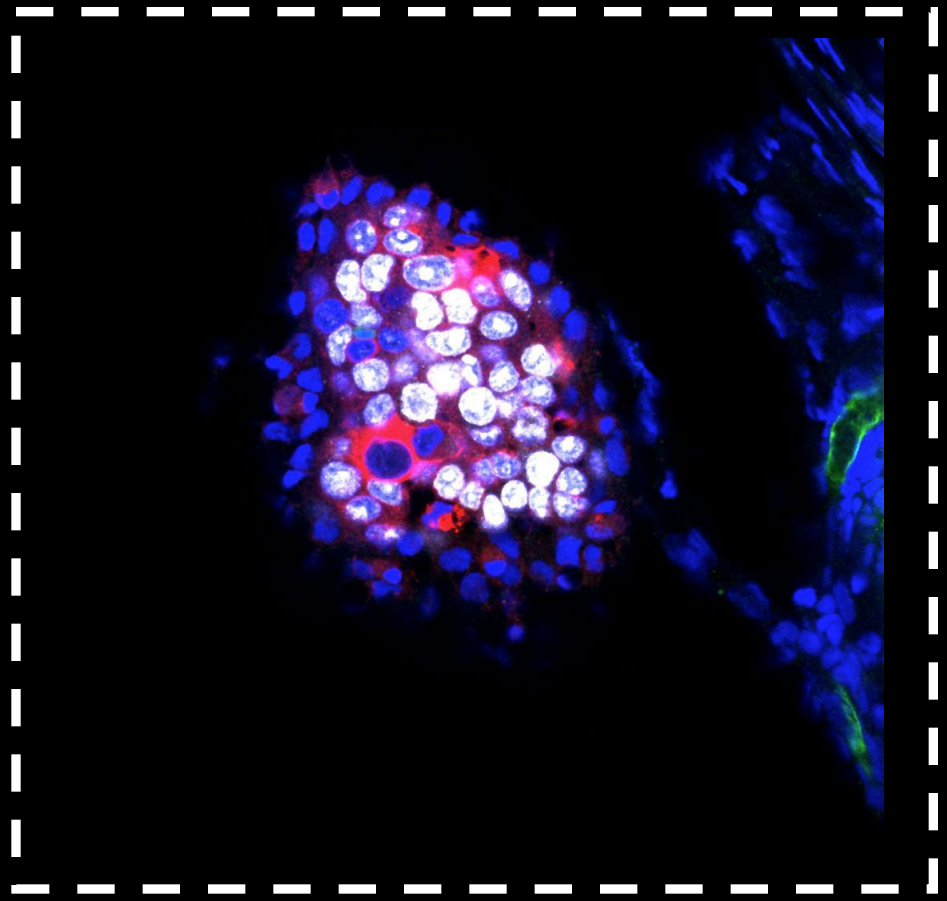


Fior et al, PNAS 2017; Costa&Ferreira et al, EBiomedicine, 2019; Rebelo deAlmeida et al Comm Biol, 2020; Costa&Estrada et al, Cells, 2020; Varanda et al, Cancers, 2020; Martinez Lopez et al, JoVE 2021; Tavares Barroso et al, Cells, 2021; Póvoa et al Nature Communications 2021; Costa et al Current Protocols 2022; Costa et al Frontiers in Oncology 2022; Martinez Lopez et al BioArch in revision; Costa et al Nature Communications 2024

CONFOCAL IMAGING



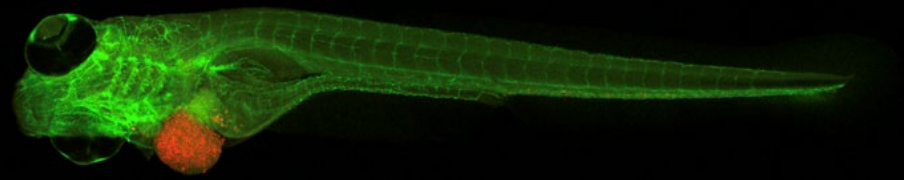
SINGLE-CELL RESOLUTION

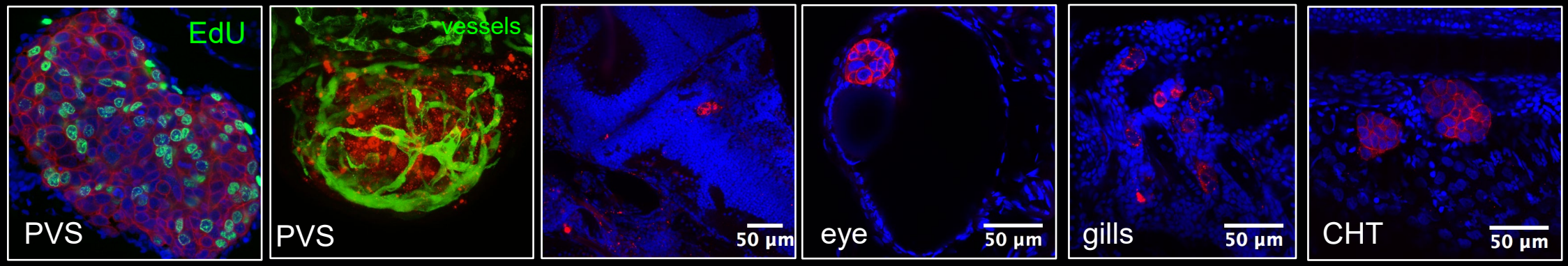


NUCLEI KI67 TUMOR CELLS

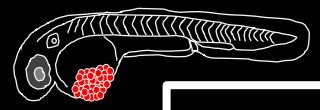
eha Sf(PM)

Human tumor cells proliferate in zebrafish & invade distant sites

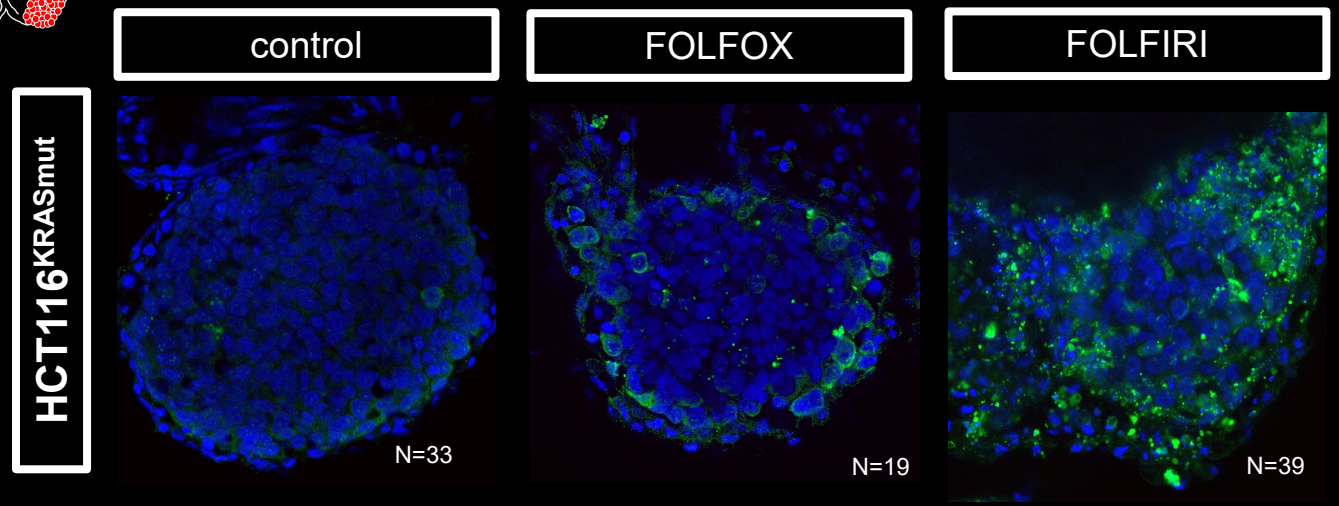


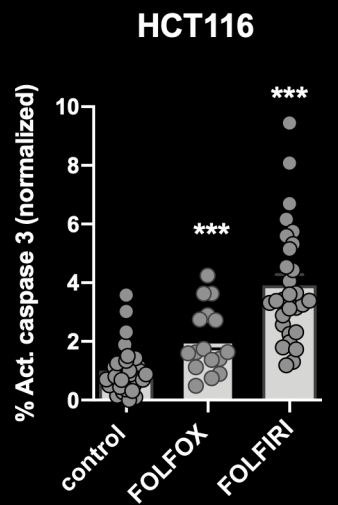


Different Chemotherapy sensitivity *in vivo*



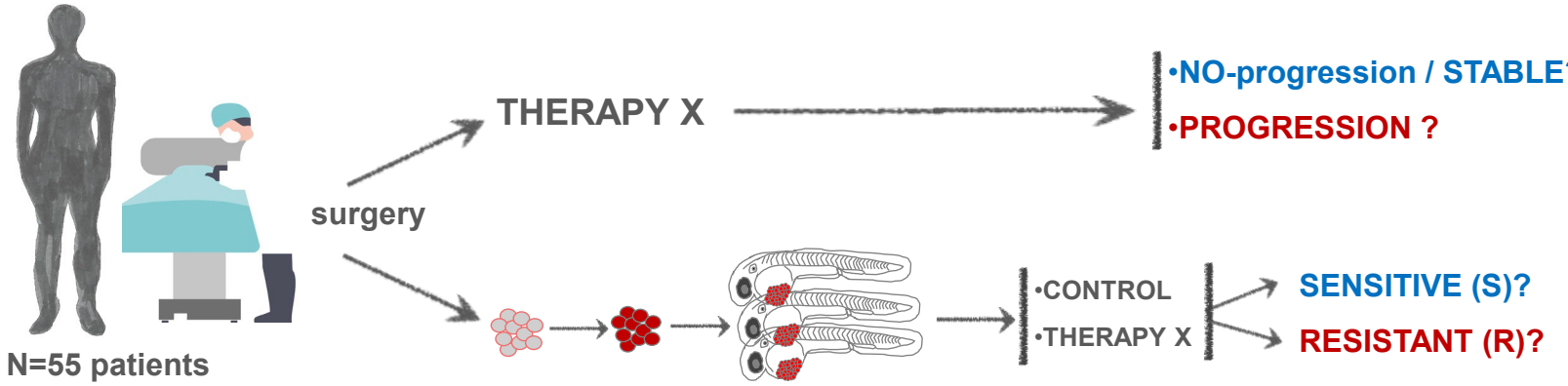
Activated caspase3 nuclei (DAPI) 4dpi 3dpT

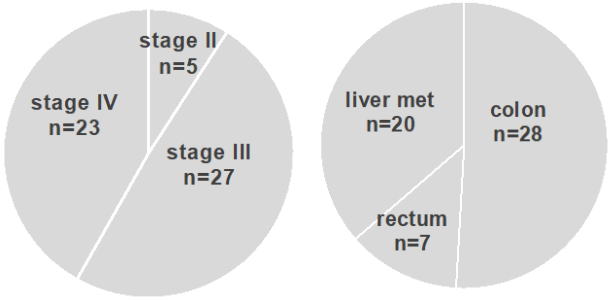


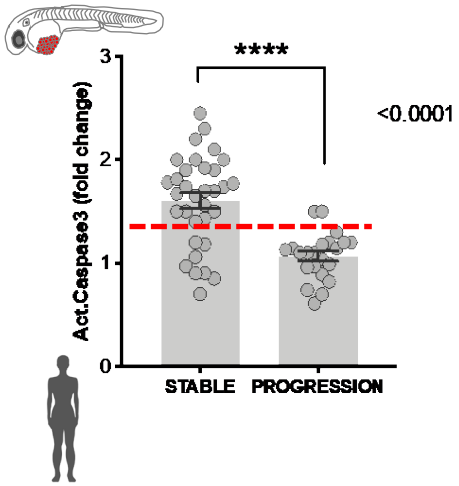


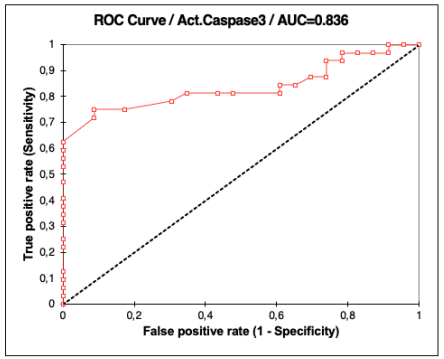
Fior et al, PNAS 2017

CRC co-clinical study comparing the patient's clinical response to treatment with their matching zAvatars









Colorectal Cancer		S	R
Response to therapy	NO-progression	25	8
	Progression	2	20

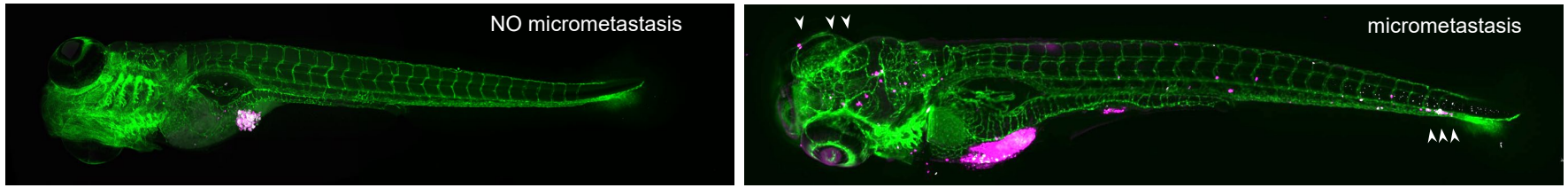
POSITIVE predicted value=92%
NEGATIVE Predictive value=71%

Bruna Costa et al Nature Comm 24

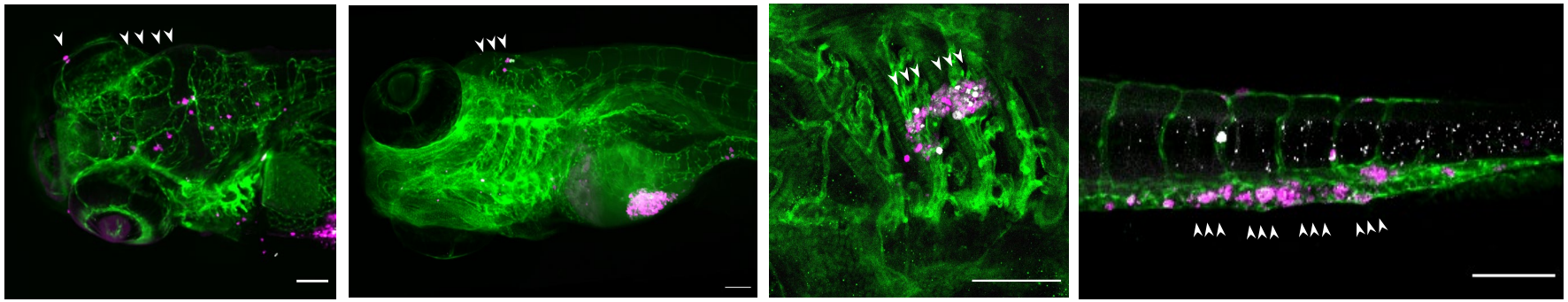
eha Sf(PM)

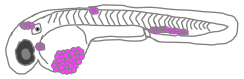
Formation of micrometastasis in zAvatars is related with patient clinical progression

CRC patient tumor cells hMITO *Tg(fli1:eGFP)* *3dpi*

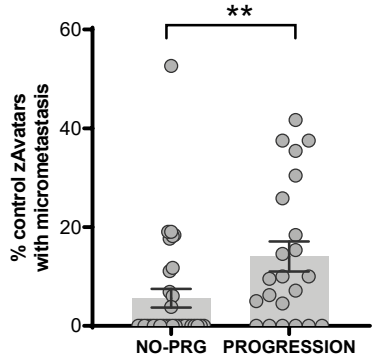


micrometastasis hMITO *Tg(fli1:eGFP)* *3dpi*





CRC patients		NO MET	MET
Stage	II/III	21	11
	IV	7	16

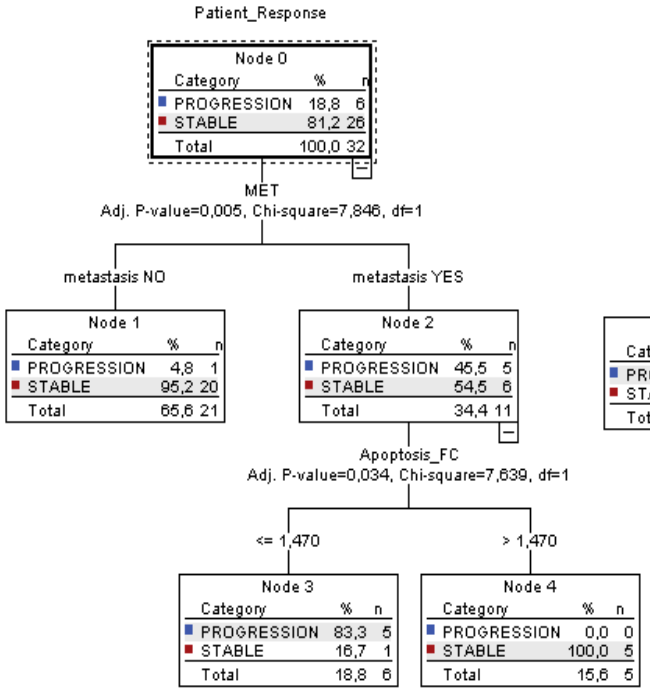


Bruna Costa et al Nature Comm 24

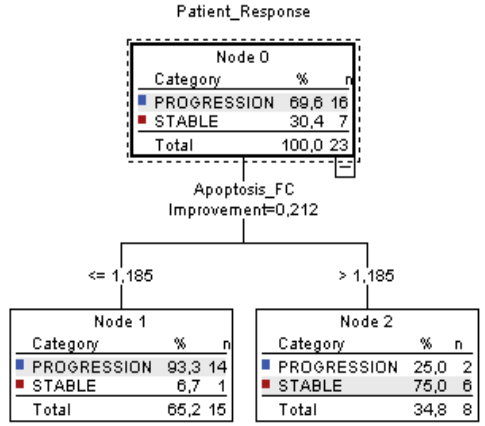
eha Sf(PM)

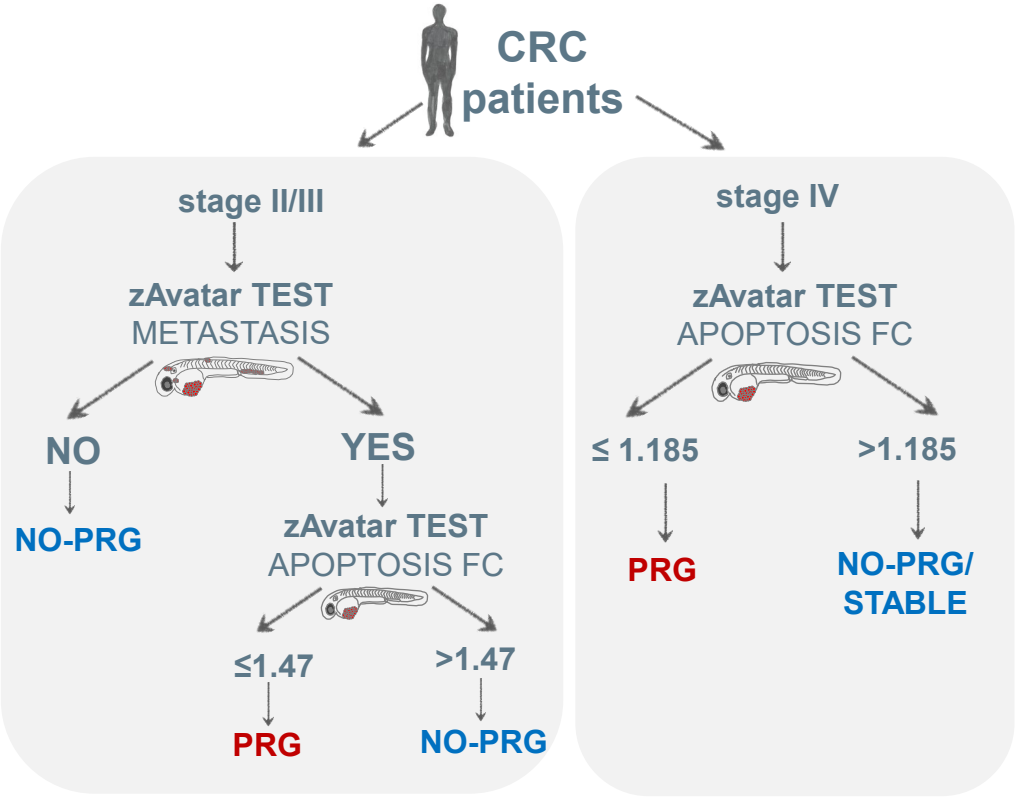
Decision-tree model improves the predictive value of the zAvatar-test

Stage



Stage IV





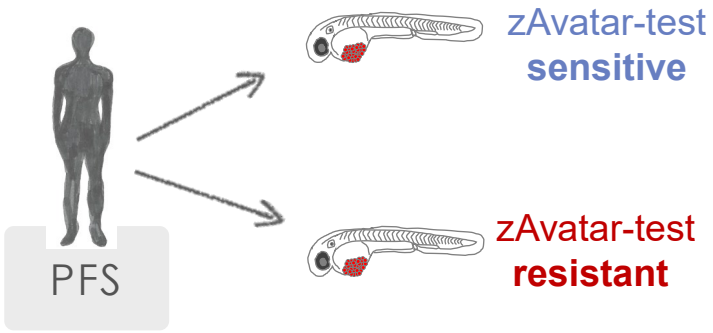
CRC patients		S	R	Total
Response to therapy	Stable	**31**	2	*33*
	Progression	3	**19**	*22*
	Total	*34*	*21*	*55*

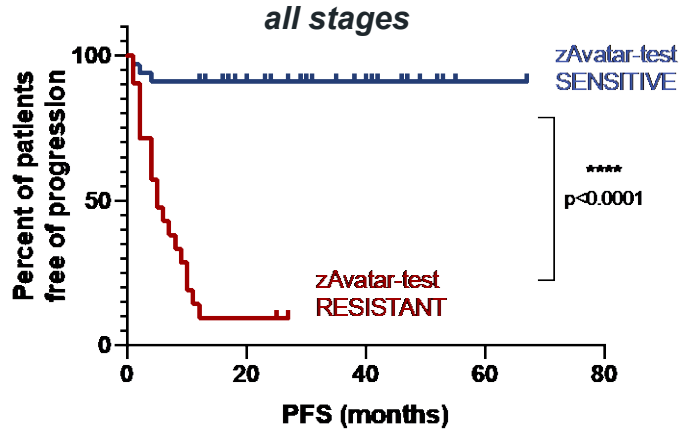
Analysis	Result
sensitivity	94%
specificity	86%
PPV	91%
NPV	90%

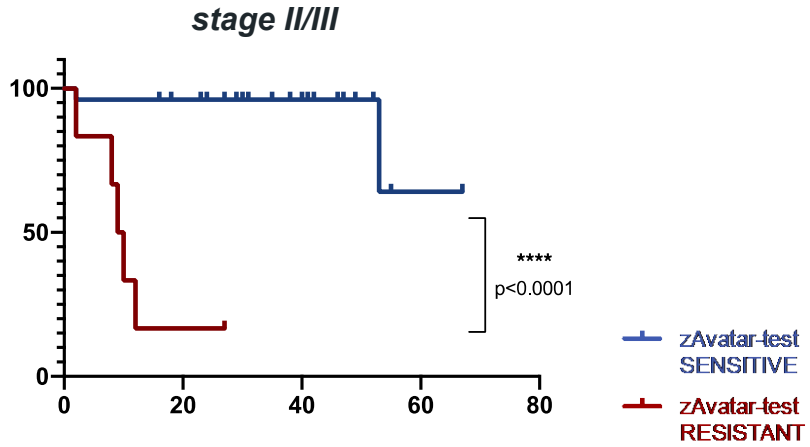
Bruna Costa et al Nat Comm 24

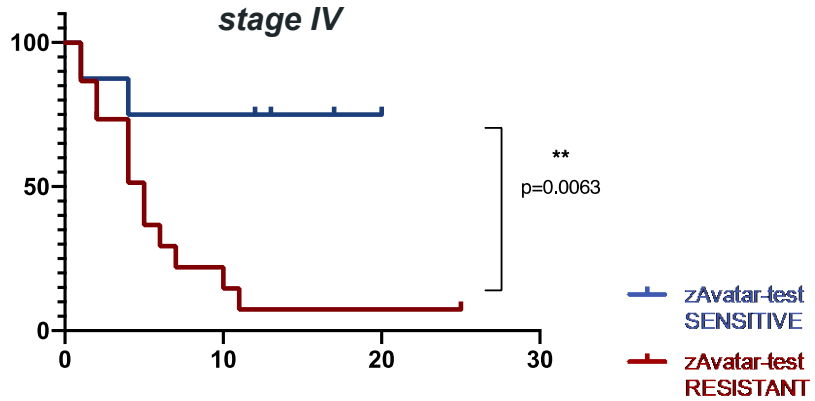
eha Sf(PM)

CRC patients whose zAvatars were sensitive to treatment have significantly longer progression free survival





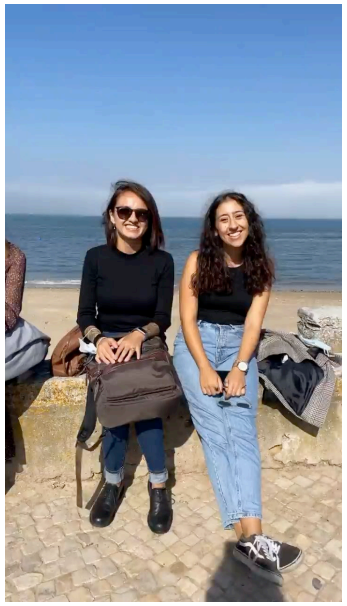




Bruna Costa et al Nature Comm 24

eha Sf(PM)

ACKNOWLEDGMENTS



TEAM

Bruna Costa
Raquel Mendes
Marta Estrada
Vanda Póvoa
Catia R. Almeida
Ana Beatriz Machado
Marcia Fontes
Filipa Amorim
Salvador Ferreira
Sara Cardoso

FORMER STUDENTS

Ines Oliveira
Mariana Rebordão
Mayra Martinez Lopez
Rita Almeida
Luis Leite
Ana Lograd o
Mariana Barroso
Micaela Domingues
Beatriz Varanda
Mariana Maia Gil
Magda Negrão
Miguel Fuzeta

COLLABORATORS

- Stefan Kauffman
- Alexandra Leroy
- Luis Costa
- A.Rita GRosso
- Pedro Moura Alves
- Valerie Paradis
- Gonçalo Bernardes
- João Barata
- Sergio Dias
- Marta Pojo
- António Jacinto

VIDEO:

Alexandre Azinheira
Hedi Young
Marta Correia
Marta Estrada

MENTORSHIP

- Leonor Saúde
- Maria de Sousa

PATIENTS & their FAMILIES

COLLABORATORS

- Digestive Unit- N. Figueiredo, C. Carvalho, P. Fidalgo, R Rio Tinto, L Fernandez, J. Azevedo, M Bispo
- Breast Unit - Fátima Cardoso, J. Ribeiro, MJ Cardoso, MJ Brito, H. Gouveia *et al*
- Radiotherapy Unit - Carlo Greco, Oriol Pares, Sandra Vieira
- Gynecology unit - H. Nabais, L Batarda, F Silva *et al*
- Neuro-Oncology unit- J Bravo Marques, Daniela Garcez, Catarina Viegas et al
- Lung Unit – Dr. Nuno Gil, Dr. Susana Simões
- Urology Unit - Jorge Fonseca *et al*
- Hematology Unit - Cristina João *et al*
- Histopathology Unit
- Molecular and Experimental Pathology Laboratory /BIOBANK- Mireia Castillo

- HPFF-Amadora Sintra - Dr. António Gomes *et al*

- FISH PLATFORM- C. Certal, J. Monteiro et al
- BIOBANK-M. Castillho et al
- Rodent Platform- I Campos et al
- Pharmacy- P. Bustorf et al
- Clinical Trials Unit- Manuela Seixas et al..
- ABBE Platform- D Arccardi et al
- Histology Platform- T.Carvalho et al
- CF Pre-award Team- Bruno Cena et al

REAGENTS

- Monica B-Dias, IGC,
- Lars Jansen, IGC
- Steven Renshaw
- Farida Djouad