

"Best Practice in Personalised Medicine" Recognition 2019

**A Liquid Biopsy 'hub':
integrating
nano-technologies
to improve cancer
diagnosis and therapy**

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ICPerMed
INTERNATIONAL CONSORTIUM

Escuela Nacional de Sanidad National Institute of Health Carlos III,
Monforte de Lemos 5, Madrid, November 5th-6th

 **IRE**
ISTITUTO NAZIONALE TUMORI
REGINA ELENA

Liquid biopsy, nanotechnology, precision cancer diagnosis, nanotherapy

Liquid Biopsy

- ❖ Predicting outcome by LB (lead time)
- ❖ Discovery adaptive resistance to clinical HER2 blockade
- ❖ Assign target therapy based on LB
- ❖ Moving liquid biopsy into nanophotonics

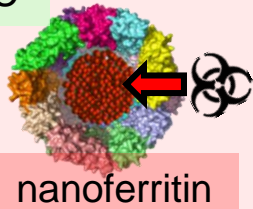
tissue and liquid biopsies

- Standard of Care
- Real-Life trials



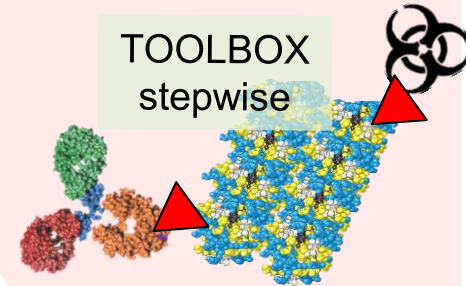
nano-drugging
nano-delivery

nano ADC

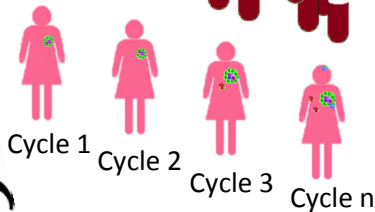


nanoferritin

TOOLBOX
stepwise



GIM21 multi-center



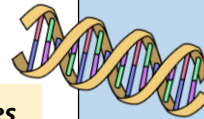
Her2 Br Ca
longitudinal



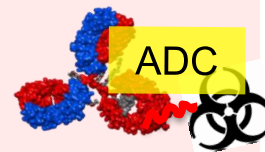
Molecular
Tumor Board



ctDNA signatures
on progression



- Beyond
Standard
of Care



Liquid Biopsy



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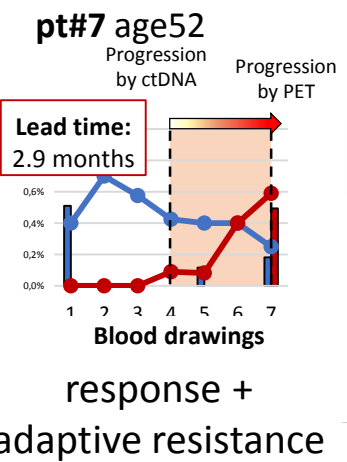
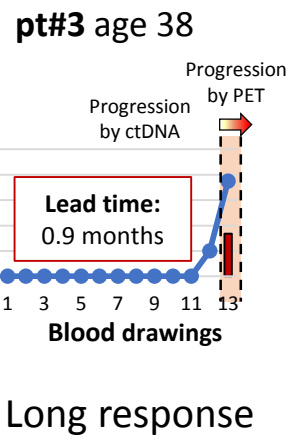
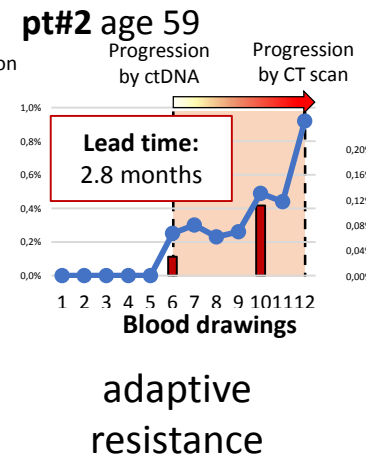
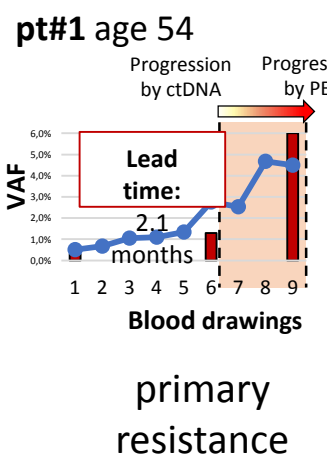
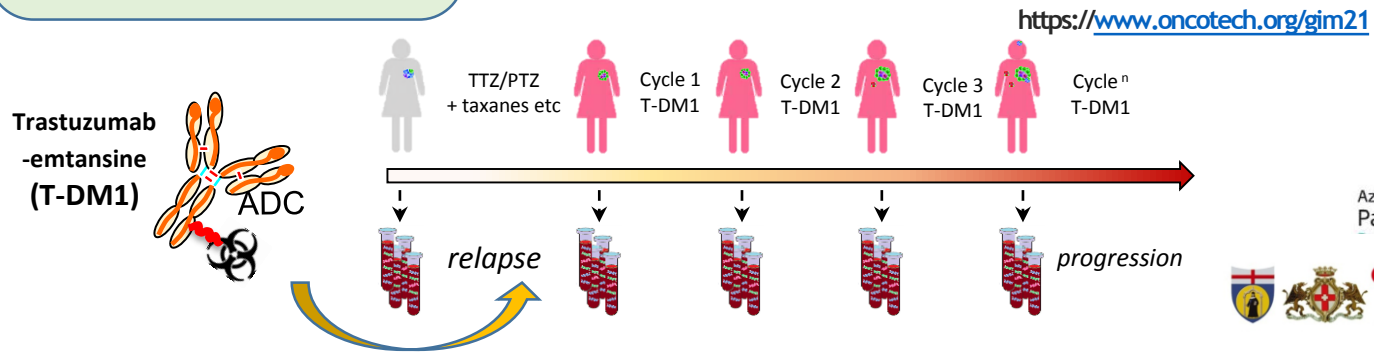
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ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

Monitoring T-DM1 treated patients by liquid biopsy



Azienda Ospedaliera Papa Giovanni XXIII

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Ospedaliero-Universitaria di Modena Policlinico

IST

IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA

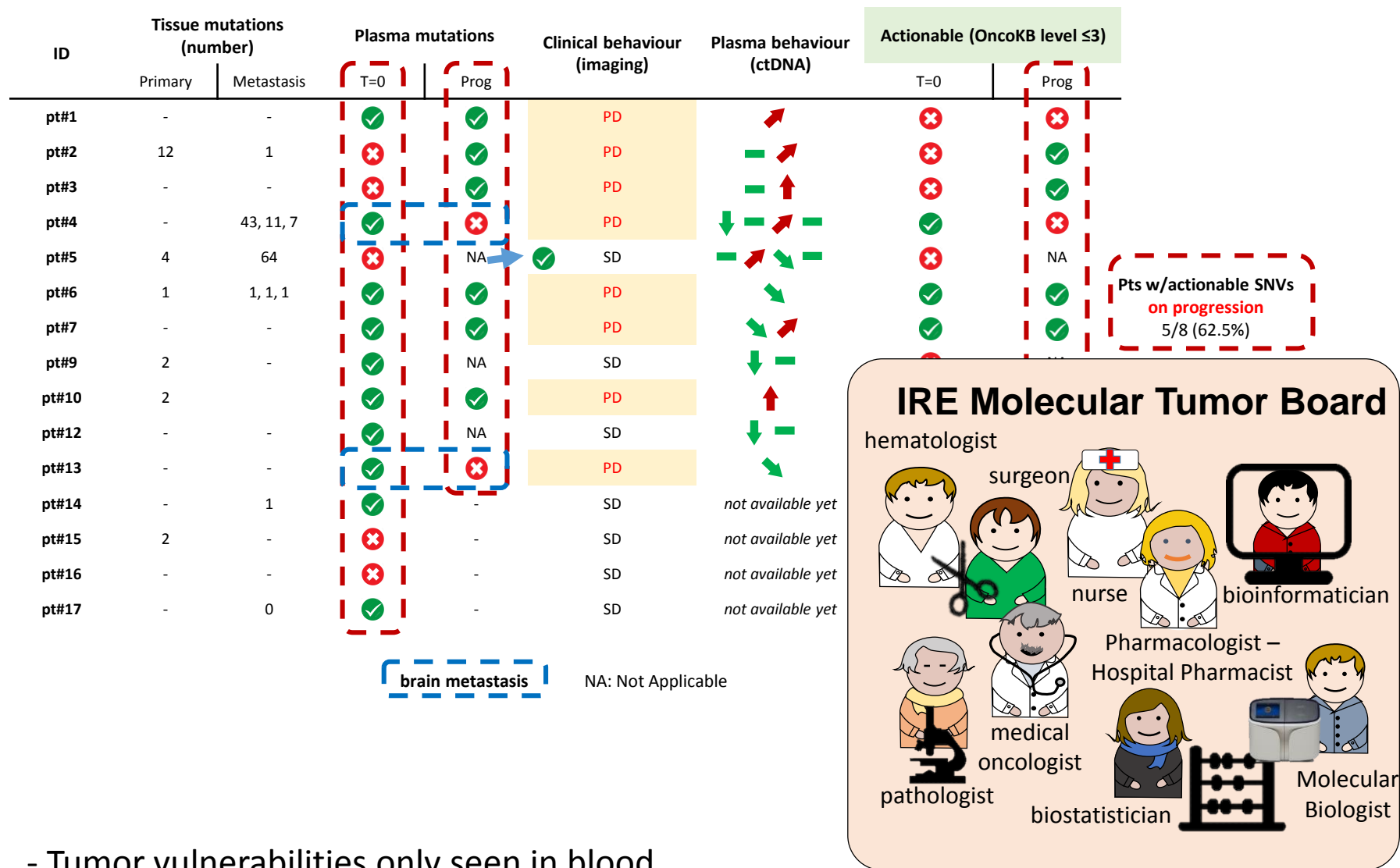
AZIENDA OSPEDALIERO-UNIVERSITARIA SANT'ANDREA

Aiom Associazione Italiana di Oncologia Medica

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

Allegretti, M. ... and Fabi, A. 2019, in preparation

Liquid biopsy reveals new vulnerabilities not present in archival tumor tissues



- Tumor vulnerabilities only seen in blood
- Tumor vulnerabilities not present at the beginning of T-DM1 treatment

Liquid Biopsy by Nanophotonics



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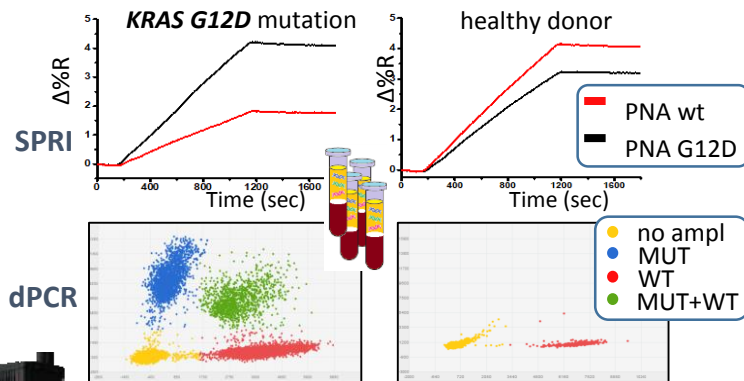
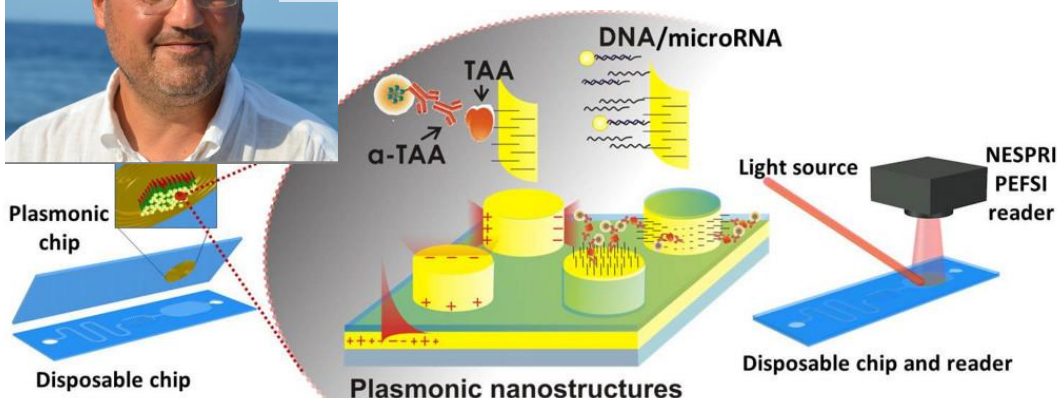
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

— **ULTRAPLACAD: ULTRAsensitive PLAsmonic CANcer DIagnosis** —



Giuseppe Spoto

Since October 24th 2018 a compact plasmonic **industrial prototype** is installed at IRE.



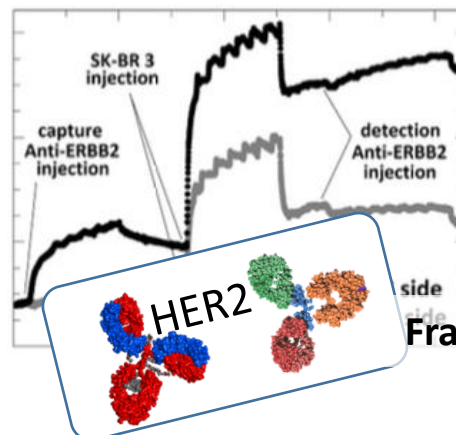
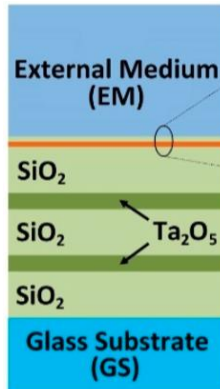
ULTRAPLACAD



www.ultraplacad.eu

EU H2020 Grant no: 633937

— **TURNOFF** —



Francesco Michelotti

Nano-therapy



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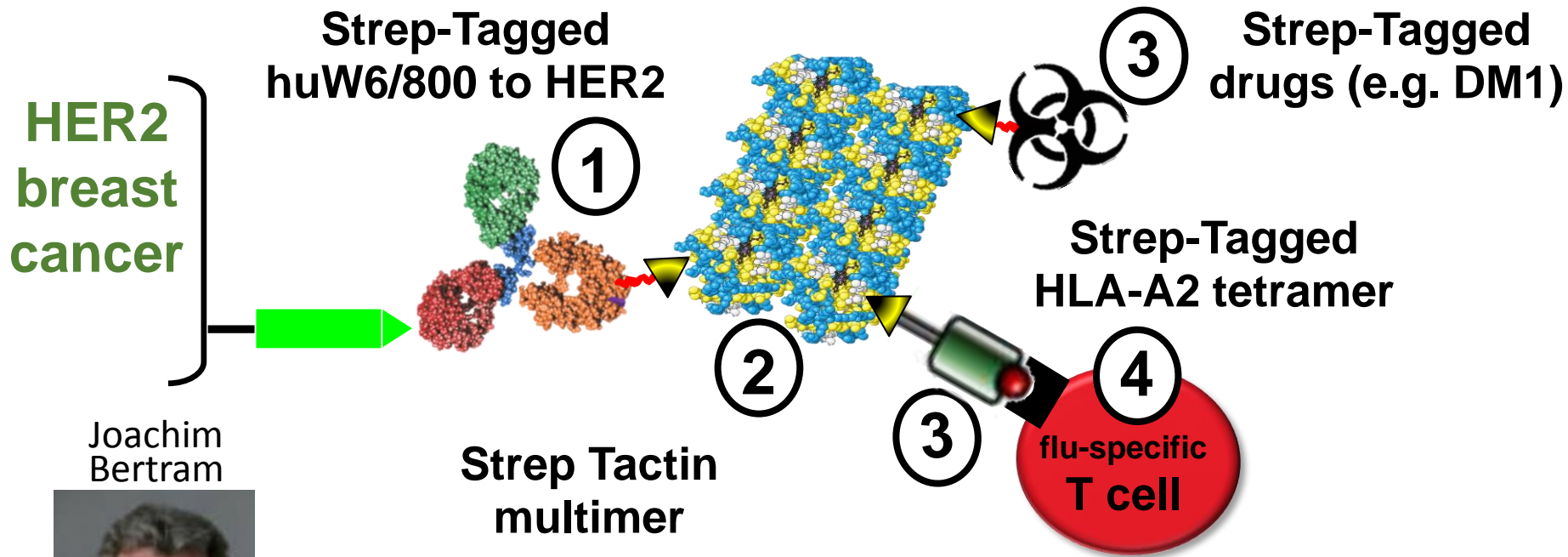
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ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

TOOLBOX: modular objects for step-wise nano-therapy



Joachim Bertram



Karl Heinz Friedrich

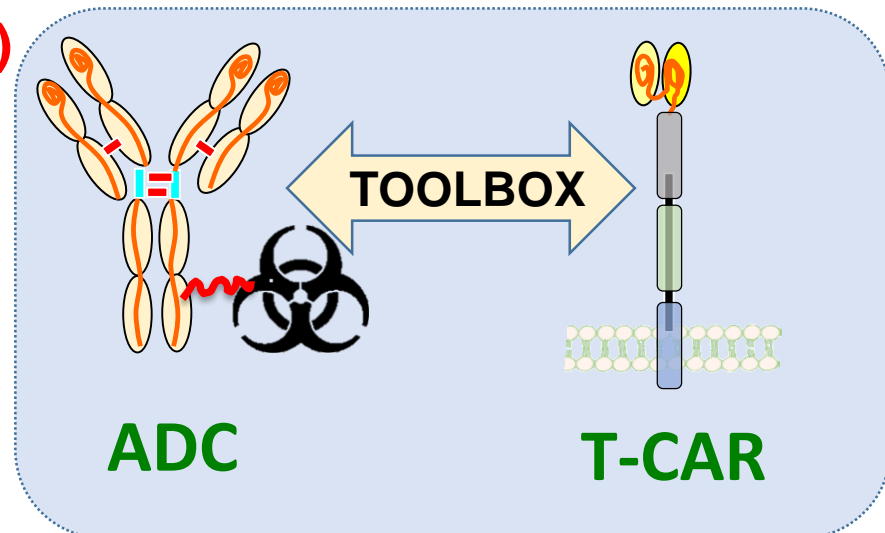


Leonardo Sibilio



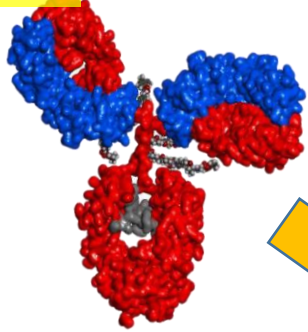
Loredana Cecchetelli

(5-10 nm)

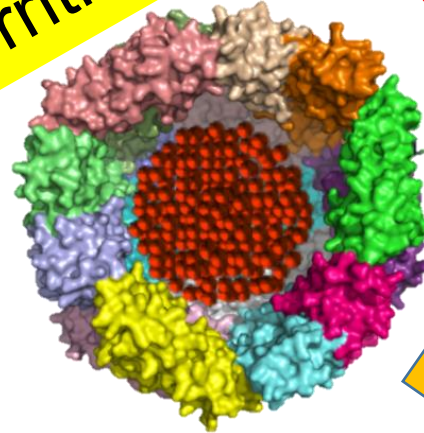


– From ADCs to α DCs –

ADC



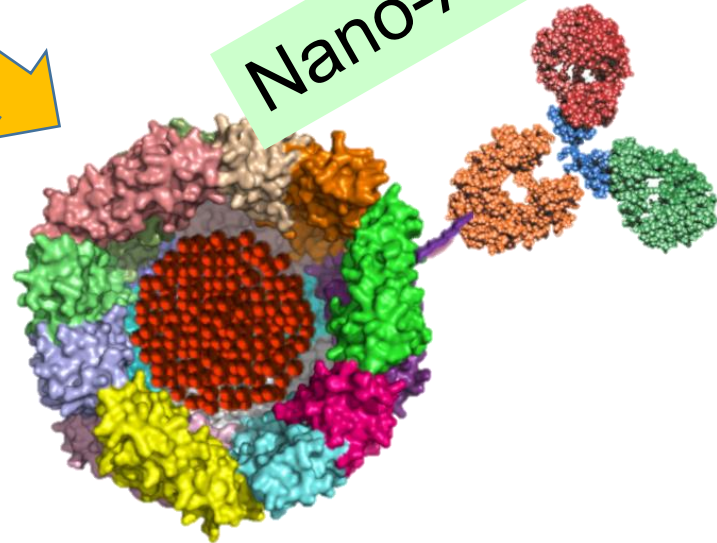
Ferritin (Hft)



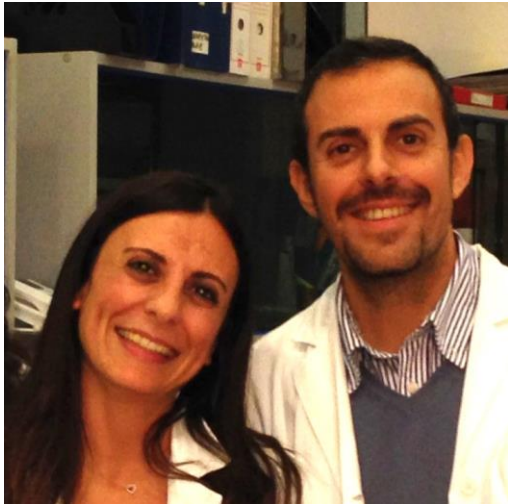
(13 nm)



Nano-ADC

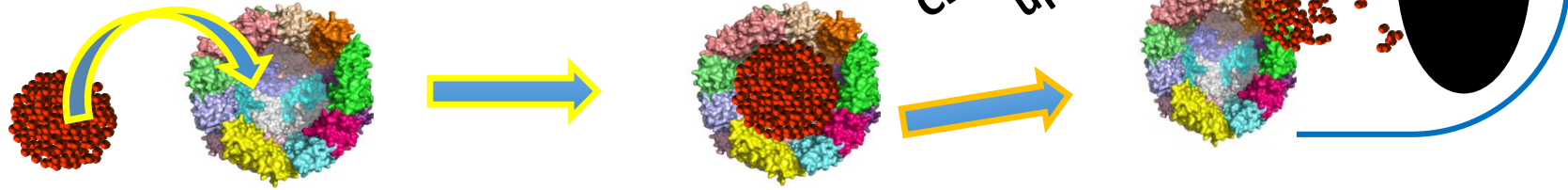


Pierpaolo Ceci



Elisabetta Falvo

H-nanoferritin (HFt): cage and carrier for antiproliferative payloads



- ferritin is a **natural** non-toxic **protein** selected during evolution to be stable in body fluids and pass body barriers
- Made of 24 subunits (H and L chains), it is produced **in recombinant form** as **HFt** (24 heavy chains)
- **HFt (heavy chains only)** is produced in high yields (5 g/L) in **E. Coli**, it is **stable at 75 °C and at pH=2.0**
- HFt **entraps** more **drug** molecules inside its cavity (**30-200** mol depending on the drug) as compared to albumin (HSA) or ADCs.
- HFt is actively uptaken through its natural **receptor (CD71, the transferrin receptor)**. This is adaptively **over-expressed** (**10-100** fold) in cancer cells

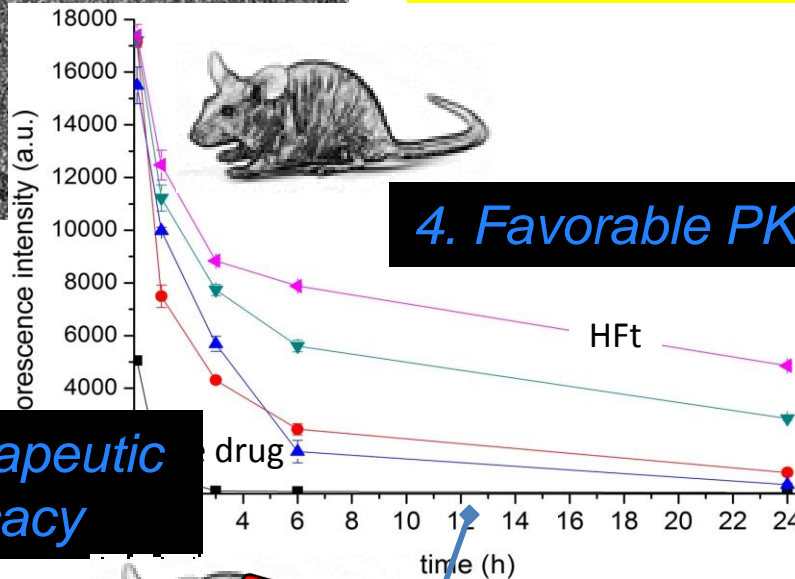
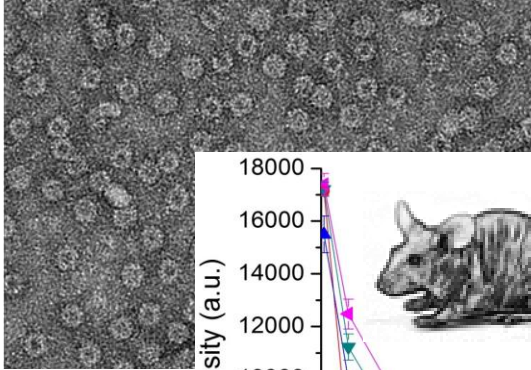
— Recombinant HFt in vivo —

2. Wide Drug nano-caging spectrum

1. Innovative industrial process

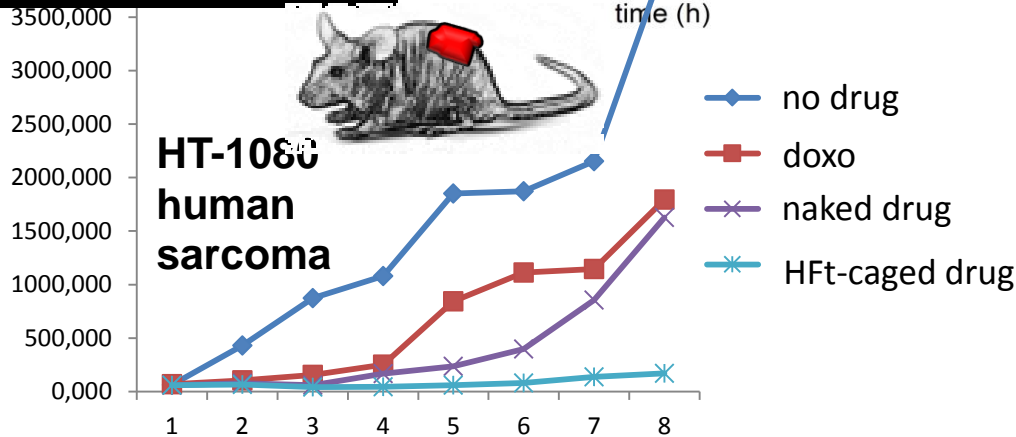
Bacteria 5g/L
Autoassembly
Double drug loading surface
Up to >100 drugs/molecule
Shelf-life
lyophilization

- Cisplatin
- Doxorubicin
- Doxorubicin analogues
- MMAE
- Mitoxantrone
- Topoisomerase inhibitors



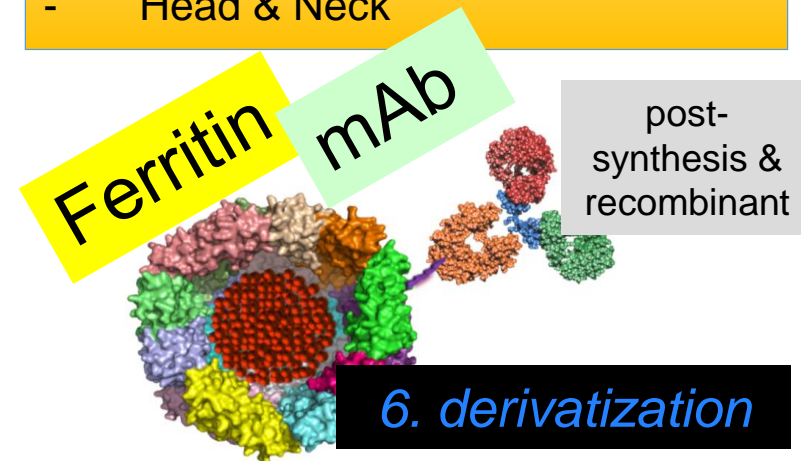
4. Favorable PK

5. Therapeutic efficacy



3. Wide spectrum of potential tumor targets

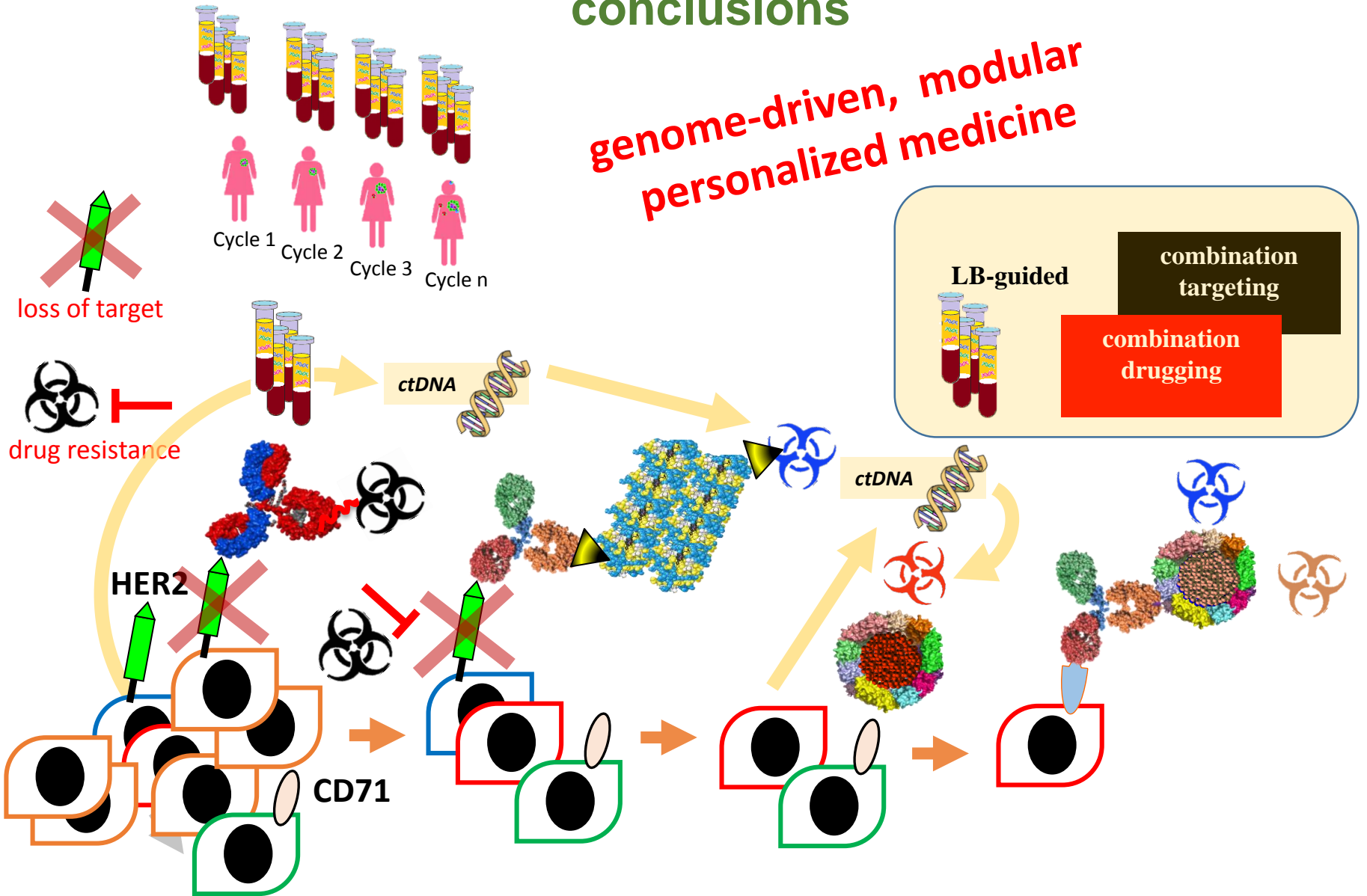
- Pancreas adenocarcinoma
- Melanoma
- Breast Carcinoma 3N
- Sarcoma
- Colorectal Carcinoma
- Head & Neck



6. derivatization

A Liquid Biopsy 'hub': integrating nano-technologies to improve cancer diagnosis and therapy: conclusions

genome-driven, modular personalized medicine



Acknowledgements and disclosure of potential conflicts of interest

main academic partners



non-profit support

- H2020 RIA and MSCA



- Lazioinnova



main industrial partners

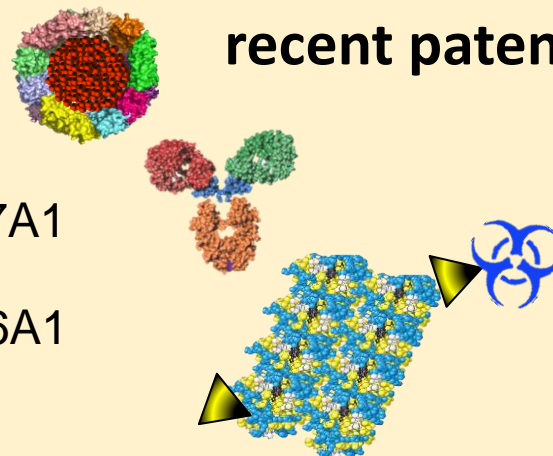


EP3186192B1

WO2017167967A1

WO2018138676A1

recent patents



A 'Precision Oncology open day'

- To be held in Rome Q1 2020.
- Co-supported and co-sponsored by the **ICPerMed recognition prize award**
- The purpose will be to raise awareness about the new **mutational oncology model** and the precision oncology potential
- Target audience: **specialists and non-specialists**, e.g. surgeons, medical oncologists, radiologists, pathologists etc, science writers and journalists, patients and patient advocacy organizations, entrepreneurs, the general public, policy makers and the Italian and EU Institutions
- Short introductory talks for both specialists and non-specialists about genome-driven oncology, its tools (molecular diagnosis report, the Molecular Tumor Board, off-label treatment), and relevant financial, regulatory, deontological, and ethical issues
- **Duet-talks** by patients and their physicians: exceptional responders, liquid biopsy therapy assignee, Lazarus responders etc seen by **the Regina Elena MTB**.

Final agenda to be assembled: **ICPerMed, the Italian Ministry of Health, and the local Health Authorities in Rome**