

# 21° Congresso Nazionale



Società Italiana di Tossicologia

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Cliniche

Nanoparticelle proteiche impiegate  
nell'imaging e nel trattamento di tumori solidi:  
il caso della ferritina nanocage.

[www.sitox.org](http://www.sitox.org)

**BOLOGNA**

20-22 Febbraio 2023

# H-ferritin (HF<sub>n</sub>) is a tumor targeting nano-delivery agent

Thermal and chemical stability

Engineered human H chains nanocage

Endogenous protein

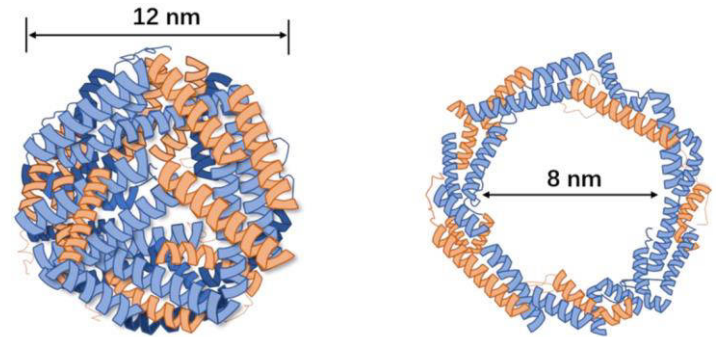
safety

Disassemble/reassemble in a shape memory way

loading capacity

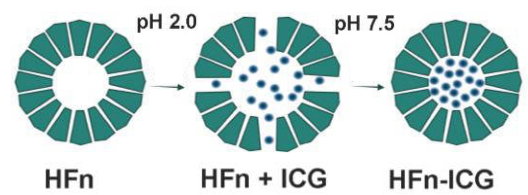
Human transferrin receptor 1 (TfR1) specific recognition

tumor homing

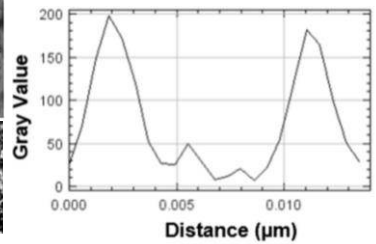
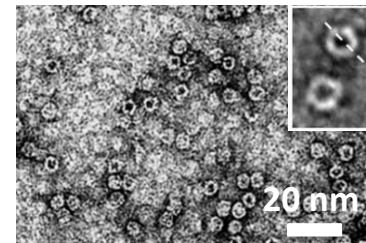
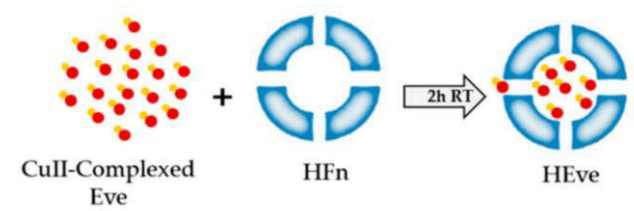


# HFfn loading: the pH disassembly-reassembly and metal affinity methods

**pH method**  
(hydrophilic molecules Dox, ICG)

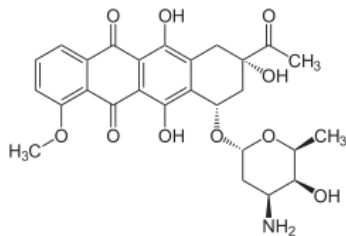


**Metal affinity method**  
(hydrophobic molecules Everolimus, Navitoclax)

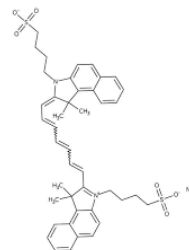


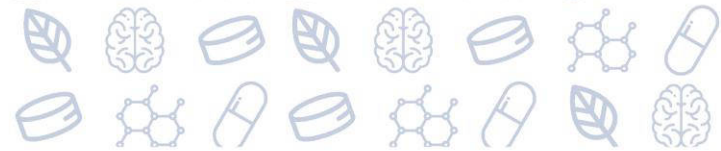
# H-ferritin (HF<sub>n</sub>) is a tumor targeting nano-delivery agent

DOXORUBICIN



INDOCYANINE GREEN

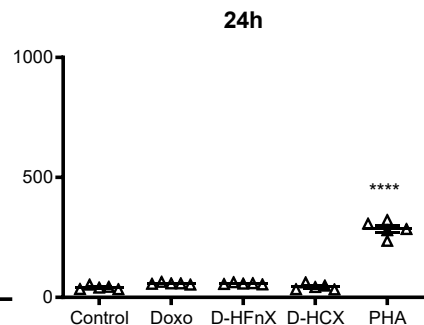
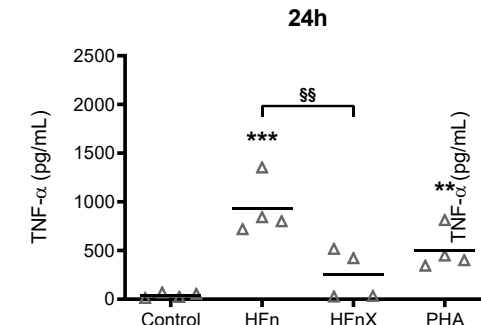
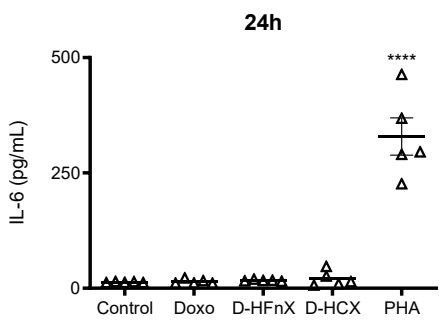
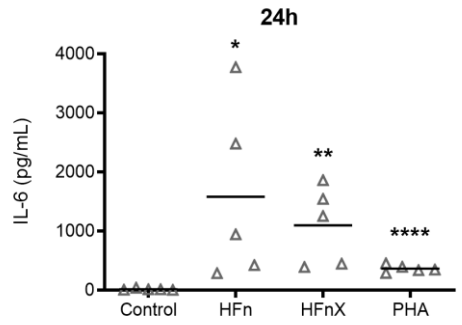
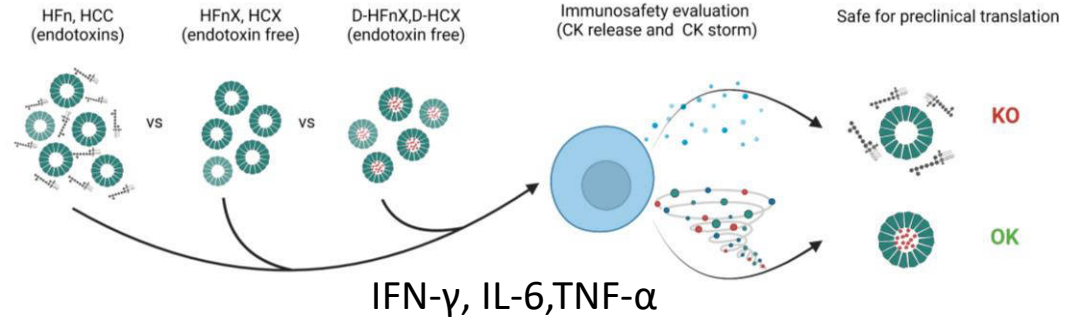




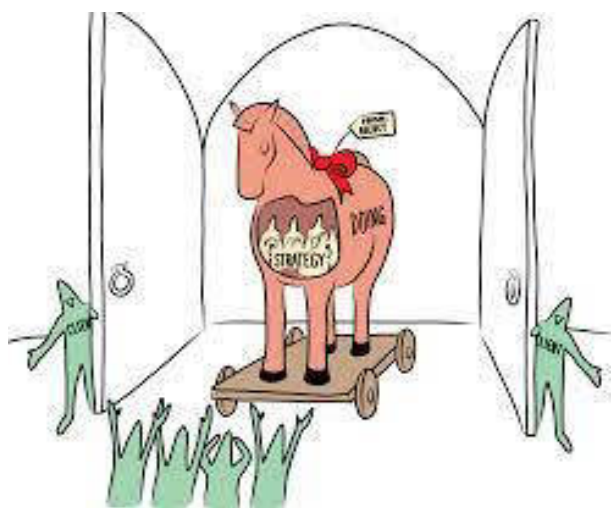
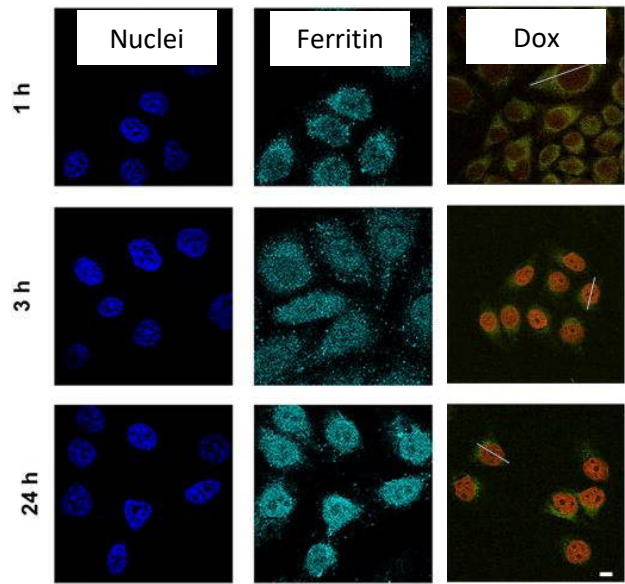
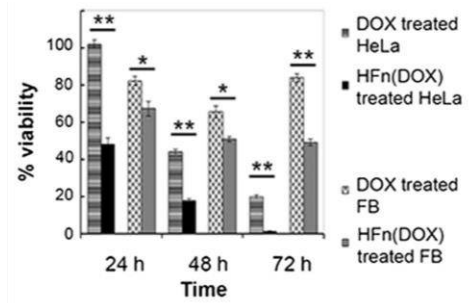
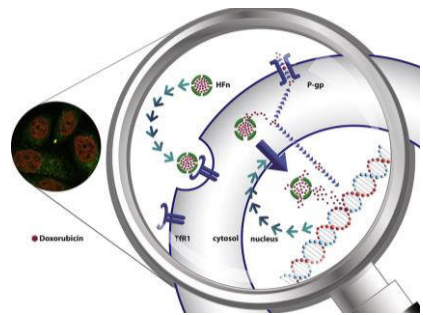
# Endotoxin free, loaded HFn is a safe nanovector for in vivo studies

**BC Bioconjugate Chemistry**

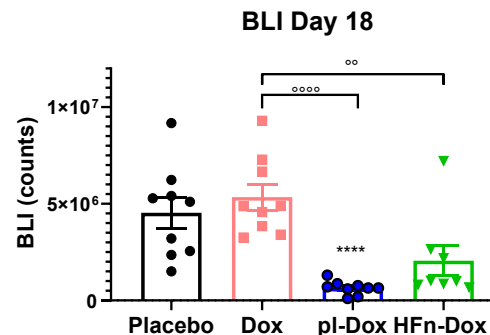
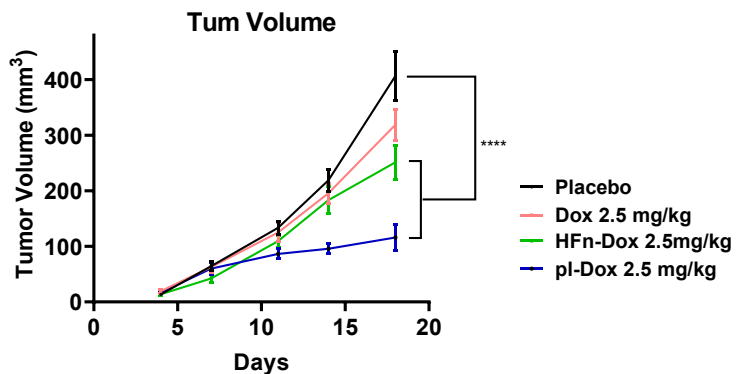
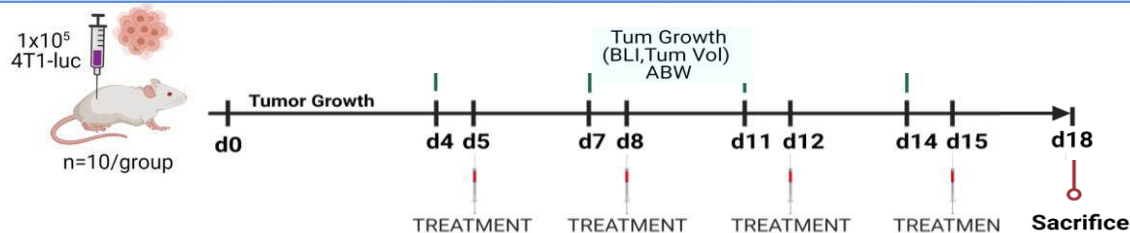
Sitia, Galbiati et al. 2023 ACCEPTED



# HFfn drives nuclear Dox release, while Fn levels increase



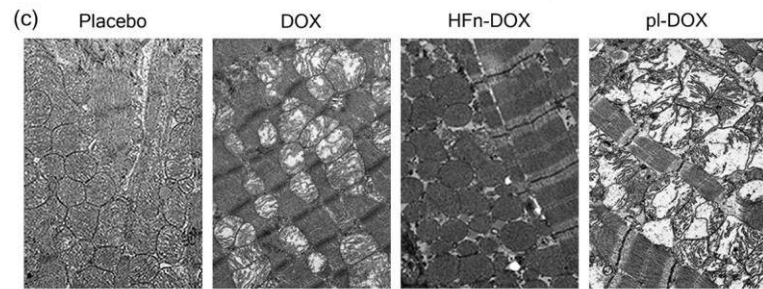
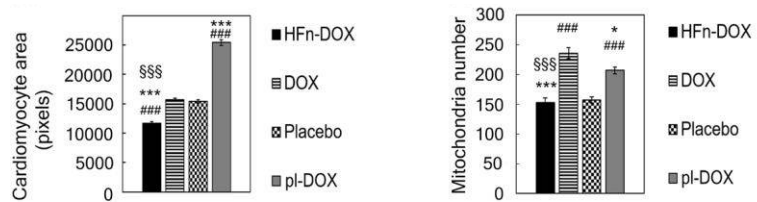
# HFn-Dox inhibits tumor growth in triple negative breast cancer



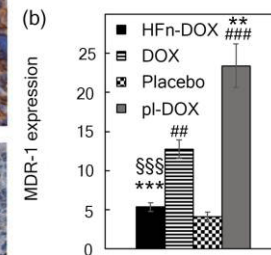
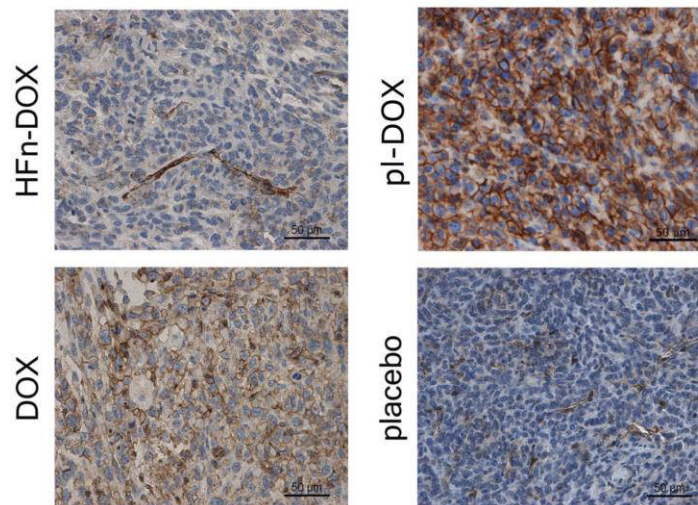
Model: 4T1-luc, TNBC model, Balb-c mice. Treatment: 2.5 mg/kg, 2xw, day 18

Manuscript in preparation

# HFfn-DOx limits DOx related toxicity and resistance induction



HFfn-DOx protects cardiomyocytes from DOx induced Hypertrophy (1.25 mg/kg, day 21)

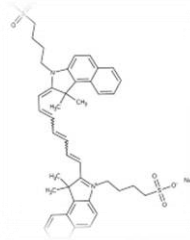


Reduced MDR-1 expression compared with DOx and pl-DOx



# H-ferritin (HF<sub>n</sub>) is a tumor targeting nano-delivery agent

## INDOCYANINE GREEN



# HFn-ICG to be used for fluorescence guided surgery



*Lancet Oncol 2019; 20: e354–67*

## Clinical need

Specific identification of tumor margins,  
positive lymph nodes and unknown  
micrometastases

## Indocyanine green (ICG) fluorescent dye



Nontoxic, water-soluble

Sentinel lymph node mapping

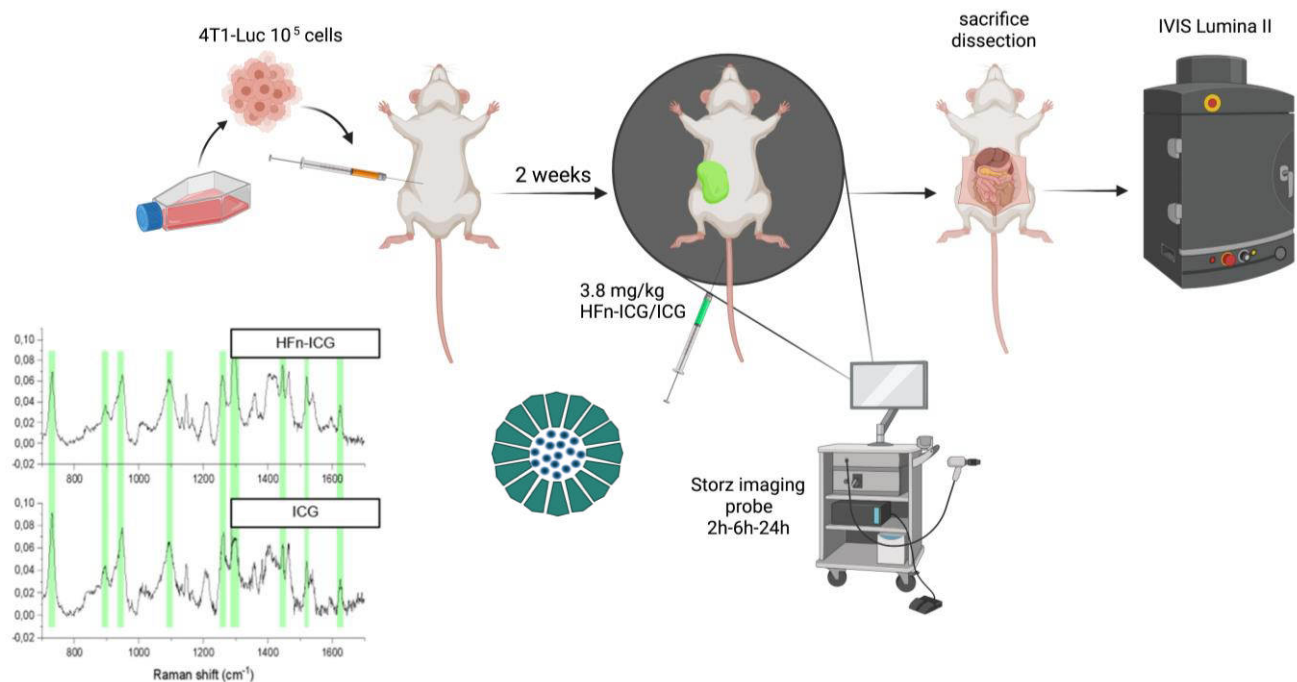


Lack of tumor targeting specificity

Rapid degradation and elimination



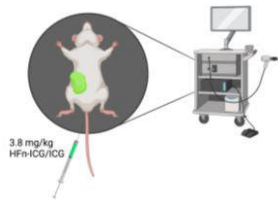
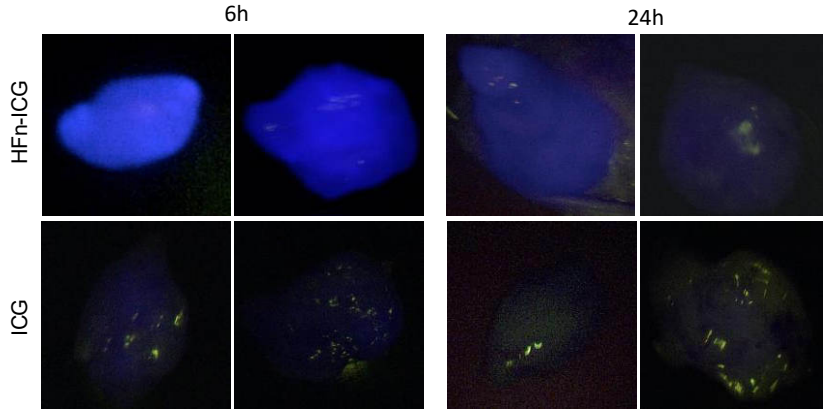
# HFn-ICG to be used for fluorescence guided surgery



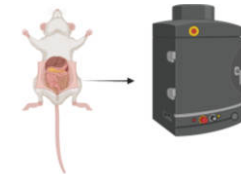
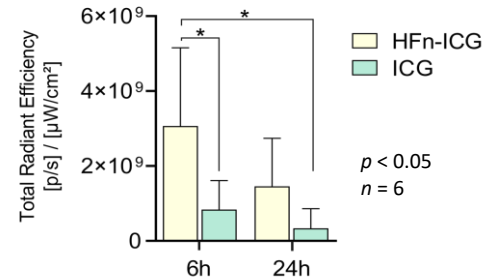
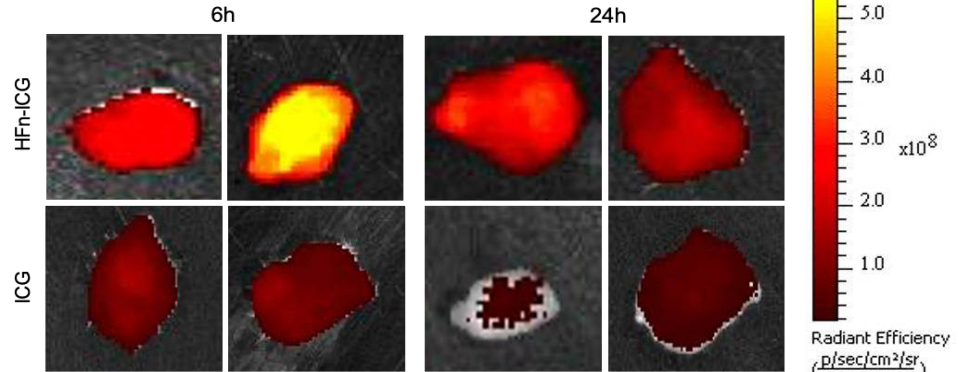
## HFn-ICG to be used for fluorescence guided surgery



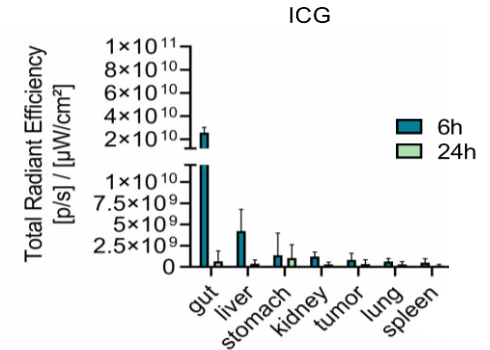
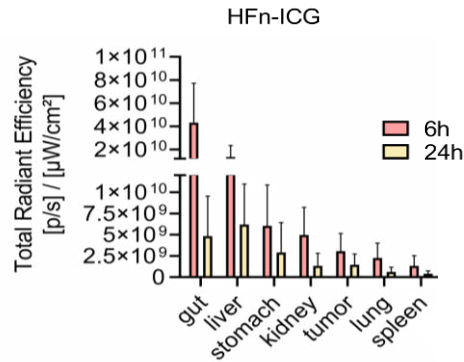
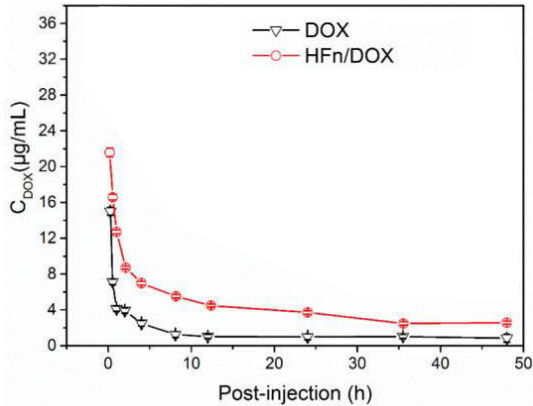
### Ex vivo imaging of the tumor by Storz probe



### Ex vivo imaging of the tumor by IVIS Lumina II



## So far, so good. However...



**Blood half life and off target biodistribution need to be improved**

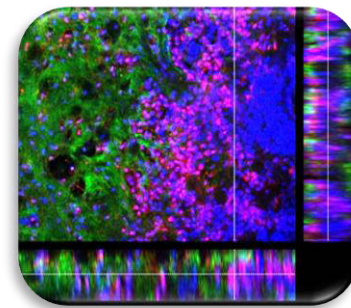
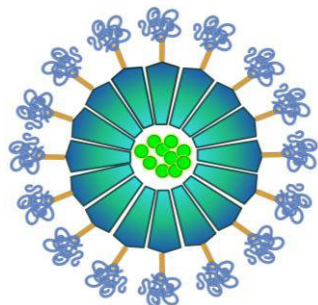
## Next steps

Improve HFn  
design

Targeting  
metastases

Interactions with  
patient tissues (PDOs  
or slices)

HFn-PASE





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**Department of Pharmacological and Biomolecular Sciences**

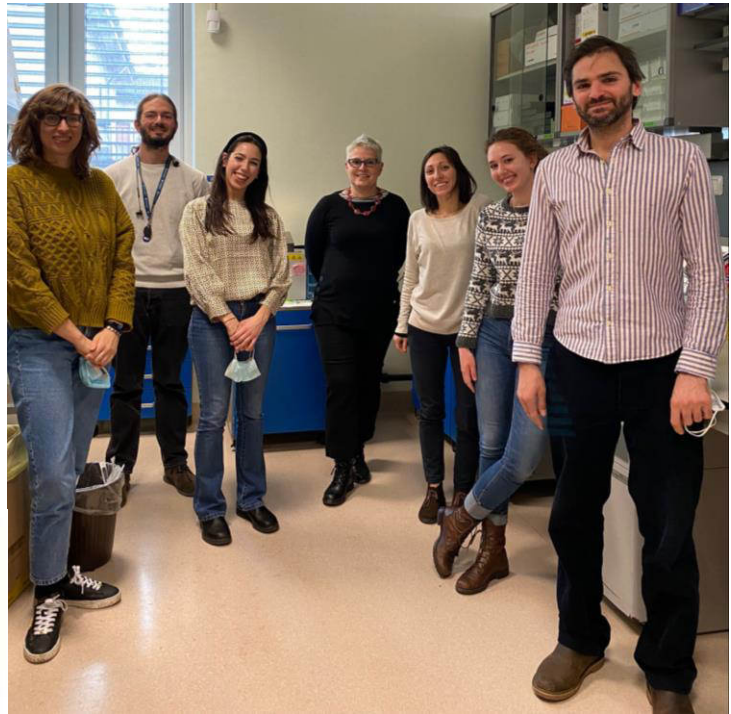
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 Dr. Valentina Galbati



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IG 2022 ID: 27107