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# Exploration of breast cancer models at Centre d'Imagerie du Petit Animal (CIPA) – CNRS - PHENOMIN-TAAM

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CIPA is part of CNRS TAAM Unit and member of National Infrastructure PHENOMIN. It is committed to servicing the scientific community. It performs state of the art multimodal in vivo explorations by high resolution X ray Computed Tomography (CT), Bioluminescence and Near-Infrared Fluorescence Tomography, Tomo Scintigraphy (SPECT), PET, and high resolution Echography coupled to Photoacoustic imaging. Certification ISO 9001:2008. NFX50-900. The team is recognized as expert in preclinical and translational research in oncology.

## Available models at CIPA

### In mouse :

- 4T1 luc (bioluminescent) syngenic model, mammary fat pad implantation with spontaneous metastasis (immunocompetent mice)
- human cell lines : MDA-MB231 luc (triple negative) and MCF7 luc, mammary fat pad implantation (immunodeficient mice)
- other cell lines can be studied upon specific request

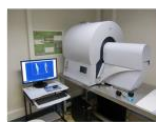
### In rat :

MDA-MB-231 luc, mammary fat pad implantation or injection in forepaw to study lymphatic drainage areas

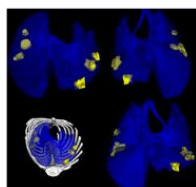
### Other models :

In collaboration with Ecole Vétérinaire de Nantes (ONIRIS) : spontaneous tumors in dog or aged rabbit – CIPA has developed a mobile device for per operative near infra red fluorescence

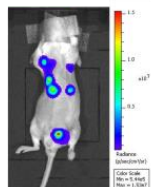
## Detection of spontaneous metastases in 4T1 Luc tumor engrafted in mammary fat pad



X Ray Computed Tomography (CT), with respiratory or ECG triggering

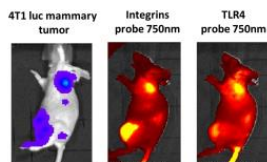


Lung metastases around 1,5-2mm detected by CT imaging, without contrast agent



Detection of metastases with bioluminescence imaging

## Photonic imaging : molecular imaging

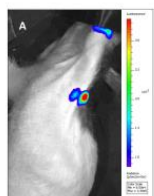


S. Roger et coll. INSERM U1069, Tours

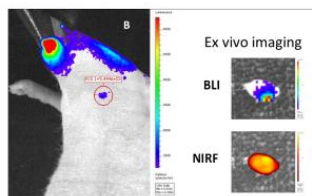
CIPA has developed a mobile device for bioluminescence and per operative near infra red fluorescence in order to manage that type of study in partners labs

## Development of models for minimally invaded sentinel lymph node (500-5000 cellules) in immunodeficient rat (A) or mouse (B)

Bioluminescence imaging allows in vivo quantification of tumor cells for each lymph node before inclusion in the protocol

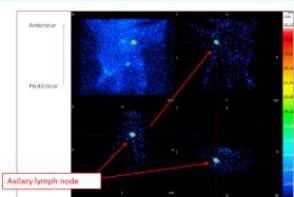


Axillary (5000 cells) and brachial lymph nodes (1500 cells)

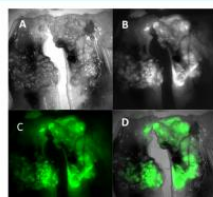


Axillary lymph node(1000 cells)

## Spontaneous mammary tumor in the aged female rabbit highlighted by lymphoscintigraphy (99mTc labelled colloids) and assessment of tumor foci by near infrared fluorescence (J Abadie, N Chouin, Oniris Nantes)



Lymphoscintigraphy with 99mTc-colloids to evidence axillary sentinel lymph node of the tumor in the same animal



Ex vivo fluorescence imaging of a spontaneous mammary tumor in the female rabbit 24h after iv injection of a RGD peptidomimetic labeled with Cy5.5. A/ photographic image, B/ raw image in NIRF, C/ fluorescence image with artificial color, D/ co-registration of fluorescence and photographic images

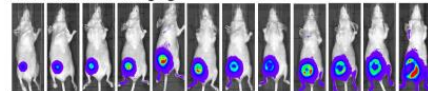
## Multimodality imaging of tumor in a model of MDA-MB231 luc in mice

### Ultrasound – 3D imaging



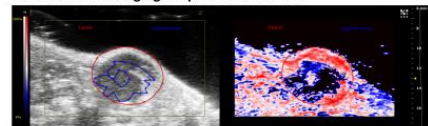
Sizing of tumor volume > 2 mm3

### Bioluminescence imaging

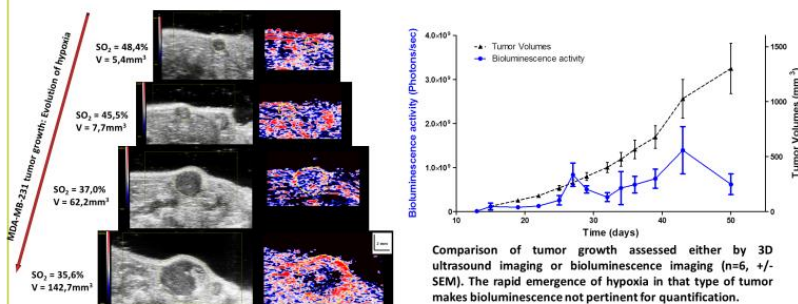


Quantification of proliferation if non hypoxic tumor  
Detection of metastasis with high sensitivity

### Photoacoustic imaging coupled to ultrasound



Exploration of tumor hypoxia  
Measurement of hemoglobin SaO2 during tumor growth and therapeutic response



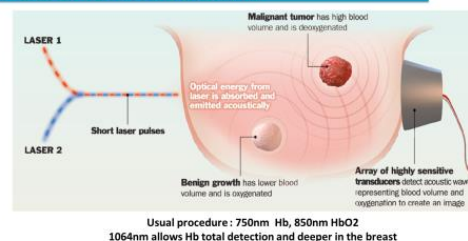
Targeting the Tumour Microenvironment with Enzyme-Responsive Drug Delivery System for Efficient Therapy of Breast and Pancreatic Cancers. Renoux et al., Chemical Sciences 2017

## Ultrasound and photoacoustic imaging

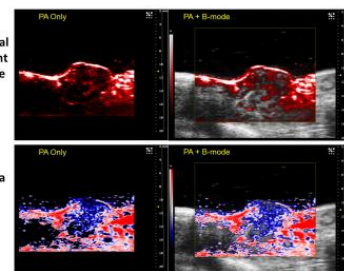


### Principle:

- Photoacoustic (PA) imaging is a real-time noninvasive imaging modality
- It combines laser pulse tissue excitation and ultrasonic detection of the tissue response
- Typically, the ultrasound image is obtained by irradiating tissue with a nanosecond pulsed laser. Optical absorption induces a rapid thermoelastic tissue expansion that generates a wideband ultrasound wave detectable by an ultrasound transducer.



### Application in mice engrafted with MDA-MB231 cells



### Applications of photoacoustic in oncology

- Quantification of hypoxia with hemoglobin SaO<sub>2</sub>
- Biodistribution of O<sub>2</sub> in tumors
- Aging and oxygenation of skin
- Melanoma and other cutaneous cancers
- Evaluation of hemoglobin content
- Gradation of tumor
- Identification of lymph nodes and lymphatic vessels
- Tumor vascularization
- Ischemia
- Molecular imaging (labelling of contrast agents, fluorochromes...)
- Translational research

Visualization of total hemoglobin content in order to improve small tumors detectability

Imaging of hypoxia biomarker

### Contacts :

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### Discover PHENOMIN:





# Exploration of colorectal and pancreatic cancer models at Centre d'Imagerie du Petit Animal (CIPA) – CNRS - PHENOMIN-TAAM

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## Cell lines :

### Colorectal cancer

- human HCT116 luc bioluminescent cell line (Kras mutation)
- human HT29 luc bioluminescent cell line (Braf mutation)
- human SW48 luc bioluminescent cell line (Kras wild type, Braf wild type) (under development)

### Pancreatic cancer:

- human MiaPaCa luc bioluminescent cell line

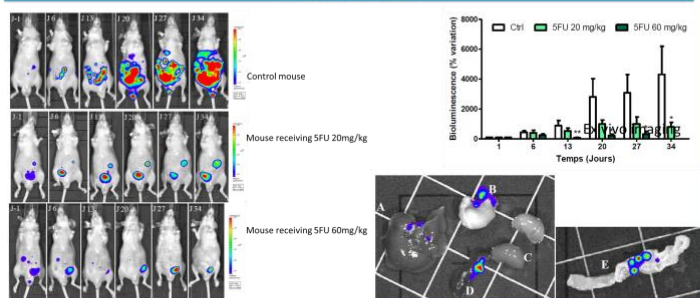
Other cell lines or induction of colorectal cancer with specific agents (AOM for example) can be studied upon specific request

Animal strains : immunodeficient mice or rats

## Models:

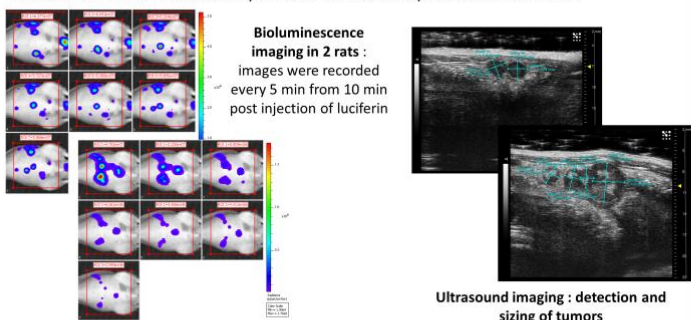
- colorectal tumor graft in the caecum
- peritoneal carcinomatosis
- liver metastases after injection of tumor cells in the spleen
- orthotopic graft in the pancreas

## Bioluminescence imaging for validation of a colorectal cancer model with peritoneal carcinomatosis (HCT116 Luc) and response to a reference chemotherapy



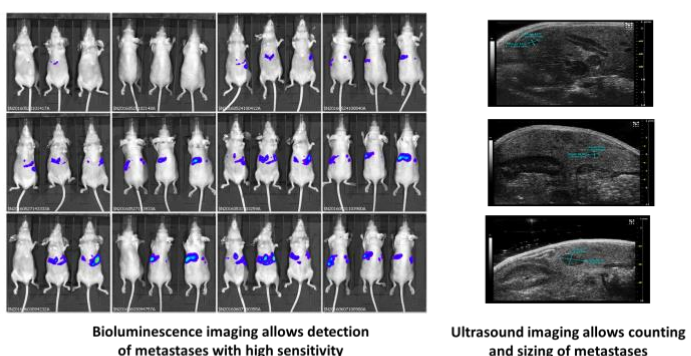
## Development of a rat model of peritoneal carcinomatosis

Rat models are becoming more and more relevant and are sometimes needed when larger models than mice have to be implemented to address a specific scientific issue



## Liver metastases in the mouse

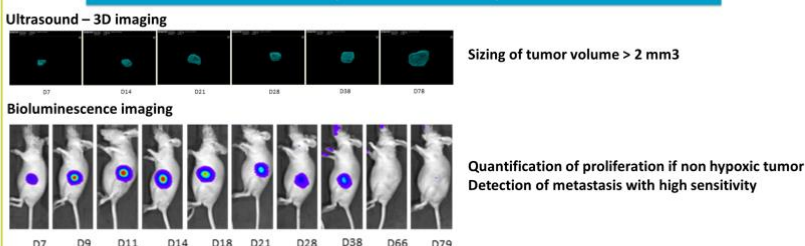
Liver metastases are obtained after injection of tumor cells in the spleen



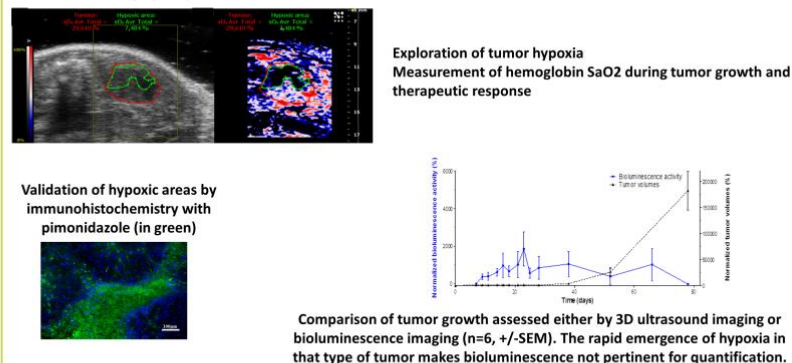
## Echo guided injection of tumor cells in the caecum



## Multimodality imaging of tumor in a model of pancreatic adenocarcinoma (MiaPaca Luc cells) in mice

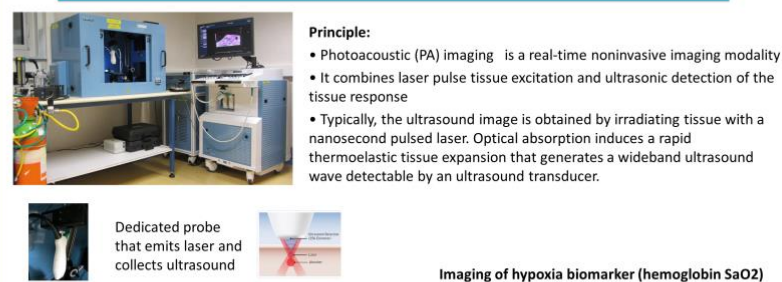


## Photoacoustic imaging coupled to ultrasound



Targeting the Tumour Microenvironment with Enzyme-Responsive Drug Delivery System for Efficient Therapy of Breast and Pancreatic Cancers. Renoux et al., Chemical Sciences 2017

## Ultrasound and photoacoustic imaging

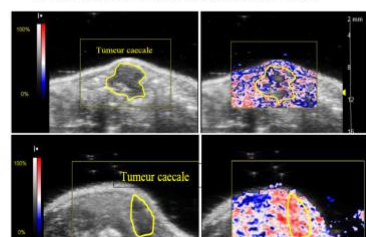


## Imaging of hypoxia biomarker (hemoglobin SaO<sub>2</sub>) in HCT116 or HT29 colorectal tumor model

- Applications of photoacoustic in oncology
- Quantification of hypoxia with hemoglobin SaO<sub>2</sub>
  - Biodistribution of O<sub>2</sub> in tumors
  - Aging and oxygenation of skin
  - Melanoma and other cutaneous cancers
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HT29 model

HCT116 model



Discover PHENOMIN:



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