
BIENVENUE AUX
6es journées
BIOSARC
12 & 13 octobre 2017
CHU Lapeyronie, Montpellier
GROUPE
SARCOME
FRANÇAIS

Etudes fondamentales :

Voies de signalisation
microenvironnement tumoral

Développement de Nouveaux modèles d'études
In vitro, in vivo

Modèle 3D : sphéroides
Modèles souris : PDX

Développement de nouvelles techniques

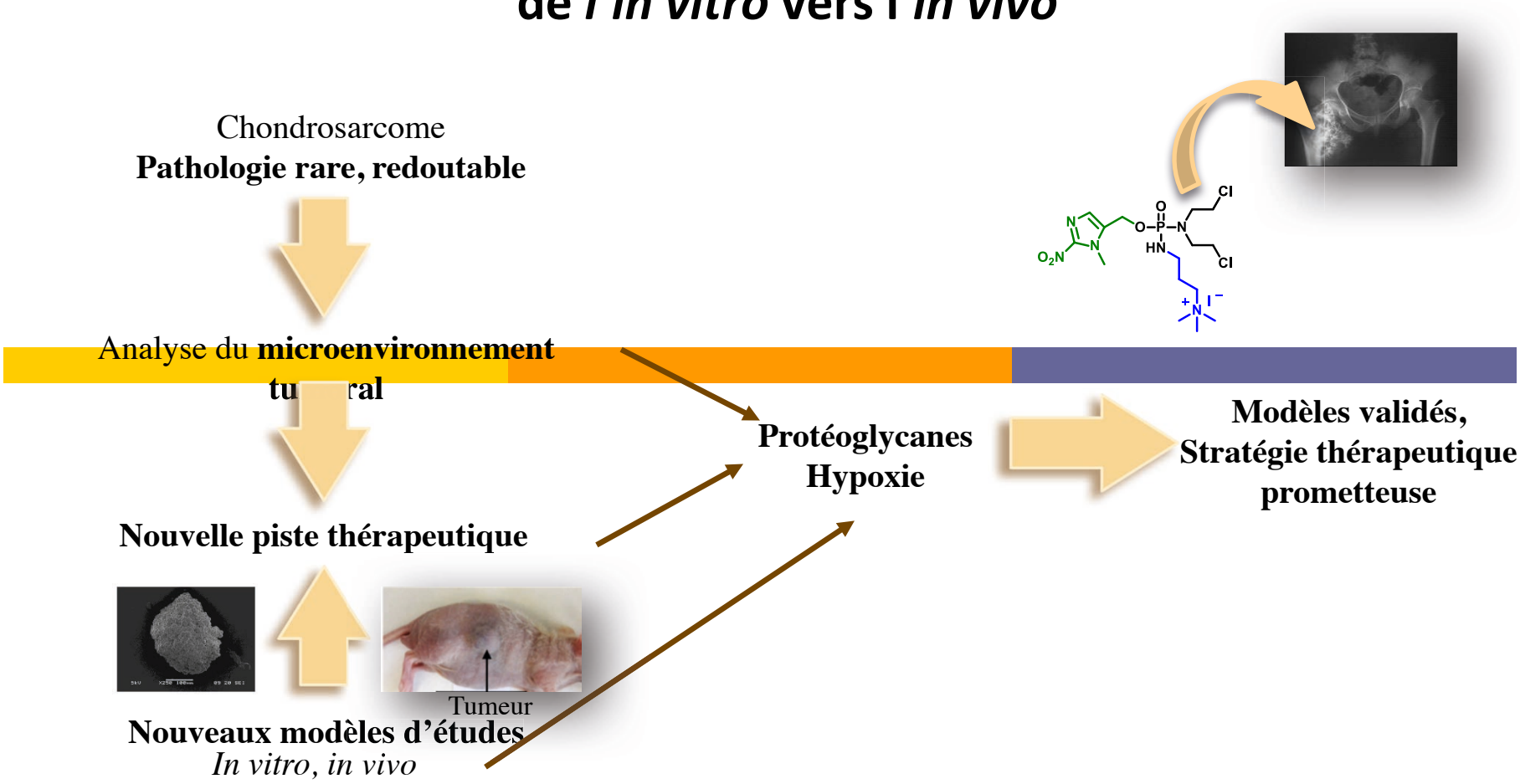
The SpiderMass^{TM} system : analyses lipidomiques par spectrométrie de masse en temps réel

Stratégies thérapeutiques prometteuses

Potentialisation de la chimiothérapie par combinaisons avec des inhibiteurs de protéines ciblées

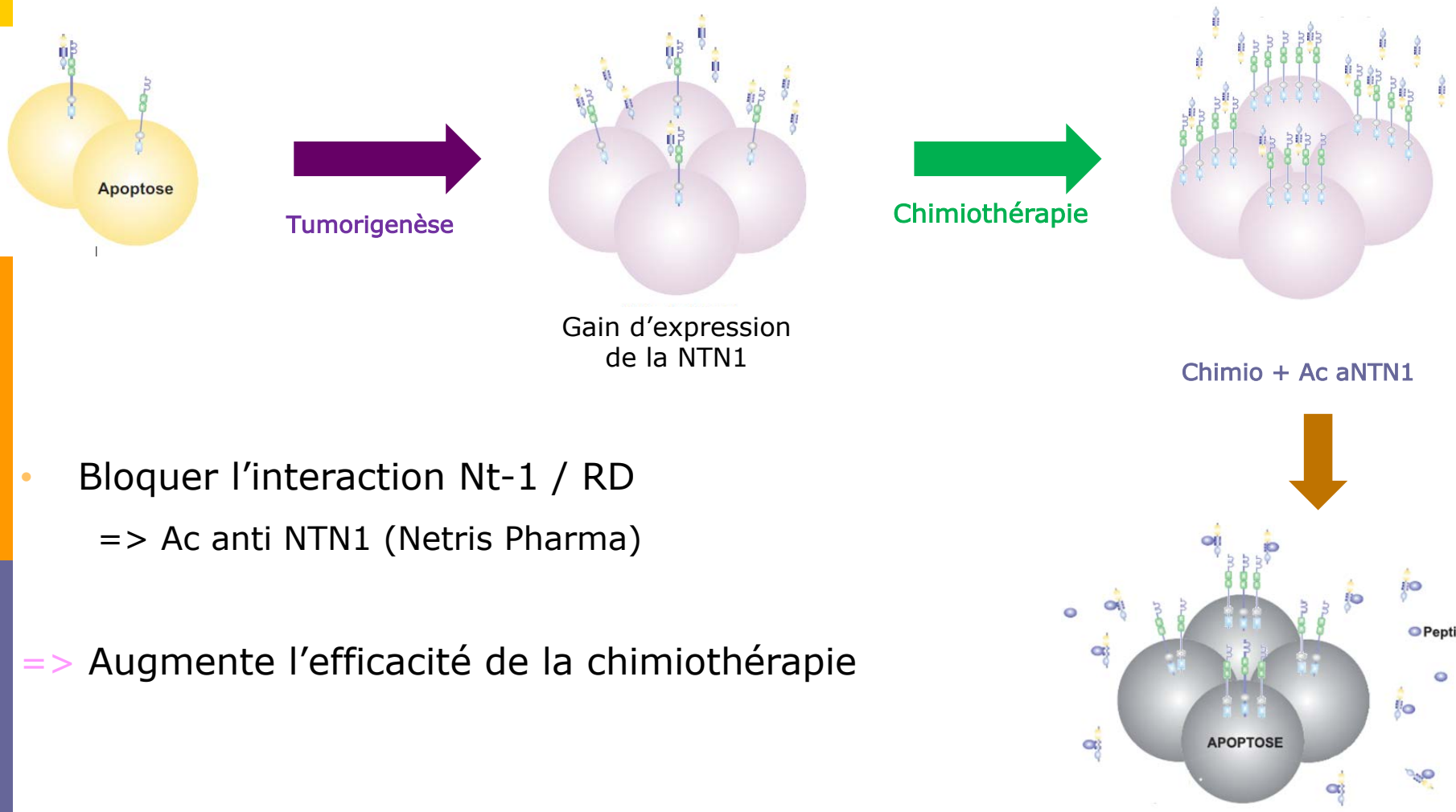
Etudes des regulations épigénétique dans la chimioresistance

Validation d'une Stratégie Thérapeutique ciblant les Protéoglycanes et l'Hypoxie du Chondrosarcome par une Approche Sphéroïde : de *l'in vitro* vers l'*in vivo*



Elise Maubert, UMR 1240 Inserm, IMoST/Université Clermont Auvergne

Potentialisation de la chimiothérapie par interférence avec la NTN1



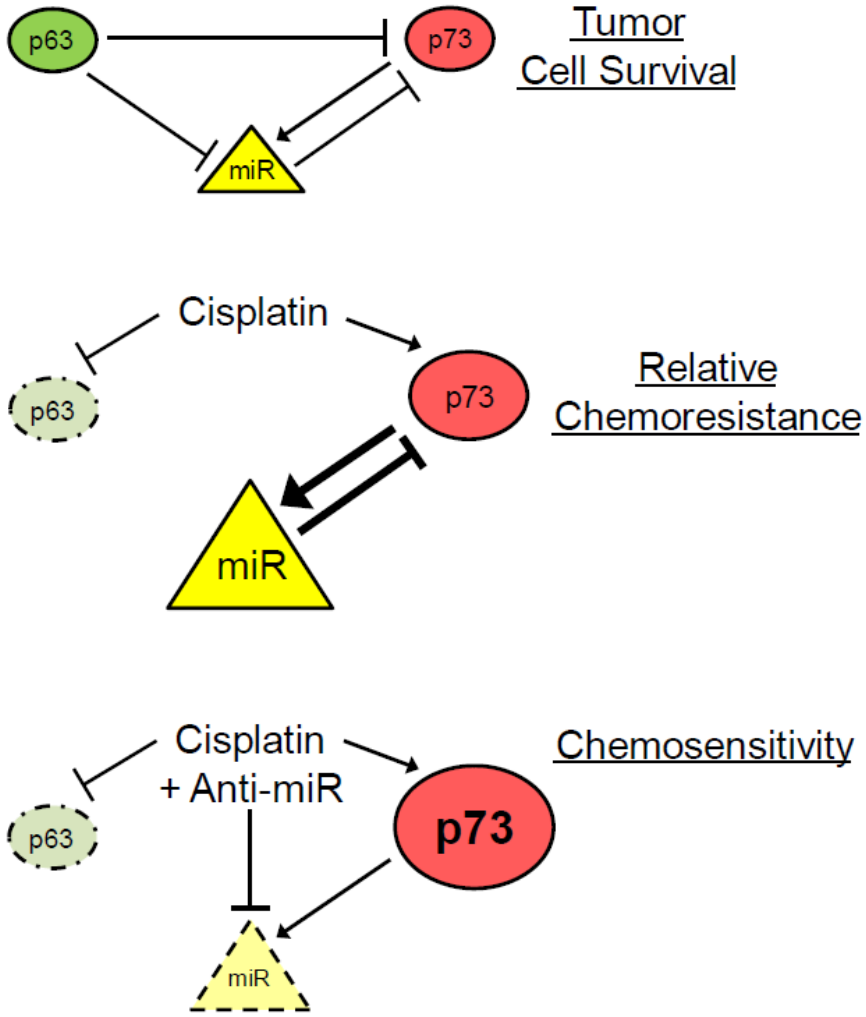
- Bloquer l'interaction Nt-1 / RD

  => Ac anti NTN1 (Netris Pharma)

=> Augmente l'efficacité de la chimiothérapie

Morgane MONCHANIN – équipe DUTOUR, Apotosis and Sarcoma Team – CRCL

Epigenetic regulation of chemoresistance to cisplatin



Dr **Benjamin Ory,** U1238 Equipe 3 / **EpiStress, Nantes**

Real-time and *ex-vivo* lipidomic analyses by mid-infrared laser ablation ambient mass spectrometry applied to dog sarcoma pathology:

The SpiderMass™ system for diagnosis, classification and margin detection

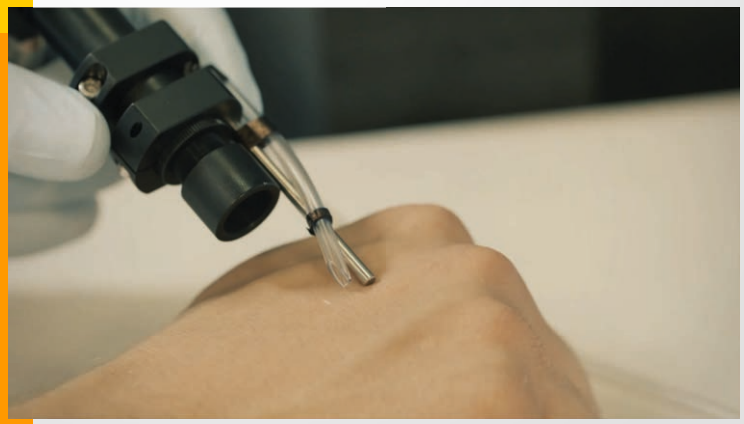
Philippe SAUDEMONT

Proteomique, Réponse Inflamatoire & Spéctrométrie de Masse (PRISM)
INSERM U1192 - Université de Lille

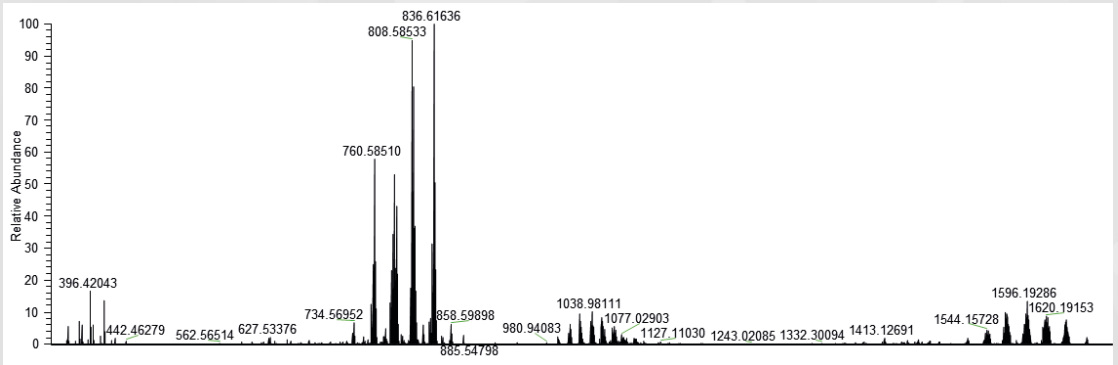
www.laboratoire-prism.fr

Spidermass provide real-time in-vivo molecular profiles with low invasiveness

Laser impact on skin



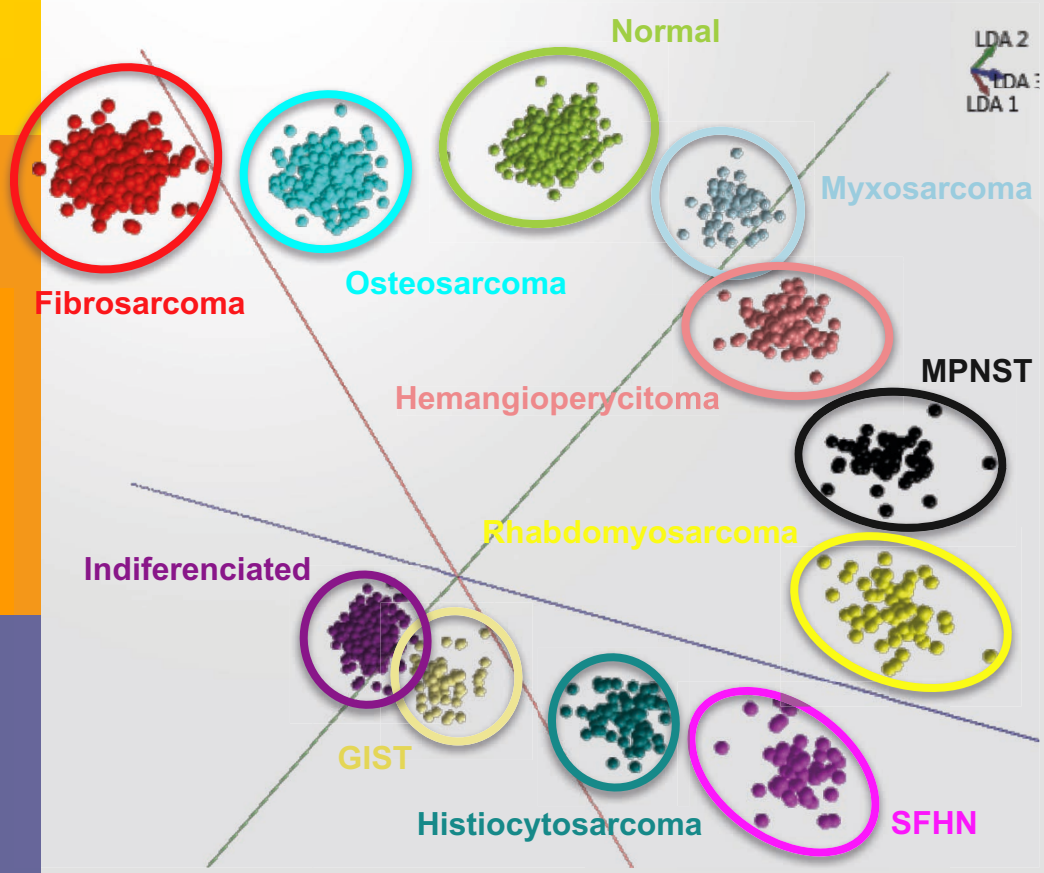
Obtained lipid profile



- **Painless and almost no destruction**
- **Identification of different classes of lipids (fatty acids, diacyglycerols, phospholipids,…)**

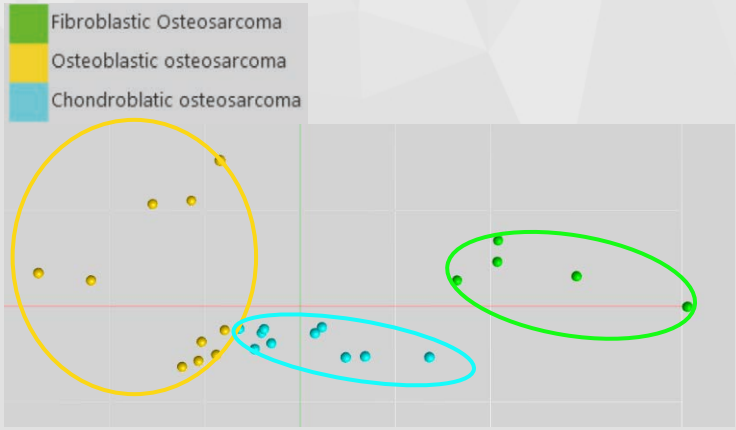
Lipids are enough to obtain information on the tissue physiology and pathology,

Spidermass molecular barcoding allows to classify dogs sarcoma



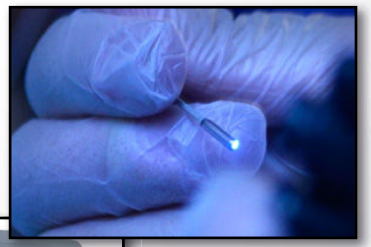
Saudemont P. et al. Sci. Trans. Med. (2017) submitted

- Separation of the biopsies according to their type
- Separation of the subtypes of osteosarcomas



The SpiderMass is able to distinguish the different types and subtypes of sarcomas

Long term development



SpiderMass

Faiblement invasif

Indolore

Détermination du grade et des marges

Nombreuses applications

Deuxième laser

Traitement

Couplage à des systèmes d'endoscope

Couplage à des robots chirurgicaux

Da Vinci

Speed	S
Profiling	P
Innovative	I
Diagnostic	D
Endoscopy	E
Real-time	R
Mass spectrometry	M
Amazing	A
Straightforward	S
Sensitivity	S

PRISE EN CHARGE DES SARCOMES: DE LA CLINIQUE AU TRANSLATIONNEL

TABLE RONDE MEDECINS / CHERCHEURS

Nelly Firmin, Carmen Llacer-Moscardo, Sébastien Carrère

Institut de Recherche en Cancérologie de Montpellier

http://www.ircm.fr

PDX models of sarcomas

Inserm
Institut national
de la santé et de la recherche médicale

ICM
Institut régional du Cancer
Montpellier | Val d'Aurelle

Université Montpellier

BioCampus Montpellier

Montpellier Cancer

PDX models of Sarcomas

Sarcomas

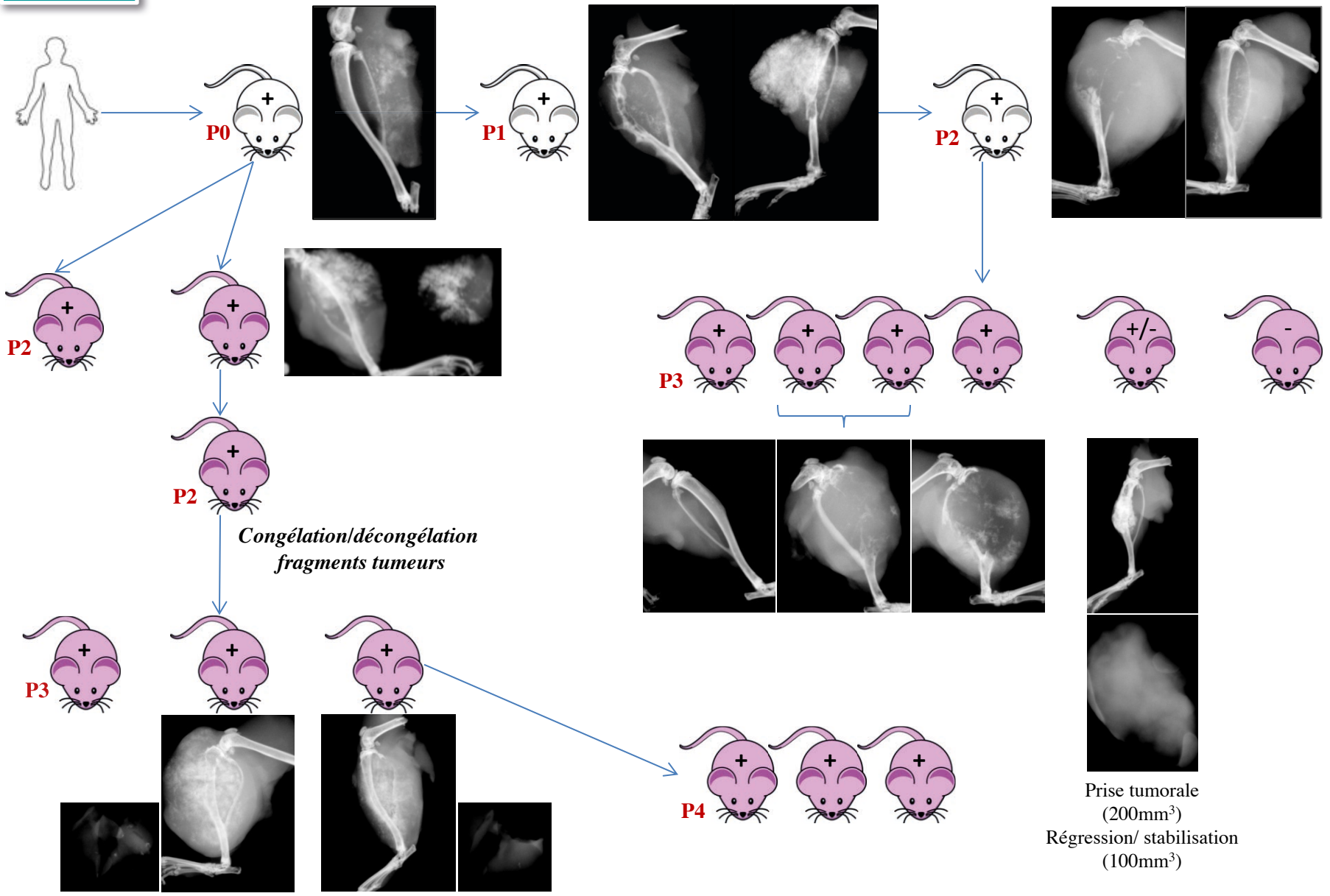
Soft tissues sarcomas

Laëtitia Linares, Montpellier

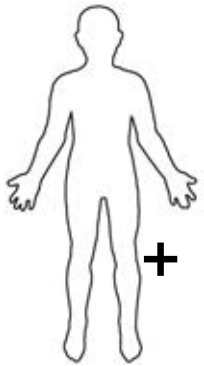
osteosarcomas

Françoise Rédini, Nantes

PDX-OS : Importance de la zone tumorale greffée



PDX-OS : Prise tumorale P0 (SCID)

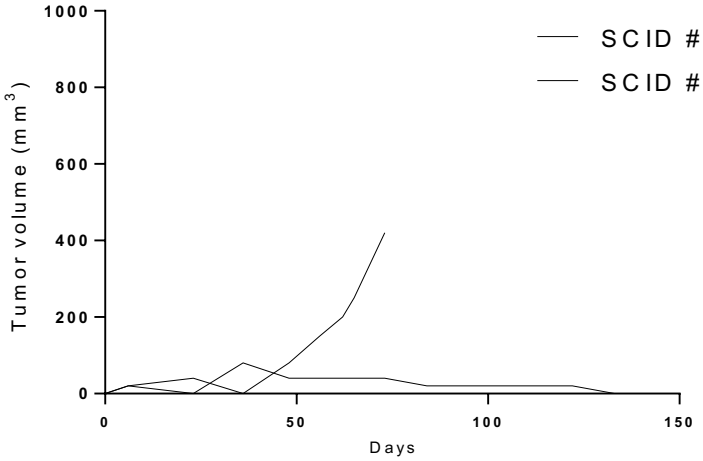


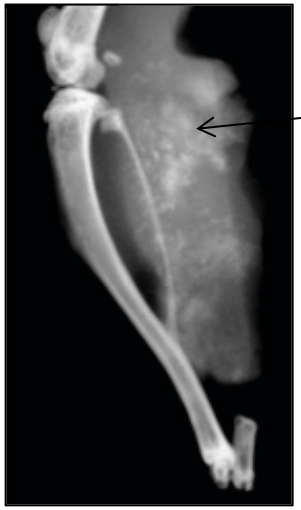
73 jours

400 mm3

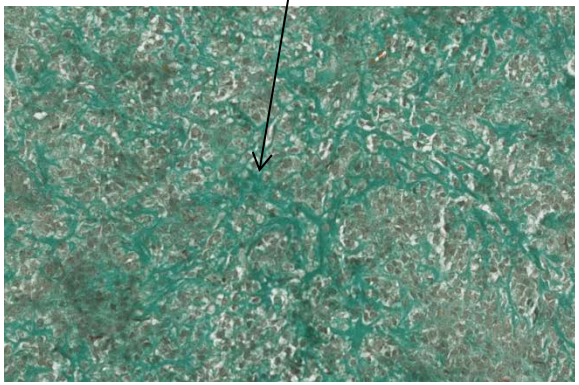
Tum⁻
Metapulm⁺

P0

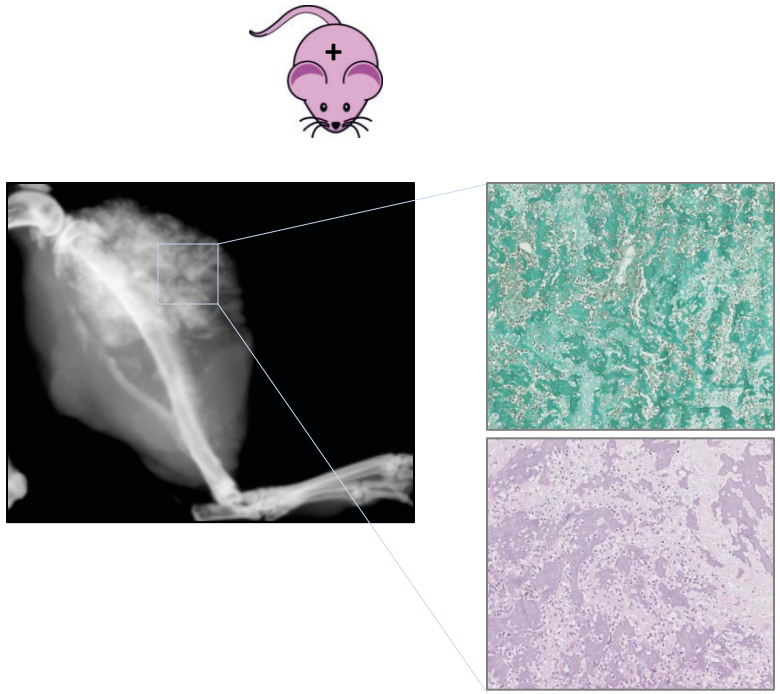


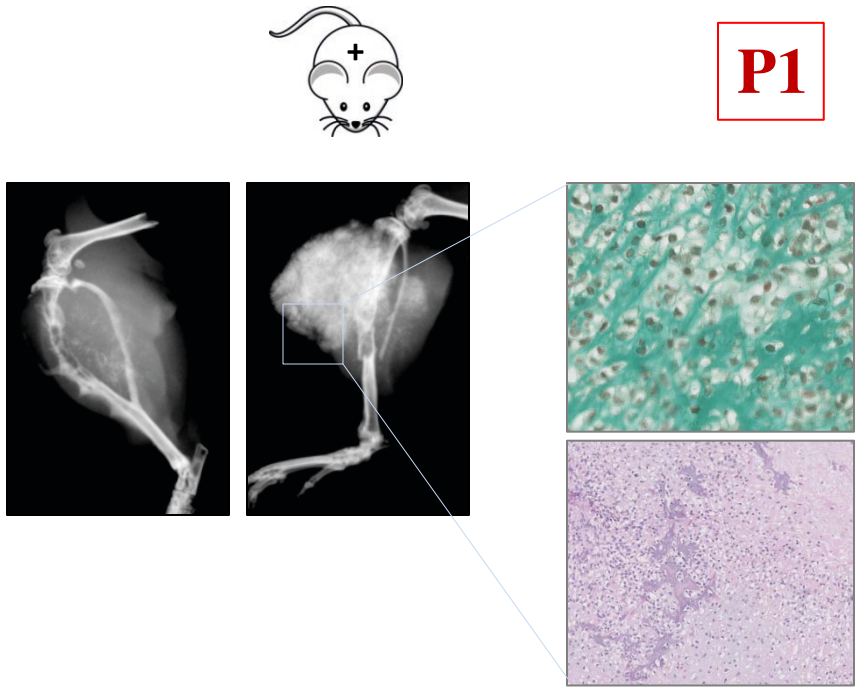


Tumeur minéralisée



PDX-OS: caractérisation histologique et radiologique



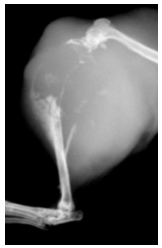


P1

NMRI/NUDE : atteinte osseuse et formation d'os ectopique dans la tumeur

SCID : **Sur un même animal** deux types d'atteintes:
- droite: lyse osseuse (fracture) + formation massive d'os ectopique dans la tumeur
- gauche: atteinte osseuse importante avec fort remodelage, formation d'os ectopique quasi inexistante

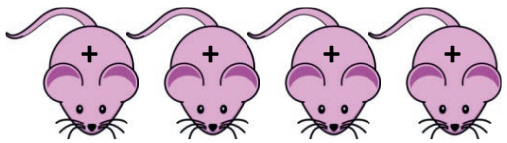
PDX-OS : Homogénéité discutable des tumeurs

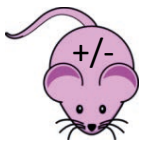


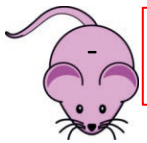
P2

65-80 jours

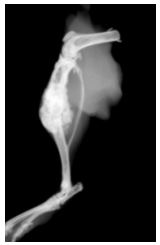
500 mm3

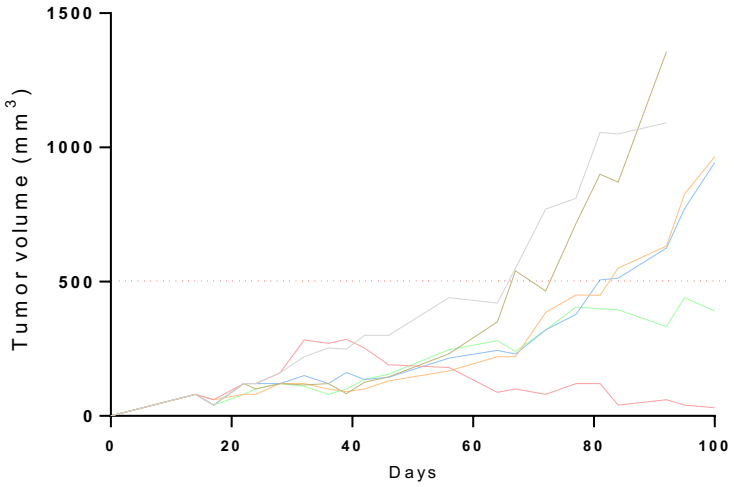






P3

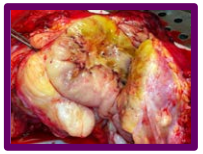




6/6 prises tumorales ± homogènes

→ 1/6 a régressé puis stagné (80 mm^3). A l'euthanasie : métastases multiples (poumons, foie, rate) ± minéralisées

PDX models of soft tissues sarcomas



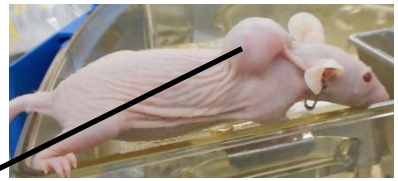
Patient tumor fragment

PDX = Patient Derived Xenograft

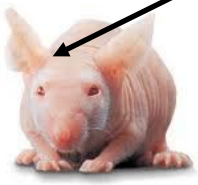
graft

Immuno compromise mice

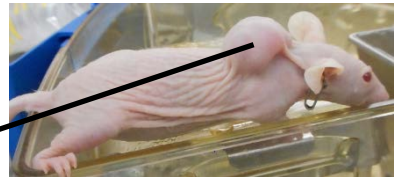
Tumor growth



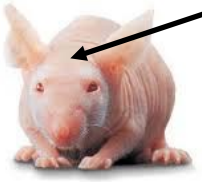
P1



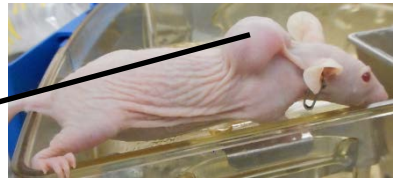
Tumor growth



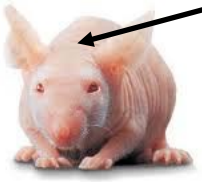
P2



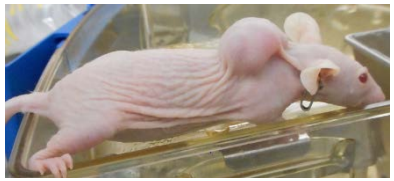
Tumor growth



P3



Tumor growth



Establishment from
P0 to P3
6 to 18 month

Passage 3 = saved model
Frozen stock
characterization

BCB SARCOME

Informations Administratives

Institut régional du Cancer de Montpellier – (ICM)

Coordonnateur Principal
Dr Nelly FIRMIN - Oncologue Médicale,

Médecins co-coordonnateurs
Dr Sébastien CARRERE – Chirurgien - ICM
Dr Carmen LLACER-MOSCARDO – Radiothérapeute - ICM

Coordonnateur Scientifique
Dr Laetitia LINARES – Chercheur IRCM

Centre de Ressources Biologiques – CRB

Mr Pierre-Arnaud FAYE
Mme Blandine MASSEMIN
Mme Catherine VIGLIANTI

Services d'Anatomopathologie

Dr Marie-Christine château
Dr Aurélie MARAN-GONZALEZ

Services Annexes

Bloc opératoire
Service des consultations

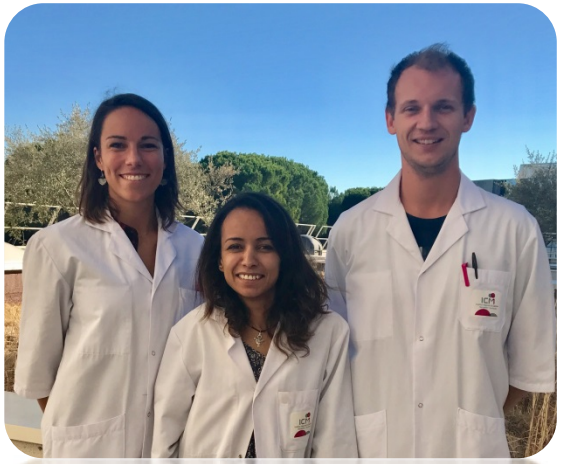
Direction de la Recherche Clinique et de l'Innovation – DRCI

Mr Jean Pierre Bleuse - **Responsable de la DRCI**

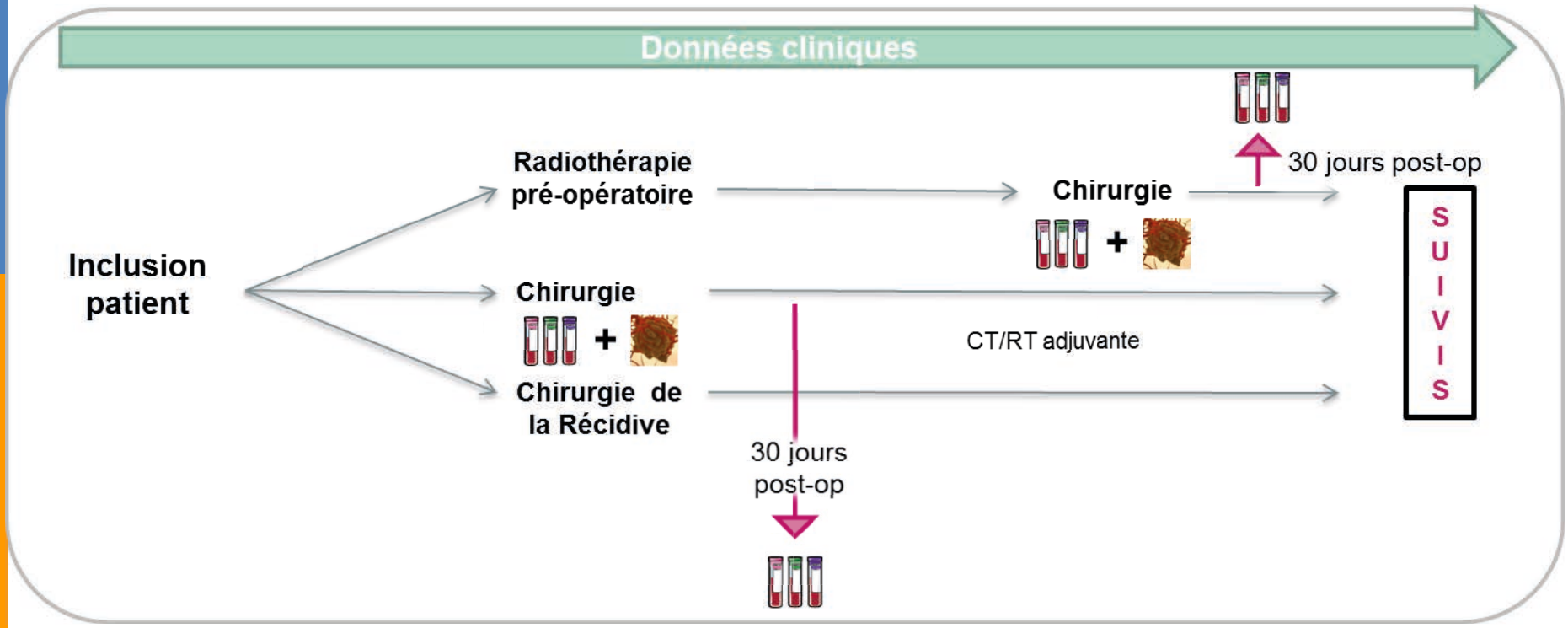
Mr Matthieu MERLOT – **Chef de Projet – ICM**

Mme Nabila BOUAZZA – **Chef de projet – ICM**

Mme Aurore MOUSSION – **Chargé de Projet – ICM**



BCB Sarcomes



Blocs histologiques

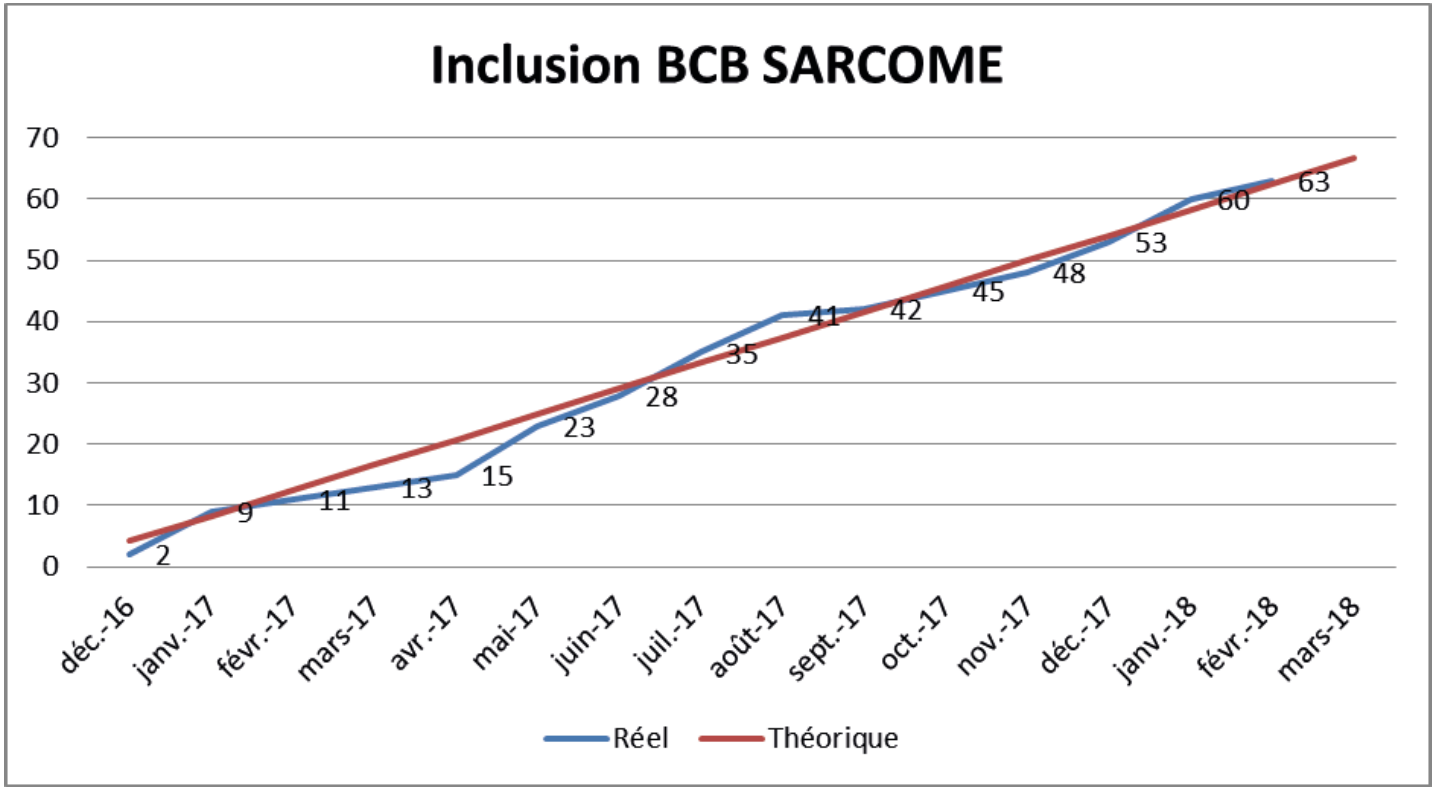
Modèles PDX

Échantillons congelés (proteines, ARN…)

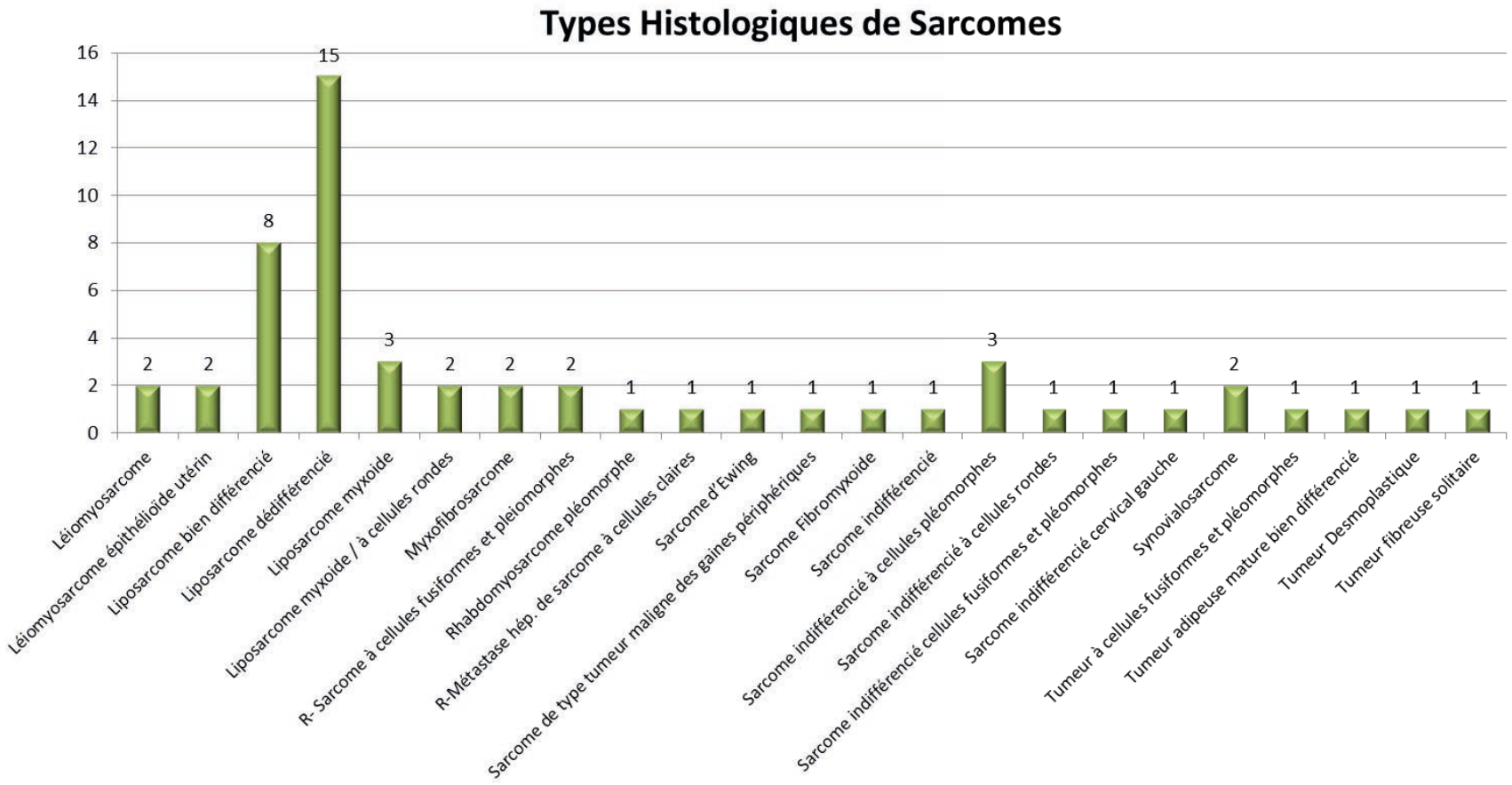
Plasma et serum

BCB Sarcomes

ETAT D'AVANCEMENT DU PROJET AU 15/0310/2018



BCB Sarcomas



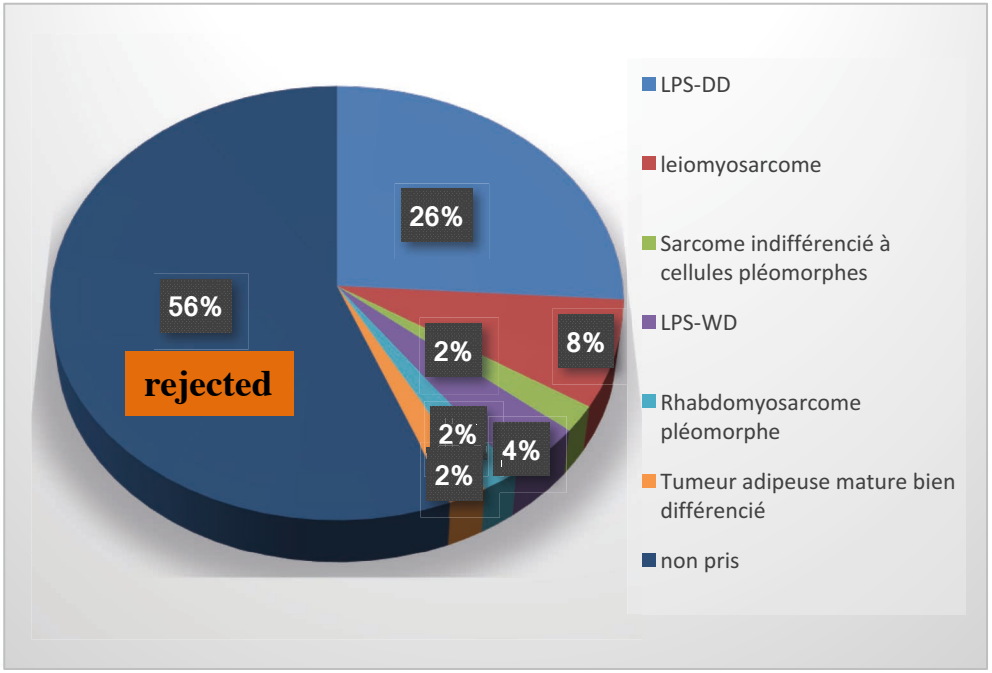
Sarcoma PDXs

January 2018

Duration of establishment

average	min-max
around 12 month	(6-23 month)

Number of tumors engraft : 59 tumors



+ 10 models ongoing

21 established models

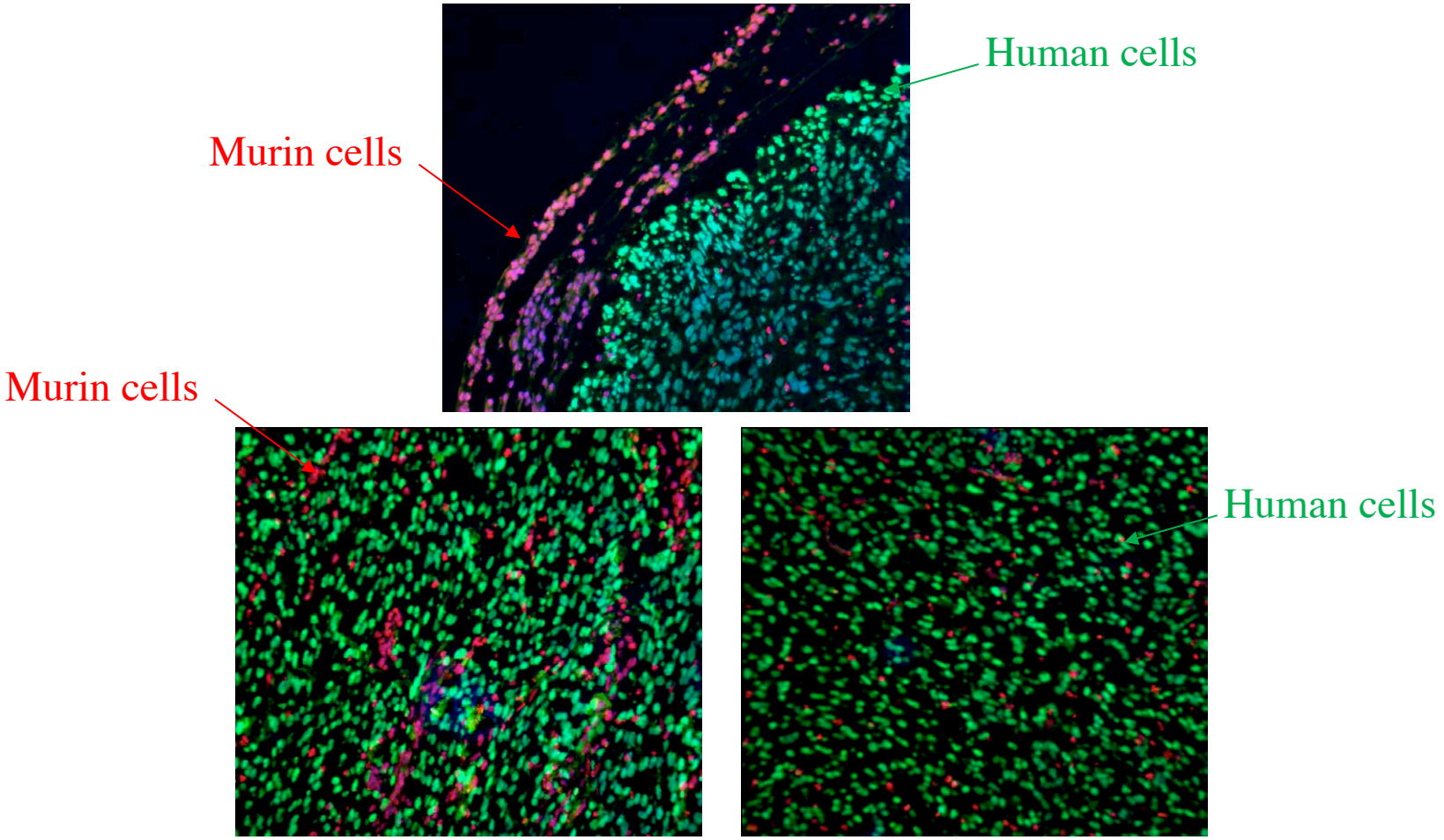
Characterization : Histology - genes Expression - Mutations

Objectives : development of PDXs corresponding to the different classes of sarcoma

PDXs : characterization

COT-FISH:

Comparison between human tumor and murine stroma



PDXs : characterization

Histological characterization :

Comparison between human sample and PDX samples at P3 and more

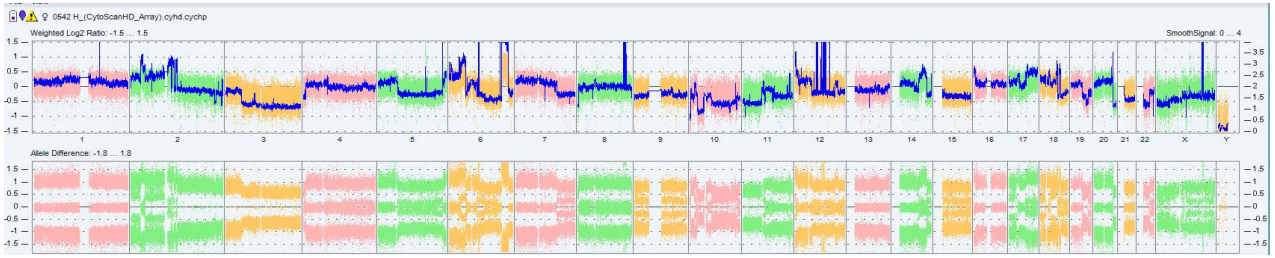
	DD-LPS	WD-LPS	Leiomyosarcoma
Différentiation	Stable	More dedifferentiated from 1 to 2	Stable
Nécrosis	Stable	Stable	Stable
Number of cells per mm3	Increased by 20%	Increased by 30%	Stable
Number of mitosis per mm3	Increased by 30%	Stable	Increased by 30%
Tumoral stage	grade 2 to 3 or stables	stable	Stable
Ki67	Increased by 7,5%	Stable	Increased by 17,5%

PDXs : characterization

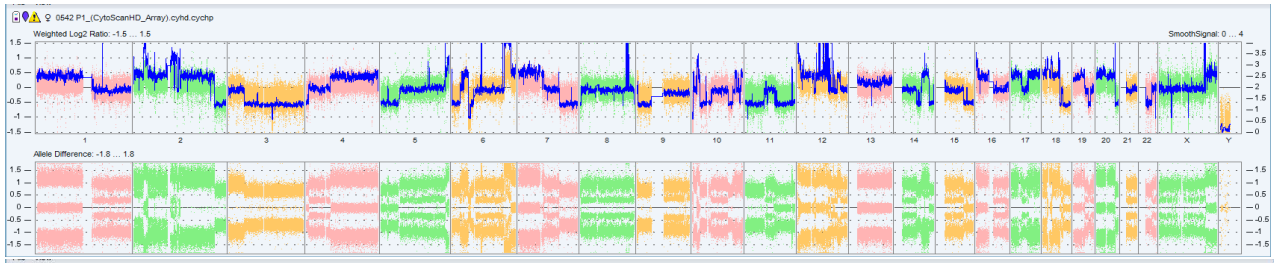
Genomic characterization by CGH :

STABLE

(Human)



(P1)

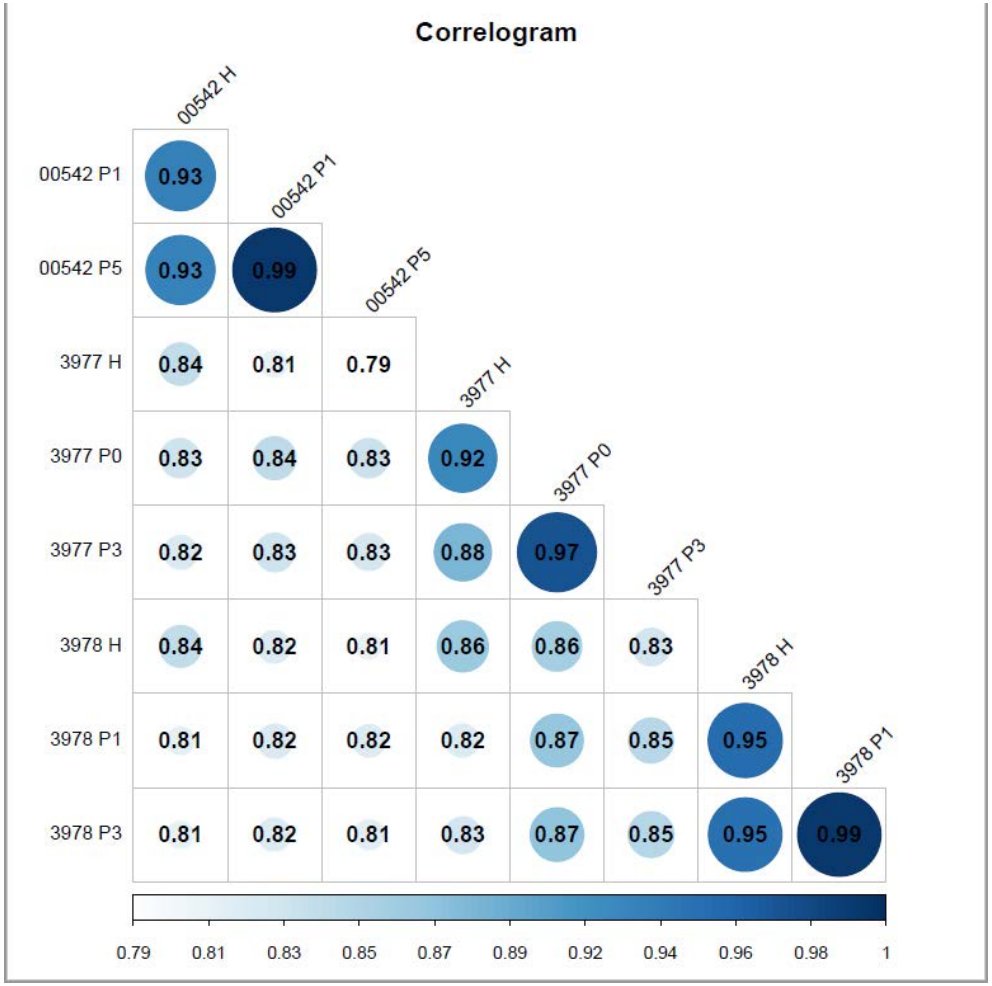


(P5)

PDXs : characterization

Genomic characterization by RNA seq :

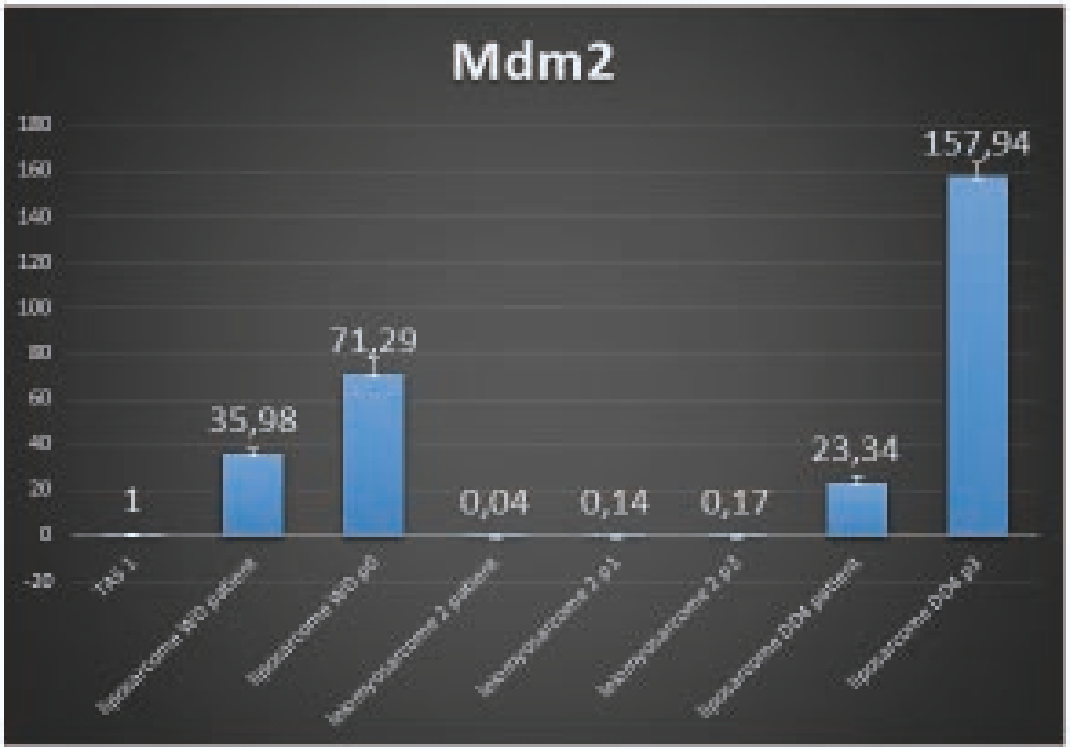
STABLE



PDXs : characterization

Genomic characterization

by Mdm2 amplification for liposarcoma



Projects…

New therapeutic strategies

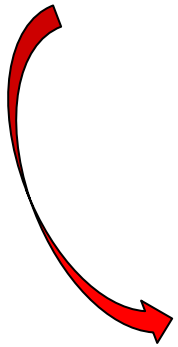
Sarcoma PDX mice

Treatment

The future of sarcomas PDX models

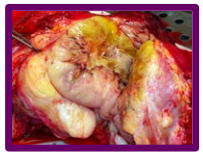
PDX models available for the French community of sarcomas

- Creation of an experimental PDX platform
- PDX database : PDX available and characterization



opening for September 2018

PDX experimental platform



Patient tumor fragment

graft

Tumor growth

Tumor amplification

Passage on X mice

10 mice per group

control

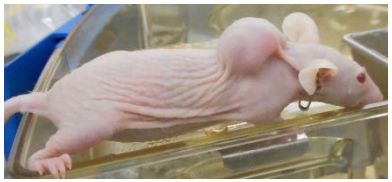
Treatment 1

Treatment 2

….

PDX experimental platform

control Treatment 1 Treatment 2



Dissection : tumor and other organs if needed

Tarification: about 3500 euros per groups of 10 mice for academic partner
(including mice and accommodation, staff and experimentation)

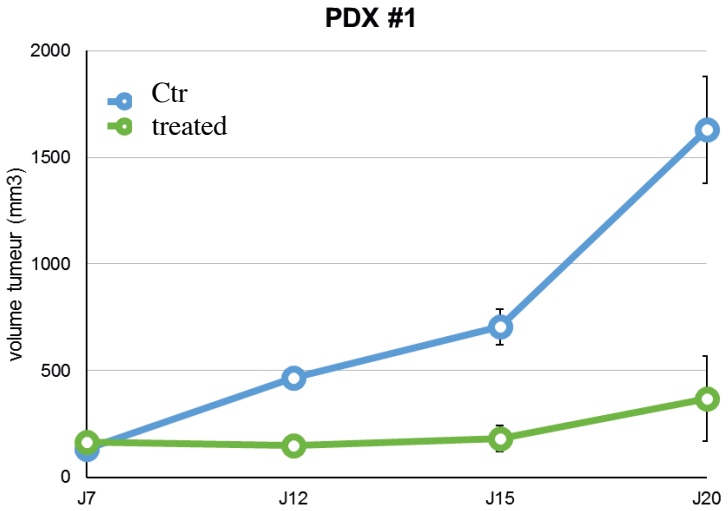
PDX experimental platform

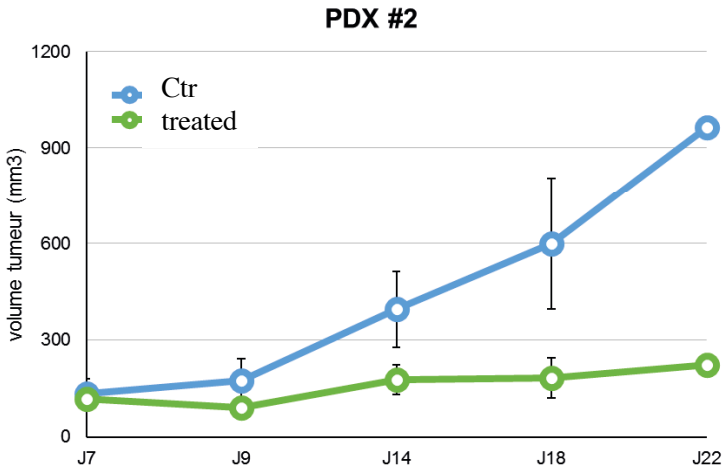
Additional services in association with other platform

RHEM : Histology : blocs – IHC ….

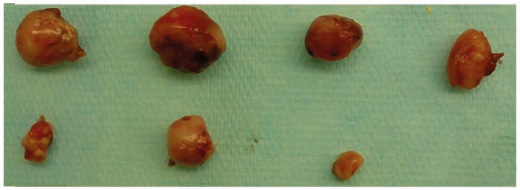
IPAM : Life imaging : Bioluminescence, spect-CT

Example: New target for therapy in liposarcomas





ctr treated



CTR

treated

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PDX experimental platform

Amplification : 12 weeks / 10 mice – 20 hours work

experimentation : 15 weeks / 10 mice per group / 80 hours work