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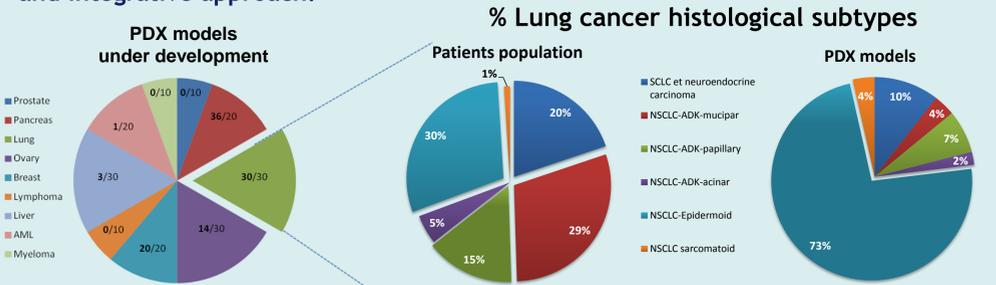
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What about IMODI

The national IMODI (Innovative MODEls Initiative) consortium includes 25 partners (pharma, SMEs, academic research labs and clinical centers) with the aim of developing more predictive tools to improve the selection of new effective treatments to combat 9 cancer pathologies. These developments include:

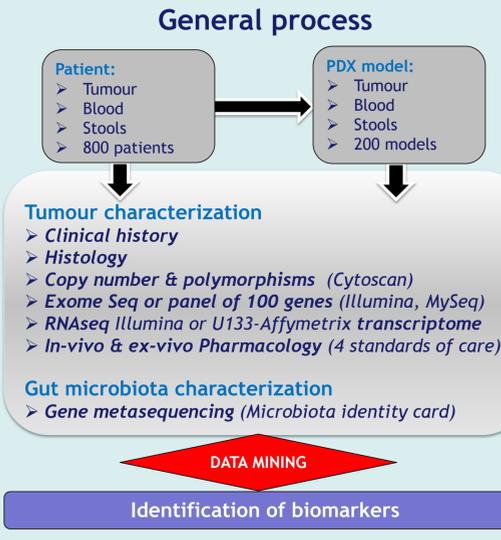
- Collection of *in-vivo* PDX models (procedures were approved by Animal Care Committees, according to ethical guidelines for animal care and handling)^{1,2},
- Collection of *in-vitro* derived cell lines,
- 2D & 3D *ex-vivo* assays,
- In-vivo* humanized models (immune system, liver and tumour stroma),
- Characterization of tumour histology, gene mutations, gene expression, pharmacological responses and gut microbiota,
- Biobanks of tumours, blood, serum and stools (patient specimens were obtained from 7 clinical centers with written informed patient consent for providing surgical tumor samples and for HIV1&2, HTLV1&2, HBV and HCV serological status testing),
- Central database,
- Datamining,

Results on NSCLC lung cancer xenograft developments, molecular and pharmacological characterizations and data analysis are presented as an example of the IMODI holistic and integrative approach.



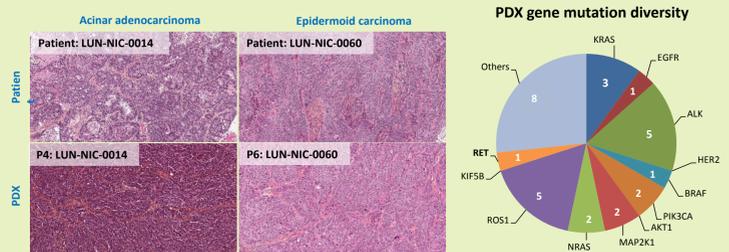
Products & Services

- In-vivo models:** Tissue microarray, Services on *in-vivo* models
- Ex-vivo assays:** Cancer stem cell lines, Services on cell lines
- Data Mining:** Tumour Biomarkers
- Data Base software:** Data Base software
- Stool and serum biobank:** Gut microbiome biomarkers, Services for microbiota analysis



Histology and Genomic Characterization

- Example of a well characterized NSCLC PDX collection
- Highly conserved phenotype and genotype
 - Histological PDX profiles are in concordance with those observed in patient tumours
 - Major molecular subtypes are represented in the NSCLC collection
 - EGFR-mutated models are under development

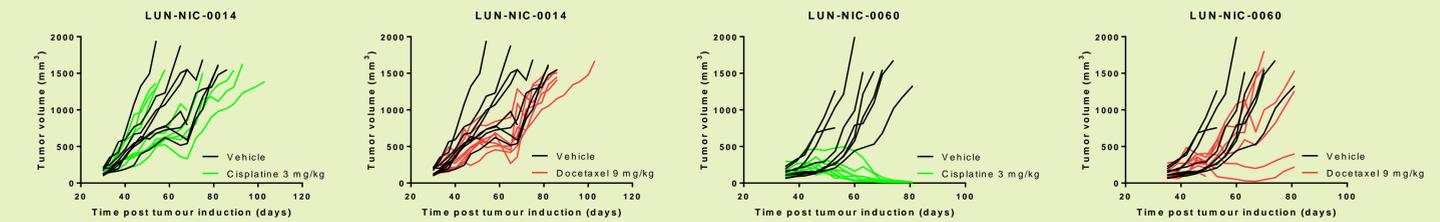


In-vivo Pharmacological Response to Standards of Care

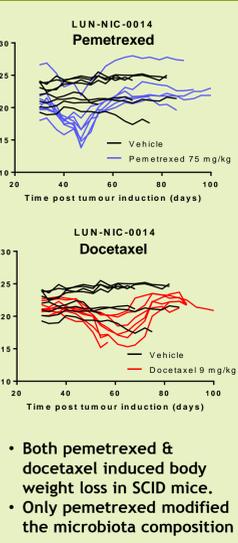
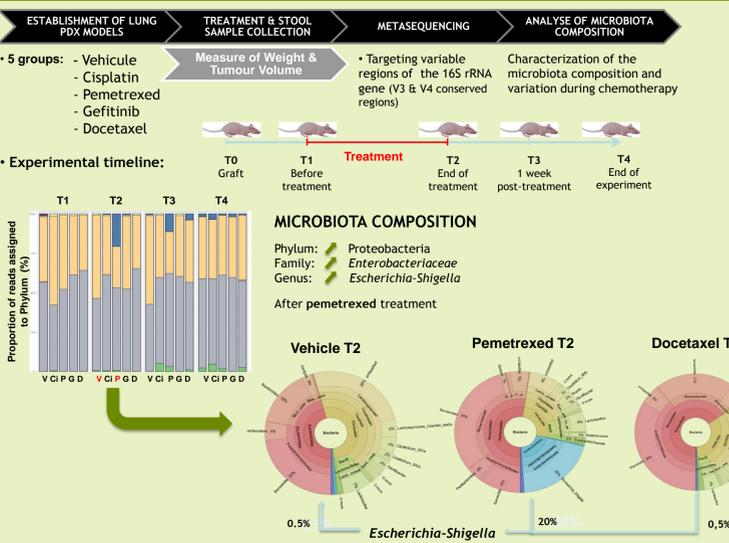
- Significant efficacy of cisplatin and gemcitabine on the LUN-NIC-0060 epidermoid model
- Marginal activity of gefitinib on the LUN-NIC-0014 acinar adenocarcinoma model (EGFR wt, KRAS wt, BRAF wt, ALK wt, ROS1 wt)
- LUN-NIC-0014 PDX resistance to cisplatin and docetaxel correlates with patient outcome (non responsive to cisplatin + docetaxel)

Drugs	ΔT/ΔC (%) (LUN-NIC-0014)	ΔT/ΔC (%) (LUN-NIC-0060)
Cisplatin 3 mg/kg	64	-4
Pemetrexed 75 mg/kg	51	Non-tested
Gefitinib 100 mg/kg	37	Non-tested
Docetaxel 9 mg/kg	59	75
Gemcitabine 120 mg/kg	Non-tested	-10

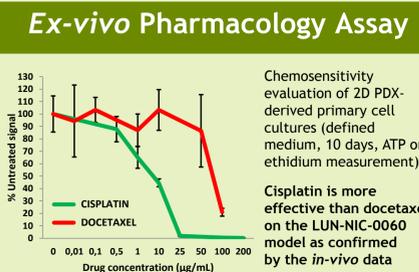
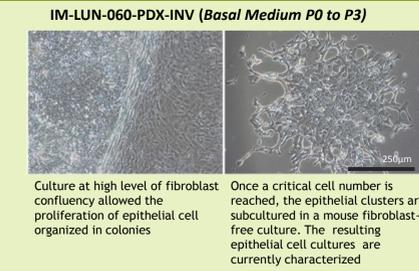
Legend: High antitumor activity (with regression) (Green), Marginal antitumor activity (Orange), No antitumor activity (Red)



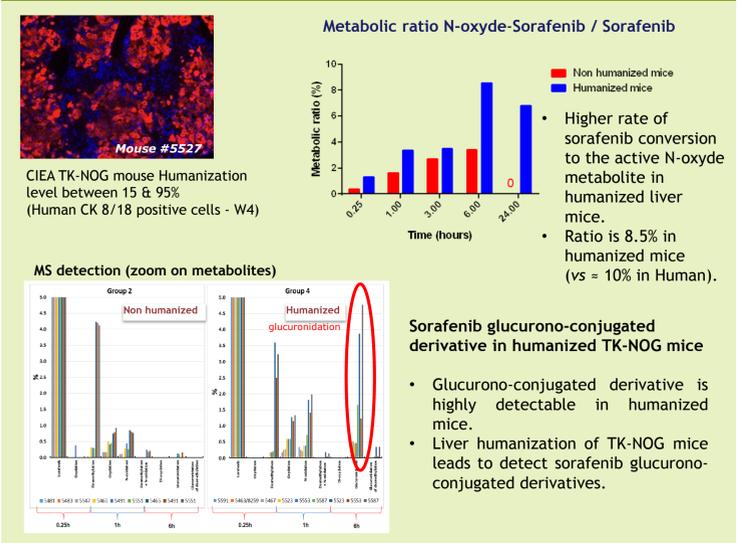
Gut Microbiota Analyses



In-vitro PDX-Derived Cell Line



Liver-Humanized Microenvironnement



Conclusion and perspectives

- IMODI is an operational consortium with the goal to continuously delivering new predictive models in regards to specific clinical needs and diversity,
- All cancer models and associated results are commercially available for cancer research community, scientific publications, new therapeutic and diagnostic candidate selection,
- IMODI has developed *ex-vivo* models/assays that can accurately predict *in-vivo* standard of care sensitivity in lung PDX models,
- The effects of chemotherapeutic agents on microbiota composition, and the impact of the microbiota on drug efficacy and toxicity are currently being evaluated,
- IMODI develops a platform of 2nd generation PDX models in mice humanized with human liver to better evaluate the ADME-Tox profile of new compounds.

(1). European Directive 2010/63 and its national transcription "Décret 2013-118 du 1^{er} Février 2013 relatif à la protection des animaux utilisés à des fins scientifiques"/ (2). Guidelines for the welfare and use of animals in cancer research. Workman *et al.*, Br. J. Cancer. 2010; 102(11): 1555-1577.