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 (specimens were approved by Animal Care Committees, according to ethical guidelines for animal care and handling) [1,2]
- Collection of in-vivo 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 HVR18, HVR182, IRB and HCV serological status testing,
- Central database,
- Data mining,
- 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.

**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

**Gut Microbiota Analyses**

- 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)

**In-vitro Pharmacological Response to Standards of Care**

<table>
<thead>
<tr>
<th>Drug</th>
<th>DFOX (µg/mL)</th>
<th>DFOX (%)</th>
<th>DFOX (µg/mL)</th>
<th>DFOX (%)</th>
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<tr>
<td>Cisplatin</td>
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<td>100</td>
<td>32</td>
<td>100</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>25</td>
<td>100</td>
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<tr>
<td>Gefitinib</td>
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<tr>
<td>Docetaxel</td>
<td>10</td>
<td>100</td>
<td>10</td>
<td>100</td>
</tr>
</tbody>
</table>

**Liver-Humanized Microenvironment**

- Sorafenib glucurono-conjugated derivative in humanized TK-NOG mice
- Ex-vivo Pharmacology Assay
- Liver humanization of TKLNOG mice leads to detect sorafenib glucurono-conjugated derivatives.

**Conclusions 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 results are available for selection of new therapeutic and diagnostic candidates.
- IMODI has developed ex-vivo models/assays that can accurately predict in-vivo standard of care sensitivity in lung PDX models.
- The effects of chemotherapy 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.