Introduction

The humanization of mice with various tissues named Chi-mice® aimed to reproduce the human situation to be more predictive than conventional models. Despite significant progress in identifying malignancy of cancer cells, a more detailed understanding of tumor generation is needed. Xenograft of tumor cells into immunodeficient rodents has constituted the major preclinical screen for the development of new drugs. These models have identified efficacious agents, but their chemosensitivity, genetic drift and clonal selection induced by cell culture have been part of the high attrition rate observed in the clinical development. Patient-derived tumor xenograft (PDX) obtained in xenografting fresh patient tumor samples in mice are reported as being more predictive to the clinical situation in maintaining the histopathology and molecular diversity of the patient tumors. The PDXs collection has been set up under ethical agreement with informed consent of patients. The patients have been screened for absence of HCV, HBV and HIV. The anonymized patient’s clinical history and tissue banking (including normal tissue when available) are centralized in our internal biological resource center. Tumor samples were freshly explanted in nude or SCID mice. Cryopreservation of the PDX is performed at early passages allowing using these PDX only at low passage. The histopathology, HER, ER and PR status for breast carcinomas and tumor growth characteristics of these PDX are being performed. Lymphoma characterization was performed using immunohistochemistry (HCD20, m/Ki67). Lymphoma detection, probably related to EBV infection, leads to switch to nude mice for xenografting.

To create a highly diversified panel of PDX, we organized a global process from multiple centers. These PDX are currently being used in preclinical development of new therapies and clinical positioning including biomarkers identification.

Material and Methods

Collection of human biological resources by registered Oncodesign BRC and establishment of in vivo tumorgraft models in mice.

Results

388 samples (116 SCID mice and 272 nude mice) were xenografted with 26 kidney tumor samples (29 on SCID mice, 1 on nude mice, 25/1), 30 liver tumor samples (21/9), 20 pancreas tumor samples (14/6), 68 prostate tumor samples (41/27), 17 stomach tumor samples (15/2), 31 bladder tumor samples (14/17), 178 breast tumor samples (5/178) and 18 lung tumor samples (5/18).

A tumor take rate of 30.8% was observed for kidney, 13.3% for liver, 20.0% for pancreas, 41.2% for stomach, 32.1% for bladder, 9.6% for breast and 38.9% for lung on immunodefficient mice.

Among 29 tumor growth after human tumor fragment engraftment in SCID mice, 17 (44%) human lymphoma were characterized using human CD20 and murine Ki67 antibodies. No human lymphoma detection was observed among 41 tumor growth after human tumor fragment engraftment in nude mice.

Conclusion

The use of nude mouse strain has inhibited the occurrence of lymphoproliferative malignancies.

We are creating a highly diversified and broad range of PDX tumor models representative of human pathologies.