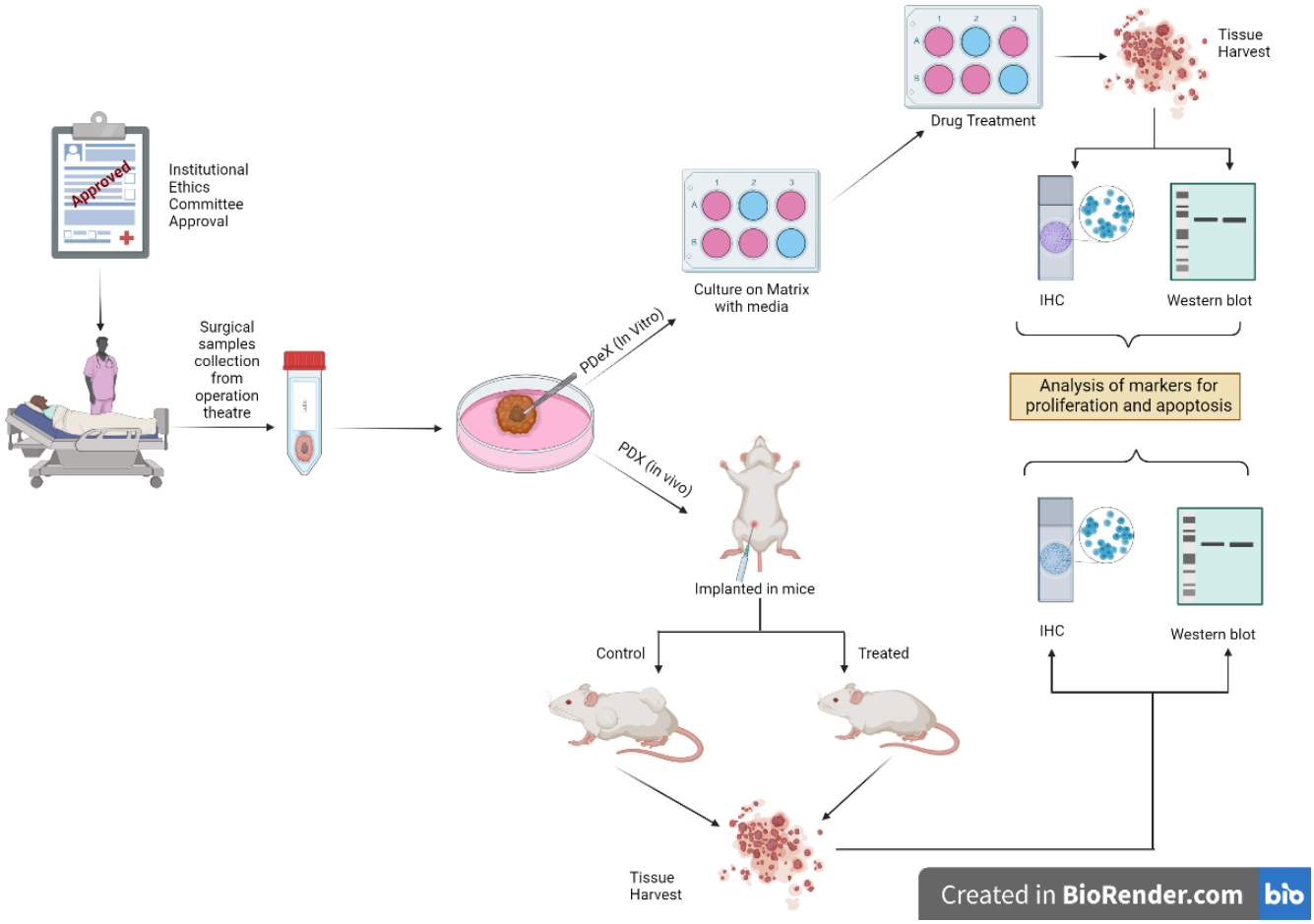
Generation of PDEx& PDX Model systems



Drug discovery process for cancers requires concerted efforts of chemists, biologists and pharmacologists. Rewards for drug discovery eludes on several occasions due to lack of the most appropriate testing systems. Though cell line-based systems remain as gold standard, several drug discovery efforts fail after pre-clinical testing and in clinical trials. Hence there is a need for developing appropriate model systems that can identify promising leads from pre clinical studies. The reason for failure of drugs has been attributed to the cell lines that were derived several years ago and have undergone changes due to long passaging in culture. Recent years have shown that patient derived cultures are the best way to test drugs on cells derived from tumors directly. Fresh tumor tissues obtained from patients at the operation theatres can be the most versatile source for drug testing. These tissues can be used under in vitro culture systems as well as in vivo in athymic mice, referred as Patient derived explants (PDEx) and Patient derived xenografts (PDX) respectively. The advantage of these models is that the tumor cells are preserved in their microenvironment and the response to drugs is best understood. The Molecular Oncology Laboratory at IIT M Biotechnology has done pioneering work in the arena of understanding cancer drug response and drug resistance. The lab activities revolve around

developing new therapeutic entities for drug resistant and hard to treat tumors like pancreatic ductal adenocarcinoma (PDAC) and triple negative breast cancers. Our efforts in this direction are supported by publications in acclaimed journals and award grants from funding agencies.

PDEx& PDX Model systems- How we do it?

All our studies are initiated with obtaining ethics approval & patient consent for collection of human tumors from cancer patients. These tumor samples will be processed:

For the PDEx models, the collected tissue samples will be washed and cultured on special matrices using specialized culture media optimized with autologous serum. The tissue samples will be exposed to drugs and controls and processed for endpoints as desired. We decide on the end points depending on the project and we use a combination of immunoblotting, immunohistochemistry, Q-PCR for markers pertaining to cell proliferation, apoptosis.

For the PDX models, the samples will be processed similarly and will be implanted into the subcutaneous tissue of athymic mice. These mice will develop solid tumors in 4 weeks which can be serially transplanted and maintained as colonies. Following the drug treatment regimen, themice will besacrificed and tumors, organs, blood are collected and processed as required for desired end-points.These tumor bearing mice are available for studies for academia and industry for drug testing.