



Scientific Abstract

SU2C-Dutch Cancer Society Tumor Organoids Dream Team:

“A New Preclinical Model for Drug Sensitivity Analysis”



Future cancer therapy will rely on treatment with drugs that are specific for individual tumors and patients. However, predicting clinical responses from genomic data remains highly challenging. Recently, systematic screens utilizing large panels of tumor cell lines have been used to correlate drug sensitivity with tumor genotype to identify predictive genomic markers of drug response. However, tumour cell lines have several drawbacks including being of limited genetic diversity; pre-clinical models that are more representative of the 'natural' mutational diversity of cancer are urgently required.

The laboratory of Hans Clevers, MD, PhD, developed methods for long-term culture of human primary tissues and cancers ('organoids'). By establishing a large collection of tumour-specific organoids, the genetic spectrum of tumours can be captured as a pre-clinical model. This will allow stratification of tumours based on their genomic footprint and drug sensitivity, and may reveal correlations between drug sensitivity and this footprint.

The aims of this proposal are:

- 1) To build and validate a large 'living' biobank for colon, pancreas and now breast cancer using organoid technology, thus capturing the genetic variability of these three tumour types.
- 2) To correlate drug sensitivity with genotype and gene expression *in vitro* to identify putative biomarkers of drug sensitivity.
- 3) To validate the dual 'genetic/organoid' approach as a predictor of drug response for individual cancer patients.
- 4) To identify the cause of elusive drug sensitivity and resistance.

