horizon

precision genome editing

Leaders in Providing Oncology Drug Discovery Services

Identifying the right drugs for the right patients

Cellular assays

GROWTH ASSAYS

- Proliferation
  - Metabolic read-out
  - Biomass
  - DNA synthesis
  - Dual live / dead
- Colony formation (2D)
- Soft agar colony formation (3D)
- Methylcellulose colony formation (3D)
- Combination assays
- Cell panels

TARGET VALIDATION

- siRNA
- RNA / cell pellet / lysate preparation

STANDARD MECHANISTIC ASSAYS

- Apoptosis assays
- Immunofluorescence
- Western blotting
- Cellular ELISA
- FACS
- Invasion and migration assays
- Comet assay

SPECIALIST ASSAYS

- Hypoxia assays
- 3D spheroid assays
- Senescence assays
- Autophagy assay
- Reactive oxygen species assays

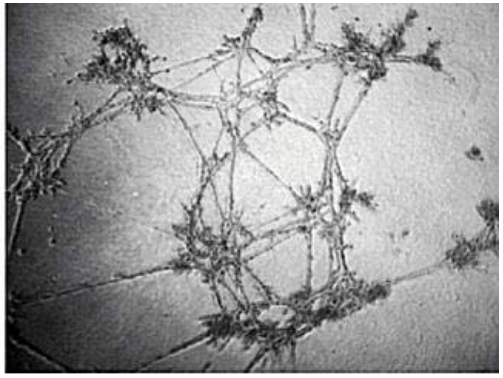
Tumour microenvironment studies

Experts in running hypoxia, 3D and nutrient-depletion assays that address the issue of how drugs will behave in the complex microenvironment that surrounds a solid tumour.

Phenotypic matrigel assay

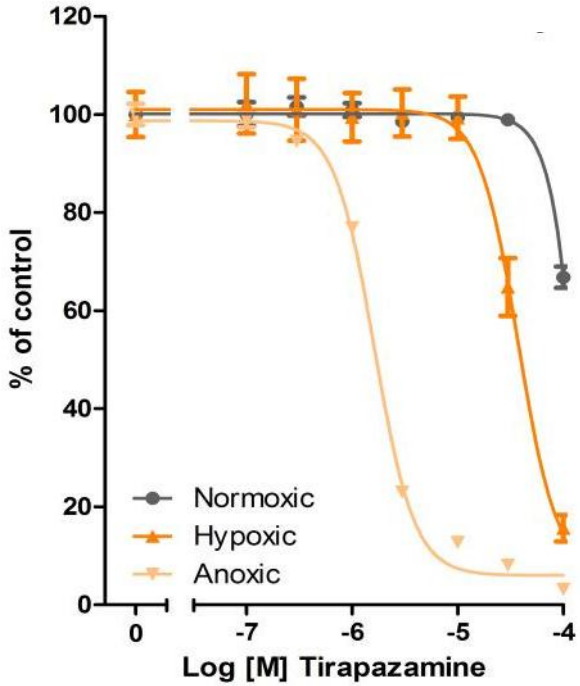
Parental Cells

PI3Kα H1047R Mutant Cells



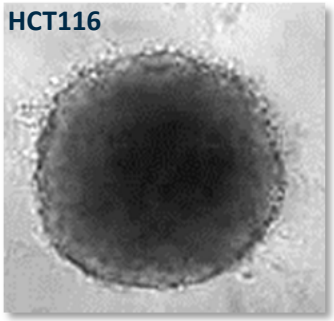
In 3D culture conditions the outgrowth phenotype of the PI3Kα mutant cells is dramatically different to the wild type parental cells

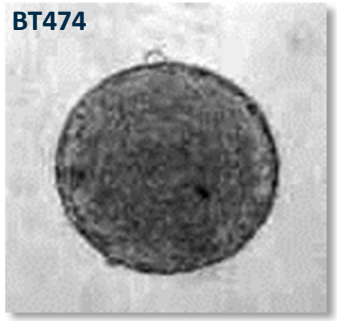
Hypoxia selective assays



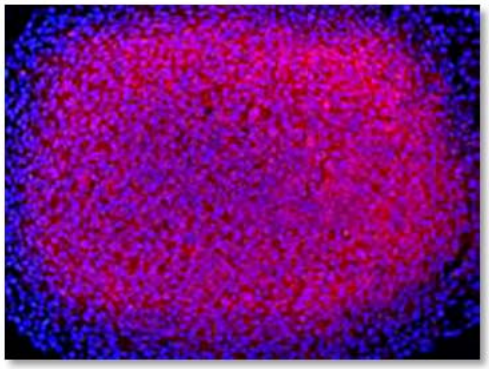
The bioreductive drug Tirapazamine shows minimal anti-proliferative effect under normoxia, with increasing potency as the level of oxygen is reduced

Spheroids formed from different cancer cells





Immuno-cytochemical staining of spheroids



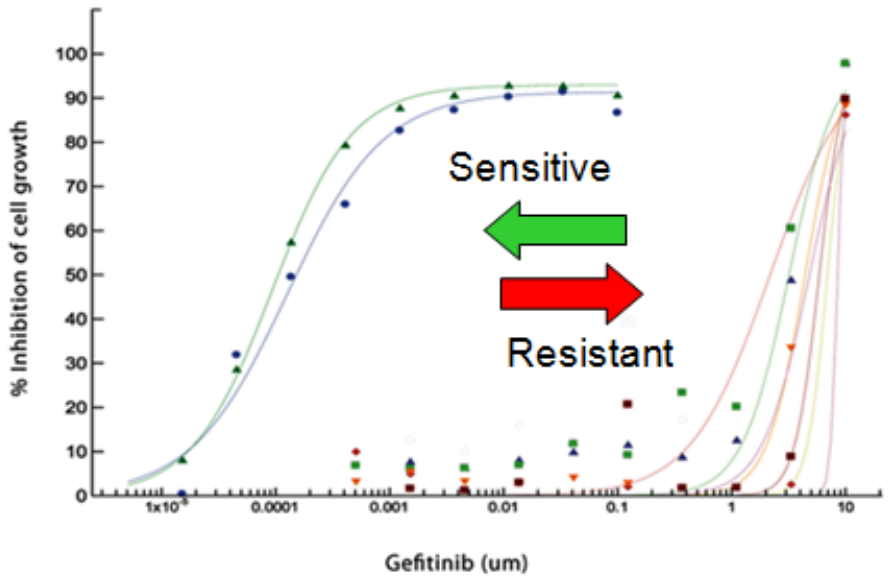
HCT116 spheroids were treated with the hypoxic marker pimonidazole, embedded and sectioned. Cell nuclei were detected with Hoechst 33258, hypoxia using Hypoxyprobe.

Compound screening in cellular assays: Standard or X-MAN™ cell panels

Access to standard cancer cell lines as well as the entire X-MAN™ panel, allowing screening in patient-relevant isogenic cell models

X-MAN™ gene-X, Mutant And Normal isogenic human cell lines

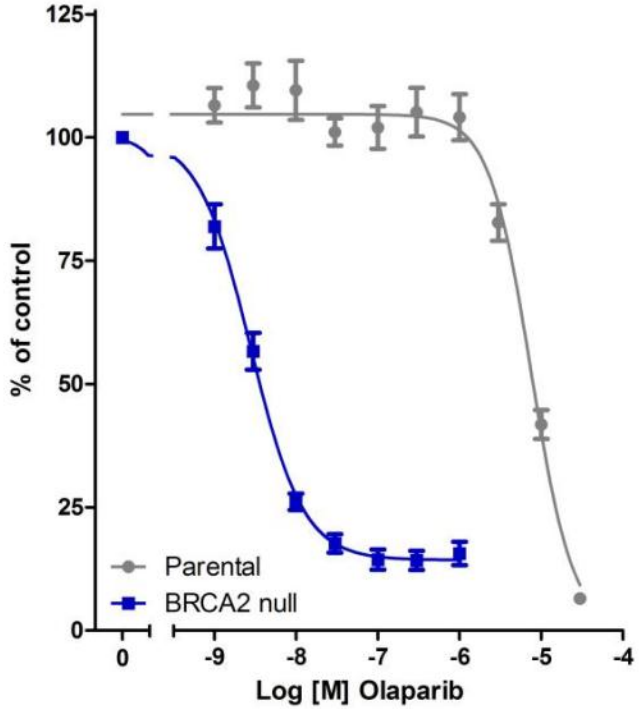
Gefitinib (Iressa®) profiling on the HME X-MAN™ panel



A panel of HME lines containing knock-in mutations of EGFR, PI3K, K-Ras or B-Raf were screened in a standard proliferation assay format.

EGFR knock-in lines are approximately 1,000-fold more sensitive to the EGFR-targeted inhibitor Gefitinib.

PARP inhibitor profiling on BRCA2 null X-MAN™ cells



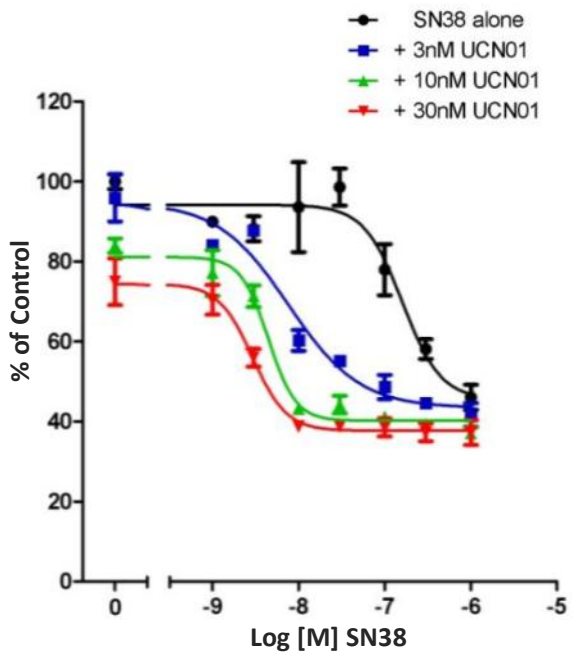
DLD-1 parental and BRCA2 null paired isogenic cell lines were screened in a 10-day quantitative colony forming assay.

BRCA2 null cells are a 1,000-fold more sensitive to the PARP inhibitor Olaparib.

Mechanistic assays & bespoke assay development

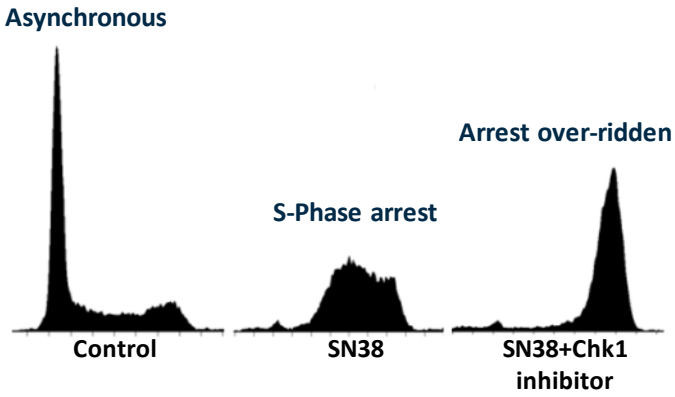
- Wide range of optimised assays validated with control compounds available
- Data is presented in an industry-standard reporting format with expert analysis from our team of cellular pharmacologists

Combination proliferation assay



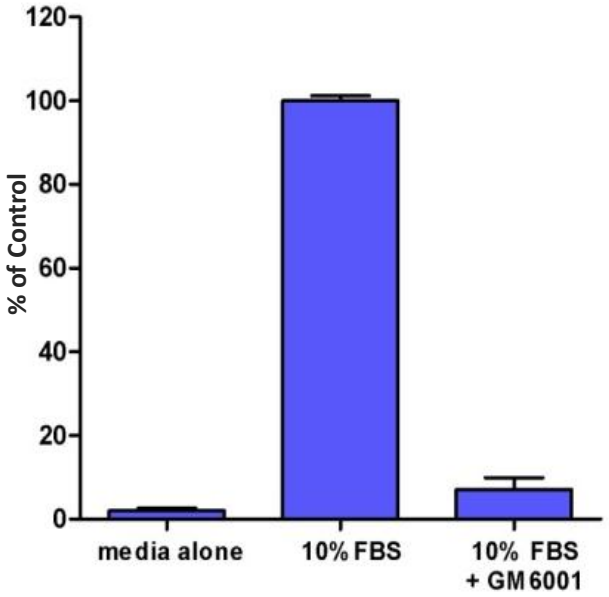
The Chk1 inhibitor UCN01 sensitises the response of HT29 cells to SN38, resulting in a >30-fold increase in potency.

Cell cycle profiling



Cell cycle profiling shows that SN38 causes HT29 cells to arrest in S phase, while addition of a Chk1 inhibitor overrides this arrest.

Quantitative cell invasion assay



HT1080 cells seeded into the top well of a Boyden chamber are able to invade through BME towards chemo-attractant. Invasion is prevented by the MMP inhibitor GM6001.

Identifying the *right drugs* for the *right patients*

IMMEDIATELY AVAILABLE CELL LINES

- Over 70 cancer cell lines, covering many of the NCI-60 panel
- Access to entire **X-MAN™** panel on a per-compound, per-project or per-FTE basis
- Non-cancerous 'control' cell lines

CELLULAR ASSAYS

- Extensive range of validated assay systems
- Bespoke assay design
- Target validation and compound screening
- Covers all major assays used in oncology drug discovery

SPECIALIST ASSAYS

- Validated tumor microenvironment assays
- 3D spheroids, hypoxia , anchorage independent assays

Enabling shorter, more focused clinical trials, based upon the unique genetic mutations that define their disease

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GENESIS™ PRECISION GENOME EDITING

Homologous recombination-mediated human gene editing platform exploiting rAAV targeting vectors

X-MAN™ gene-X, Mutant And Normal isogenic human cell lines

Patient-relevant, isogenic somatic models of human genetic diseases *"patients in a test-tube"*

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