We saw the start of PRECISION-Panc, a dynamic and coordinated research platform to define, understand, test and implement stratified therapeutic strategies for pancreatic cancer (PDAC). The initiative is centred on discovery and preclinical and clinical development, and is supported by a 5-year award of £10M from Cancer Research UK along with substantial additional funding from industry partners.

For discovery (Lead: Andrew Biankin), the consortium holds the world’s most accurate and comprehensive molecular catalogue of pancreatic cancer data, generated as part of the International Cancer Genome Consortium from a prospective observational cohort of patients with pancreatic cancer with extensive clinico-pathological, treatment and outcome information. These in-depth analyses have uncovered the detailed molecular pathology of PDAC and its potential underlying vulnerabilities. The initial focus for clinical studies will be on defects in the DNA damage response pathway, apparent in approximately 20% of PDAC, and extend into overlapping vulnerabilities through targeting of the immune system.

For preclinical studies (Lead: Olivier Sanson), Jeff Evans and Juan Valle, Manchester). The ultimate aim is to develop a multi-drug, multi-sub-study, biomarker-driven family of clinical trials that use state-of-the-art genomic profiling to match patients to sub-studies testing targeted investigational therapeutics, coordinated by the CRUK Glasgow Clinical Trials Unit (CTU). The first trials are not dependent on rapid turnaround time for molecular testing, but include mandatory tissue sampling for patient recruitment, and the initial focus will be on streamlining the processes for rapid analyses during the course of the initial trials (PRECISION-Panc Master Protocol - Lead: David Chang). These trials include a safety study of a CCR2 inhibitor in combination with an anti-PD-1 antibody, sponsored by AstraZeneca, which has completed recruitment and a randomised phase II study in unselected patients with metastatic PDAC comparing FOLFOX plus nab-paclitaxel with Gemcitabine plus nab-paclitaxel combinations, which has opened to recruitment.

In 2017, the Translational Pharmacology Laboratory (led by Fiona Thomson) was also selected by the CRUK Centre for Drug Development (CDD) as one of its four Biomarker Centres of Excellence to develop and perform biomarker studies within the CDD’s clinical trials portfolio, while the CRUK Clinical Trials Unit (Director: Rob Jones) underwent a successful quinquennial review. The CTU develops, coordinates and delivers national and international multi-centre studies. A particular highlight this year was the publication of the final disease-free survival of the SCOT study (an international phase III randomised, non-inferiority trial comparing 3 versus 6 months of oxaliplatin-based adjuvant chemotherapy for resected stage III colon cancer). The CTU also supports the TASTER Clinical Trial and Experimental Medicine Programme in Chronic Myeloid Leukaemia (Mhari Copland and David Vetrie). Management of CML requires life-long tyrosine kinase inhibitors (TKIs) that can cause significant side effects. While TKIs induce remission, they are rarely curative due to persistence of TKI-resistant leukaemic stem cells (LSC) that evolve to drive TKI resistance and disease progression. Recently, research teams at the Paul G’O’Gorman Leukaemia Research Centre have identified survival factors that can be exploited therapeutically to eradicate TKI-resistant LSC and manage untreated clinical need in CML. This forms the basis of a new Experimental Medicine Programme funded by CRUK, combining a phase II clinical trial (TARGETing Stem cell Resistance; TASTER) with a precision-medicine-based scientific programme, investigating the safety and efficacy of HDAC2, EZH2 or BET inhibitors in combination with TKI in patients with all phases of CML. Exploratory objectives include investigation of how LSC clonal architecture changes during drug treatment and whether these changes can be computationally modelled to predict drug response. The scientific programme will also determine whether TKI-resistant LSC clones exist at low levels in CML drug-naive diagnostic samples and, using in silico models as predictors at the point of diagnosis, will determine the efficacy of standard-of-care or the novel therapies.

A number of our early-career researchers were successful this year. Ross Carruthers was awarded a CRUK Clinician Scientist Fellowship that has allowed him to establish a new research group investigating elevated DNA replication stress in glioblastoma and neural stem cells and exploring its therapeutic potential, while Peter Bailey, Senior Lecturer in Cancer Systems Biology, and Patricia Roxburgh, Senior Clinical Lecturer and Honorary Consultant in Medical Oncology, have an interest in early-phase clinical trials and ovarian cancer, joined the ICS as principal investigators. Lisa Hopcroft was awarded Fellowships by Leuka and the Kay Kendall Leukaemia Fund, Gillian Horne was awarded the Thomas Smellie prize for the best PhD thesis by a clinician, and Evangelos Giampazolias was awarded the prize for the best non-clinical PhD thesis. During 2017 Ian McInnes also left to undertake a prestigious position at Imperial College, London.