GLASGOW COLLABORATIVE COLORECTAL INITIATIVE

GROUPING AND STRATEGY
OUR GROUPING

The Cancer Research UK Glasgow Centre is a partnership between the Beatson West of Scotland Cancer Centre, the CRUK Beatson Institute, NHS Greater Glasgow and Clyde and the Universities of Glasgow and Strathclyde.

One cancer the centre has chosen to focus on is colorectal cancer and as part of this we have developed the Glasgow Collaborative Colorectal Initiative (GCCI), which is a collaborative grouping of experts in colorectal cancer research based in Glasgow, UK. The GCCI brings together individual groupings from within Glasgow University, the CRUK Beatson Institute and NHS Greater Glasgow and Clyde, all with a common interest in colorectal cancer. By combining our strengths in discovery, translational and clinical research we have the foundations to develop personalised treatment strategies for colorectal cancer patients in a true bench to bedside manner. The team is managed by a multidisciplinary collaborative grouping of translational scientists (Dr Joanne Edwards and Professor Donald McMillan), discovery scientists (Professor Owen Sansom and Dr Seth Coffelt), academic surgeons (Mr Campbell Roxburgh and Professor Paul Horgan) and oncologists (Dr Janet Graham).

Since the initial formation of this collaborative grouping, the team has strengthened its academic resources by developing large comprehensive patient cohorts of linked clinical data along with extensive in vivo models and investing in state-of-the-art equipment for genomic analysis. The success of such an approach has been demonstrated in the research outputs that resulted in all members of the management team being returned in the 2014 REF.
The aim of the GCCI is to better understand the determinants of short and long-term outcomes in patients with colorectal cancer. In particular, the relationship between the local and systemic inflammatory responses, tumour microenvironment and cell signalling is being examined with a view to taking such knowledge into the routine clinical management of colorectal cancer. Our collective aim is to develop novel treatment strategies to establish a personalised medicine approach for colorectal cancer.

To achieve these aims strong academic collaborations have been established to utilise the expertise of the colorectal cancer community:

- Professor JP Medema and Dr Louis Vermeulen, AMC, The Netherlands
- Dr Christian Kersten, Sørlandet Hospital Norway
- Dr Marty Weiser, Memorial Sloan Kettering, USA
- Professor Keiran Sheehan and Dr Liz Ryan, University of Dublin, Ireland
- Professor Ishizuka and Kubota, Dokkyo Medical University, Japan
- Professor Stephen Clarke, University of Sydney, Australia

The group also has a working relationship with the NHS Tissue Biorepository and Safe Haven, allowing access to important clinical trial specimens and data. Furthermore, an industrial partnership with BioClavis will give the grouping access to exciting new technologies to push colorectal cancer research forward.
The GCCI has a wealth of expertise across discovery, translational and clinical science allowing us to quickly move from bench to bedside.

The CRUK Beatson Institute hosting Professor Owen Sansom and Dr Seth Coffelt is a world-leading centre for basic colorectal cancer research. Their research focuses on the drivers of colorectal metastasis. Central to this work is the use of novel inducible models of colorectal tumourigenesis that allow the study of functions related to specific genes and inflammation.

The Wolfson Wohl Cancer Research Centre is a state-of-the-art translational science facility hosting the teams of Professor Andrew Biankin, Dr Joanne Edwards and Mr Campbell Roxburgh. Their work focuses on linking genomics, the tumour microenvironment and signal transduction mechanisms to inform on response to therapy. Central to this work is large colorectal tissue microarrays allowing identification of clinically relevant prognostic and predictive biomarkers and a state-of-the-art genomics suite allowing assessment of the genomic landscape of the tumours.

The Glasgow Royal Infirmary is a leading centre for clinical research hosting the team of Professors McMillan and Horgan. Their work has highlighted the importance of the systemic and local inflammatory response in colorectal cancer. This has led to the introduction of the Glasgow Prognostic Score (GPS) and Glasgow Microenvironment Score (GMS) as prognostic markers for colorectal cancer. Central to this work is the large clinical databases created by the team. The Beatson West of Scotland Cancer Centre is the second largest cancer treatment centre in Europe, serving a population of 2.6 million. The treatment centre has ECMC status and hosts the CRUK Clinical Trials Unit, providing access to colorectal cancer clinical trial specimens and data. Dr Janet Graham’s team takes a lead on a broad portfolio of early and late phase colorectal trials within the centre.

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<thead>
<tr>
<th>Beatson Institute of Cancer Research</th>
<th>Wolfson Wohl Cancer Research Centre (UoG)</th>
<th>Greater Glasgow and Clyde</th>
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<tbody>
<tr>
<td>• World renowned CRUK-funded centre for basic research into cancer development and progression</td>
<td>• State of the art centre for translational cancer research</td>
<td>• Leading hospital-based centres for clinical cancer research</td>
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<tr>
<td>• GEM and xenograft models for colorectal cancer research</td>
<td>• Large colorectal cancer tissue resources</td>
<td>• Large clinical databases and tissue collection</td>
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<td>• Drug discovery programme to identify novel cancer therapeutics</td>
<td>• Polyomics and Genomic expertise</td>
<td>• Access to NHS Research Scotland’s GGC tissue Biorepository: colorectal tumour specimens such as the SCOT clinical trial</td>
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<td>• Expertise in cell function and signalling</td>
<td>• Expertise in biomarker research</td>
<td>• Clinical expertise in colorectal cancer surgery and oncology</td>
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<td>• Collaborative research between scientist and clinicians</td>
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RESEARCH

DISCOVERY RESEARCH

Research Interests

• Understanding the early changes associated with intestinal neoplasia to identify novel markers of disease and new targets for therapy
• The role of the APC gene in sporadic cancers
• The use of novel inducible mouse models of colorectal tumourigenesis to study the functions of specific tumour suppressor genes
• The study of the dichotomous roles of immune cells and how tumours control immune cell behaviour
• Understanding how immune cells participate in the metastatic process to develop new immunotherapies that counteract metastatic lesions

Resources

• In vivo mouse models of colorectal tumourigenesis
• GEM models of consensus molecular subtypes and metastatic disease
• Orthotopic xenograft models
• Colorectal and immune cell lines

Selected Publications

TRANSLATIONAL RESEARCH

Research Interests

• Assessment of tumour-associated inflammation and stromal infiltration as prognostic biomarkers
• The development of strategies to pre-operatively assess the tumour microenvironment
• The relationship between signal transduction and inflammatory response in relation to patient outcome
• The use of tumour signalling pathways to predict prognosis and response to therapy
• Development of a clinically translatable subtyping method based on histological analysis to classify patient by prognosis and predict response to therapy
• The use of genomics to evaluate RNA expression and DNA mutational landscaping of cancers to provide biomarkers to inform clinical trial design
• Characterising the genomic, transcriptomic and epigenomic aberrations in cancer, and extending this to a personalised model of cancer care, where molecular characteristics guide treatment decisions.

Resources

• Established 274 stage I-III colorectal cancer patient tissue microarray with matched clinical data from Glasgow Royal Infirmary 1997-2007
• Established 750 stage I-IV colorectal cancer patient tissue microarray with matched clinical data from Western Infirmary and Stobhill hospitals from 1997-2007 (MSI data available for all patients)
• New 1000 stage I-III colorectal cancer patient tissue microarray with matched clinical data from Glasgow Royal Infirmary from 1997-2013
• New 190 T1-T2 screen detected colorectal cancer patient tissue microarray with matched clinical data from Greater Glasgow and Clyde Hospitals from 2009-2011
• State-of-the-art genomics suite with custom 150 and 250 cancer mutation panels

Selected Papers

CLINICAL RESEARCH

Research Interests

• Prognostic value and determinants of pre-operative cancer-associated systemic inflammation
• Worldwide comparisons of systemic inflammation in colorectal cancer
• The role of post-operative systemic inflammation in short and long-term outcomes
• Can immune cell responses and expression of MHC-1, PD-1 and PD-L1 be measured on sequential tumour biopsies to provide an assessment of patterns of immune priming in response to chemoradiotherapy?
• Are there gene signatures that can be applied to stratify a subset of patients by degree of immunogenicity present at baseline and during treatment?
• Assessment of different treatment regimens in colorectal cancer clinical trials

Resources

• Population-level clinicopathological data for patients diagnosed with colorectal cancer in West of Scotland (2011-2014)
• Clinicopathological data from first round of National Bowel Screening Programme NHS GG&C (2009-2011)
• Prospectively maintained dataset of patients undergoing resection of colorectal cancer in Glasgow Royal Infirmary (1997-onwards, 1700 patients to date)
• SCOT trial tissue specimens, blood samples and patient data

Selected Papers

• Andrea Cercek, Campbell SD Roxburgh, et. al. (2017) Total neoadjuvant chemotherapy to facilitate delivery and tolerance of systemic chemotherapy and response in locally advanced rectal cancer. Journal of Clinical Oncology. 35:15_suppl, 3519-3519.
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TEAM

Senior Management Team
J Edwards  C Roxburgh
A Biankin  O Sansom
D McMillan  P Horgan
S Coffelt  J Graham

Senior Lecturers and Lecturers
A Roseweir  J Park
D Chang  P Bailey
C Steele  S McSorley
D Mansouri  Liz Musgrove

Researchers
Research Associates/Post docs
PhD students
Clinical Research Fellows
Bioinformaticians

Technical Staff
Scientific officers
Technicians
Data Managers
Developers

CONTACT US

Discovery Research  o.sansom@beatson.ac.uk
                    s.coffelt@beatson.ac.uk

Translational Research  joanne.edwards@glasgow.ac.uk
                        antonia.roseweir@glasgow.ac.uk

Clinical Research  campbell.roxburgh@glasgow.ac.uk
                    james.park@glasgow.ac.uk
                    janet.graham@ggc.scot.nhs.uk

Wolfson Wohl Cancer Research Centre, Garscube Estate, Glasgow, Scotland, G61 1QH, UK