GeCIP Detailed Research Plan Form

Background

The Genomics England Clinical Interpretation Partnership (GeCIP) brings together researchers, clinicians and trainees from both academia and the NHS to analyse, refine and make new discoveries from the data from the 100,000 Genomes Project.

The aims of the partnerships are:

1. To optimise:

- clinical data and sample collection
- clinical reporting
- data validation and interpretation.

2. To improve understanding of the implications of genomic findings and improve the accuracy and reliability of information fed back to patients. To add to knowledge of the genetic basis of disease.

3. To provide a sustainable thriving training environment.

The initial wave of GeCIP domains was announced in June 2015 following a first round of applications with expressions of interest in January 2015. These will be used to ensure that the plans are complimentary and add real value across the GeCIP portfolio and address the aims and objectives of the 100,000 Genomes Project. They will be shared with the MRC, Wellcome Trust, NIHR and Cancer Research UK as existing members of the GeCIP Board to give advance warning and manage funding requests to maximise the funds available to each domain. However, formal applications will then be required to be submitted to individual funders. They will allow Genomics England to plan shared core analyses and the required research and computing infrastructure to support the proposed research. They will also form the basis of assessment by the Project's Access Review Committee, to permit access to data.

Domain leads are asked to complete all relevant sections of the GeCIP Detailed Research Plan Form, ensuring that you provide names of domain members involved in each aspect so we or funders can see who to approach if there are specific questions or feedback and that you provide details if your plan relies on a third party or commercial entity. You may also attach additional supporting documents as relevant (optional).

Additional members can apply to join the GeCIP domain by completing the form on our website found here: http://www.genomicsengland.co.uk/join-a-gecip-domain/.

Genomics England Clinical Interpretation Partnership (GeCIP) Detailed Research Plan Form

Application Summary	
GeCIP domain name	**Sarcoma cancer**
Project title *(max 150 characters)*	**Sarcoma cancer research in the 100,000 Genomes Project**

Objectives. *Set out the key objectives of your research. (max 200 words)*

This dataset and accompanying analytical models will contribute significantly to the development of new diagnostic algorithms and new diagnostic strategies for undifferentiated tumours and cancers of unknown primary.

This domain will:

1. Advise on sarcoma diagnosis and treatment, engage with the national sarcoma community (via Genomic Medicine Centers), to recruit patients, and to advise on the most relevant phenotype and –omics data to capture.
2. To inform clinical reporting and data interpretation to ensure return of optimal data to NHS clinicians and patients.
3. Engage NHS clinical sarcoma services and in particular the 5 national commissioning group bone sarcoma centers.
4. Deliver training opportunities for medical, nursing, and the allied health workforce, to address the implementation of genomics into the NHS. In addition, the research opportunities provided by the 100,000 genomes project will be explored in terms of single cell sequencing, circulating tumour DNA analysis and epigenetics for identifying new methodologies for diagnosis and monitoring disease.
5. Align itself with the Genome Medical Centers (of which some working group leads are participants), the Wellcome Trust Sanger Institute, eMedLab and the Farr Institute to establish pathways for contributing existing and future heterogeneous datasets of large number of patients with sarcoma for integration and analysis for patient benefit.

Lay summary. *Information from this summary may be displayed on a public facing website. Provide a brief lay summary of your planned research. (max 200 words)*

- Sarcomas are rare cancers (accounting for 1% of malignancies ~ 3500 cases/year in the UK) that can occur at almost any anatomical site and as such represent diagnostic and therapeutic challenges, often presenting with delayed diagnosis and poor clinical outcomes for patients compared to those with common cancer types.
- Amongst the various categories of rare cancer types defined by the both the European rare cancer network and National Specialist Commissioning Group, sarcomas are amongst the most diverse and different cancer types with more than 100 subtypes known.
- Sarcomas are treated in a small number of specialist units. This lends itself to good sample and data collection, and standardised quality of care. Soft tissue sarcomas, being more common, are also treated in a limited number of units.
- The clinical outcome of these diseases has improved little since the 1980s. However, research into rare cancers has been shown to be informative, particularly for some sarcomas.
- Genomic data from the 100,000 genomes project will serve to promote the characterisation of different tumours based on the genetics, their appearance, and their response to treatment.

Expected start date	**Q2 2017**

Expected end date	**Q2 2020**

Lead Applicant(s)	
Name	Professor Adrienne M Flanagan MB BCH BAO FRCPath PhD FMedSci
Post	Professor of Musculoskeletal Pathology, UCL Head of Academic Department of Pathology (research) UCL Cancer Institute Pathology Clinical Lead for the London Sarcoma Service Honorary Consultant Histopathologist at Royal National Orthopaedic Hospital Trust NHS Trust & Nuffield Orthopaedic Centre, Oxford Director of UCL Advanced Diagnostics
Department	
Institution	UCL
Current commercial links	

Subdomains	Subdomain leads
Optimal samples, pathology, consent and clinical data	Prof. Jeys, Mr. Gerrand, Dr. Pillay, Prof. Hassan, Prof. Judson
Building capacity in bioinformatics	Prof. Campbell, Prof. Luscombe, Prof. Balloux, Dr. Herrero
Epigenetics, circulating tumour cells, circulating DNA and single cell sequencing	Prof. Beck, Prof. Voet, Dr. Van Loo, Dr. Forshew, Dr. Rankin
Training Group	Prof. Luscombe, Prof. Flanagan, Dr Van Loo, Prof. Campbell, Prof. Jeys, Prof. Shipley
Molecular tumour	Prof. Flanagan, Prof. Shipley, Prof. Campbell
Paediatric sarcoma	Prof. Flanagan, Prof. Shipley, Dr. Chisholm

GeCIP domain - Expression of interest

Full proposal

Title *(max 150 characters)*	**Sarcoma cancer research in the 100,000 Genomes Project**

Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*

The sarcoma unit led by Prof. Flanagan at RNOH has a strong track record in this regard being a founding partner with the ICGC bone tumour project at the Wellcome Trust Sanger Institute that has already performed whole genome and whole exome sequences of 400 tumours. The ICGC project has been successful and resulted in being able to provide more accurate diagnosis for a number of primary bone tumour types because of the identification of a number of specific genetic diagnostic biomarkers viz, diagnostic assays being developed for *IDH1/2* and *H3.3* mutations for chondrosarcomas and giant cell tumours of bone respectively.

Additional sarcoma genomic data sets (from paired tumour and matching non-neoplastic tissue) will be delivered from ongoing sarcoma sequencing projects (Prof Flanagan and Dr Pillay) – 50 malignant peripheral nerve sheath tumours (whole exomes), 50 myxofibrosarcomas (whole exomes) and 25 undifferentiated tumours (whole genomes) including sequencing projects from Birmingham, Oxford and the Royal Marsden Hospital. This existing genomic data is incredibly powerful when combined with carefully curated clinical outcome data and imaging. This approach is crucial because to unravel the genomic complexity and correlate this with clinical data will require the comparative analysis of thousands if not tens of thousands of genomes.

This is evidenced by the fact that despite whole genome/exome sequencing of 140 osteosarcoma there is neither a diagnostic biomarker for osteosarcoma, the most common primary bone tumour, nor is there is biomarker to predict which osteosarcoma would respond to neoadjuvant chemotherapy; this is an unmet need with the survival of patients with osteosarcoma remaining stagnant since the introduction of neoadjuvant chemotherapy in the 1980s.

To facilitate this integrative big data approach, these genomes and associated metadata are being deposited in eMedLab, a £9m strategic award from the MRC. The eMedLab is a shared offsite data center with close links to the FARR Institute, UCL Partners and Genomics England. Prof. Flanagan and Prof. Luscombe together with Dr Javier Herrero and Dr Peter Van Loo are already developing projects for osteosarcoma. Prof. Campbell will be assisting by contributing gold-standard variant annotation algorithms and expertise in cancer genome sequencing. They aim to harness this unique group of patients' datasets to develop reference data for future studies. They will use the histology, genotypes and imaging phenotypes and develop sophisticated machine-learning models to integrate and analyse these heterogeneous datasets with the aim of generating algorithms to distinguish the tumour types on imaging, and to determine which osteosarcomas are likely to response to neoadjuvant chemotherapy. Furthermore, these primary bone tumour datasets can be correlated with a full set of images including X-rays, CT scan and MRIs from 100s of patients with metastatic carcinoma and lymphoma.

When combined with the 100,000 genome data, this dataset and accompanying analytical models will contribute significantly to the development of new diagnostic algorithms. This existing genomic scaffold with metadata is likely to contribute significantly to the development of new diagnostic strategies for undifferentiated tumours and cancers of unknown primary, particularly when analytical clustering models are performed.

Updated experimental approach and analysis:

1. Development of assays for surveillance:
   We would like to undertake genetic profiling of cell free DNA as well as profiling of promoter DNA methylation in cell free DNA for the purposes of surveillance of patients and correlate with methylation profiling to determine which would be the most useful approach. In certain instances, for instance, in patients with germline alerations, the profiling could be used for diagnostic purposes and or screening.

2. Understanding tumour heterogeneity:
   We will undertake single cell RNA and DNA sequencing and whole genome bisulphite sequencing from frozen and samples processed at the time of surgery for the purpose of understanding tumour heterogeneity. This will be compared to single cell sequencing of fetal tissue in order to understand the cell of origin of tumours.

3. Mechanism by which the disease may develop and progress:
   We will undertake additional analysis (methylation, transcriptomic, proteomic) on the same samples from which WGS was undertaken by GE and correlate genetic, epigenetic, transcriptomic and proteomic data with clinical outcomes and response to therapies.

4. The generated methylation data will be used for classification of disease.

5. We also wish to undertake immune profiling of the tumours and immunohistochemistry which may involve multiplexing technology.

6. We will employ artificial intelligence and machine learning on digitised images to improve diagnostic criteria: the data from the image files will also be integrated with other multi-omic datasets and correlate with clinical outcome

7. We will study the inherited genomic data accrued in conjunction with a global initiative to identify and validate pathological genetic variants that could increase sarcoma risk.

8. We will undertake analysis of germline DNA from the Sarcoma GeCIP patients and determine if
   - these are specific to a sarcoma subtype
   - these result in a specific pattern of cancers
   - these are similar to alterations that occurs sporadically

9. World-wide collaborations:
   We will correlate our genomic data with that generated from other research groups across the world such as with The International Sarcoma Kindred Study (ISKS) the Chief Investigator of which is Professor David Thomas Sydney, Australia, who is a Sarcoma GeCIP member.

10. Functional studies:
    We will develop mouse and in vitro models such as inducible pluripotent stem cells and mesenchymal stem cells to study the functional impact of genetic alterations identified in sarcomas through whole genome sequencing

Collaborations including with other GeCIPs. *Outline your major planned academic, healthcare, patient and industrial collaborations. This should include collaborations and data sharing with other GeCIPs. Please attach letters of support.*

Network of participating hospitals

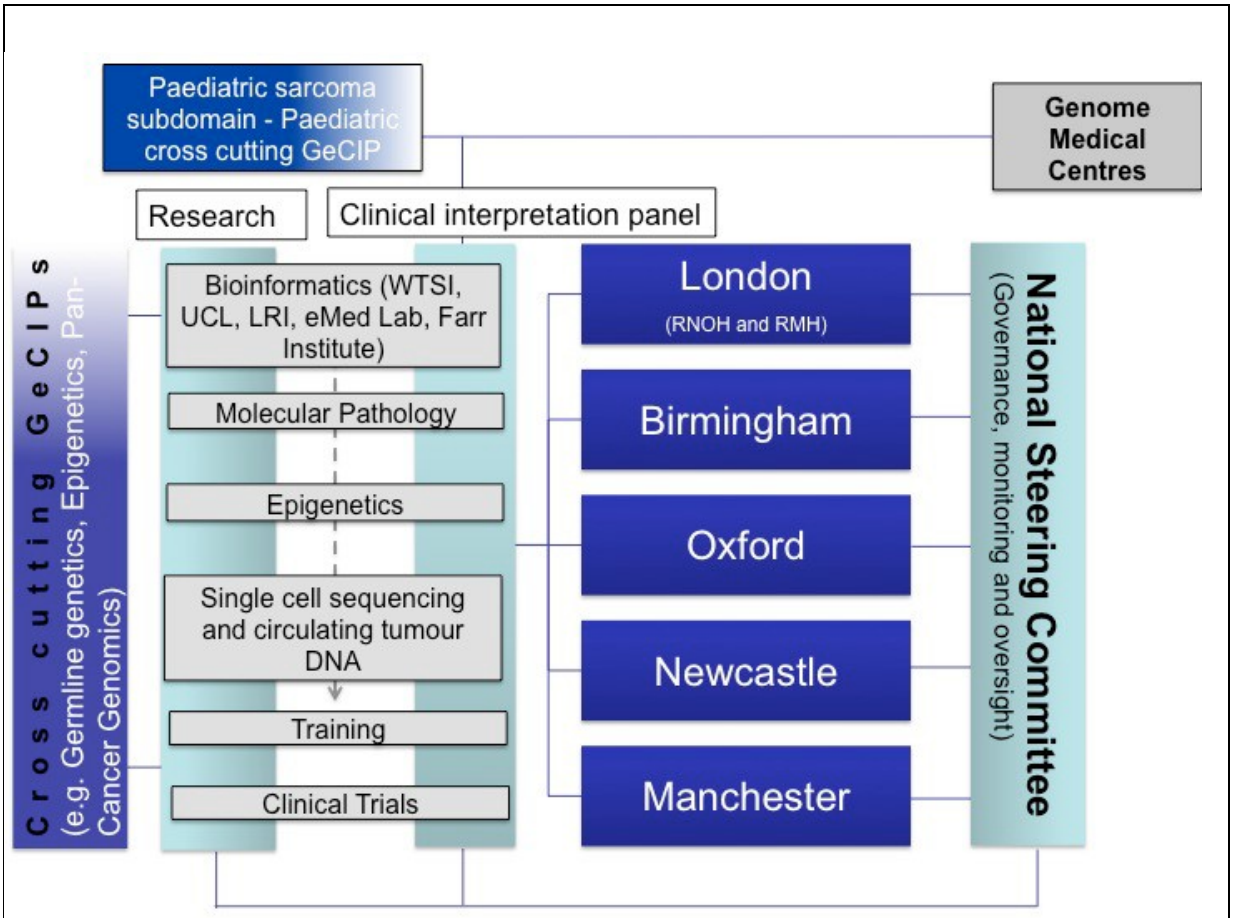
1. The **London Sarcoma Service (LSS)**, combining the teams at University College Hospital and the Royal National Orthopaedic Hospital, treats the whole range of soft tissue and bone, extremity, thoracic, abdominal and retroperitoneal sarcomas, and is one of the largest bone tumour units in Europe. Professor Flanagan is the clinical – pathology lead for the **International Cancer Genome Consortium (ICGC) bone tumour project** performed at the Sanger Institute, which has generated the **400 sarcoma exome/ whole genome sequences** which can be linked with imaging, histology and clinical outcome datasets generated longitudinally. The LSS also is one of the largest recruiters to national and international clinical trials in sarcoma across Europe. Its oncologists Whelan, Strauss and Seddon have extensive experience of conducting early and late phase clinical trials. Opportunities to develop collaborative studies exist through engagement with the NCRI sarcoma clinical studies group and bone sub-group as well as international collaborative clinical trials through consortium such as the European and American Osteosarcoma study group, Euramos, (http://www.ctu.mrc.ac.uk/euramos), Euroewing consortium (EEC), Whelan, Strauss (http://www.euroewing.eu), and EORTC STBSG, (http://www.eortc.org), and globally through Sarcoma Alliance for Research through Collaboration (SARC, http://www.sarctrials.org). These collaborations provide a platform for engagement with industry to facilitate development of clinical trials based on GeCIP findings.
2. Soft tissue sarcomas (STS) are a major focus for genomics research at The **Royal Marsden Hospital (RMH) / Institute of Cancer Research**, where a project is being conducted to investigate patients with multiple cancers including sarcomas to help determine the role played by genetic predisposition in the aetiology of sarcomas (Dr. Clare Turnbull) and a collaboration, also involving colleagues at UCH, is studying families with a strong history of cancer, including sarcoma. This project, the International Sarcoma Kindred Study, is led by a team at the Peter McCallum Cancer Centre in Melbourne. In both studies, DNA and comprehensive family histories will be available for additional studies. The unit has a prospectively maintained clinical database that includes ~7000 patients with STS and a large clinical practice, including many patients with rare, genetically determined, STS subtypes. [The local clinical research lead is Prof. Ian Judson]. RMH is also a leading EORTC Centre for sarcoma, and has been pivotal in a number of practice changing clinical trials. Prof. Janet Shipley's laboratory (Paediatric sarcoma subdomain) at ICR also has a strong research interest in adult sarcomas and has a sequencing project in the pipeline comparing dedifferentiated and well diff liposarcomas (Sarcoma UK funded). They are also interested in epigenetic changes associated with the differentiation of liposarcomas and its regulation including histone modifications and identifying mutations involved. In addition, an EU proposal currently being considered includes the genetics associated with differences in outcome of synovial sarcomas occurring at different ages (indicated in a French study) that could represent a prognostic biomarker. Levels of genetic change as well as actionable mutations would be of similar interest to sequence in other soft tissue sarcomas through obtaining these samples with the appropriate consent that as required by Genomics England.
3. The **Oxford Sarcoma Service** is a comprehensive bone and soft tissue sarcoma NHS service supported by the Oxford Biomedical Research Centre Oncology theme and

Oxford Musculoskeletal Biomedical Research Unit. OxSarc is a major partner in EuroSarc, a European FP& network of translational trials in sarcoma. The translational objectives are early phase biomarker and Bayesian designed trials in Ewing and Osteosarcoma, and next generation sequencing sarcoma diagnostics. The latter is in conjunction with the Oxford Molecular Pathology service and genomics centre, and hot-spot panels have been combined with known sarcoma translocation capture panels. The local research lead is Prof Bass Hassan.

4. Manchester and Newcastle: These services see patients with sarcomas in all anatomical locations, including bone and have established programs in tissue banking, donation and clinical data collection which will support this initiative.

Attachment I: Organisation of the proposed National Sarcoma GeCIP

- The proposed National Sarcoma GECIP incorporates the largest NHS clinical sarcoma centers in the UK and has aligned itself with national and internationally recognised researchers, particularly in the areas of cancer genome sequencing, bio-informatics, single cell sequencing and epigenetics. It also aligns itself with the Paediatric sarcoma subdomain, whose researchers also have an interest in adult sarcomas.
- The establishment of a working group for sample and data collection aims to harness existing infrastructure in the different sarcoma centers and build new structures for consenting, tissue and data collection where needed. It will also utilise existing tissue biobanks for assessment of longitudinal sample collection.
- The formation of a Molecular tumour board will be responsible for data interpretation in a clinical context that will facilitate the implementation of genomics into NHS clinical practice. In particular there is a Training working group that will be responsible for guiding the next generation of clinicians and health workers in the science of genomic medicine.
- This GeCIP also aims to guide future development of innovative therapeutic clinical trials partnering with both academia and pharmaceutical companies.
- Oversight and management of the Sarcoma GECIP will be through the National Steering Committee. The Sarcoma GECIP Steering Group will be constituted by the key stakeholders in the treatment of sarcoma, the leads of the working groups, the molecular tumour board and working groups, and representation from the Genome Medical Centers.
- Funding opportunities to support the management and running of the Sarcoma GECIP will be explored with agencies such as CRUK, Sarcoma UK and the Bone Cancer Research Trust.



Organogram depicting structure of Sarcoma GeCIP

WTSI – Wellcome Trust Sanger Institute
UCL – University College London

LRI – London Research Institute

Detailed research plan – Subdomain

Full proposal (total max 1500 words per Subdomain)	
Title *(max 150 characters)*	**Optimal samples, pathology, consent and clinical data**

Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*

London Sarcoma service:

1. Retrospective series of ~2500 high quality frozen sarcoma samples with matched normal tissue many of which have longitudinal sampling, and multi---regional sampling for investigations of genomic heterogeneity.
2. All patients consented for genomics and tissue donation, including germ line DNA. Approximately 60 patients are consented per month, associated with plasma, blood, and tumour collections. In addition, valuable clinical metadata such as pathology, staging, imaging, outcome etc. is collected.
3. Plasma is also collected for a selection of high and low grade sarcomas longitudinally.
4. This service averages 20 high grade sarcoma per month.

Royal Marsden NHS Trust (RMH):
The RMH sees ~ 1000 new patients a year with sarcoma. Currently RMH is banking 200 fresh frozen samples per annum and planning to store blood samples and matched normal tissue. There are currently >3000 frozen samples in the tissue bank. There is a comprehensive clinical database supporting the tissue collection.

Oxford Sarcoma Service:

1. Retrospective collection of ~150 sarcomas.
2. All patients consented for genomics and tissue donation, including germ line DNA.
3. All fresh frozen tissue collected with BRISQ criteria with documentation, all in theatre with only of minutes ischaemic time.
4. All samples in RNA Later with collections of buffy coat/ plasma.
5. This service averages 7 high grade sarcoma per month.

Birmingham:

1. Retrospective series of ~3000 frozen sarcoma samples with matched normal tissue.
2. This service average 20 high grade sarcoma per month and all patients consented for tissue donation.

Newcastle

1. ~40 matched normal and bone and soft tissue sarcomas per annum.
2. Annotated clinical metadata.

Full proposal (total max 1500 words per Subdomain)	
Title *(max 150 characters)*	**Building capacity in bioinformatics**

Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*

The Bill Lyons Informatics Centre, headed by Dr. Herrero will provide bioinformatics expertise in the processing and analysis of the different -omics data. The team will contribute to the analysis of SNVs, CNAs and other somatic aberrations from the genome sequences. Further research proposals will be based on relating these genomic data to additional data including epigenomics (Prof. Beck) and compare the somatic mutations from the samples with the ctDNA and single cell genomic sequences. Lastly, they will work on the statistical models to integrate clinical imaging data, namely x-rays, MRI and CT scans (with Prof. Luscombe). The Bill Lyons Informatics Centre is supported by the UCL CRUK Centre grant and will use the MRC-funded eMedLab computational infrastructure for developing new analysis pipelines and integrative models. Prof. Campbell and his team will assist with expertise in gold-standard variant and driver annotation and in developing models to integrate the disparate –omics datasets. Prof. Balloux's research will focus on characterising "blood microbiomes" and searching for cryptic pathogens from non-human reads. His team also has expertise in bioinformatics and computational biology on human genomes. As such, they can also contribute to the core analyses that may be of more immediate interest to other members of the domain.

Full proposal (total max 1500 words per Subdomain)	
Title *(max 150 characters)*	**Epigenetics, circulating tumour cells, circulating DNA and single cell sequencing**

Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*

Prof. Beck: Despite large sequencing efforts in cohorts of bone sarcoma (ICGC) it has been identified that a substantial number of cases still show no recurrent genetic driver mutations. There is therefore a strong argument for investigating the epigenetics of these tumours. Prof. Flanagan has an on-going collaboration with Prof. Beck (Epigenetics) at UCL who will support our genomics effort with analysis and the expertise of his group should this sarcoma GeCIP obtain funding.

Dr. van Loo and Prof. Voet: Molecular archaeology of sarcoma: inferring intra-tumour heterogeneity and timelines of cancer development and evolution

We can construct life histories of thousands of sarcomas from their genome sequences, using both driver and passenger mutations. By obtaining detailed timelines of many cancers' evolutionary histories that include driver mutations, copy number changes, rearrangements and mutational processes, we will identify the initiating events of cancer development, and the events that are selected for later in a cancer's lifetime, including those that drive late clonal expansions and that may play a role in tumour malignancy. In addition, these analyses will allow blueprints of the subclonal architecture across cancer types in unprecedented detail and on an unprecedented number of cases, allowing a glimpse into a tumour's future. We've recently shown that such molecular archaeology approaches allow enhanced and unique insights into cancer evolution, particularly when genome sequencing of multiple samples is generated, over multiple time points (Bolli et al. (2014), Nature Communications 5:2997), through multi-region sequencing (Cooper et al., Nature Genetics, in press)), or across multiple metastases (Gundem et al., Nature, in press). As such, we are particularly interested in applying these approaches across cases with multiple samples (either temporal and/or spatial).
We would like to complement these bulk sequencing analyses with single-cell genomics (and potentially transcriptomics as well) of dozens or hundreds of cells from different regions or time points, across a selected subset of the tumours, to dissect in minute detail sarcoma

subclonal architecture, and gain insight into tumour evolution and metastasis.

Dr. Forshew: It is now well established that many solid tumours release DNA into the circulation. Dr Forshew was part of the team that first demonstrated non-invasive solid tumour mutational profiling by direct sequencing of this circulating tumour DNA (ctDNA). Prof. Flanagan and Dr Forshew have demonstrated for the first time that a range of sarcoma including osteosarcoma, chondrosarcoma and giant cell tumour of bone release mutant DNA into circulation (unpublished findings).

By comparing the results from the 100,000 Genomes Project with those obtained through the genetic analysis of serially collected blood samples it will be possible to test the utility of ctDNA in a range of potential applications. These include whether ctDNA can be used for non-invasive diagnosis, prognostication, and disease burden monitoring or relapse detection. We will also test whether ctDNA analysis can be used to detect heterogeneity and evolution of sarcoma.

Dr. Rankin is leading a multicentre trial in Newcastle investigating the detection of circulating tumour cells.

Full proposal (total max 1500 words per Subdomain)	
Title *(max 150 characters)*	**Training group (including Bio---informatics, Data interpretation and molecular pathology)**
Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.* Dr. Behjati through his PhD in cancer genomics has contributed significantly to the delivery of the ICGC bone sarcoma project at the Sanger Institute. Dr's Pillay (PhD) and Mifsud (PhD) are histopathologists who have both spent training time at the Sanger Institute on the bone sarcoma project and will continue developing these skills as part of the Sarcoma GeCIP. Dr's Parry and Ford are surgical trainees with research interests in sarcoma.	

Full proposal (total max 1500 words per Subdomain)	
Title *(max 150 characters)*	**Molecular Tumour Board (MTB) for clinical reporting and data interpretation**
Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.* Key function: Building capacity and experience in the identification of actionable mutations, correlation with histopathology, radiology, development of clinical trials and clinical outcome data and monitoring.	

Full proposal (total max 1500 words per Subdomain)	
Title *(max 150 characters)*	**Molecular tumour board paediatric sarcoma**
Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*	

Sarcomas are rare, aggressive tumours with unmet need that frequently affect the young. This sub-group of the sarcoma GeCIP aims to collaborate with the paediatric sarcoma subdomain as young patients with these tumours are of mutual interest with implications for both domains in terms of molecular diagnosis, research and treatment. Prof. Flanagan is represented in the paediatric sarcoma domain.

Data and informatics requirements
All GeCIP Domains have contributed to the construction of the data model for their tumour type and have contributed to ongoing efforts within Genomics England to develop the clinical and research informatics infrastructure.

Data access and security	
GeCIP domain name	Sarcoma cancer
Project title *(max 150 characters)*	

Applicable Acceptable Uses. *Tick all those relevant to the request and ensure that the justification for selecting each acceptable use is supported above.*

X *Clinical care*

X *Clinical trials feasibility*

X *Deeper phenotyping*

X *Education and training of health and public health professionals*

X *Hypothesis driven research and development in health and social care - observational*

X *Hypothesis driven research and development in health and social care - interventional*

X *Interpretation and validation of the Genomics England Knowledge Base*

X *Non hypothesis driven R&D - health*

X *Non hypothesis driven R&D - non health*

X *Other health use - clinical audit*

X *Public health purposes*

X *Tool evaluation and improvement*

Information Governance

X The lead for each domain will be responsible for validating and assuring the identity of the researchers. The lead may be required to support assurance and audit activities by Genomics England.

Any research requiring access to the embassy will be required to complete IG Training and read and sign a declaration form. Access will only be granted once these requirements have been met.