HaemOnc Network of Excellence

Angela Hamblin
Polly Talley

Summary of aims of the Networks of Excellence

Prenatal Genomic Medicine Network of Excellence

To ensure equity of access to high quality pre- and perinatal genomic medicine for all families across England, whilst capitalising on new technological developments to ensure access to state-of-the-art testing for more conditions.

Circulating Tumour Biomarker testing for rapid, effective cancer diagnostics and monitoring

To provide an evidence-driven framework to expedite the evaluation and introduction of ctDNA and other liquid biopsy tests into clinical diagnostic service in England.

Haemato-Oncology Work Packages

To utilise expertise within the GLHs and GMSAs and ultimately allow implementation of new technologies and assays across all geographies for the equitable benefit of patients with or at risk of haematological malignancies.

NHS Rare and Inherited Disease Genomic Network of Excellence

To develop and deliver a sustainable network to accelerate delivery of the clinical and diagnostic ambitions of the Rare Diseases Action Plan 2023 and UK Rare Diseases Framework for all NHS patients and families affected by rare genetic conditions

Severe Presentation of Infectious Disease Genomic Network of Excellence

To transform the understanding and management of patients with life threatening infectious disease, through the application of novel genomic technologies in pathogen detection and host immunity profiling.

Improving the identification and outcomes for individuals with inherited and acquired cardiovascular disease

To pilot approaches to improve the identification of individuals at risk of both inherited and acquired CVD through using genomics to improve outcomes in a well-established and phenotyped cohort of patients

Pharmacogenomics and Medicines Optimisation

To support the expansion and extension of the PROGRESS programme across the NHS GMS Alliance footprint and other healthcare settings.

Genomics AI Network: GAIN

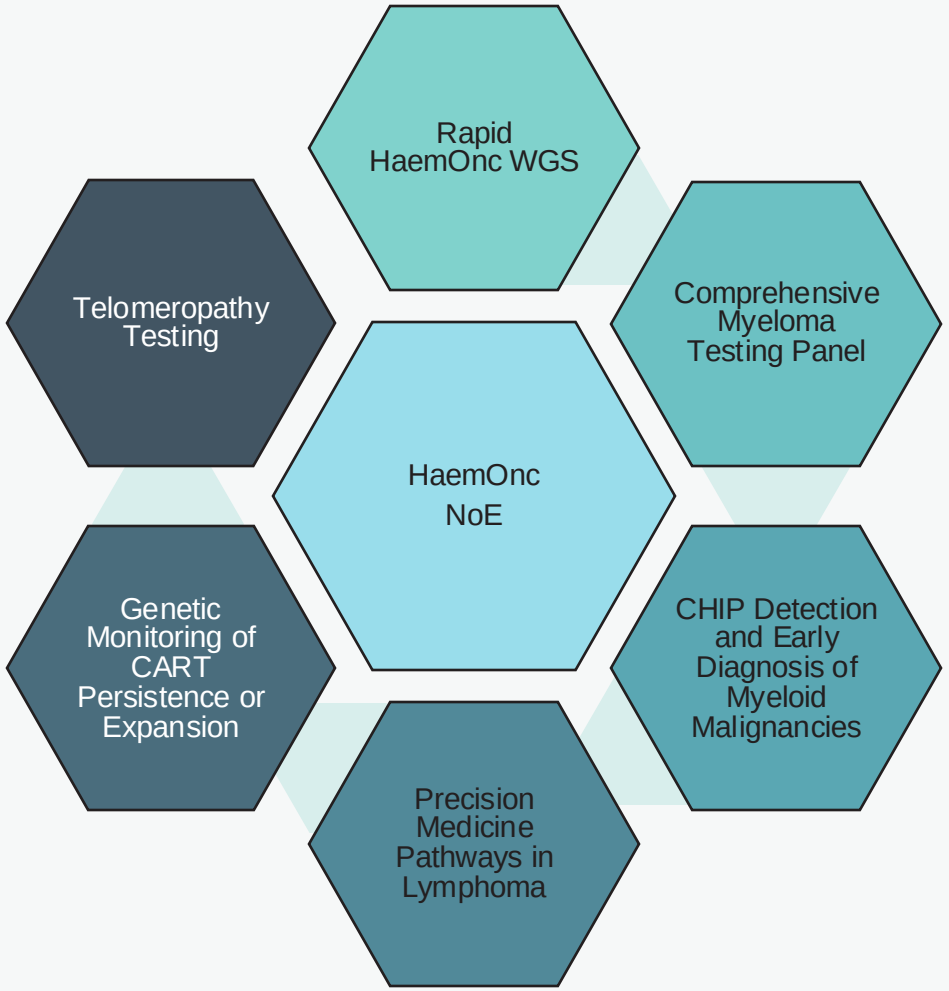
To build a national community in genomics and AI, create frameworks to support AI deployment, and deliver exemplar accelerator programmes to develop the evidence required to adopt AI for the benefit of NHS patients, including improved and accelerated diagnosis and personalised medicine.

HaemOnc Network of Excellence

Rapid HaemOnc SR WGS
SIHMDS straight to sequencing lab, transfer data to GEL
?Domain 0 to speed up analysis
Tumour first / early
Further phases to explore local pipelines, RNA seq and LRS.
Aiming for TAT of ~7 days
A Hamblin (C&S)

Accreditation of telomere length assay (ddPCR)
Utility in diagnosis of aplasia and bone marrow failure syndromes
Gap in test provision in NHS in England
D Yallop (SE) & J Bartram (NT)

Validation and accreditation of ddPCR light chain assay to monitor CAR-T
Correlation with clinical response and inform where to implement augmentation strategies
D Yallop (SE) & C Wragg (SW)



Single DNA panel determines SNV / CVs / SVs in broad range of myeloma targets
Current provision of genomic testing is by FISH – high failure rate & limited data return
Enhanced prognosis and in-time therapy choice
A Hamblin / S Gooding / K Ramasamy (C&S)

Development of guidelines of who to screen for CH
Implementation of MN risk prediction tool
Development of national database
Implementation of high through-put screening panel
C Cargo (NEY) G Vassiliou (E)

Implementation of GEP for diagnosis / prognosis
Implementation of NGS panels
Development of ctDNA
Broader implementation of WGS
C Burton (NEY) L Raso-Barnett (E)

Rapid HaemOnc WGS – WP1

- Rapid HaemOnc SR WGS – specifically requested from NHSE
- Originally to be a transformation project, now back in the NoE
- Multi-phase proposal – initial plan is sample to be sent from SIHMDS straight to sequencing lab, initiate request, perform sequencing, transfer data to GEL for annotation with their pipeline, data returned to the portal, ?for domain 0 to speed up analysis
- To start with tumour first / early – but facility to later send matched germline for sequencing with subsequent tumour-normal subtraction
- Further phases to the project include exploring local pipelines, RNA seq and LRS
- Aiming for initial TAT of sample receipt in sequencing lab to data in the portal of ~7 days

Dr Angela Hamblin (C&S)

Comprehensive Myeloma Panel Testing – WP2

- Large (single) panel designed to cover SNV, SVs, CNVs in myeloma
- Able to detect *IGH* rearrangements from DNA; uses two sets of probes; higher concentration of probes for SNVs / CNVs, lower concentration of probes for SVs
- Single sequencing output with single bioinformatics pipeline able to call all variant types (performs favourably compared to FISH & WGS; published in Clin Cancer Res. 2022; 28:2854).
- Being used in RADAR trial and other research consented patient samples – plan to sequence >1000 samples in next 18 months
- Currently uses a germline sample; work underway to optimize bioinformatics so this is not required (reduce cost and work involved)
- Bid for some additional bioinformatics funding for above – plan to submit for ISO accreditation
- Once accredited can share design / SOPs / bioinformatics pipelines with other GLHs or run as a <7 GLH test

Dr Angela Hamblin, Sarah Gooding & Dr Karthik Ramasamy (C&S)

CHIP Detection & Early Diagnosis of Myeloid Disease – WP3

- CHIP and CCUS now recognised entities in the WHO and ICC
- Individuals with CH have significantly higher risk of progression to myeloid malignancies and worse overall survival
- Currently no clear guidance on patient screening or clinical management
- Development of predictive tools and markers
  - CHIP - MN-predict (Gu *et al*, Nature Genetics, in press)
  - CCUS (manuscript in preparation)

Aims:

- To harmonise the detection and management of patients with CHIP and CCUS nationally
- To translate the extensive research into the clinical field
- Build on national work ongoing in this area

Project plan:

- Define clinical and laboratory criteria for selecting and screening patients
- Application and improvement of predictive tools
- National database of CH patients
- Development of rapid screening tool for detecting CHIP

Dr Catherine Cargo & Dr George Vassiliou

Precision Medicine Pathways in Lymphoma – WP4

AIMS:

- Optimisation of sampling pathways and use of available tissue
- Incorporation of molecular diagnostics into standard of care
    - Improve diagnostic precision / Define clinical behaviour of molecular subgroups / Targeted therapy/personalised medicine
- Explore new models of genomic service delivery

OUTCOMES:

- Sustainable tissue processing pathway optimised for genomic testing nationally
- Standardised GEP and HTS approaches within lymphoma genomics
- Optimised reporting of clinical results & sharing of research data via molecular knowledge bank
- Novel technologies for profiling & MRD assessment
- Prospective assessment of minimum testing requirements, both targets and modalities, to inform Test Directory

Dr Cathy Burton and Dr Lívia Rásó-Barnett

Genetic Monitoring of CART Persistence / Expansion – WP5

- We plan to further develop and validate ddPCR assays to measure CAR-T levels in patients who receive one of the NHSE licensed CAR-T products (Tisagenlecleucel, Axicabtagene ciloleucel and Brexucabtagene autoleucel).
- ddPCR is a technique which offers the ability to monitor and evaluate cellular therapy at a highly sensitive level and can be undertaken on peripheral blood with a rapid turnaround time, all of which make it ideal for routine clinical practice
- The plan is within 12 months the project will be transitioned into routine clinical practice as part of the national genomic test directory as a <7 GLH test
- The scope of the NOE may be expanded beyond its original aims to create a framework to allow ddPCR to be developed prospectively as new CAR-T products become available, with a view to universal CAR monitoring strategies

Dr Debby Yallop (SE) & Chris Wragg (SW)

Accreditation of Telomeropathy Assay - WP6

- Telomere length, alongside the sequencing of associated variants in key genes (R91), is a valuable tool for screening patients with suspected telomeropathies, including those with inherited bone marrow failure which can lead to the development of haematological malignancies.
- Telomere length also finds use in prognostic scoring in various other haematological malignancies, solid tumours and systemic disorders such as pulmonary fibrosis and cirrhosis of liver.
- Significant implications for treatment and prevention of complications of this multi-system disorder. Additionally diagnosis in a proband may have wider implications for family screening and monitoring.
- Currently KCH receives approximately 600 test requests for telomere length assessment annually where a multiplex qPCR test is performed alongside the TGC gene panel (R91). Due to under-recognition of the clinical phenotype, the current sample request is an underestimation of the true burden of disease
- Gap in test provision in NHS in England
- The project aims to standardize, validate and accredit qPCR telomere length assessment across adult and paediatric cases and accredit the test and offer as a <7GLH test to all GLHs

Dr Debby Yallop (SE) & Dr Jack Bartram (NT)