Central England Haemato-Oncology (and Oncology) Research Biobank (CEHRB)

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Annual Report

April 2014 to March 2015

CEHRB
C/o West Midlands Regional Genetics Laboratory
Birmingham Women’s Hospital
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Fax: 0121 627 2711

Website: http://www.bwnft.nhs.uk/wmrgs/regionalgenetics/biobank-cehrb/

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PART 3 - Targets

3.1 Review of Targets for 2014-2015
1.1 CEHRB Staff

The following staff members, from the West Midlands Regional Genetics Laboratory contribute to CEHRB activities.

**Director**
Prof Mike Griffiths  Email: mike.griffiths@bwnft.nhs.uk

**Manager and HTA Designated Individual**
Sally Jeffries  Email: sally.jeffries@bwnft.nhs.uk

**Technical and Admin Support**
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**Health and Safety Officer**
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**Information and Technology Manager**
Gareth Masson  Email: gareth.masson@bwnft.nhs.uk

**Chief Technology and Information Officer**
Chris Kotara  Email: chris.kotara@bwnft.nhs.uk
1.2 Steering Committee

**Prof Charles Craddock (Chair and Representative for Cure Leukaemia)**
Consultant Haematologist
Centre for Clinical Haematology
University Hospital Birmingham NHS Foundation Trust
Email: charles.craddock@uhb.nhs.uk

**Dr Richard Chasty (Lymphoma Group)**
University Hospital North Staffordshire
Hilton Road
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**Dr Guy Pratt (Myeloma Group)**
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Heartlands Hospital
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**Dr Jeff Neilson (Ethics Representative)**
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**Alan MacWhannell (Myeloid Group)**
Royal Wolverhampton Hospital
Wolverhampton Road
Heath Town
Wolverhampton
WV10 0QP
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Birmingham Children's Hospital
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Birmingham
B4 6NH
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**Kelly Hard (Research and Development)**
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Birmingham Women’s Hospital
Edgbaston, Birmingham, B15 2TG
Email: Kelly.hard@bwnft.nhs.uk

**Prof Mike Griffiths (CEHRB Director)**
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**Sally Jeffries (CEHRB Manager)**
West Midlands Regional Genetics Laboratory
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Birmingham B15 2TG
Email: sally.jeffries@bwnft.nhs.uk
1.3 Types of samples stored

Blood and bone marrow stored as

- Fixed cell suspensions
- DNA
- RNA
- Viable cells
- Plasma
- Fresh Blood and bone marrow (on request)
- Other (on request)

Solid tumours (on request)

- Fresh tissue
- FFPE slides

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**Percentage of sample types released from CEHRB between 2009-2015**

- Plasma: 32%
- RNA/cDNA: 19%
- DNA: 23%
- Fresh/Viable cells: 11%
- Fixed cells: 15%
1.4 Hospitals involved in seeking patient consent

There are 10 hospitals that have a funded Research Nurse and are currently involved in seeking patient consent

- University Hospital of North Staffordshire
- Stafford District General Hospital
- Centre for Clinical Haematology, Queen Elizabeth Hospital
- Russell’s Hall Hospital, Dudley
- Birmingham Heartlands Hospital
- University Hospital, Walsgrave, Coventry
- Worcestershire Royal Hospital
- Alexandra Hospital, Redditch
- Sandwell General Hospital
- New Cross, Royal Wolverhampton Hospital

We have also received patient consent from unfunded centres

- Priory Hospital
- Nuffield Hospital, Wolverhampton
- Mosely Hall Hospital
- Little Aston Hospital, Sutton Coldfield
- Hereford
- Princess Royal Hospital, Telford
- Kidderminster Hospital
With additional funding there is potential to seek patient consent from the additional hospitals

- Walsall Manor Hospital
- Warwick Hospital
- Rugby Hospital
- George Eliot Hospital, Nuneaton
- Royal Shrewsbury Hospital
- Queens Hospital, Burton

1.5 **Consented patient figures**

1.5.1 Monthly breakdown of patient consent

The following patient consent data are based on consent data received from 11 sites:

### Hospital List

<table>
<thead>
<tr>
<th>Code</th>
<th>Hospital Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALBR</td>
<td>Alexandra Hospital</td>
</tr>
<tr>
<td>CHCB</td>
<td>Centre for Clinical Haematology, Queen Elizabeth Hospital</td>
</tr>
<tr>
<td>EEBB</td>
<td>Heartlands Hospital</td>
</tr>
<tr>
<td>KGKI</td>
<td>Kidderminster General Hospital</td>
</tr>
<tr>
<td>NXWV</td>
<td>New Cross Wolverhampton</td>
</tr>
<tr>
<td>RUDU</td>
<td>Russell's Hall, Dudley</td>
</tr>
<tr>
<td>SDMS</td>
<td>Stafford District General</td>
</tr>
<tr>
<td>SDSA</td>
<td>Sandwell Health Care NHS Trust</td>
</tr>
<tr>
<td>UHNS</td>
<td>University Hospital North Staffordshire</td>
</tr>
<tr>
<td>WGCO</td>
<td>Walsgrave Hospital Coventry</td>
</tr>
<tr>
<td>WRWO</td>
<td>Worcester Royal</td>
</tr>
</tbody>
</table>
Overall the number of patients consenting has decreased since 2011 (by 28%), however this may be attributable to:

1) limiting resources for consenting patients
2) the assimilation of the recently amended patient consent form (V1.4).

1.5.2 Cumulative patient consent since April 2008
1.5.3 Patients consented from Individual Hospitals

Patient consent has predominantly been secured from 11 sites within 2011-2015. The table below represents ‘potential’ recruitment opportunities within these sites. The data is based on the number of presentation or staging samples received by the WMRGL from each site during the given period (which corresponds to number of ‘New’ patients at each centre). It should be noted however that patient consent is not always collected at diagnosis, it can also be obtained at follow-up, this is apparent where ‘obtained recruitment’ figures exceeds ‘potential recruitment’. As demonstrated for KGKI in the tables below.

Potential recruitment opportunities per site (Based on Presentation and Follow-up samples received within period).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
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<tr>
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<td>100</td>
<td>121</td>
<td>101</td>
<td>83</td>
<td>405</td>
</tr>
<tr>
<td>CHCB</td>
<td>679</td>
<td>869</td>
<td>989</td>
<td>939</td>
<td>3476</td>
</tr>
<tr>
<td>EBEB</td>
<td>504</td>
<td>498</td>
<td>571</td>
<td>655</td>
<td>2228</td>
</tr>
<tr>
<td>KGKI</td>
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<td>6</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
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<td>558</td>
<td>436</td>
<td>604</td>
<td>591</td>
<td>2189</td>
</tr>
<tr>
<td>RUDU</td>
<td>232</td>
<td>239</td>
<td>230</td>
<td>188</td>
<td>889</td>
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<tr>
<td>SDMS</td>
<td>367</td>
<td>273</td>
<td>396</td>
<td>472</td>
<td>1508</td>
</tr>
<tr>
<td>SDSA</td>
<td>141</td>
<td>139</td>
<td>125</td>
<td>144</td>
<td>549</td>
</tr>
<tr>
<td>UHNS</td>
<td>25</td>
<td>30</td>
<td>94</td>
<td>86</td>
<td>235</td>
</tr>
<tr>
<td>WGCO</td>
<td>207</td>
<td>190</td>
<td>280</td>
<td>279</td>
<td>956</td>
</tr>
<tr>
<td>WRWO</td>
<td>263</td>
<td>247</td>
<td>274</td>
<td>307</td>
<td>1091</td>
</tr>
<tr>
<td>Grand Total</td>
<td><strong>3082</strong></td>
<td><strong>3042</strong></td>
<td><strong>3670</strong></td>
<td><strong>3752</strong></td>
<td></td>
</tr>
</tbody>
</table>
Actual Consent obtained per site (Based on number of consent forms received within period).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ALBR</td>
<td>2</td>
<td>34</td>
<td>41</td>
<td>44</td>
<td>121</td>
</tr>
<tr>
<td>CHCB</td>
<td>179</td>
<td>124</td>
<td>178</td>
<td>51</td>
<td>532</td>
</tr>
<tr>
<td>EEBB</td>
<td>12</td>
<td>35</td>
<td>0</td>
<td>5</td>
<td>52</td>
</tr>
<tr>
<td>KGKI</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>NXWV</td>
<td>190</td>
<td>179</td>
<td>70</td>
<td>120</td>
<td>559</td>
</tr>
<tr>
<td>RUDU</td>
<td>8</td>
<td>61</td>
<td>71</td>
<td>14</td>
<td>154</td>
</tr>
<tr>
<td>SDMS</td>
<td>136</td>
<td>97</td>
<td>141</td>
<td>86</td>
<td>460</td>
</tr>
<tr>
<td>SDSA</td>
<td>53</td>
<td>34</td>
<td>32</td>
<td>27</td>
<td>146</td>
</tr>
<tr>
<td>UHNS</td>
<td>16</td>
<td>0</td>
<td>7</td>
<td>11</td>
<td>34</td>
</tr>
<tr>
<td>WGCO</td>
<td>8</td>
<td>0</td>
<td>14</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>WRWO</td>
<td>19</td>
<td>14</td>
<td>12</td>
<td>76</td>
<td>121</td>
</tr>
<tr>
<td>Other*</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Grand Total</td>
<td>623</td>
<td>579</td>
<td>566</td>
<td>468</td>
<td></td>
</tr>
</tbody>
</table>

*Other includes consents from unfunded centres but excludes BCCB (Paediatrics).
Consent data for each site as a percentage of potential recruitment (actual consent v presentation and follow-up)

<table>
<thead>
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<th></th>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
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<td>ALBR</td>
<td>2.0</td>
<td>28.1</td>
<td>40.6</td>
<td>53.0</td>
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<tr>
<td>CHCB</td>
<td>26.4</td>
<td>14.3</td>
<td>18.0</td>
<td>5.4</td>
</tr>
<tr>
<td>EEBE</td>
<td>2.4</td>
<td>7.0</td>
<td>0.0</td>
<td>0.8</td>
</tr>
<tr>
<td>KGKI</td>
<td>0.0</td>
<td>-</td>
<td>0.0</td>
<td>125.0</td>
</tr>
<tr>
<td>NXWV</td>
<td>34.1</td>
<td>41.1</td>
<td>11.6</td>
<td>20.3</td>
</tr>
<tr>
<td>RUDU</td>
<td>3.4</td>
<td>25.5</td>
<td>30.9</td>
<td>7.4</td>
</tr>
<tr>
<td>SDMS</td>
<td>37.1</td>
<td>35.5</td>
<td>35.6</td>
<td>18.2</td>
</tr>
<tr>
<td>SDSa</td>
<td>37.6</td>
<td>24.5</td>
<td>25.6</td>
<td>18.8</td>
</tr>
<tr>
<td>UHNS</td>
<td>64.0</td>
<td>0.0</td>
<td>7.4</td>
<td>12.8</td>
</tr>
<tr>
<td>WGCO</td>
<td>3.9</td>
<td>0.0</td>
<td>5.0</td>
<td>1.1</td>
</tr>
<tr>
<td>WRWO</td>
<td>7.2</td>
<td>5.7</td>
<td>4.4</td>
<td>24.8</td>
</tr>
</tbody>
</table>

Note: Patients are not necessarily targeted at presentation and consent may be completed at a different site to clinic visits.

1.6 Promotion of the Biobank

- Poster – Central England Haemato-oncology (and oncology) Research Biobank: aims and contribution to cancer research, Sally Jeffries, Kim Piechocki, Mike Griffiths, ACGS Spring Meeting April 29-30 2015, Austin Court, Birmingham.

1.7 Sustainability of CEHRB

- Collaboration with Trans-Hit Biomarkers, a worldwide company based in Canada who provide high quality samples to research groups globally.
- Grant submitted to Wellcome Trust: rejected on basis of number of applicants. Suggested that should approach charities for funding.

PART 2: Projects and Publications

- The total number of samples sent out to ethically approved projects for April 2014 – March 2015 is 572 (295 in 2014). Details are provided below.
  - 13 projects have received samples from CEHRB.
    - 2 new projects and 11 existing projects.
  - 5 new projects were approved
  - 9 sample requests were rejected due to limited resources, unable to provide material or information.
- Since Sept 2009 CEHRB has provided 2818 samples to 54 projects. Some of these projects continue to receive samples.
### 2.1 Existing projects that have received samples from CEHRB between April 2014 and March 2015

<table>
<thead>
<tr>
<th>Project No.</th>
<th>Project Title</th>
<th>Principal Investigator</th>
<th>Laboratory Address</th>
<th>Sponsor</th>
<th>Samples Sent</th>
<th>Type</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Histone deacetylase inhibitors, a new class of anti-tumour agents in AML.</td>
<td>Dr Tatjana Stankovic</td>
<td>CRUK Institute for Cancer Studies</td>
<td>Kay Kendall Leukaemia Fund</td>
<td></td>
<td>Marrow</td>
<td>11</td>
</tr>
<tr>
<td>18</td>
<td>Prospective study of trough Imatinib levels in newly diagnosed Chronic Myeloid Leukaemia patients and its correlation with response.</td>
<td>Professor Deepak Chandra</td>
<td>University Hospital North Staffordshire</td>
<td>Novartis</td>
<td></td>
<td>Plasma</td>
<td>30</td>
</tr>
<tr>
<td>31</td>
<td>Dissecting Mechanisms of Regulation of Gene Expression in Human Leukaemia</td>
<td>Prof Peter Cockerill and Constanze Bonifer</td>
<td>IBR Medical School, University of Birmingham</td>
<td>Leukaemia and Lymphoma Research</td>
<td></td>
<td>Blood</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Marrow</td>
<td>5</td>
</tr>
<tr>
<td>34</td>
<td>Validation of Cytocell Ltd. FISH probes for diagnostic use in haematological oncology referrals.</td>
<td>Dom McMullan</td>
<td>WMRGL</td>
<td>Cytocell</td>
<td></td>
<td>Fixed Cells</td>
<td>124</td>
</tr>
<tr>
<td>41</td>
<td>The MYB Family of Proteins in Myeloid Disease</td>
<td>Prof Jon Frampton</td>
<td>Institute for Biomedical Research, College of Medical and Dental Sciences, Birmingham University</td>
<td>Not Stated</td>
<td>Blood/Marrow</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Page</td>
<td>Title</td>
<td>Author(s)</td>
<td>Institution(s)</td>
<td>Research Areas</td>
<td>Type</td>
<td>References</td>
<td></td>
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<td>--------</td>
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<td></td>
</tr>
<tr>
<td>42</td>
<td>Constitutional Genetics in the Aetiology and Prognosis of AML</td>
<td>Dr James Allan</td>
<td>Newcastle-NICR</td>
<td>Leukaemia and Lymphoma Research</td>
<td>DNA</td>
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<tr>
<td>43</td>
<td>Mechanisms of Clonal Progression and New Therapeutic Approaches in B cell Chronic Lymphocytic Leukaemia with a DNA Damage Defect</td>
<td>Dr Nicholas Davies</td>
<td>Birmingham-ICS</td>
<td>Leukaemia and Lymphoma Research</td>
<td>Blood/Marrow</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>Study of the Effects of Donor Lymphocyte Infusion on the Promotion of GVL and GVHD Responses Following Haematopoietic Stem Cell Transplantation.</td>
<td>Mr Ben Abbotts</td>
<td>Birmingham-ICS</td>
<td>Leukaemia and Lymphoma Research</td>
<td>DNA</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>Genetic definition of the BCR-ABL1- like sub-group in acute lymphoblastic leukaemia</td>
<td>Ms Claire Schwab</td>
<td>Leukaemia Research Cytogenetics Group, Northern Institute for Cancer Research, Newcastle University</td>
<td>Leukaemia and Lymphoma Research</td>
<td>Fixed Cells</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>Genomic analysis of primary refractory AML</td>
<td>Professor Paul Ferguson/Susanna Akiki</td>
<td>BWH</td>
<td>University of Birmingham</td>
<td>DNA</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>Defining Molecular Mechanisms underlying the Pathogenesis of APL and Therapy-Related Leukaemias</td>
<td>Prof David Grimwade</td>
<td>Grimwade-Guy</td>
<td>Leukaemia and Lymphoma Research</td>
<td>DNA</td>
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<td>Fixed Cells</td>
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</tr>
</tbody>
</table>
### 2.2 Newly approved projects that have received samples from CEHRB Between April 2014 and March 2015

<table>
<thead>
<tr>
<th>Project No.</th>
<th>Project Title</th>
<th>Principal Investigator</th>
<th>Lab. Address</th>
<th>Sponsor</th>
<th>Samples Sent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Genomic analysis of diagnostic AML patient samples to identify molecular markers of disease relapse following haematopoietic stem cell transplantation</strong></td>
<td>Professor Charles Craddock/ Dr Paul Ferguson</td>
<td>The Weatherall Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital</td>
<td>DNA</td>
<td>150</td>
</tr>
<tr>
<td>52</td>
<td><strong>Comparative genomic analysis of AML patients at diagnosis and relapse following stem cell transplant as part of the FIGARO Clinical trial</strong></td>
<td>Professor Charles Craddock/ Dr Paul Ferguson</td>
<td>School of Cancer Sciences, University of Birmingham</td>
<td>University of Birmingham</td>
<td>DNA/RNA Collating Samples</td>
</tr>
<tr>
<td>53</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.3 List of publications/presentations that have used samples from CEHRB

- Since 2009 there have been 17 publications and at least 9* oral presentations that have used samples received from CEHRB (* data on oral presentations collated since 2010).
- There were 4 publications during the 2014-2015 period; detailed below.

Publications (2014/2015)


Oral presentations and meeting abstracts (2014/2015)

1. “Activating FLT3-ITD receptor mutations in AML are associated with a specific epigenetic signature composed of a discrete subset RUNX1-bound DNase1 hypersensitive sites enriched for AP-1 and C/EBP motifs.” Pierre Cauchy, Sally James, Jason Piper, Anetta Ptasinska, Joaquin Zacarias-Cabeza, Maria-Rosaria Imperato, Martina Canestraro, Salam Assi, Maarten Hoogenkamp, David Westhead, Sascha Ott, Constanze Bonifer and Peter Cockerill. Modern Trends in Leukemia and Cancer, Wilsede, Germany, June 21-24, 2014.

2. “Chronic FLT3-ITD signaling in Acute Myeloid Leukemia is connected to a specific chromatin signature.” Molecular Haemopoiesis17 meeting, London October 17 2014

3. SSBP2-CSF1R is a Recurrent Fusion in B-Other Acute Lymphoblastic Leukaemia with Variable Clinical Outcome Claire Schwab, Rebecca Andrews, Lucy Chilton, Alannah Elliott, Stacey Richardson, Sarra Ryan, Amy Logan, Adele Fielding, Nicholas Goulden, Ajay Vora, Anthony V Moorman, Christine Macartney and Christine J Harrison (Abstract)
PART 3: Targets

3.1 Review of targets and other achievements for 2014-2015

Targets Achieved

- Approve and supply samples to 5 or more projects
- Review SOPs for sample selection and send out of material, ensuring better understanding of consent by staff.
- Renewal of ethics for further 5 years.
- Secured ethical approval to receive samples for specific projects. Previous was for excess diagnostic material only.
- Amended consent forms to include consent for data retrieval from patient notes.
- Secured collaboration with a company based in Canada who provide samples to research groups.

Targets Not Achieved

- Extend consent to children (requires amendment to ethics)
  - To remove from targets. Significant barriers to prevent this.
- Secure additional funding
  - Unable to secure from grants and charity requests.
  - To include in next year’s targets
- Ensure continued improvement in patient recruitment by liaising with RRN.
  - Limited resources have enabled this.

3.2 New targets for 2015-2016

- Approve and supply samples to 5 or more projects
- Ensure continued improvement in patient recruitment by liaising with RRN.
- Secure additional funding
- Seek to establish further collaboration with global Biobank networks to increase income and research portfolio.

Sally Jeffries, BSc, DipRCPath
Manager of CEHRB