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

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Annual Report

April 2014 to March 2015

CEHRB
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PART 1- Staff and Consent

PART 2 - Projects and publications 2014-2015

PART 3 - Targets

PART 1- Staff and Consent

1.1 CEHRB Staff

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

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1.2 Steering Committee

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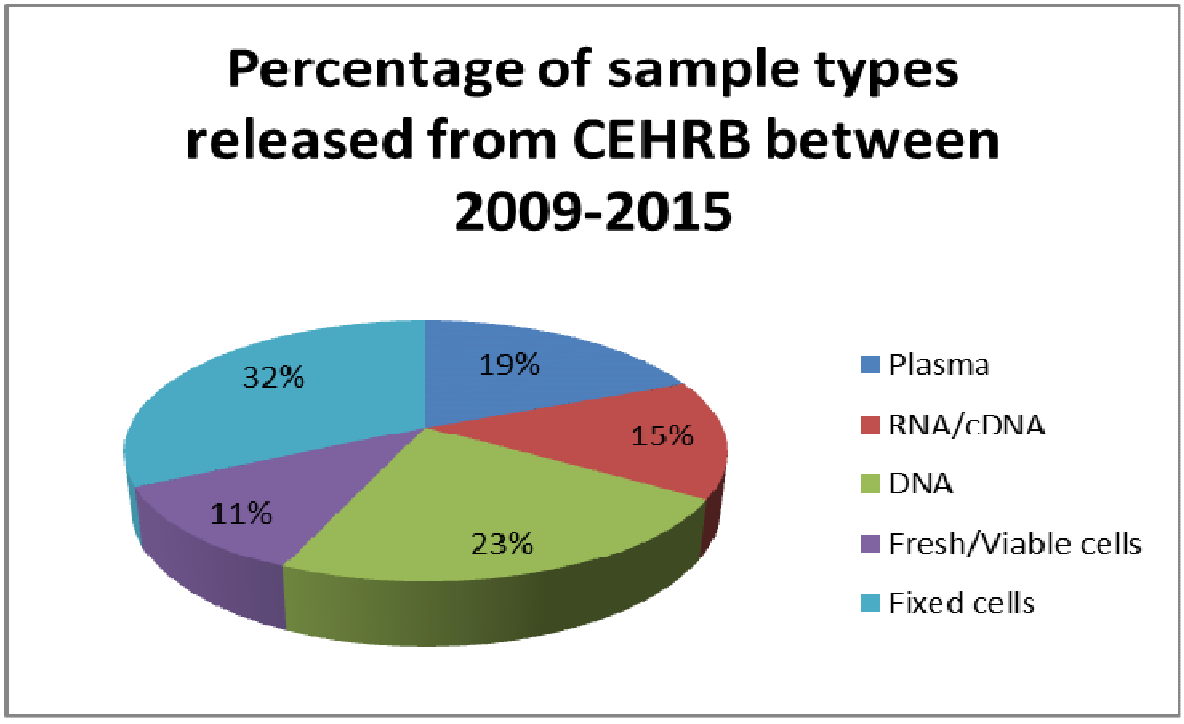
1.3 Types of samples stored

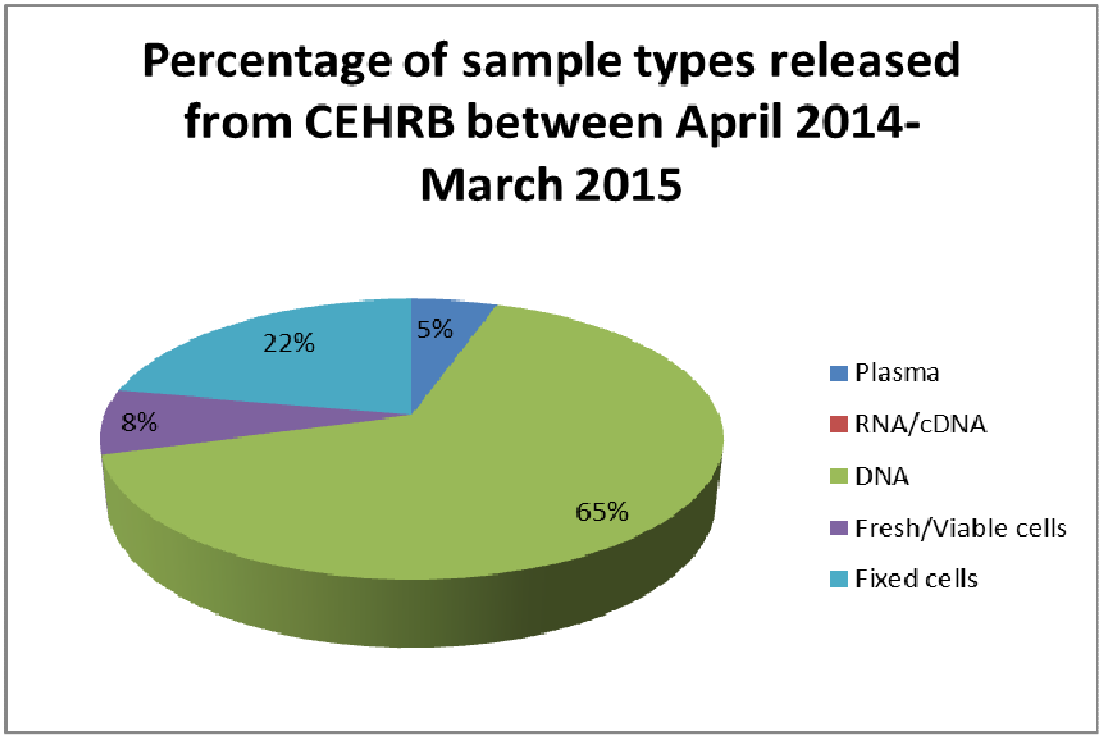
Blood and bone marrow stored as

- 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





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

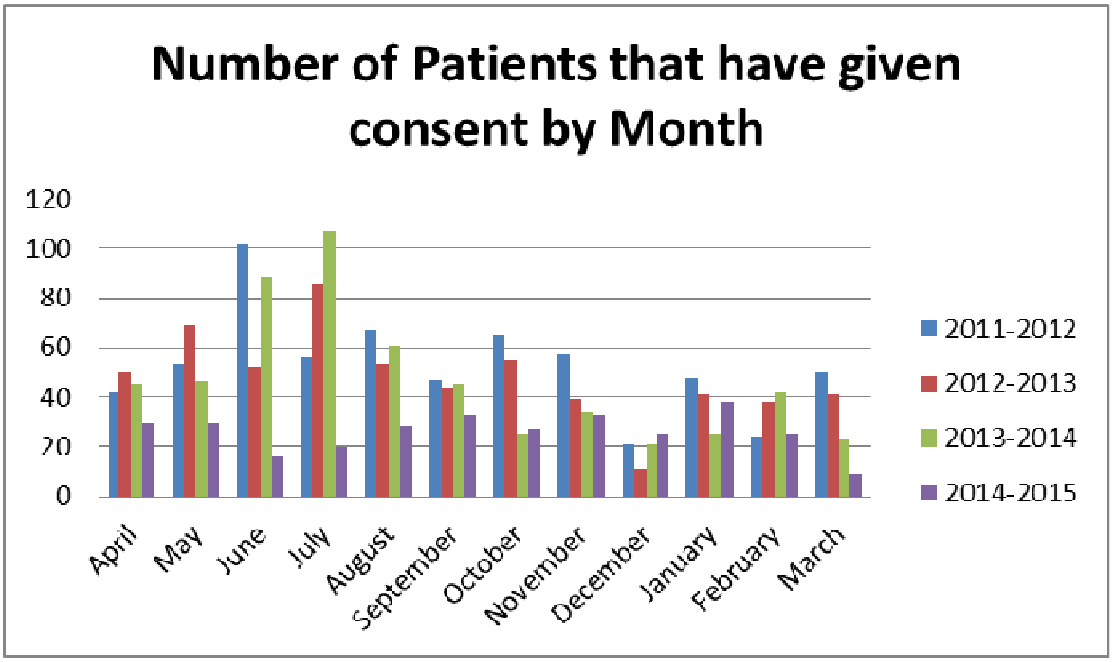
1.5 Consented patient figures

1.5.1 Monthly breakdown of patient consent

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

Hospital List

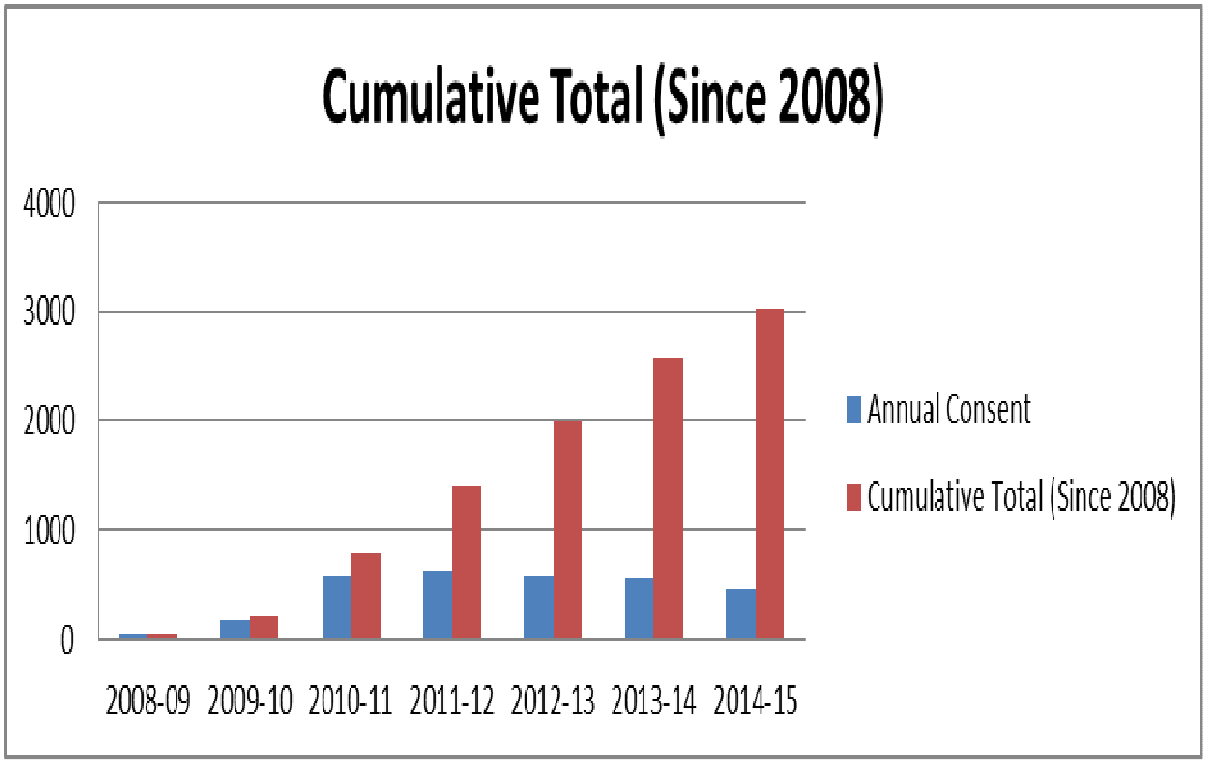
ALBR	Alexandra Hospital
CHCB	Centre for Clinical Haematology, Queen Elizabeth Hospital
EBEB	Heartlands Hospital
KGKI	Kidderminster General Hospital
NXWV	New Cross Wolverhampton
RUDU	Russell's Hall, Dudley
SDMS	Stafford District General
SDSA	Sandwell Health Care NHS Trust
UHNS	University Hospital North Staffordshire
WGCO	Walsgrave Hospital Coventry
WRWO	Worcester Royal



- 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.

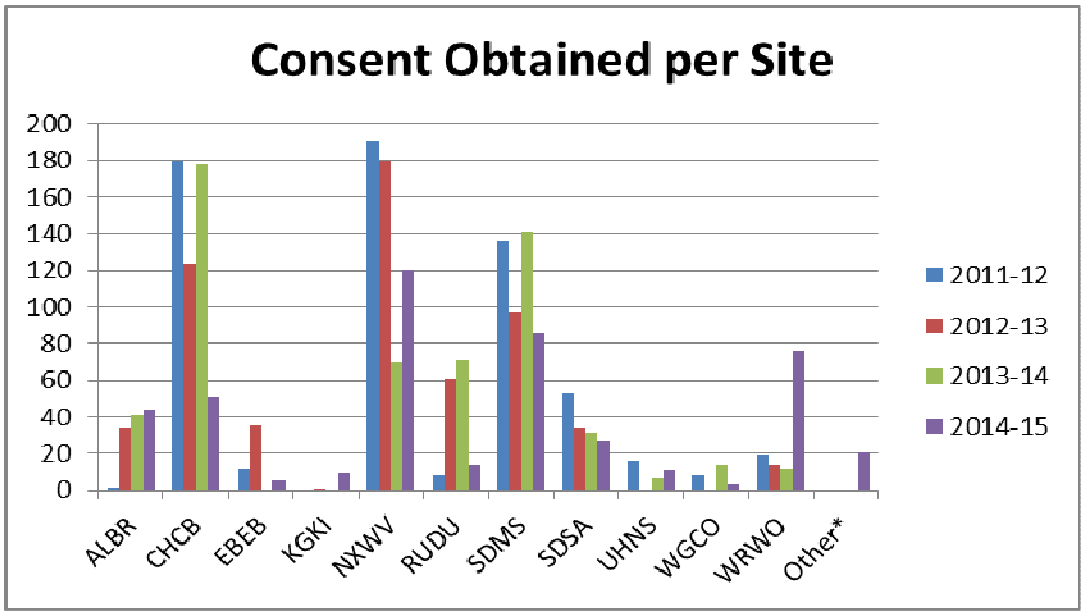
Potential recruitment opportunities per site (Based on Presentation and Follow-up samples received within period).

	2011-12	2012-13	2013-14	2014-15	Total between 2011-15
ALBR	100	121	101	83	405
CHCB	679	869	989	939	3476
EBEB	504	498	571	655	2228
KGKI	6	0	6	8	20
NXWV	558	436	604	591	2189
RUDU	232	239	230	188	889
SDMS	367	273	396	472	1508
SDSA	141	139	125	144	549
UHNS	25	30	94	86	235
WGCO	207	190	280	279	956
WRWO	263	247	274	307	1091
Grand Total	**3082**	**3042**	**3670**	**3752**	

Actual Consent obtained per site (Based on number of consent forms received within period).

	2011-12	2012-13	2013-14	2014-15	Total between 2011-15
ALBR	2	34	41	44	121
CHCB	179	124	178	51	532
EBEB	12	35	0	5	52
KGKI	0	1	0	10	11
NXWV	190	179	70	120	559
RUDU	8	61	71	14	154
SDMS	136	97	141	86	460
SDSA	53	34	32	27	146
UHNS	16	0	7	11	34
WGCO	8	0	14	3	25
WRWO	19	14	12	76	121
Other*	0	0	0	21	21
Grand Total	**623**	**579**	**566**	**468**	

*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)

	2011-12	2012-13	2013-14	2014-15
ALBR	2.0	28.1	40.6	53.0
CHCB	26.4	14.3	18.0	5.4
EBEB	2.4	7.0	0.0	0.8
KGKI	0.0	-	0.0	125.0
NXWV	34.1	41.1	11.6	20.3
RUDU	3.4	25.5	30.9	7.4
SDMS	37.1	35.5	35.6	18.2
SDSA	37.6	24.5	25.6	18.8
UHNS	64.0	0.0	7.4	12.8
WGCO	3.9	0.0	5.0	1.1
WRWO	7.2	5.7	4.4	24.8

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

Project No.	Project Title	Principal Investigator	Laboratory Address	Sponsor	Samples Sent	
					Type	Number
3	**Histone deacetylase inhibitors, a new class of anti-tumour agents in AML.**	Dr Tatjana Stankovic	CRUK Institute for Cancer Studies	Kay Kendall Leukaemia Fund	Marrow	11
18	**Prospective study of trough Imatinib levels in newly diagnosed Chronic Myeloid Leukaemia patients and its correlation with response.**	Professor Deepak Chandra	University Hospital North Staffordshire	Novartis	Plasma	30
31	**Dissecting Mechanisms of Regulation of Gene Expression in Human Leukaemia**	Prof Peter Cockerill and Constanze Bonifer	IBR Medical School, University of Birmingham	Leukaemia and Lymphoma Research	Blood	3
					Marrow	5
34	**Validation of Cytocell Ltd. FISH probes for diagnostic use in haematological oncology referrals.**	Dom McMullan	WMRGL	Cytocell	Fixed Cells	124
41	**The MYB Family of Proteins in Myeloid Disease**	Prof Jon Frampton	Institute for Biomedical Research, College of Medical and Dental Sciences, Birmingham University	Not Stated	Blood/Marrow	13

42	**Constitutional Genetics in the Aetiology and Prognosis of AML**	Dr James Allan	Newcastle-NICR	Leukaemia and Lymphoma Research	DNA	164
43	**Mechanisms of Clonal Progression and New Therapeutic Approaches in B cell Chronic Lymphocytic Leukaemia with a DNA Damage Defect**	Dr Nicholas Davies	Birmingham-ICS	Leukaemia and Lymphoma Research	Blood/Marrow	11
48	**Study of the Effects of Donor Lymphocyte Infusion on the Promotion of GVL and GVHD Responses Following Haematopoietic Stem Cell Transplantation.**	Mr Ben Abbotts	Birmingham-ICS	Leukaemia and Lymphoma Research	DNA	18
49	**Genetic definition of the BCR-ABL1- like sub-group in acute lymphoblastic leukaemia**	Ms Claire Schwab	Leukaemia Research Cytogenetics Group, Northern Institute for Cancer Research, Newcastle University	Leukaemia and Lymphoma Research	Fixed Cells	1
50	**Genomic analysis of primary refractory AML**	Professor Paul Ferguson/Susanna Akiki	BWH	University of Birmingham	DNA	26
51	**Defining Molecular Mechanisms underlying the Pathogenesis of APL and Therapy-Related Leukaemias**	Prof David Grimwade	Grimwade-Guy	Leukaemia and Lymphoma Research	DNA	15
					Fixed Cells	1

2.2 Newly approved projects that have received samples from CEHRB Between April 2014 and March 2015

Project No.	Project Title	Principal Investigator	Lab. Address	Sponsor	Samples Sent	
					Type	Number
52	**Genomic analysis of diagnostic AML patient samples to identify molecular markers of disease relapse following haematopoietic stem cell transplantation**	Professor Charles Craddock/ Dr Paul Ferguson	The Weatherall Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital		DNA	150
53	**Comparative genomic analysis of AML patients at diagnosis and relapse following stem cell transplant as part of the FIGARO Clinical trial**	Professor Charles Craddock/ Dr Paul Ferguson	School of Cancer Sciences, University of Birmingham	University of Birmingham	DNA/RNA	Collating Samples

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)

1. *IGH@* Translocations Are Prevalent in Teenagers and Young Adults With Acute Lymphoblastic Leukemia and Are Associated With a Poor Outcome. *Lisa J. Russell, Amir Enshaei, Lisa Jones, Amy Erhorn, Dino Masic, Helen Bentley, Karl S. Laczko, Adele K. Fielding, Anthony H. Goldstone, Nicholas Goulden, Christopher D. Mitchell, Rachel Wade, Ajay Vora, Anthony V. Moorman, and Christine J. Harrison.* Journal of Clinical Oncology, 2014 May; 10:32 (14): 1453-62.IGH@ translocations co-exist with other primary rearrangements in B-cell precursor acute lymphoblastic leukemia *Jeffries SJ, Jones L, Harrison CJ, Russell LJ* Haematologica, 2014 Aug;99 (8):1334-42.

2. Chronic FLT3-ITD signaling in Acute Myeloid Leukemia is connected to a specific chromatin signature. *Cauchy P, James SR, Zacarias-Cabeza J, Ptasinska A, Imperato MR, Assi SA, Piper J, Canestraro M, Hoogenkamp M, Raghavan M, Loke C, Akiki S, Clokie SJ, Richards SJ, Westhead DR, Griffiths MJ, Ott S, Bonifer C and Cockerill PN.* Cell Reports (in press 2015).

3. Genetic variation at MECOM, TERT, JAK2 and HBS1L-MYB predisposes to myeloproliferative neoplasms. *William Tapper, Amy V. Jones, Robert Kralovics, Ashot S. Harutyunyan, Katerina Zoi, William Leung, Anna L. Godfrey, Paola Guglielmelli, Alison Callaway, Daniel Ward, Paula Aranaz, Helen E. White, Katherine Waghorn, Feng Lin, Andrew Chase, E. Joanna Baxter, Cathy Maclean, Jyoti Nangalia, Edwin Chen, Paul Evans, Michael Short, Andrew Jack, Louise Wallis, David Oscier, Andrew S. Duncombe, Anna Schuh, Adam J. Mead, Michael Griffiths, Joanne Ewing, Rosemary E. Gale, Susanne Schnittger, Torsten Haferlach, Frank Stegelmann, Konstanze Do¨hner, Harald Grallert, Konstantin Strauch,Toshiko Tanaka, Stefania Bandinelli, Andreas Giannopoulos, Lisa Pieri, Carmela Mannarelli, Heinz Gisslinger, Giovanni Barosi, Mario Cazzola, Andreas Reiter, Claire Harrison, Peter Campbell, Anthony R. Green, Alessandro Vannucchi & Nicholas C.P. Cross*. Nature communications, 2015 April 7; 6:6691

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 DNaseI 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

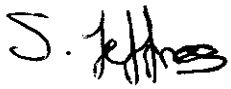
- Approve and supply samples to 5 or more projects
- Review SOPs for sample selection and send out of material, ensuring better understanding of consent by staff.
- Renewal of ethics for further 5 years.
- Secured ethical approval to receive samples for specific projects. Previous was for excess diagnostic 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.



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