MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR IMMUNOBIOLOGY
Orlando, FL
Thursday, February 20, 2020, 12:15 pm–3:00 pm

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1. Introduction

The CIBMTR Immunobiology Working Committee (IBWC) was called to order at 12:15 pm on Thursday February 20th, 2020 by Dr. Katharine Hsu. Dr. Hsu introduced the IBWC leadership and the outgoing (herself) and incoming chair Dr. Shahinaz Gadalla. Dr. Hsu continued by reviewing the goals of the working committee, areas of focus, and limitations of the IBWC. She gave a brief overview of the status of the current portfolio and number of proposals to be presented at the meeting.

2. Published and submitted papers

Due to the full agenda, the 2019 papers published or submitted were mentioned, but not presented. Eight papers were published and nine papers were submitted in the last year.

a. **IB06-05b** Role of HLA-B exon 1 in graft-versus-host disease after unrelated haemopoietic cell transplantation: A retrospective cohort study. Petersdorf EW, Carrington M, O'hUigin C, Bengtsson M, De Santis D, Dubois V, Gooley T, Horowitz M, Hsu K, Madrigal JA, Maiers MJ, Malkki M, McKallor C, Morishima Y, Oudshoorn M, Spellman SR, Villard J, Stevenson P. ***Lancet Haematology*. doi:10.1016/S2352-3026(19)30208-X. Epub 2019 Oct 25.**

b. **IB09-06s** Tang H, Hahn T, Karaesmen E, Rizvi AA, Wang J, Paczesny S, Wang T, Preus L, Zhu Q, Wang Y, Haiman CA, Stram D, Pooler L, Sheng X, Van Den Berg D, Brock G, Webb A, Pasquini MC, McCarthy PL, Spellman SR, Sucheston-Campbell LE. Validation of genetic associations with acute GVHD and non-relapse mortality in DISCOVeRY-BMT. ***Blood Advances.* 2019 Aug 13; 3(15):2337-2341. doi:10.1182/bloodadvances.2019000052.**

Epub 2019 Aug 7. PMC6693017.

c. **IB10-01c** Population Frequency of Fanconi Pathway Gene Variants and Their Association with Survival after Hematopoietic Cell Transplantation for Severe Aplastic Anemia (S Gadalla/S Savage). ***Biol Blood Marrow Transplant*. 2020 Jan 23. pii: S1083-8791(20)30022-7. doi: 10.1016/j.bbmt.2020.01.011. [Epub ahead of print]**

d. **IB10-01h** Pre-transplant short telomeres are associated with high mortality risk after unrelated donor haematopoietic cell transplant for severe aplastic anaemia. Wang Y, McReynolds LJ, Dagnall C, Katki HA, Spellman SR, Wang T, Hicks B, Freedman ND, Jones K, Lee SJ, Savage SA, Gadalla SM. ***British Journal of Haematology*. doi:10.1111/ bjh.16153. Epub 2019 Aug 19**

e. **IB10-01i** Genome-wide association study identified HLA-DPB1 as significant risk factor for severe aplastic anemia (S Savage/S Gadalla) ***Am J Hum Genet*. 2020 Feb 6;106(2):264-271. doi: 10.1016/j.ajhg.2020.01.004. Epub 2020 Jan 30.**

f. **IB15-04** Molecular correlates of socioeconomic status and clinical outcomes following hematopoietic cell transplantation for leukemia. Knight JM, Rizzo JD, Wang T, He N, Logan BR, Spellman SR, Lee SJ, Verneris MR, Arevalo JMG, Cole SW. ***JNCI Cancer Spectrum.* 2019 Dec 1; 3(4):pkz073. doi:10.1093/jncics/pkz073. Epub 2019 Sep 12. PMC6859844.**

g. **IB15-07** Multiple functional variants in the IL1RL1 region are pretransplant markers for risk of GVHD and infection deaths. Karaesmen E, Hahn T, Dile AJ, Rizvi AA, Wang J, Wang T, Haagenson MD, Preus L, Zhu Q, Liu Q, Yan L, Liu S, Haiman CA, Stram D, Pooler L, Sheng X, Van Den Berg D, Brock G, Webb A, McCarthy PL, Pasquini MC, Spellman SR, Lee SJ, Paczesny S, Sucheston-Campbell LE. ***Blood Advances*. 2019 Aug 27; 3(16):2512-2524. doi:10.1182/bloodadvances.2019000075. Epub 2019 Aug 27. PMC6712530.**

h. **IB16-01** Donor HLA-E status associates with disease free survival and transplant related mortality after non in vivo T-cell depleted HSCT for acute leukemia. Tsamadou C, Fürst D, Wang T, He N, Lee SJ, Spellman SR, Fleischhauer K, Hsu KC, Paczesny S, Verneris MR, Schrezenmeier H, Mytilineos J. ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation.* doi:10.1016/j.bbmt.2019.08.007. Epub 2019 Aug 16.**

i. **R02-40/R03-63d** KIR B donors improve the outcome for AML patients given reduced intensity conditioning and unrelated donor transplant (J Miller) **In press. Blood Advances**

j. **IB09-06b/RT09-04b** Genetic susceptibility to transplant-related mortality after unrelated donor stem cell transplant (T Hahn/L Sucheston-Campbell) **Submitted**

k. **IB09-06m** DISCOVeRY-BMT: Compare unrelated donor to Welcome Trust Case Control Consortium controls (K Onel/A Clay-Gilmour/E Karaesmen) **Submitted.**

l. **IB09-06p** DISCOVeRY-BMT: Genetics and epidemiology of Myeloid Malignancies genome-wide association (A Clay-Gilmour/K Onel/T Hahn) **Submitted.**

m. **IB14-03a** The prognostic impact of somatic mutations and levels of CXC chemokine ligands on post hematopoietic cell transplantation (HCT) outcomes in patients with myelodysplastic syndromes (MDS) (W Saber/B Dhakal) **Submitted.**

n. **IB14-04** Assessing the similarity of the T cell receptor repertoire in allogeneic hematopoietic stem cell recipients with the same single human leukocyte mismatches (EH Meyer) **Submitted.**

o. **IB15-03** Killer Immunoglobulin Receptor (KIR) gene content and pediatric acute leukemia transplant outcomes (MR Verneris/J Miller/S Cooley) **Submitted.**

p. **IB16-03** Role of recipient and donor genetic polymorphisms in interferon lambda 4 (INFL4) on outcomes after unrelated allogeneic cell transplant (S Gadalla) **Submitted.**

q. **IB18-03** Effect of HLA Class I Heterozygosity and HLA Supertypes on Outcomes Following Allogeneic HCT for Myeloid and Lymphoid Malignancies (C Camacho-Bydume/K Hsu) **Submitted.**

3. Research repository update and accrual tables *(Attachment 2)*

Steve Spellman gave a brief update on the current status of the resources and data available via the CIBMTR Research Repository. There are samples on approximately 55,000 related and unrelated donor pairs available.

4. Future/proposed studies and discussion

Dr. Sophie Paczesny reviewed the voting prioritization guidelines and introduced each of the proposal presenters.

a. Voting guidelines

HLA GENES

b. **PROP1908-01** Evaluation of the impact of HLA molecular mismatch on clinical outcomes in patients who underwent haploidentical hematopoietic stem cell transplantation (J Zou/S Ciurea) – *(Attachment 3)*

Dr. Zou presented this proposal. The hypothesis is that HLA molecular disparity quantified by mismatched eplets load (defined by the HLA MatchMaker algorithm), but not by the accumulative number of mismatched antigens or alleles, is relevant in accurate predication of clinical outcome in haploidentical transplantation. The primary objective is to investigate the impact of structural/molecular mismatch in HLA molecules on overall survival and disease-free survival. Neutrophil and platelet engraftment, acute and chronic GVHD, relapse, and non-relapse mortality are secondary outcomes of interest.

During the discussion one attendee expressed concern over the simplistic approach in that eplet and HLA mismatches are highly correlated within each locus and between loci. Another was concerned about having enough patients and suggested collaborating with EBMT to increase power.

c. **PROP1911-135** Association of immunopeptidome divergence between mismatched HLA class I alleles and outcome of 9/10 matched unrelated HCT (P Crivello/E Arrieta-Bolaños/K Fleischhauer) – *(Attachment 4)*

Dr. Fleischhauer presented this proposal. The hypothesis is that immunopeptidome divergence defines permissiveness of HLA class I mismatches in 9/10 matched HCT. Overall survival is the primary clinical endpoint of interest, while disease-free survival, non-relapse mortality, relapse, acute and chronic GVHD are secondary clinical endpoints. Patients will be stratified into 3 major groups: fully matched 10/10 vs 9/10 peptide binding motif (PBM) matched vs 9/10 PBM mismatched. Clinical associations in patients stratified according to PBM clusters will be compared with those observed in the same cohort stratified according to the previously reported HLA supertypes.

During the discussion one attendee asked for clarification regarding how mismatches were classified and whether or not observations with HLA mismatches without PBM data would be omitted. Dr. Fleischhauer responded that they will assign mismatched HLA combinations based on their corresponding PBM clusters. Regarding data omission,

Dr. Fleischhauer responded that they want to be very stringent with the data and will omit those HLA mismatch combinations without data available. She also clarified the scoring method of match versus mismatch.
Finally, one attendee commented on how this is one uniform concept for classifying supertypes as opposed to many other divergent classifications we've had before. They also suggested the team consider stratifying by conditioning intensity.

d. **PROP1911-15** HLA-Mismatches in the Setting of Post-Transplant Cyclophosphamide and Lymphomas: Are Matched Unrelated or Haploidentical Donors Still an Issue? (A Mussetti/A Sureda/A Kanate) – *(Attachment 5)*
Dr. Kanate presented this proposal. This study aims to address if the type of donor (MUD vs haploidentical) matters when a PT-Cy based strategy is used. The hypothesis is that a PT-Cy based strategy could neutralize differences between donors resulting in similar survival between haplo and MUD transplantation. This proposal has also been submitted to the Lymphoma Working Party of EBMT. If accepted by EBMT, this would nearly double the potential population for this study and would make the study feasible.
There were no further questions or comments.

SENSITIZATION AND TOLERANCE

e. **PROP1911-182** Role of Recipients' Specific anti-HLA Antibodies (RSA) in hematopoietic stem cell transplantation with Human Leukocyte antigen (HLA) mismatched donors (J Zou/K Cao/S Ciurea) – *(Attachment 6)*
Dr. Zou presented this proposal. This study aims to 1.) evaluate the incidence of RSA in HLA mismatched transplants, 2.) correlate RSA with transplant outcomes, namely GVHD and non-relapse mortality, and 3.) assess the clinical relevance of different levels of RSA/DSA. The hypotheses are that the presence of RSA in donors has a detrimental effect on transplant outcomes and that different levels of DSA at different loci is associated with inferior clinical outcome.
An attendee questioned the cost of testing for the full population. Dr. Zou commented that they plan to screen with a cheaper test that is $10/sample and then narrow down the final population from there. Later in the meeting an attendee expressed concern that the screening assays aren't as sensitive and may lead the study team to the wrong conclusion. Dr. Zou agreed that a single antigen assay would be better for specificity and that they would write a grant to cover the cost.
Another attendee asked how you will be able to tell the difference between the effect of pregnancy versus the effect of DSA. Leadership confirmed that the CIBMTR does have data on prior pregnancy that will be taken into account for the analysis.
There was discussion regarding donors that have antibodies that aren't recipient specific and that overall DSAs might be difficult to find in patients. Dr. Zou stated that patients with antibodies present that aren't recipient specific will be used as controls.
Finally, another attendee commented that it seems as if frequency of RSA in unrelated donors is low because females haven't been sensitized and asked if there was any data on this. Zou confirmed there is no data, but haplo would be best option to evaluate this question. The attendee offered that it may be best to restrict to haplo and mother/daughter and surmised that the unrelated cohort would not be informative.

OTHER-FUNDED PROPOSALS AND EXTENSIONS OF EXISITING STUDIES

f. **PROP1911-133** IB12-02D: Refinement of the T cell epitope algorithm for the definition of permissive HLA-DPB1 mismatches in allogeneic hematopoietic cell transplantation: stratification of TCE group 3 mismatches (E Arrieta-Bolaños/P Crivello/K Fleischhauer)

g. **PROP1911-172** Evaluation of Killer Cell Immunoglobulin-like Receptor - HLA class I Ligand models for donor selection- Joint Study of the Cellular Therapy and Immunobiology Working Party (CTIWP) of EBMT and the Immunobiology Working Committee (IBWC) of CIBMTR (J Schetelig/K Fleischhauer/C Chabannon)

h. **PROP1911-268** Genetic epidemiology of Adolescent, Young adult, and Adult Acute Lymphoblastic Leukemia (A Clay-Gilmour/L Sucheston-Campbell/T Hahn/E Cull)

i. **PROP1912-02** Clinical outcomes among hematopoietic stem cell transplant recipients as a function of socioeconomic status and related transcriptome differences (J Knight/J Rizzo/S Cole/K Rentscher)

DROPPED PROPOSALS

j. **PROP1904-01** The effect of HLA mismatch on the outcomes of haploidentical transplantation for hematological non-malignant disorders – *Feasibility*

k. **PROP1919-18** The impact of HLA mismatches on haploidentical hematopoietic stem cell transplant recipient outcome – *Overlap with IB19-02*

l. **PROP1911-02** Clonal hematopoiesis and hematologic ageing in long-term allo-SCT survivors- *Feasibility*

m. **PROP1911-108** An association study of Non-Hodgkin Lymphoma (NHL) subtypes and Histocompatibility Leukocyte Antigen (HLA) alleles, haplotypes, and zygosity – *Feasibility*

n. **PROP1911-140** Impact of HLA Antigen Mismatch in Haploidentical Donor Transplantation Using Post-Transplant Cyclophosphamide – *Overlap with IB19-02*

5. Studies in progress *(Attachment 7)* 1:40 pm

NK/KIR

a. **IB17-02** Donor-recipient NK cell determinants associated with survival in JMML after hematopoietic stem cell transplantation (D Lee/H Rangarahan) **Data file preparation**

b. **IB18-04** Impact of donor KIR genotype on outcome after URD TX in patients with MDS or sAML (J Schetelig/N Kröger/M Robin) **Manuscript preparation**

c. **IB19-03** Impact of the direction of NK cell alloreactivity predicted by KIR ligand mismatch on engraftment in umbilical cord blood and haploidentical stem cell transplantation (F Otegebeye/M Fernandez-Viña/M de Lima) **Protocol development**

d. **R04-74d** Functional significance of killer cell immunoglobulin-like receptor genes in HLA-matched and mismatched unrelated HCT (K Hsu) **Ongoing – <u>Update</u>**
Dr. Hsu presented this study update. This is an ongoing study looking at KIR content, KIR plus HLA combinations, and KIR alleles with HLA allele combinations. This most recent work is based on a paper published in 2017 showing a very strong interaction between KIR3DL1 alleles and HLA-Bw4 alleles associated with high relapse and lower survival. HLA-A also contains a few alleles that exhibit the Bw4 epitope, which wasn't taken into account in the first study. This study included an in-vitro analysis to measure interactions between Bw4+ HLA-A alleles and KIR3DL1. The HLA-A alleles exhibited some NK cell inhibition, but it is not to the same level as HLA-Bw4 epitopes. It was concluded that HLA-A Bw4 alleles (A*24 and A*32) contribute to NK education. HLA-A*24 can be considered as an inhibitory ligand for KIR3DL1, which impacts relapse. An effect of A*32 could not be demonstrated.

HLA GENES – CLASSICAL MATCHING

a. **IB06-05** Use of high-resolution HLA data from the NMDP for the International Histocompatibility Working Group in HCT (E Petersdorf) **Ongoing**

b. **IB14-07** Indirectly recognizable HLA epitopes (PIRCHES): a retrospective validation study on the role of indirect recognition of mismatched HLA in hematopoietic stem cell transplantation outcome (E Spierings) **Manuscript preparation**

c. **IB16-02** Use of HLA structure and function parameters to understand the relationship between HLA disparity and transplant outcomes (LA Baxter-Lowe) **Manuscript preparation – Update**

This update presentation as withdrawn prior to the meeting.

d. **IB18-01** Effect of HLA phenotypes on long term GVHD risk (C Story/M Riches/P Armisted) **Manuscript preparation – Update**
Charlotte Story presented an update. This study evaluated a novel cumulative peptide binding score derived from donor-recipient pair HLA genotypes to predict clinically significant GVHD in fully matched transplants. The hypothesis was that high affinity binding scores would increase donor T-cell activations leading to increased GVHD and lower relapse compared to low affinity binding scores. This study was negative with no significant difference found between high and low affinity binding scores in any outcomes (OS, DFS, relapse, TRM, aGVHD and cGVHD).
One attendee asked for explanation of how the scores were established. Ms. Story explained that the NetMHCpan algorithm, which is a validated algorithm, was used to determine peptide scores. Further, the population was restricted to those where the data was present for at least 4 of 6 Class I (HLA-A, B and C) alleles and 1of 2 Class II (HLA-DRB1) alleles, which were then analyzed separately.

e. **IB18-02** Impact of HLA class I risk alleles associated with AA Immune pathogenesis on allo TX outcomes in patients with SAA (D Babushok/T Olson) **Sample typing**

f. **IB19-01** The impact of ultra-high resolution HLA matching on the outcome of unrelated donor hematopoietic cell transplantation (N Mayor/S Spellman/S Marsh) **Data file preparation**

g. **IB19-02** Effect of class II HLA mismatching on the outcome of HLA-haploidentical hematopoietic cell transplantation with high dose, post-transplantation cyclophosphamide: a combined CIBMTR/EBMT analysis (S McCurdy/S Solomon/Y Kasamon/A Bashey/E Fuchs) **Data file preparation**

CYTOKINE/CHEMOKINE

a. **IB14-03c** Effect of telomere length in MDS patients without TP53/RASTK/JAK2 mutations (RC Lindsley/W Saber) **Manuscript preparation – Update**
Dr. Coleman Lindsley provided an update for this study, which leverages a previous dataset to ask questions about non-relapse mortality. Other literature in more hetergoenous populations show that telomere length in recipients was associated with non-relapse mortality. The team measured telomere length using qPCR in recipients and divided these into three categories of telomere length. Looking at the association between telomere length and patient-, disease-, and transplant-related characteristics, there are clear associations between shorter telomere length and older age. However,

there were no differences in any transplant-related characteristics. Short telomere length was independently associated with poor survival. The population was then stratified by conditioning intensity, which showed higher non-relapse mortality in shorter versus longer telomere length. In patients who recieved reduced intensity conditioning, there was increase mortality following severe GVHD in those who recieved Melphalan.

During the discussion, one attendee questioned why they were not looking at more telomere length categories that may allow them to find a stronger effect. Dr. Lindsley replied that they attempting to find the balance between parsing too much and not enough. They used an unbiased statistical approach to identify the cutpoints for this cohort, which did explain most of the variability.

Another attendee asked for clarification on the defitintion of cryptic germline mutations. Dr. Lindsley clarified taht there were patients who had no documented telomere disorder. Most of these would be considered variants of unknown signficance and the team cloned 20 novel TERT variants to address this question. These were rare variants associated clinically with shorter telomeres, younger age at diagnosis, and increased NRM.

Finally, an attendee asked what contributes to NRM. Dr. Lindsley acknowledged that this was a difficult question to answer based on the way deaths are reported. There was no specific cause of death that was associated with the finding.

OTHER GENES

a. **IB09-06/RT09-04b** Genetic susceptibility to transplant-related mortality after unrelated donor stem cell transplant (T Hahn/L Sucheston-Campbell) **Submitted – Update**

Dr. Lara Sucheston-Campbell presented an update for this study. This is a DISCOVeRY-BMT study that aims to test the effects of recipient and donor genetic variation in non-HLA regions on patient survival after HLA matched unrelated donor HCT. The population includes AML and MDS patients with unrelated donors. Donor recipient pairs were genotyped on OmniExpress in addition to a rare variant chip. This was followed by a transcriptome wide association study and Phi-C analysis, along with other bioinformatics tools available. The team recently submitted the Phase II proposal to NIH, which will include whole exome sequencing.

During the discussion one attendee questioned how they will handle the multi-ethnic dataset, which differs from the homogenous dataset previously analyzed. Dr. Sucheston-Campbell agrees that it can be difficult and there are many considerations when analyzing multi-ethnic data in that the linkage disequilibrium structure is different. Each group will be analyzed separately, and there are various methods to account for the differences when combining each of the separate analyses. Dr. Sucheston-Campbell also stated that she is comfortable with her team developing new methods to handle this data appropriately.

b. **IB10-01f** Epigenetic clock: Can this guide donor selection in HCT (S Gadalla/S Savage) **Manuscript preparation – Update**

Dr. Shahinaz Gadalla presented an update for this study, which examines aging as a marker for donor selection. The objectives are to 1.) evaluate donor DNA-methylation age (i.e epigenetic clock) or age acceleration before HCT as a predictor of survival post-HCT in patients with severe aplastic anemia and 2.) describe dynamics of DNA-methylation age in the first 100 days post-HCT and the effect of those changes on survival post-HCT. The team used the MethylationEpic array and GrimAge clock to

measure methylation age, methylation age acceleration (deviation from expected for age), and post-HCT methylation aging (difference between donor pre- and post-HCT methylation age). This analysis found no added value for donor GrimAge over chronological age in relation to survival; however, donors with high GrimAge acceleration may predispose patients to higher mortality. Post-HCT samples showed significant GrimAge acceleration, and an increase of greater than or equal to 15 years was associated with decreased OS.

During the discussion, one attendee asked if there was any correlation between post-transplant age and actual age of the recipient. Dr. Gadalla stated there was no correlation of age and was then asked if that was of any concern. She stated that she would only be concerned if the acceleration was associated with age, but that was not the case here.

Another attendee questioned how long the patients were followed. Dr. Gadalla stated they had up to 20 years of follow-up for patients and that most acceleration occurs within one year. A follow-up question was asked regarding the correlation with chronic GVHD. The team didn't have enough numbers to fully evaluate the association.

There was additional interested in how age was defined. Dr. Gadalla explained that the clock is a validated algorithm that uses machine learning approaches to identify certain markers that can identify and predict a person's age.

Finally, Dr. Gadalla was asked about other epigenetic markers to be analyzed or other mitochondrial genetics that could potentially guide donor selection. She stated that those are definitely questions that are of interest and have yet to be answered.

c. **IB14-05** mtDNA haplotypes and unrelated donor transplant outcomes (M Verneris/J Ross) **Manuscript preparation**

d. **IB17-03** Identification of genomic markers of post hematopoietic cell transplantation (HCT) outcomes in patients with myelofibrosis: A pilot study (W Saber/S Gadalla) **Data file preparation**

e. **IB17-04** Epigenetic profiling of unrelated donor-recipient pairs to improve donor selection during HCT transplants (S Beck/K Peggs/V Rakyan/A Webster) **Analysis**

f. **IB18-06** Clonal mosaicism and HCT outcomes in patients with acute leukemia and myelodysplastic syndromes (S Gadalla/T Hahn/L Sucheston-Campbell) **Manuscript preparation – <u>Update</u>**

Dr. Shahinaz Gadalla presented an update for this study, which is a collaboration with the DISCOVeRY BMT team. The objectives are to 1.) characterize clonal mosaic chromosomal alterations in acute leukemia and MDS patients, 2.) compare the pattern of detected somatic mosaicism by disease status, and 3.) evaluate the effect of detected clonal mosaic chromosomal alterations on patient outcomes. Results showed the percentage of chromosomal alterations was 5% in ALL, 15% in AML, and 35% in MDS. The team further looked into similarities and differences in de-novo and therapy related AML and MDS. They found that patients in remission but that carry copy intron loss of heterozygosity in chromosome 17p have inferior survival that is similar to patients with advanced disease. There is ongoing work to define the prognostic impact and refine risk stratification for patients with ALL, AML, and MDS.

During the discussion an attendee asked if the outcome differences were related to relapse and if the same is true for those treated without transplant. Dr. Gadalla confirmed that in AML there are clear differences in relapse incidence; however, it is unclear if the same is true for those who do not receive a transplant. We can't be sure if

these changes are occurring after chemotherapy or at diagnosis. This question can't be answered unless we have samples at diagnosis and transplant.
Another attendee asked about the specifics of the assay. Dr. Gadalla stated it was very sensitive and can detect a change as small as 5%.
Finally, an attendee questioned whether they had looked at p53 as a control. Dr. Gadalla agreed this would be interested to look at, but they do not have the sequence data to allow them to do so.

g. **IB18-07** Donor and recipient genomic associations with acute GVHD (V Afshar-Khargan) **Sample typing**

SENSITIZATION AND TOLERANCE

a. **IB19-04** Impact of donor HLA on transplant outcomes in NPM1 mutated AML (R Narayan/E Meyer/Y Chen) **Protocol development**

ONGOING AND OTHER-FUNDED STUDIES

a. **R02-40/R03-63** Acquisition of natural killer cell receptors in recipients of unrelated transplant (J Miller/E Trachtenberg) **Ongoing**
b. **IB06-05** Use of high-resolution HLA data from the NMDP for the International Histocompatibility Working Group in HCT (E Petersdorf) **Ongoing**
c. **IB09-01** Clinical importance of minor histocompatibility complex haplotypes in umbilical cord blood transplantation (E Petersdorf) **Ongoing**
d. **IB09-03** Clinical relevance of cytokine/immune response gene polymorphisms in umbilical cord blood transplantation (E Petersdorf) **Ongoing**
e. **IB09-05** Identification of functional single nucleotide polymorphisms in umbilical cord blood transplantation (E Petersdorf) **Ongoing**
f. **IB09-07** Clinical significance of genome-wide variation in unrelated HCT (E Petersdorf) **Ongoing**
g. **RT09-04/IB09-06i** DISCOVeRY-BMT: Recip, Donor Genome-wide association study Interaction with Conditioning Intensity (Myeloablative/Reduced intensity conditioning), Total body irradiation, Disease status (E Karaesemen/L Sucheston-Campbell/T Hahn) **Manuscript preparation**
h. **IB09-06j** DISCOVeRY-BMT: Additional analysis of major histocompatibility complex single nucleotide polymorphisms (S Spellman/L Sucheston-Campbell) **Manuscript preparation**
i. **IB09-06m** DISCOVeRY-BMT: Analysis of X chromosome single nucleotide polymorphisms (S Spellman/L Sucheston-Campbell) **Manuscript preparation**
j. **IB09-06o** DISCOVeRY-BMT: Genetics and Epidemiology of Myeloid Malignancies candidate gene (L Suchestion-Campbell/E Karaesmen/A Clay-Gilmour/T Hahn) **Manuscript Preparation**

DROPPED STUDIES

a. **IB18-05** Imputation of KIR in genome-wide association study and the association of KIR-HLA with outcomes following alloHCT In AML and MDS (C Camacho-Bydume/L Sucheston-Campbell/S Leslie/K Hsu) – *Lack of progress*

b. **IB19-05** Impact of donor signal-regulatory protein alpha polymorphism on outcomes of allogeneic hematopoietic stem cell transplantation (J Danska/F Lakkis) – *Lack of funding*

6. Closing Remarks

Dr. Hsu adjourned the meeting and thanked members for attending.

Working Committee Overview Plan for 2020-2021

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2020	Hours allocated 7/1/2020-6/30/2021	Total Hours allocated
HLA GENES							
IB12-02d: TCE group 3 re-analysis	Analysis	Manuscript Preparation – June 2021	130	60	0	80	**80**
IB16-02: HLA structure and function parameters in the relationship between HLA disparity and HCT outcomes	Manuscript Preparation	Published – June 2021	40	50	40	10	**40**
IB18-01: Effect of HLA phenotypes on long term GVHD risk	Manuscript Preparation	Published – June 2021	70	80	70	10	**80**
IB18-02: Impact of HLA class I risk alleles associated with AA Immune pathogenesis on allo TX outcomes in patients with SAA	Data File Preparation	Submitted – June 2021	250	250	120	150	**250**
IB18-03: Effect of HLA Class I Heterozygosity and HLA Supertypes on Outcomes Following Allogeneic HCT for Myeloid and Lymphoid Malignancies	Manuscript Preparation	Submitted – June 2020	20	20	20	0	**20**
IB19-01: Impact of ultra-high resolution HLA matching on outcome of URD HCT	Manuscript Preparation	Submitted – September 2020	70	70	0	70	**70**

IB19-02: Effect of HLA Class II mismatching on outcome of HaploHCT with high dose PTCy	Data File Preparation	Submitted – June 2021	230	230	100	130	**230**
IB19-02b: HLA-B leader in Haplo HCT	Analysis	Submitted – June 2021	90	90	0	90	**90**
IB20-01: Immunopeptidome-based matching	Protocol Pending	Analysis – June 2021	330	200	0	200	**200**
IB20-02: HLA MatchMaker in HaploHCT	Protocol Pending	Analysis – June 2021	230	100	0	100	**100**
CYTOKINE/CHEMOKINE							
IB14-03a: CXC chemokine ligands on MDS HCT outcomes	Submitted	Published – December 2020	10	**10**	10	0	**10**
IB14-03c: Effect of telomere length and telomerase gene mutations on allogenic stem cell transplantation outcomes in MDS	Submitted	Published – December 2020	10	**10**	10	0	**10**
NK/KIR							
IB17-02: Donor-recipient NK cell determinants associated with survival in JMML after HSCT	Data File Preparation	Submitted – June 2021	150	**150**	40	110	**150**
IB18-04: Impact of donor KIR genotype on outcome after URD TX in patients with MDS or sAML	Manuscript Preparation	Published – June 2021	20	**30**	20	10	**30**

IB18-04b: Impact of donor KIR genotype on outcome after URD TX in patients with MDS or AML	Data File Preparation	Analysis – June 2021	130	**20**	0	20	**20**
IB19-03: KIR ligand mismatch in UCB and haplo	Protocol Development	Manuscript Preparation – June 2021	330	**260**	100	160	**260**
OTHER GENES							
IB10-01f: Epigenetic clock and outcome	Analysis	Submitted – June 2021	70	**70**	50	20	**70**
IB14-05: mtDNA haplotypes and unrelated donor transplant outcomes	Manuscript Preparation	Published – June 2021	20	**30**	20	10	**30**
IB16-03: Role of genetic polymorphisms in INFL4 after URD HCT	Submitted	Published – December 2020	0	**0**	0	0	**0**
IB17-03: Identification of genomic markers of post-HCT outcomes in patients with myelofibrosis	Data File Preparation	Submitted – June 2021	180	**180**	50	130	**180**
IB17-04: Improve donor selection during HCT using epigenetic signatures	Analysis	Manuscript Preparation – June 2021	90	**20**	10	10	**20**
IB18-06: Clonal mosaicism in acute leukemia	Manuscript Preparation	Submitted – June 2021	70	**70**	20	50	**70**

IB18-07: Donor and recipient genomic associations with acute GVHD	Data File Preparation	Analysis – June 2021	230	**100**	100	0	**100**
SENSITIZATION AND TOLERANCE							
IB19-04: Impact of donor HLA on transplant outcomes in NPM1 mutated AML	Data File Preparation	Submitted – June 2021	230	**230**	100	130	**230**

Oversight Assignments for Working Committee Leadership

Sophie Paczesny	**IB16-03:** Role of recipient and donor genetic polymorphisms in interferon lambda 4 (INFL4) on outcomes after unrelated allogeneic cell transplant
	IB17-03 Identification of genomic markers of post hematopoietic cell transplantation (HCT) outcomes in patients with myelofibrosis (MF): A pilot study
	IB18-04 Evaluation of the impact of donor KIR genotype on outcome after unrelated donor transplantation in patients with myelodysplastic syndromes or *secondary* acute myeloid leukemia
	IB18-04b Evaluation of the impact of donor KIR genotype on outcome after unrelated donor transplantation in patients with myelodysplastic syndromes or acute myeloid leukemia
	IB18-06 Clonal mosaicism and HCT outcomes in patients with acute leukemia and myelodysplastic syndromes
	IB18-07 Donor and recipient genomic associations with acute GVHD
	IB20-02 HLA-mismatches in the setting of post-transplant cyclophosphamide and lymphomas: Are a matched unrelated or haploidentical donors still an issue?
Shahinaz Gadalla	**IB12-02b** Refinement of the T cell epitope algorithm for the definition of permissive HLA-DPB1 mismatches in allogeneic hematopoietic cell transplantation: stratification of TCE group 3 mismatches
	IB14-03a The levels of CXC chemokine ligands on post hematopoietic cell transplantation outcomes in patients with myelodysplastic syndromes
	IB14-03c Impact of telomere length and telomerase gene mutations on allogeneic stem cell transplantation outcomes in myelodysplastic syndrome
	IB17-02 Donor-recipient NK cell determinants associated with survival in JMML after hematopoietic stem cell transplantation
	IB19-03 Impact of the direction of NK cell alloreactivity predicted by KIR ligand mismatch on engraftment in umbilical cord blood and haploidentical stem cell transplantation
	IB19-04 Impact of donor HLA on transplant outcomes in NPM1 mutated AML

	IB20-03 Evaluation of the impact of HLA molecular mismatch on clinical outcomes in patients who underwent haploidentical hematopoietic stem cell transplantation
Steven Marsh	**IB10-01f** Epigenetic clock: Can this guide donor selection in HCT
	IB16-02 Use of HLA structure and function parameters to understand the relationship between HLA disparity and transplant outcomes
	IB17-04 Epigenetic profiling of unrelated donor-recipient pairs to improve donor selection during HCT transplants
	IB18-01 Effect of HLA phenotypes on long term GVHD risk
	IB18-02 The impact of HLA class I risk alleles associated with AA Immune pathogenesis on allogeneic transplant outcomes in patients with severe acquired aplastic anemia
	IB18-03 The Effect of HLA Class I Heterozygosity and HLA Supertypes on Outcomes Following Allogeneic Hematopoietic Cell Transplant for Myeloid and Lymphoid Malignancies
	IB19-01 The impact of ultra-high resolution HLA matching on the outcome of unrelated donor hematopoietic cell transplantation
	IB19-02 Effect of class II HLA mismatching on the outcome of HLA-haploidentical hematopoietic cell transplantation with high dose, post-transplantation cyclophosphamide
	IB19-02b The role of HLA-B leader dimorphism on outcome after haploidentical HCT
	IB20-01 Association of immunopeptidome divergence between mismatched HLA class I alleles and outcome of 9/10 matched unrelated HCT