BSHI
British Society for Histocompatibility and Immunogenetics
Promoting Science and Education in Transplantation

NEWSLETTER 127

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Science Watch

S. Charonis, L. James and A. Georgopoulos. Scientific Reports volume 12, Article number: 8074 (2022)

SARS-CoV-2 in silico binding affinity to human leukocyte antigen (HLA) Class II molecules predicts vaccine effectiveness across variants of concern (VOC)

Reviewed by Anthony Poles, BSHI Research Chair, NHSBT, Bristol

This publication explores the use of a predictive model to evaluate efficacy of mRNA-based vaccines against five variants of SARS-Cov-2 virus. The study evaluated peptide binding affinity with a selection of 66 HLA-Class II (DRB1, DQB1, DPB1) alleles that were defined as common. The definition of common was >0.01 frequency using Global Allele frequencies *(http://www.allelefrequencies.net)*. In addition to the wildtype SARS-Cov-2 virus, viral variants analysed included Alpha, Beta, Gamma, Delta, and Omicron.

The proposed epitopes for analysis were defined as consecutive linear 15-, 18- and 22-mers peptide sequences selected from the spike protein sequence from each variant. Each linear peptide was treated as a potential epitope which was subsequently analysed for binding affinity with each HLA allele. The epitopes were selected as overlapping sequences using a sliding window approach, detailed in Figure 1.

Supported by
Alpha Biotech Ltd,
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Savant Ltd,
StemCell Technologies,
VH Bio Ltd,
CareDX
and Miltenyi Biotec.

Binding affinities for all potential peptides (five million) with the 66 different HLA-Class II alleles were performed. Subsequent analysis only used combinations of specific peptides that were predicted to possess higher affinity with HLA-Class II alleles, as these would be more likely to enable CD4+ T-cell response.

A literature review gathered data on vaccine effectiveness for two doses of mRNA vaccines (BNT162b Pfizer & mRNA-1273 Moderna). Results are summarised in Tables 3 and 4, to summarise effectiveness was greater against the wildtype virus and declined to a lesser degree against Alpha, Beta, Delta, and Omicron respectively.

Data analysis was based on the hypothesis that the clinical effectiveness of a vaccine caused by different variants was dependant on the level of binding affinity of the various variant specific proteins presented by the common HLA-Class II alleles. To test the hypothesis, a linear regression analysis was performed where the dependant variable was clinical effectiveness, and the independent variable was the percentage of HLA high affinity bindings using the in-silico method. A statistical analysis using the Monte Carlo approach was also performed which tested the data and potential association further.

The association between vaccine effectiveness and HLA binding affinity is presented in Figure 2 which illustrates the close association with predicted efficacy of vaccine using the HLA binding affinity data. The data also demonstrates the reduction in efficacy of the vaccine with the different variants in combination with the data from HLA binding affinity. The relative binding affinity for each allele was also presented which provided specific information for each allele assessed, ranging from high binding affinity for DPB1*04:02 compared to least relative binding affinity for DRB1*01:02.

Learning points

The model developed underlines the use of bioinformatics to aid analysis of the potential immune response, specifically in this case to specific vaccine proteins.

Data from such studies may enable more focussed vaccine development, such as evaluation of the 18 epitopes shared by all variants that possessed high affinity to the common HLA-Class II alleles.

This model demonstrated good correlation between estimated efficacy and published efficacy of the vaccine and, in addition, also permitted analysis to determine efficacy against emerging variants.

Please note study limitations detailed at end of the publication

End

Editorial

Welcome to the Winter edition of the Newsletter, which is packed full of content to see you through the dark nights ahead! With that in mind, I will keep this brief; our bursary recipients have outdone themselves in providing detailed coverage from the BSHI 2022 conference, and there are several topical articles covering vaccine effectiveness, the use of Imlifidase, and sustainability in transplantation from Anthony Poles, Brendan Clark and me.

We also have a chance to 'visit' Leeds in the first of our virtual lab visits. The pride the writers have for their lab and team is woven throughout the article, showing strong *esprit de corps* and an excellent advertisement for the lab. The aim of these segments was to foster a sense of community between our different labs; I hope this example spurs others into also submitting a virtual lab visit to the Newsletter.

Finally, on behalf of the Editorial Team and the past Editors, I'd like to recognise the huge contribution our publisher, Stephen Bates of Ptarmigan Design, has made to the Society. Steve has had a long partnership with the Newsletter, always presenting our material well and being exceedingly patient with any delays or last-minute changes! With his upcoming retirement in December, this super-sized edition marks the final issue he will produce for us. Thank you, Steve!

Mohammad Ali Rafique

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Chair's Report

Dear Colleagues

Sadly, on 8th September Her Majesty Queen Elizabeth II passed away after a reign of over 70 years. The Nation entered a period of official mourning which culminated in the State Funeral on Monday 19th September. The H&I community marked their respects to the late Queen at the start of the BSHI Conference on 12th September, with a minute's silence and reflection of a lifelong commitment to public service. Also, since I last wrote in the Newsletter, we are on our third Prime Minister. The UK has been on a roller-coaster ride and there's certainly not been a dull moment. I note that recently the word **"Permacrisis"** meaning an extended period of instability and insecurity, especially one resulting from a series of catastrophic events has been named one of Collins "Word of the Year 2022". Alex Beecroft, head of Collins Learning added it "sums up just how truly awful 2022 has been for so many people". It is true we are facing some challenging times as we head towards winter; however, we have a bumper edition of the Newsletter for you enjoy and a chance to remind you of our first face to face BSHI conference since 2019 – something to be celebrated!!!

I would like to thank all the contributors who have put together a fantastic summary of the sessions at this year's BSHI conference. This was my first conference as BSHI Chair, and it was so lovely to see so many faces (old and new) in the room together. I thoroughly enjoyed the science that was so wonderfully presented by all our excellent speakers and the chance to catch up with friends and make new ones during the conference dinner and networking event.

Also, in this edition of the newsletter, we have the first of what we hope will be a series of virtual lab tours. If you've ever wondered what it's like to work in Leeds (and believe me, I have on numerous occasions!!) Katherine and Adrienne's report will give you an insight into the varied transplant programmes supported and great innovative work the lab is undertaking.

Science Watch, by Anthony Poles reviews the paper "SARS-CoV-2 in silico binding affinity to human leukocyte antigen (HLA) Class II molecules predicts vaccine effectiveness across variants of concern (VOC)" by authors Spyros A. Charonis, Lisa M. James & Apostolos P. Georgopoulos. The paper explores the use of a predictive model to evaluate efficacy of mRNA-based vaccines against five variants of SARS-Cov-2 virus.

I'm sure many of you will be aware that NICE have recently approved a new therapeutic agent, Imlifidase, as a desensitisation treatment for highly sensitised adults awaiting a kidney transplant. H&I experts are working with transplant colleagues to develop guidelines on the safe implementation of Imlifidase for kidney transplantation, which will be ratified through BSHI/BTS. To find out more about this exciting development and the implications for H&I laboratories, please take a look at the article **Imlifidase: The solution (…and a problem?)** by Brendan Clark and Adrienne Seitz

Ali Rafique attended the 50th Anniversary Congress of the British Transplantation Society (BTS) in Belfast and has submitted an article on sustainability in transplantation reviewing an emotive debate on how 'organ allocation should be redirected locally to minimise the carbon footprint of transplantation.' In his article Ali also describes how clinical laboratories can help to move towards more sustainable practices, which I'm sure will be critical for healthcare provision in the future.

On 2nd November the BTS announced with sadness the death of Professor Sir Peter Morris at the age of 88. Peter worked for many years as the Nuffield Chair of Surgery in Oxford where he established the Oxford transplant programme. He was the third Honorary President of BSHI from 1994-1996 and you can read more about Sir Peter's contribution to transplantation in James Douglas' History of BTS and Presidents' biographies and listen to Sir Peter talking about the early days of BTS and transplantation in the BTS 50th Anniversary film, all found here https://bts.org.uk/about-bts/fifty-years-of-the-bts/.

Finally, the nights are certainly drawing in now and the Festive Season will soon be upon us. I hope everyone has the chance to spend time over Christmas with those that are near and dear to you, and I wish you a Happy 2023.

Deborah Sage

End

Carla Rosser - BSHI Secretary Report

BSHI Secretary Report

BSHI Main Committee meeting – 12th September 2022

BSHI Committee in attendance:

Chair: Deb Sage (DS); *Secretary:* Carla Rosser (CR); *Treasurer Elect:* Corinna Freeman (CF): *Chair BEB:* Sarah Peacock (SP); *Membership Secretary:* Emily Ryan (ER); *Meetings Secretary:* Helena Lee (HL); *Ordinary members:* Rachel Smith (RS), Franco Tavarozzi (FT) and Jessie Martin (JM). *Apologies from Treasurer:* Mian Chen (MC) and *Chair BPAG:* Richard Battle (RB).

BSHI Chair's Report [DS]:

Academy of Healthcare Science Professional Bodies Council - A review of standards is taking place and a workshop is due to be held to discuss views. DS has contacted several H&I colleagues about writing a contribution to the VOX newsletter – timeline to be confirmed. The AHCS has appointed an Equality, Diversity and Inclusivity (EDI) ambassador. Potential initiatives being created to develop future leaders.

NHS England - Reviewing workforce information in the healthcare system.

Healthcare Professions Council - Review of HCPC standards survey received.

Secretary's Report [CR]:

Committee elections - Turnout of 47% to vote for the four positions advertised in May 2022. Dan Eggleston will join the committee after the 2022 AGM as FT steps down. Requests for nominations to the TDE were recently requested but elections are not required for these posts.

BSHI 2022 Bursaries - There were 25 bursaries awarded for BSHI 2022 at a cost of £5,600.

ACS Assessor: An application for Tim Key to become an ACS assessor was supported by the committee.

Website improvements - The certificate of competency and BSHI Diploma application forms are now web forms that can be completed on the website.

MailChimp performance - Changes have been made to the mail out email settings and hopefully have reduced the issues with emails reaching members. This will continue to be monitored.

Treasurer's Report [MC absent]:

No update.

Membership Secretary [EH]:

Membership - We have 362 active BSHI members with 12 new members since the last meeting.

Invoices - Introduced a reconciliation process with EBS to ensure timely invoicing and payment for job adverts and group memberships. Agreed that, in future, all job adverts with the same job reference will be allowed one reminder/ re-advert email without further payment.

Continued on next page

BSHI Committee Members (from 2021 AGM)

Chairperson: *Deborah Sage*
Start: AGM 2020 Finish: Sept 2023
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Secretary: *Dr Carla Rosser*
Start: AGM 2021 Finish: AGM 2024
Email: secretary@bshi.org.uk

Treasurer: *Mian Chen*
Start: AGM 2022, End AGM 2025
Email: treasurer@bshi.org.uk

Treasurer Elect: Corinna Freeman

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Chair BEB: *Sarah Peacock*
Start: AGM 2018 Finish: AGM 2024
sarah.peacock@addenbrookes.nhs.uk

IT Consultant: *James Robinson*

Archivist: *Richard Battle*

BSHI Secretary Report... continued

Meeting Secretary's Report [HL]:

EBS Conference update - There were 149 attendees at the time of the report but there have been some late registrations. The exhibition hall is full with 14 trade stands and all lunchtime sessions have been filled. Anticipating a small profit.

National Mourning for Her Majesty, Queen Elizabeth II - It was agreed by the committee that the conference should proceed as planned and delegates will be emailed to confirm.

BSHI AGM - To be held on 07/12/2022 from 10:00-13:00 and will include a patient talk along with the Next Generation Scientist winner presentation.

BSHI Education Board (BEB) Chair's Report [SP]:

RE Update - The RE have SIGs in the planning stage. They have been updating their Terms of Reference (TOR) and the constitution was also updated to reflect current practice.

IBMS-BSHI relationship - The second meeting was held in June. The BSHI diploma will be reviewed alongside the specialist IBMS portfolio to streamline the process for those wishing to complete the diploma; subject to IBMS approval.

BSHI Professional Advisory Group (BPAG) Chair's Report [RB absent]:

PAG Representative reports – a full report on the Kidney Advisory group (KAG) was provided.

Consultations update – no open consultations at the moment. Uncertainty remains regarding the impact of the MDR/IVDR law change in 2023. A consultation is expected in October 2022 from HCPC standards.

Workforce Planning – workforce data was presented to the H&I Network group in July.

BSHI Alloantibody guidelines – met in September and progressing.

BSHI Coeliac guidelines – to be reviewed by the committee.

Equality, Diversity and Inclusion (EDI):

General – Discussion about how/if BSHI should collect EDI data on BSHI membership. To be considered at future meetings.

Professional Bodies Council – EDI data is being collected from other member organisations and DS will provide an update in the future

Any Other Business:

Newsletter – Ali has suggested that "virtual lab visit" articles may be a useful way to generate new content for the newsletter (Newsletter 125).

End

Advertorial

LABScreen™ Extended Panels: Disentangling epitopes from antibody profiles

Mohammad Ali Rafique, VH Bio Ltd.

Introduction

The success of transplantation is inextricably linked with measures implemented to reduce rejection. Human leukocyte antigens (HLA) have a crucial role in defence via antigen presentation but, in the context of transplantation, are responsible for recognition of non-self thus initiating an immune response.

Patients can form anti-HLA antibodies in response to pregnancy, transfusion, or against transplant-mismatched antigens; however, these may also form following pro-inflammatory events such as surgery, trauma, infections, and vaccinations. Antibody characterisation remains an integral part of histocompatibility testing to support clinical transplantation.

HLA antibody screening

Unacceptable antigens (UAs) to which there is pre-existing antibody reactivity can be defined from patient antibody profiles; organs expressing UAs are censored during organ allocation. For highly sensitised patients (HSPs), this limits the donor pool creating a barrier to timely transplantation; instead, definition of antibody-epitope reactivity may allow for a reduction in the number of listed UAs.

Comparison between a donor's HLA type and the patient antibody profile have been increasingly used to perform virtual crossmatches (VXM); these represent a risk assessment tool capable of replacing the need for physical crossmatching assays and their accompanying delay to solid organ transplantation.

The association of donor-specific antibodies (DSA) with subsequent graft loss suggests that routine post-transplant screening can lead to early intervention to improve graft outcomes.

From antigens to epitopes

The number of known HLA alleles now stands at over 30,000 with that number increasing year on year, however only ~30% of these have been reported commonly in unrelated individuals (*CWD catalogue v2.0.0, Mack et al 2013*).

The classic LABScreen™ Single Antigen Bead (SAB) products have been designed to give breadth of antigen coverage across all serological specificities. However, while multiple HLA alleles can encode a specific serological group (e.g., the HLA-B44 antigen is encoded by B*44:02 and *44:03 alleles), scientific theory has moved beyond antigens to epitopes.

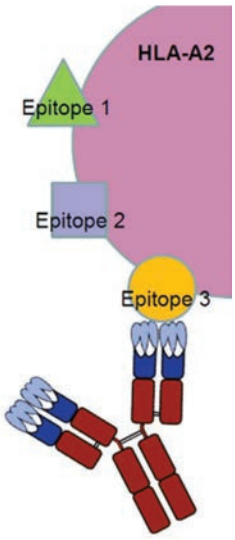

Figure 1. Illustrative schematic showing a single antigen (HLA-A2) with several different epitopes.

Antigens refer to any substance capable of stimulating an immune response, and the specific parts that interact with antibodies are called epitopes; these can either be small sequences of amino acids (linear), or unique sites formed by protein tertiary structure (conformational). Functional epitopes (*Duquesnoy, 2006*) interact with antibody paratopes, therefore changes in amino acid sequence directly impact antibody binding affinity/strength.

One antigen will display many different epitopes, which may be specific to the antigen alone (private) or found on several antigens (public). Public epitopes shared by several HLA antigens help explain cross-reactivity between different antigen groups (*Rodey et al, 1987*).

Extended panels

One Lambda are renowned for introducing new technology to advance the field of HLA and remain the global leader for HLA antibody detection. Listening to customers, they released the next evolution in HLA diagnostic reagents.

LABScreen™ Extended Panels	Compatible instruments
Supplement	Luminex 200
ExPlex	Luminex 200, FlexMAP3D

In terms of use, the Extended Panels fit easily into the laboratory workflow by following the same setup and analysis protocols as other products in the LABScreen™ range.

When used in concert with the classic LABScreen™ SAB products, they form the largest panel for detection of HLA antibodies, including many alleles not displayed by competitor products.

Advertorial

LABScreen™ Extended Panels: Disentangling epitopes from antibody profiles

Mohammad Ali Rafique, VH Bio Ltd.

Why use them?

The Supplement and ExPlex products aim to benefit transplant patients through improved risk management. They increase the depth of antigen coverage whilst also developing breadth and depth of epitope coverage; as such, they better complement molecular typing results.

The patient populations most likely to benefit from these products include multiparous females, patients receiving second or third transplants, HSPs, and patients that received transplants from donors with incomplete typing.

This is primarily achieved due to improved antibody profiling for better informed VXMs, increased accuracy in DSA monitoring, identification of permissible alleles, and the use of epitope-based analyses to clarify antibody-epitope reactivity.

As the number of alleles available on the panels have increased, further reducing the likelihood of missed reactivity, there is also increased representation for ethnically diverse alleles; this can help promote health equity, especially important given increased HLA diversity within local patient populations. Figure 2 uses global heat-maps to illustrate the frequency of population-specific alleles by geographical region.

Hands-on laboratory experience

Several labs have presented their experience with these extended panels, which can be viewed via the One Lambda Learning Centre.

ASHI 2021 - Dr Kelley Hitchman
San Antonio, USA,

EFI 2022 - Dr Rob Liwski
Halifax, Canada.

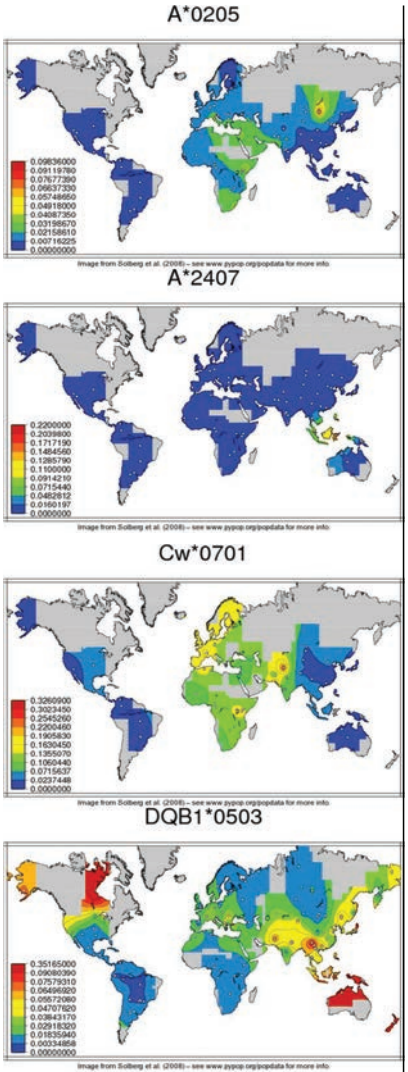

Figure 2. Population frequencies for several LABScreen™ Extended Panel alleles, (Solberg, 2008).

Examples in practice

This first example of LABScreen™ Extended Panels in clinical use re-examined a sensitised patient using ExPlex. Reactivity was detected against B*48:02 and C*16:02 alleles, despite B*48:01 and C*16:01 alleles (present on classic LABScreen™ SAB panels) remaining negative.

The additional allele information provided by ExPlex usage enabled identification of two epitopes covering most of the profile, 163LW and 80K, which are not displayed by either B*48:01 or C*16:01 antigens.

This case highlights the caution required when using surrogate markers of reactivity; while they are low-frequency, B*48:02 and C*16:02 are still common therefore could have presented in a potential donor.

This second example covers an unexplained positive flow crossmatch re-examined using the LABScreen™ Extended Panels. Previous antibody screening had detected reactivity against B*57:01, B*57:03, and B*58:01 antigens, which were not DSAs.

Using ExPlex, antibodies were detected against the donor A*02:05 antigen while other HLA-A2 antigens (A*02:01, *02:03 and *02:06) remained negative. Epitope-based analysis revealed the likely cause for this profile to be antibodies specific for the 62GRN epitope, which is displayed by A*02:05, B*57:01, B*57:03 and B*58:01 antigens.

Like the previous example, A*02:05 is not uncommon and can present in many populations but is not present on classic LABScreen™ SAB panels.

What next?

VH Bio Ltd. are happy to support your evaluation of the LABScreen Extended Panels to demonstrate their value in interrogating HSPs and identifying the cause of unexplained positive crossmatches. Please get in touch for more information!

REFLECTIONS AND FUTURE DIRECTIONS

13th – 14th September 2022
Park Regis, Birmingham

Day 1

Plenary Session 1: Post-pandemic reflections – Lessons learnt

Coverage by Susan Fagan, Dublin

This session was chaired by Arthi Anand and Carla Rosser, and the first speaker was Stephanie Ascough; an academic immunologist from the Department of Infectious Disease, Imperial College London, who presented her research on 'HLA polymorphisms and virus-specific immune responses in Controlled Human Infection Models (CHIMS).' CHIMS are safe and well-tolerated models of studying human infection, with the advantage of infecting volunteers with a known amount of pathogen at a set time then monitoring the progression of selected compartments of pre-existing immune responses; however, a disadvantage can be that strains used may differ from those naturally occurring and induce only a mild or moderate disease. The combination of a CHIM and a vaccine study can be less time-consuming than Phase 2 clinical trials. To date, the team successfully established challenge models for influenza (H1N1 and H3N2), Respiratory Syncytial Virus (RSV) and SARS-CoV-2. The study focussed on the relatively poorly understood role of the adaptive immune response, specifically T cells, to these acute respiratory viruses, both pre- and post-infection. A multi-parameter flow cytometry panel was used to identify virus-specific T cells in peripheral blood and BAL's from healthy volunteers whose HLA alleles were known. The polymorphic nature of HLA, combined with natural variation between individual volunteer immune responses and low-frequency virus-specific T cells, makes characterisation of CD4+ and CD8+ T cell immunity complicated; however, the ability to isolate soluble MHC protein monomers from the viral proteome can overcome the unreliable, low-binding affinity of MHC class II epitopes. Monomers can be multimerised to form tetramers or pentamers, allowing for stable binding of multiple TCR's on the CD4+ or CD8+ cell surface including pentamers and tetramers from a pre-alpha SARS-CoV-2 strain. These multimers were used in the flow cytometry panel, thus giving the ability to characterise populations of low-frequency virus-specific T cells. So far, one novel finding was that post-RSV and influenza infection, virus-specific CD8+ T cells are more plentiful in the respiratory tract than in peripheral blood; indeed, the airway cells typed as CD69+ CD103+ T resident memory (Trm) and could have a role in protection against severe respiratory disease. As CHIM studies, by name, are more controlled than observational studies of naturally acquired infections, lower numbers of participants were required to achieve strong statistical results. Combining this with the use of multimers expressing virus-specific MHC epitopes enabled a unique manner of probing the immune response to viral respiratory infections. These challenge models have a role in testing efficacy of novel vaccines without the potential risks and costs associated with Phase II/III vaccine trials.

Next up was Nana-Marie Lemm, who is undertaking a clinical PhD programme at Imperial College London. Her group investigate mucosal and systemic immunity to aerosolised SARS-CoV-2 vaccination and human experimental infection, and she presented on 'HLA polymorphisms and responses to aerosolised COVID-19 vaccination.' As all licensed COVID-19 vaccines to-date are intramuscular, the COVAXAER01 study sought to investigate the use of a nasal spray/inhaled vaccine against SARS-

Continued on next page

COV-2 (which is primarily a respiratory pathogen). This was a Phase 1 dose escalation, non-randomised study focussing on safety and initial immune response of 30 healthy volunteers to the aerosolised adenoviral vector vaccine booster AZD1222 (AstraZeneca). It was noted that the group were aware of the importance of achieving a balance of ethnicity within the target volunteer population. Peripheral blood samples and 3 BAL's (bronchoscopy) were taken from the volunteers at 3 time points during the study, and varying techniques were used to assess the antigen-specific immune responses to the booster; flow cytometric immunophenotyping examined antigen-induced T-cell response in peripheral blood mononuclear cells while HLA-specific staining of pentamers and tetramers assessed epitope-specific responses. Early conclusions have provided novel insights into both systemic and local cellular immune responses, in particular that there appears to be a difference in the memory T-cell populations between the PBMC & BAL cell preparations. Further studies are needed but could provide insights to deepen the understanding of a specialised mucosal immunity to SAR-COV-2 and further develop vaccination modality.

The next talk, 'OTDT and the Pandemic', was a summary of organ donation and transplantation activity in the UK during the COVID-19 pandemic, presented by Lisa Mumford of NHS Blood and Transplant (NHSBT). Lisa is the Head of Organ and Tissue Donation and Transplantation (OTDT) Studies within the NHSBT Statistics and Clinical Research Department. In the 10 years prior to the pandemic, OTDT had reported a 15% fall in waiting times and a 10% increase in transplants. However, there was an immediate impact on organ donation and transplant activity on 11th March 2020, when COVID-19 positivity was considered a contraindication to donation. By the end of March, donor age restrictions were applied, the pancreas service was suspended, and centre-based allocation was introduced. During April, DBD age restrictions were increased from >60 to >75 years while DCD remained at >50 years; this change in donor characteristics was introduced to enable more organs to be donated by fewer, younger donors. Non-urgent and some older patients were suspended from the active waiting lists. Elective liver offers were suspended at the beginning of May. Opt-Out legislation was passed in England on 20th May 2020, which may have been poor timing relative to donations numbers. Overall, heart activity was maintained while lung activity was severely decreased, and a small number of renal centres could maintain activity. For example, Belfast could move their theatre to another centre, unlike London & Portsmouth who were unable to continue with their transplant programme. The living donor programme was cancelled. OTDT recognised that they quickly needed to start rebuilding the service so twice-weekly medical team meetings were held, allowing them to rapidly respond to any transplant-related issues around the UK. At this point it was noted that the incidence of COVID-19 infections in the transplant cohort was no different to the general population; however, the severity of infection was increased. By July/August 2020 the service resumed a level of normality only then to be hit with the next wave of infections. OTDT used their ability to divert organs to centres that were able to maintain a transplant service, and April 2021 saw the service once again resuming. Staffing issues, mainly sick leave, was the next blow to the service which still linger. In 2021, the changes to the tightened donor age characteristics were reversed to again include older donors. Non-urgent and older patients were reactivated to the waiting lists, in addition to newly activated patients. Considering there was a 3% decrease in family consent last year, deceased donor activity and transplantation has almost returned to pre-pandemic levels. The living donor programme for kidneys and partial livers was reactivated, accounting for 40% of total organ donation in 2021. Overall, there was a 27% decrease in transplants during the COVID-19 period. Heart services were relatively maintained, lung severely decreased, pancreas cancelled and renal fluctuated. Despite the return to donation and transplantation activity, the service must now manage increased numbers on the waiting lists and the aftermath of the pandemic disruptions, not least the nationwide staffing shortages.

In December 2021, the MELODY (Mass Evaluation of Lateral Flow Immunoassays for the Detection of SARS-CoV-2 antibody responses in immunosuppressed people) Study opened to recipients of solid organ transplants. Almost 13,000 patients have registered to look at the effectiveness of 3rd and 4th doses of vaccinations in the transplant population. The study will further be opened to those with rare autoimmune diseases and blood cancers. The study is being led by researchers at Imperial College London and is employing home blood finger prick antibody tests.

The final speaker for the session was Ines Ushiro-Lumb who presented to us via recorded session on 'Reflections on the path to recovery: donor infection and recipient immunisation.' Ines is a Consultant Clinical Virologist at NHSBT, where she is the Lead Clinical Microbiologist for Organ Donation and

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BSHI conference... continued

Transplantation, and Clinical Director of the Virology Reference Laboratory. We were presented with a reflection on what has happened, where we are currently, and where we are going from two aspects: firstly, that of donor risk assessment for SARS-CoV-2 transmission, and secondly of COVID-19 vaccine efficacy within immunosuppressed populations. During the initial stages of the pandemic, SARS-CoV-2 positivity was a contraindication to donation as it was unknown what the risk of viral transmission to solid organ transplant (SOT) recipients might be. As the pandemic progressed, a better understanding of disease dynamics emerged. The interpretation of virus screening results has changed with national guidelines published in March 2022; asymptomatic donors testing positive for SARS-CoV-2 can proceed to donation. Of the 4316 potential donors, 84 tested positive and all organs were offered with the exception of lungs. To date, there is no evidence of donor to recipient virus transmission through non-lung SOT. We await the publication of the outcomes of recipients who received organs from SARS-CoV-2 RNA positive donors at the time of screening. Due to the global diversity of SARS-CoV-2 epidemiology and populations across the world experiencing different variants, the search for effective anti-virals is ongoing but, in terms of producing a viable vaccine, 11 months has been a spectacular achievement. Relative to the recommended UK vaccination schedule, the bivalent COVID-19 vaccines have been shown to be effective at preventing severe disease and death. Compared with the general population, vaccine efficacy in immunosuppressed patients has been shown to be slightly less but effective nonetheless in reducing hospital admissions. During the Delta variant surge in the UK, the vaccination schedule was 3 initial doses instead of 2 for those SOT patients receiving immunosuppression. The additional dose was proven to provide extra protection for those unable to mount a sufficient immune response to protect them from serious illness. Defined clinical end points have been essential in order to monitor efficacy and the length and level of vaccine protection has been variable. Worldwide, we cannot forget that less than 1% of the population of some countries have been vaccinated.

Trade Exhibition

Coverage by Hannah Kenworthy and Helen Sansom, Oxford

CareDx showcased their AlloSeq HCT NGS system for engraftment monitoring post-hematopoietic stem cell transplant. This measures the relative percentage of the recipient and the donor DNA in the recipient's post-transplant specimen and can assist in detecting disease relapse and graft failure. The kit-based system analyses DNA from peripheral blood or cells against 202 bi-allelic SNPs for recipient and donor and is compatible with Illumina MiSeq and iSeq analysers. CareDx discussed the benefits of using their NGS system compared to current technology: SNPs are balanced across ethnic groups, increased sensitivity, and the ability to distinguish 3 genomes. The Session gave an interesting insight into a new technique for an important post monitoring assay.

Ben Adams from VH Bio ran a session looking at antibodies against epitopes. This was supported by discussion of the tools to support antibody definition including the LABScreen Extended Panels (Supplement and ExPlex) and HLA Matchmaker. The Extended Panel SAB kits provide broader antibody coverage, including against more ethnically diverse HLA, to evaluate eplet patterns. HLA Matchmaker, available with HLA Fusion software, can be used to determine the degree of eplet mismatching between donor and recipient and to facilitate the definition of antibody/epitope specificities through epitope-based analysis. These tools may enable easier identification of a 'window of opportunity' for highly sensitised recipients and, in recipients with multiple donor options, facilitate the selection of the donor with fewest epitope mismatches. The Oxford laboratory followed up this talk by inviting Ben to give us a more in-depth talk on the features of HLA Matchmaker which will stand us in good stead when the LABScreen Extended Panels are introduced to the laboratory.

Immucor showcased their LIFECODES® Non-HLA Antibody Assay. Multiple studies have demonstrated the impact of non-HLA antibodies in transplant rejection and decreased graft survival. To help further the detection and understanding of the role of non-HLA antibodies, the kit provides a way to detect IgG antibodies to an extensive list of 60 non-HLA-autoantigens. The clinical impact of these antibodies was discussed along with the benefits of expanding the understanding of the role on non-HLA antibodies.

Christine Barr from STEMCELL Technologies gave a talk on automated cell isolation to achieve higher lab efficiency, skipping centrifugation and

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isolating cells directly from whole blood in 8-20 minutes. The EasySep Direct works by negative selection, immunomagnetically depleting RBCs and other unwanted cells in a single step; omitting the need for density centrifugation, RBC lysis or other pre-processing which may alter cellular function and increase processing time. This standardised technique has been formulated for the isolation of highly purified cells for use in crossmatch analysis, HLA serological typing and chimerism analysis. Depending on your laboratory throughput this technique can be used with a single sample or up to 16 samples by combining EasySep Direct with the EasyEights EasySep Magnet. Full automation can also be achieved using the RoboSep.

Paul Sinnott Next Generation Scientist Award

Coverage by Louise Walsh, Dublin

Following an excellent lunch and several informative trade exhibitions, we reconvened in the Sky Gallery in the afternoon for the presentations for consideration for the Paul Sinnott Next Generation Scientist award. The session was chaired by Martin Howell and Deborah Pritchard, and we were treated to six excellent talks from scientists from around the UK.

To kick us off, Christopher Byrnes presented research from the Blood and Bone Marrow unit at Hammersmith Hospital where they carried out a retrospective analysis to evaluate the impact of donor KIR B motifs on recipient outcomes in haploidentical HPCT. By separating 77 donor and recipient pairs into neutral or better and best groups based on KIR B motif content the group sought to determine the impact if any on relapse free survival, overall survival, and infection amongst other outcomes. The KIR B motif was not found to be a good predictor of positive outcomes and was not added to the haploidentical donor selection criteria for the unit. The group identified that further studies are required into the benefits of KIR and HLA incompatibilities in HPCT.

We were introduced to a new research tool called the Mismatch Data Aggregator (MDA) by Rebecca Cope from Cambridge University Hospitals. The MDA was used with HLA screening results and typing data to retrospectively identify mismatches and to assess the impact of de novo DSA on a cohort of heart transplants carried out between 2009 and 2015. The lab found that almost a third of the cardiac transplant patients developed dnDSA which had a detrimental effect on outcomes. dnDSA patients had a 3-fold risk of developing chronic allograft vasculopathy and a slight risk of antibody medicated rejection. Antibodies to HLA-DQ were the most commonly identified dnDSA especially DQ2 and DQ7. The group identified a need for more research involving larger multicentre studies and further analysis on immunogenicity relating to donor antigens.

Rachael Cole from NHSBT presented results of a retrospective analysis of 200 patients who received HSCT from donors who were only mismatched at HLA-DPB1. Using a revised T-cell epitope matching algorithm (TCE-FD), DP mismatches were classified as permissive or non-permissive. Within the study, the level of DPB1 mismatching was found to significantly influence the incidence of Grade I-II acute graft-versus-host-disease. Those that were HLA-DPB1 matched showed a trend towards better survival overall. Having identified and developed deeper understanding of the role of HLA-DPB1, the centre is now using information about HLA-DPB1 locus to help guide donor selection strategy in order to optimise unrelated HSCT outcomes.

Sean Druce presented a challenging case study from NHSBT involving a patient with an inherited bleeding disorder which produces defects in platelet membrane glycoproteins GPIIb/GPIIIa called Glanzmann's thrombasthenia. The patient required mitral valve replacement surgery which posed an increased and life-threatening risk of bleeding. Platelet selection was complicated by the presence of class I HLA antibodies (cRF>95%). Deteriorating response to HLA-selected platelets led to the discovery that the patient also had antibodies directed against GPIIb/GPIIIa. Plasma exchange was successfully used to reduce GPIIb/GPIIIa antibodies enabling platelet transfusion and allowing surgery to go ahead. The interesting case study was presented as an example of successful multidisciplinary team effort

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requiring collaboration and cooperation involving multiple specialities including haematology, multiple H&I labs and NHSBT to result in a successful clinical outcome.

Katie Whittle from the Welsh Transplantation and Immunogenetics Laboratory discussed validation of SAB technology to detect anti-HLA IgM antibodies. This involved using LABScreen Mixed and SABs coupled with an IgM conjugate; 22 CDC-defined IgM positive sera were tested, and cut-offs determined. The tests were then used to screen a cohort of non-sensitised and sensitised patients for anti-HLA IgM antibodies. A total of 96 samples were screened to discover that 36% of the 'sensitised' and 16% of the 'non-sensitised' patients had IgM anti-HLA antibodies identified, with the majority co-existing with IgG. The results indicated that the most accurate results would be obtained from IgM testing based on SAB testing alone. However, the team questioned whether the cost would be worthwhile as the significance of anti-HLA IgM antibodies is uncertain and clinical application to virtual crossmatch strategy and unacceptable antigen listing is in question.

MICA is the most polymorphous non-HLA antigen and expression is up regulated in times of cellular distress. As there is greater expression of MICA antigens on the pancreas epithelium, Deeya Balgobin from Viapath at Guy's Hospital presented work which investigated whether antibodies to donor-specific MICA might play a role in the rejection of the pancreas and not the kidney following simultaneous pancreas and kidney (SPK) transplantation. 25 SPK donor-recipient pairs were included in the study; 20 pairs where differential rejection of the pancreas was suspected in the absence of HLA antibodies and 5 rejection-free pairs. The pairs were MICA genotyped and pre-transplant and date of rejection sera were screened using LABScreen MICA SABs. No significant difference in the detection of MICA DSA was noted between the suspected rejection group and the control pairs. This study was limited not only by small sample size but also because the most common MICA antigen (MICA*008) was absent from the LABScreen screening kit. Further work recommended by the team before discounting the significance of MICA DSA in pancreas rejection post-SPK was a larger scale study including NGS typing of SPK pairs and a screening kit to include MICA*008.

Rebecca Cope was announced as the very worthy recipient of the Paul Sinnott Next Generation Scientist award at the conference dinner held that evening.

Plenary Session 2: Current Novel Therapies

Coverage by Aisling O'Brien, Dublin

The first talk in this session was delivered by Dr Martin Howell, Head of H&I Service Development, NHSBT. He began by stating that provision of drug therapy is the second highest expense to the NHS, and it has been accepted that drug efficacy may reach up to 90% in 30-50% of patients receiving drug therapy. Monitoring of drug efficacy for the same dose and same effect may lead to changes in prescription dose or to try an alternative drug between different patients. Adverse drug reactions (ADRs) result in approximately 1 in 11 hospital admissions and affect 1 in 6 hospital in-patients. ADRs are broadly divided into type A; the expected effect on the body was different than anticipated such as occurs with 'overdose', or type B; an unexpected or "off-target" effect, such as an immunological reaction against the drug as noted with drug hypersensitivity. In terms of specific HLA allele drug hypersensitivity reactions, known notable associations are Abacavir in the presence of HLA B*57:01, Carbamazepine in treatment of epilepsy patients with HLA A*31:01 or B*15:02, and the development of drug induced liver injury with Flucloxicillin treatment in patients with B*57:01. Genetic variants are also accepted to impact drug interactions in the body, one of the most studied includes cytochrome p450, which has been noted to downregulate some interactions while upregulating others. The metabolism of the immunosuppressant Tacrolimus has been shown to be impacted by cytochrome p450 3A5 (CYP3A5). A study involving screening for CYP3A5 and measuring Tacrolimus level in paediatric post-transplant renal patients has shown metabolism of Tacrolimus was increased when one or more copies of the CYP3A5 allele is present, thus a higher dose may be required to be effective and maintain a stable therapeutic level in these patients. Dr Howell further discussed the outcome of studies to determine the

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strength of genetic association and drug reactions. The Netherlands and the US have identified a number of "actionable drug interactions" linked to specific alleles in patients (60 and 100 respectively). NHS England has similarly established a pharmacogenetics group to determine gene-drug interactions. The Pharmacogenetics and Stratified Medicines Society was additionally recommended as an important educational resource in this area.

The second talk in this session was 'Universal CAR-T cell therapies for haematological malignancies' by Dr Kanchan Rao, paediatric consultant and BMT lead at Great Ormond Street Hospital (GOSH). The introduction of the talk focused on the potential negative characteristics of using autologous CAR-T cell therapy for the treatment of haematological malignancies including leukaemia; these included the derivation process as it is expensive, patient deterioration while CAR-T cells are processing, and possible suboptimal quality of the product as it is derived from the leukaemic patient. The use of CAR-T cells from allogeneic healthy donors may overcome these limitations and permit availability when needed, but an important possible negative impact of allogeneic CAR-T cells is the development of GVHD or rejection by the recipient's immune system. Genome editing of the allogeneic CAR-T cells may prevent GVHD and immunogenicity. The speaker outlined a patient case study involving the infusion of universal CAR19-T cells in which TALEN was used to 'knock-out' the CD-52 /TCR receptor on the T cells into a paediatric patient with B-ALL with the aim to induce deep remission. Infusions were performed in 2016 and 2017 and the patient then underwent follow-up a bone marrow transplant. A second follow-up study involving more patients has since begun. Examples of possible adverse drug reactions included toxicity to the infusion and failure of cellular expansion and persistence of the cells in the patient. The potential use of CRISPR edited CAR-T cells was also outlined. CRISPR gene editing can be used to knockout the TCR only and is associated with fewer "off-target" changes in the cells in contrast to TALEN gene editing. The treatment protocol was described as patient leukodepletion, infusion of the CRISPR CAR-T cells, cellular expansion, and remission. Engraftment was expected by 28 days post-infusion but levels were not maintained and bone marrow transplant must follow the treatment. The use of CRISPR-CAR7 T cells as a "last line" treatment for T cell acute lymphoblastic leukaemia followed by BMT is also under investigation for paediatric patients in GOSH.

The final talk in this session 'The influence of HLA genotype on the development of metal hypersensitivity following joint replacement surgery' was delivered by Mr. David Langton from ExplantLab. Increasing levels of arthritis in the aging population may lead to an increase in the number of hip replacements required. An immune response against the metal implant following exposure to the metal in the joint may result in metal hypersensitivity. Notably, delayed metal hypersensitivity to the cobalt chrome (CoCr) components in hip joints has been associated with resultant tissue damage. If there is only macrophage involvement then minimal damage has been noted, but with both macrophage and T lymphocyte involvement damage may be extensive up to tissue necrosis; it may take 3 to 4 years for development of the damage. Mr. Langton's study was performed to identify HLA alleles associated with metal hypersensitivity against CoCr hip replacements. The following characteristics were considered in the algorithm to predict the resistance or susceptibility to CoCr hypersensitivity: age, gender, HLA genotype, levels of cobalt and chromium in the blood. Hip replacement patients recruited were either known to have aseptic lymphocyte dominated vasculitis association lesion (ALVAL) and without ALVAL. HLA-DQ and HLA-DRB1 typing was performed using NGS. The haplotype showing the strongest susceptibility to ALVAL was DQB1*02:02-DQA1*02:01 while DQB1*05:01-DQA1*01:01 was found to be most resistant. No relationship was found with DRB1 alleles. Mr. Langton further pointed out the use of CoCr implants was noted as frequent for knee replacements, thus the issue is not limited to a small number of patients. In future, an alternative approach may be to pre-emptively type class II HLA and use different metals in the joint replacement.

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Festenstein Lecture

Coverage by Claire Lenehan, Dublin

In this session, Dr Asquith focused on Killer immunoglobulin-like receptors (KIRs) and their influence on HLA disease associations. KIRs are a polymorphic family of surface receptors expressed on Natural Killer (NK) cells and some T cells and are specific for major histocompatibility complex (MHC) molecules. Upon engagement with HLA class I molecules, KIRs inhibit NK cell activation (iKIRs). iKIRs and HLA molecules are inherited independently and the number of functional iKIRs (i.e. both receptor and ligand present) inherited varies from 1 to 4 in the general population.

Dr Asquith and her team use a combination of genetic data analysis with mechanistic mathematical data modelling and assays of *in vitro* and *in vivo* T cell dynamics to investigate the relationship between iKIRs, T cell dynamics and human health. Three observational studies were presented in relation to viral infections and class I HLA disease associations along with the level of functional iKIRs expressed: HCV, HTLV-1 and HIV-1. In all three cases, the presence of higher levels of functional iKIRs enhanced the protective or detrimental effect the HLA allele had on disease progression.

However, this raises the question how can the same mechanism enhance both protective and detrimental effects? The hypothesis is that iKIRs enhance HLA associations by enhancing CD8+ T cell survival. To investigate this theory three separate approaches were used; longitudinal HIV viral loads, quantifying of T cell age using CD57 and *in vivo* survival studies using stable isotope labelling to estimate the rate of T cell proliferation. The results of these studies showed a positive correlation between T cell life span and the number of functional iKIRs present, and suggested that the mechanism of how iKIRs enhance T cell dynamics is via an indirect pathway.

Finally, the role of KIRs in autoimmunity was discussed. Since the 1970s there has been an established link between HLA and the risk of developing type I diabetes (T1D). iKIRs have been shown to modify protective HLA class II associations in T1D but have no impact on detrimental associations.

KIRs enhance T cell survival and this in turn impacts on clinical outcomes in viral infections (HCV, HTLV-1, HIV-1) and autoimmunity (type I diabetes) with a direct consequence for human health.

Poster Session

Coverage by Amber Cox and Eamonn Cudworth, Barts

This year's poster session was a bustling event with 26 posters on display to be viewed with a glass of bubbles and delicious canapes. This sociable event provided a great opportunity to discuss the posters with their authors as well as with fellow colleagues and delegates. The large number of posters on display involved a range of important and informative topics from summaries of scientific research to implementation of an alternative quality strategy.

A poster from the Cambridge team exploring the immunological relevance of pre-transplant HLA DSA in intestinal and liver transplantation was this year's poster award winner. Their retrospective study included development of two novel programs to aid in DSA identification, the Patient Single Antigen Bead (SAB) Combiner and Mismatch Data Aggregator, both of which have been made publicly available for use in other centres. Their results found for patients with class I DSA, risk of mortality appeared to be reduced by 59% in patients receiving liver inclusive transplantation compared to those receiving liver exclusive transplants. The discussion highlighted how this data is suggestive that the liver may show some resistance to class I DSA, and that future studies confirming this could provide clinically important findings.

Another poster exploring DSA was from NHSBT Tooting, questioning if complement-fixing DSA are more clinically relevant. They investigated whether using Immucor LIFECODES C3d detection assay could improve the prediction of a flowcytometric crossmatch (FCXM) outcome. The study determined that of the 20 positive FCXMs evaluated 100% were SAB positive but only 68% were C3d positive. Conversely, of the 38 negative FCXMs evaluated 57% were SAB positive however only 17% were C3d positive demonstrating improved concordance. Using the C3d assay may aid in understanding the clinical significance of DSA rather than relying on MFI levels alone

A different evaluation of antibody testing was provided by the Welsh Blood Service, with a poster examining the case of false

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negative DQ2 antibody screen results. One Lambda LABScreen Mixed (LSM) kits had provided a negative CII result for a patient with historic DQ2; on further testing with LABScreen SABs the results were positive for all DQ2 beads. Comparative testing with the Immucor screening assay also provided a positive CII result, indicating this disparity was specific to the LSM assay. Although unable to identify the cause, this poster demonstrated the importance of up-to-date SAB testing.

The Manchester team delivered a poster focusing on improving the reporting of STR chimerism data. They developed a novel in-house program for analysis and reporting of chimerism results and evaluated the effect of its implementation on improved laboratory efficiency. Saving a calculated 23 minutes per patient which equates to ~68 working days a year, this implementation should ensure turnaround times are met and free up staff to work in other laboratory areas.

Away from the 'technical side', the Manchester team also produced a poster focussed on laboratory quality. The poster entitled 'Implementation of a Flexible Scope of Accreditation' reported a single centre study that analysed potential implementation of Flexible Scope accreditation compared to the currently employed Fixed Scope accreditation. The first phase of the study identified evidence-based quality indicators that could be measured pre- and post-implementation of the Flexible Scope approach, and suggested benefits to this change including potential cost savings and improved staff experiences.

The transplant laboratory at the Royal London presented an interesting case study which highlighted the evolving role of how H&I labs can help facilitate thymus transplantation. The patient in the case presented originally underwent a thymus transplant in 2019, but no HLA matching of patient or donor was performed at the time of transplant and unfortunately there was no thymic epithelium detected from post-transplant biopsies or immune reconstitution at 1-year post-transplant. There were no DSAs detected at the time of transplant, however de novo DSA were later detected >5,000 indicating possible acute rejection. The patient was due to go for a second transplant, this time the H&I lab performed HLA typing of the patient and potential donors, as well as antibody detection and definition. The first five donors were not considered suitable due to the presence of DSA. A sixth donor was considered suitable, and the transplant proceeded; the patient was monitored weekly and, after two weeks, de novo DSAs were detected. In this instance the patient was treated for rejection with rituximab and three cycles of plasma exchange. This resulted in a lowering of DSA levels, with the antibody levels later stabilising and the patient became clinically well.

The laboratory at Hammersmith outlined the danger of leukemic cell infiltration in non-blood derived samples. It is well known that leukemic cells can cause errors in HLA typing when performing typing from peripheral blood samples especially if the patient is undergoing a blast crisis. It is often recommended to confirm HLA typing from a buccal sample, skin plug or haplotype analysis of relatives where errors are expected. In this case, an AML patient exhibited a novel mutation in exon 1 of A locus resulting in an HLA A*31:01 novel null allele, with the second allele an A*24:02. Due to the presence of a null allele, the patient was considered as being A*24:02 homozygous when performing an unrelated donor search. To confirm this mutation a buccal swab was obtained to confirm the somatic HLA type, however the NGS typing showed leukemic infiltration, therefore the lab resorted to using a skin plug sample. This sample also showed an infiltration of leukemic cells, however thankfully to a lesser degree that it was possible to determine the correct HLA type of the patient. This shows the danger of performing unrelated donor searches when there is the chance there may be an inaccurate patient HLA type as a result of leukemic cell infiltration, possibly causing mismatched donors to unexpectedly be selected.

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Day 2

Plenary Session 3: Future Directions

Coverage by James Cashin, Madeleine Harris, Julie Johnson, Rebecca McGuire, and Radvile Prialgauskaite, Manchester

The day opened with a talk from Dr Ray Fernando who provided an update from the 18th International HLA and Immunogenetics Workshop, focussing on defining the clinical relevance of non-HLA antibodies in rejection. The aim of the workshop was to produce a multi-centre pilot study of non-HLA assays from One Lambda and Immucor that utilise the Luminex® platform. The results showed that patients with specific non-HLA antibodies pre- or post- transplant were at increased risk of being early rejections (CSF2, CXCL9, GSST1, and IL-8, CSF2 respectively). The study also revealed that the presence of persistent non-HLA antibodies were associated with rejection episodes. However, MFI values were not significantly different when comparing the control and rejection groups. This talk revealed the headway that has been made into understanding the role of non-HLA antibodies, concluding that larger studies are necessary to determine the clinical relevance and utility of non-HLA antibody assays in the future.

The presentations that followed were from Professor Simon Kay and Dr Brendan Clark, who delivered a noteworthy talk on the Leeds programme for Vascularised Composite Allotransplantation (VCA), or hand transplantation to the uninitiated! For many of us this was a first insight into the fascinating VCA programme, and the dynamic pair offered a captivating overview of both the surgical and scientific considerations for this newly emerging area of transplantation.

The first talk on the VCA programme was given by Professor Simon Kay, a plastic surgeon and hand surgeon at Leeds General Infirmary. In this talk, Professor Kay went through the history of hand transplantation and milestone cases. He then went through the UK cases and spoke about the Leeds hand transplantation programme which started in December 2012. There was a great emphasis on prevention of the psychological rejection; Professor Kay explained the psychological preparation process for patients that is carried out in Leeds which takes approximately a year and involves multiple steps, assessments and interviews. This intense workup has contributed to only 6 patients undergoing VCA out of the 52 referrals within the first 5 years of the programme. Simon touched upon the ethical dilemma of hand transplantation. Some may not view the hand as an essential organ; you can survive without them and the effects of immunosuppression can be more detrimental than living without a limb, especially when prosthetics are offered as an effective alternative (although Professor Kay provided a convincing argument against the latter). Professor Kay explained the risks related to hand transplantation such as fungal infections, immunosuppression, metabolic issues or potentially ineffective transplant. However, he explained that fungal infections are manageable, and that the outcome is still good despite complications. Professor Kay also highlighted that it is important to consider an individual's mental wellbeing, as bilateral hand loss is likely to damage socialisation, employment, self-esteem, and integration. Finally, Professor Kay outlined characteristics of hand transplantation that make it superior over prosthetics such as motility, sensate, always attached, and self-repairing.

Dr Clark then discussed the pros and cons of HLA matching in the context of VCA, and whilst HLA matching may play a role in the clinical risk assessment at the time of offer, donor availability, surgical feasibility and issues relating to cosmesis (wanting the graft to have a certain appearance) in the recipient are the primary factors considered. Next, the role of HLA antibodies was outlined. Most patients are accepted onto the programme with some degree of HLA sensitisation due to multiple skin grafts and transfusions to treat the underlying issue. The majority of VCA patients were not transplanted across donor-directed antibodies. HLA mismatching is associated with DSA production, followed by rejection of the graft. A case of rejection in the Leeds VCA programme was controlled with altered immunosuppression. Crossmatching was initially carried out by performing a “wet” crossmatch, but all hand transplants at Leeds now proceed on the basis of a virtual crossmatch. Another important consideration in the VCA programme is a phenomenon known as split rejection, where alloreactivity may occur in two vectors: host vs. graft and graft vs. host, in addition to the possible development of delayed-type hypersensitivity in the donor or recipient tissue. This is in part due to the complex immune environment in the hand, including donor bone marrow in the bones of the graft, the

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large antigenic load present in the graft, the high immunogenicity of the skin and a considerable proportion of APCs and other immunocompetent cells in the graft. Dr Clark also outlined the ethical considerations of hand transplantation; for example, a life-enhancing as opposed to life-saving intervention, clinical risk versus benefit evaluation, the requirement for life-long immunosuppression and the psychological resilience required by the recipient.

Best Abstracts

The best abstract session opened with a presentation by Dr Richard Issitt from GOSH who described an exciting new desensitisation methodology for cardiothoracic transplant patients. Cardiothoracic transplant patients who are supported by Ventricular Assist Devices (VAD) are at an increased risk of developing HLA antibodies, therefore widening the donor pool is essential. Furthermore, there is a calling for an effective consensus desensitisation method in patients requiring cardiothoracic transplant patients as the paediatric waiting list continues to grow. In an experiment which mimicked paediatric patients undergoing cardiac transplant, the team at GOSH were able to create a bypass system with the ability to separate plasma. This system contained a secondary immunoadsorption system to deplete plasma of HLA antibodies. Here it was demonstrated how desensitisation could be performed with this intraoperative system, by dramatically reducing MFI values, resulting in flipping of flow cytometric crossmatches from positive to negative in this theoretical ex vivo setting. Intraoperative technologies such as this immunoadsorption bypass system have already proved their efficacy and have facilitated ABO-incompatible heart transplantation at GOSH. It is hoped that the experiments described by Dr Issitt during this talk will facilitate HLA-incompatible transplantations and reduce waiting times for patients in need of cardiac transplantation.

The second talk was given by Professor Graham Davis, also from GOSH. He presented the work completed by his team to perform over 60 thymus transplants since 2009, at one of only two centres in the world performing this surgery. His talk included an impressive depiction of the methodology for thymic transplantation; slices of cultured thymic tissue are implanted into the quadricep muscle, with patients receiving approximately 30 thymic slices that will develop into tissue that is indistinguishable from normal thymic tissue. Professor Davis presented retrospective data, showing that HLA matching is associated with an increase in T-cell receptor excision circles (a surrogate marker for T cell production and maturation). Preliminary data also suggested that HLA matching is associated with fewer incidences of autoimmunity post-transplant. This developed into a discussion of a potential future direction for thymus transplantation, whereby cultured thymic tissue could be cryopreserved in a biobank, facilitating prospective HLA matching in this transplant setting. This concept would allow the possibility of improving outcomes in this fascinating area of transplantation.

The next talk was given by Jessica Brookes from NHSBT Filton, a centre that provides a national HNA genotyping service. Using their PCR-SBT method, the laboratory team was able to identify a potentially new polymorphism (NM_000570.4: c.197T > G p.Leu66Arg) in a donor sample. After retrospectively testing 229 samples, nearly a quarter of the samples tested carried this potentially novel allele with up to three different polymorphisms at this position. Interestingly, further testing by long-range amplification using FCGR3B-specific primers revealed that the polymorphisms were only observed in the FCGR3A; it can be challenging to

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identify polymorphisms unique to each of the FCGR3 genes as they are co-amplified during PCR. Jessica finished the talk by discussing how using the FCGR3B-specific method can therefore be utilised to remove ambiguities as well as confirm null genotypes, negating the need for phenotyping assays.

The second half of the Best Abstract Session began with an informative depiction delivered by Matthew Hopkins, NHSBT, of how the Filton laboratory utilised the HITAlert (IQ Products, Groningen, Netherlands) assay to aid in the diagnosis of vaccine-induced thrombotic thrombocytopenia (VITT) following the ChAdOx1 CoV-19 vaccine (AstraZeneca). This phenomenon, usually observed in the context of heparin, involves the generation of antibodies to platelet factor 4, resulting in inappropriate clot formation. As the biological mechanisms of VITT is thought to be comparable to heparin-induced thrombocytopenia (HIT), assays used to diagnose HIT were explored as a possible diagnostic avenue for VITT. The current method of detecting HIT at Filton was an ELISA (Immucor HAT45G) based method; however, it was noted that not all cases of VITT could be detected this way. They reported that the HITAlert assay, a functional platelet flow cytometry assay, enabled a definitive functional test for VITT. Unlike in HIT, where platelets are only shown to be activated on the flow cytometry plot after heparin exposure, with this activation reduced with excess heparin, in VITT the platelets are activated in the absence of heparin. Overall, this talk demonstrated the innovative use of an existing assay, repurposed to allow for improved service offering during an unprecedented time.

Following on from this talk, we heard about a very interesting case of donor cell derived myelodysplastic syndrome (MDS) following an allogenic haematopoietic progenitor cell transplant (HPCT) from Betia Nouri of Imperial College Healthcare NHS Trust. Donor cell leukaemia (DCL) is a rare occurrence, accounting for 2-5% of relapsed cases. The H&I laboratory and the specialist integrated haematological malignancy diagnostic service (SIHMDS) presented their multidisciplinary approach in diagnosing DCL MDS post-paternal haploidentical HPCT for a patient with therapy-related AML. This patient appeared to have a successful HPCT, achieving MRD negativity by flow and cytogenetics as well as displaying >97% donor chimerism post-transplant. However, within months there was evidence of cytogenetic relapse despite maintaining morphological remission and high donor chimerism. After performing STR and NGS chimerism monitoring, FISH, karyotyping, flow cytometry and further HLA typing, this MDT determined the cause of relapse to be DCL MDS. It was decided that the best treatment plan for this patient was a second HPCT, matching the patient's initial type and not that of their donor to exploit the graft-versus-leukaemia effect. This case clearly highlights the importance of working in MDT to solve rare diagnoses and ensure continued patient care.

The final talk in this session also involved a patient with a haematological malignancy. In this case, presented by Dario Merlo, Anthony Nolan, a 27-year-old female was being assessed for a HPCT to treat T-ALL. NGS analysis (GenDx NGSgo®-AmpX v2) of a peripheral blood sample revealed a distinct subpopulation of reads for the HLA-DRB1*13 allele, accounting for 17%. This subpopulation differed by a single SNP (C > T), corresponding to an amino acid change (Thr > Met) at position gDNA 5421. HLA mutations are seen in malignancy, usually in the form of loss of heterozygosity; however, SNPs can also occur. Notably, the patient was undergoing a blast crisis at the time of peripheral blood sample collection, with a lymphoblast count of 91% in the bone marrow. To this end, they requested a buccal sample to determine whether the origin of the mutation was germline or somatic (cancer-derived). The buccal sample showed no evidence of the mutation, leading the laboratory to conclude that the SNP was specific to the malignant cells. In the wake of COVID-19, where the practice of using buccal samples to confirm initial types may have been temporarily lost, this talk highlights their importance in confirming suspected novel alleles in patients with haematological malignancies. It also sparks an interesting debate into whether buccal samples should be incorporated into routine practice to verify the types of all patients with haematological malignancies. It will be interesting to witness any changes made because of this case.

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Trade Exhibition

Coverage by Charlotte Cambridge and Dario Merlo, Anthony Nolan

Omixon presented NanoTYPE, an upcoming multiplex sequencing kit compatible with Oxford Nanopore's MinION platform which can generate HLA typing results to third field resolution due to long-read sequencing. This method will take under five hours to obtain HLA results from a DNA sample. NanoTYPE has a simplified workflow compared to short read NGS and is flexible (between 1 and 24 samples can be processed). A beta study (15 laboratories) comparing concordance rate at second field resolution found that overall concordance was excellent with little difference observed between various sample sources. All novel alleles were confirmed, homopolymer sequencing errors were quite low and 'off target' ambiguities were only detected at DRB1 and DRB3 loci. In conclusion, this kit should provide good sequencing coverage, allele balance and SNR, but an area to improve on will be class II coverage.

Alpha Biotech introduced GenDX, who presented several products including qPCR (39 indel markers) and NGS (34 indel markers) chimerism monitoring assays and an upcoming multiplex sequencing kit compatible with Oxford Nanopore's MinION platform. NGStrack has advantages over the qPCR kit for chimerism monitoring as it needs only one sample measurement while sample measurement using KMRtrack needs to be repeated for each test. The use of indels provides superior detection than SNPs, as this approach is less prone to sequencing errors, and they can be detected below noise levels. NGStrack has a sensitivity of 0.5% and is suitable for both low and high throughputs. GenDX also announced their multiplex sequencing kit, NGSTurbo, which is compatible with Oxford Nanopore's MinION platform; this should be available (for research purposes) in 2023. The aim of the product will eventually be to provide second field resolution typing results within 4 hours but is still in development.

Anna Barker presented a session from Promega, giving a talk entitled 'Engraftment monitoring using STRs following repeat haematopoietic stem cell transplantation'; this focussed on the use of the Promega GenePrint® 24 System in an H&I laboratory setting. The kit is a 24-locus short tandem repeat (STR) based system for mixed sample analysis, allowing distinct identification of highly similar samples and examination of specific cell lineages. Here, we heard how the GenePrint® 24 System can be used for chimerism monitoring in patients post-HCT. Several case studies were presented on patients who had undergone repeat HCT from related and unrelated donors; in these cases, the patient samples would be a complex mix of DNA from several sources, containing closely related individuals. Despite this, the 24 STR loci amplified by the kit provided a panel of informative markers to detect chimerism levels in repeat transplant settings, with quick turnaround times rivalling NGS methods.

Carrying on with a similar theme, Connor Dove from Devyser presented their new NGS kit for chimerism monitoring. The kit targets 24 indel markers (population-independent), enabling a one-size-fits-all approach. The main benefit of the kit is the sensitivity to detect down to as little as 0.05% fraction of chimerism, which Devyser says 'allows earlier detection of graft rejection and disease relapse.' The current gold standard in chimerism monitoring uses RT-PCR and STR fragment analysis for detection and monitoring; this NGS method condenses this down to a single workflow which can be performed in a single tube, increasing efficiency, and reducing hands-on time in the laboratory. Having heard its application in a clinical setting during the Best Abstracts session, I'm sure we'll see routine use of Devyser's Chimerism NGS kit in the laboratory in the future.

Continued on next page

BSHI conference... continued

BSHI MDT: Solid organ and HSCT case study presentations

Coverage by Manchester (credits above)

The first talk of the MDT Solid Organ and HSCT Case Study Presentations was delivered by Sarinder Day, Bristol, who reported their second HNA-3a antibody patient case identified for renal transplantation and the first planned HNA-3a antibody incompatible case which used HLA/ABO antibody removal protocols including plasma exchange and administration of Rituximab. HNA-3a antibodies have been shown to be associated with early and chronic rejection with graft loss in some cases. In this case, the patient was a 49-year-old woman with polycystic kidney disease whose genotype was HNA-3b3b while the donor's genotype was HNA-3a3a. After applying HNA-3a antibody removal protocols, they monitored the patient by T cell flow cytometry which showed reduction of T and B cell relative mean fluorescence in serum titrations.

The second case was presented by Katherine Mounsey, Leeds, where a 17-month-old patient with renal dysplasia had potentially developed HLA antibodies after receiving a live vaccine against Varicella Zoster; this vaccine is propagated from an MRC-5 human cell line which was HLA-A2 positive. In this case, patient had not undergone any sensitising event; however, antibody screening revealed HLA-A2 and A28 antibodies. To investigate the functionality of these antibodies, a flow cytometry crossmatch was performed between the patient and his father which was T and B cell positive. This case resulted in further investigation of 9 other paediatric patients who had received a vaccine; unfortunately, these were difficult to analyse as several had received blood products after the vaccination. They found two patients with previous transfusion history and two without sensitising events who had developed HLA-A2 antibodies.

The third talk was delivered by Sandra Lloyd, WTAIL, who presented a case where a 55-year-old male had returned to the deceased donor transplant list after the failure of the first kidney transplant; antibody screening revealed allele-specific antibodies against DQB1*06:02, *06:03, *06:09. They performed sequence-specific typing which showed that the patient was DRB1*15-DQB1*06:01 rather than the more common DRB1*15-DQB1*06:02. Unfortunately, listing DQ6 would severely reduce the patient's chance of receiving a donor kidney due to complex antibody profile. However, listing DRB1*15 could be used as a surrogate for DQB1*06:02 due to strong linkage disequilibrium; this would reduce, but not eliminate, the chance of positive crossmatch but the patient could still receive incompatible offers of DRB1*13:01-DQB1*06:03 or DRB1*13:02-DQB1*06:09 donors. It was decided to list DRB1*15 as an unacceptable antigen after discussion at the MDT meeting, which resulted in two incompatible donor offers until the patient was transplanted with a crossmatch negative donor.

A case study reflecting the update to the BTS/BSHI Guidelines relating to Liver transplantation was presented by Sarah Peacock, Addenbrooke's Hospital. The current version of the guidelines does not consider HLA-DSA in the liver setting, in spite of increasing evidence that pre-formed donor-specific antibodies are associated with an increased risk of adverse outcomes in liver recipients. Post-transplant survival is reduced by around 50% if a patient is transplanted across a positive crossmatch. A patient was listed for their 3rd liver graft in 2021. Antibody screening revealed a high level of sensitisation, mainly to HLA class II specificities, which was a concern as there appears to be a stronger link with HLA class II in terms of rejection. The decision was taken to avoid previous HLA class II mismatches at MFI >20,000 due to this. Eventually, the patient was transplanted and had no detectable DSA 3-months post-transplant. This update to the Guidelines proposes a recommendation to consider circulating HLA-specific donor-directed antibodies (likely to cause a positive crossmatch) should be avoided in re-transplant patients following discussion with the clinical team and careful risk vs. benefit evaluation.

Alison Logan from Manchester followed with a presentation on HPCT following antibody removal of high-level donor-specific antibodies. The patient presented with high-risk AML and following work-up of potential related donors, both shared an HLA haplotype with the patient. A search of unrelated and cord donor registries yielded no suitable matches. The lack of suitable donors and clinical urgency of the case compelled the clinical team to select one of the related donors with antibody removal performed in the recipient pre-transplant. Both potential donors were CDC and flow cytometry crossmatched against the recipient. The relative who had the lowest level of donor-specific antibodies directed against them was selected as the donor of choice. The patient underwent several cycles of plasma exchange and was eventually transplanted. Post-transplant chimerism monitoring showed the patient had successfully engrafted and

Continued on next page

continues to be fit and well with no apparent rejection.

Finally, Dr Anna Barker, also from Manchester, presented a case concerning a patient with myelodysplasia who was referred for an urgent unrelated donor HPCT. Five donors were identified for the patient, 3 of whom were 10/10 matched at HLA-A, B, C, DRB1 and DQB1. The remaining two donors were HLA-DPB1 mismatched. One of the three 10/10 donors was found to have a discrepant type (HLA-A*01, 02) from that issued by the registry (HLA-A*02 homozygous). HLA antibody screening of the recipient defined donor-specific antibodies against HLA-DPB1*02:01, *04:02 and HLA-A*01. Due to the urgency of the transplant, crossmatching bloods were requested from both HLA-DPB1 mismatched donors; unfortunately, both crossmatches were B-cell positive. Two further donors were ordered who were HLA-DPB1 matched with the recipient. However, during work-up for transplant, the patient relapsed. Dr Barker stressed the significance of receiving samples for HLA antibody screening during work-up in an appropriate timeframe so that selection of the most suitable donors is not compromised, facilitating the shortest possible time to transplant for urgent patients.

Terasaki Lecture

David Briggs from NHSBT Birmingham.

The final lecture of the conference, the Terasaki Lecture, given by Professor David Briggs from NHSBT Birmingham.

"David started his career in H&I in 1980 at Guy's hospital. He worked at Guy's, then as Head of Lab at the Middlesex Hospital in London before becoming Head of Lab in Birmingham in 1996. He has always combined running a clinical service with a very active R&D role, with a wide range of interests including complement genes & KIR as well as many aspects of HLA. His most notable achievement has probably been in the field of HLA incompatible transplantation, working with colleagues in Coventry to successfully implement a programme to transplant patients who would not otherwise have been able to receive a transplant."
Deb Sage, BSHI Chair

Having started in the field at Guy's hospital in 1980, Professor Briggs has worked in H&I for over 40 years, 25 of which have been based at NHSBT Birmingham. This presentation was a culmination of his years spent working with antibodies and antibody incompatible transplantation. To begin with, we went all the way back to Terasaki & Patel's landmark paper from 1969, which correlated a positive CDC crossmatch caused by cytotoxic antibodies with graft failure. From here, Professor Briggs moved on to discussing different approaches to dealing with and treating the issue of antibody incompatible transplantation. It was a wide-ranging presentation covering the profile and dynamics of a donor-directed antibody response, the differences seen across the population in this phenomenon and how to treat AMR. Of particular interest, Professor Briggs mentioned that although pre-transplant plasma exchange is effective at preventing graft rejection, delayed graft loss is still a possibility for these patients. This led on to a discussion whether all antibodies are equal, considering the function, subclass, specificity and MFI level of the antibody, the properties of the cellular target, and the number of anti-HLA antibodies. The final message was an important one, considering the balance of risk versus reward when it comes to transplantation across donor-specific antibodies. A better understanding of these factors will enable us to better stratify transplant risk in future.

End

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Share Your CPD With Others - Our CPDme Dashboard allows you to share and access free CPD opportunities that you or others within the community have found beneficial. Regularly access the shared area for daily updates and recommended development opportunities.

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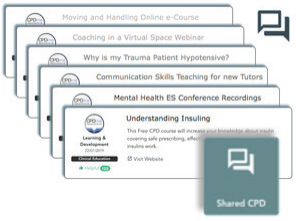

We will be hosting live webinar in November to guide you through getting started with your CPD Portfolio as well provide you with some top tips in capturing your development. A copy of the recording will also be available for you to catch-up.

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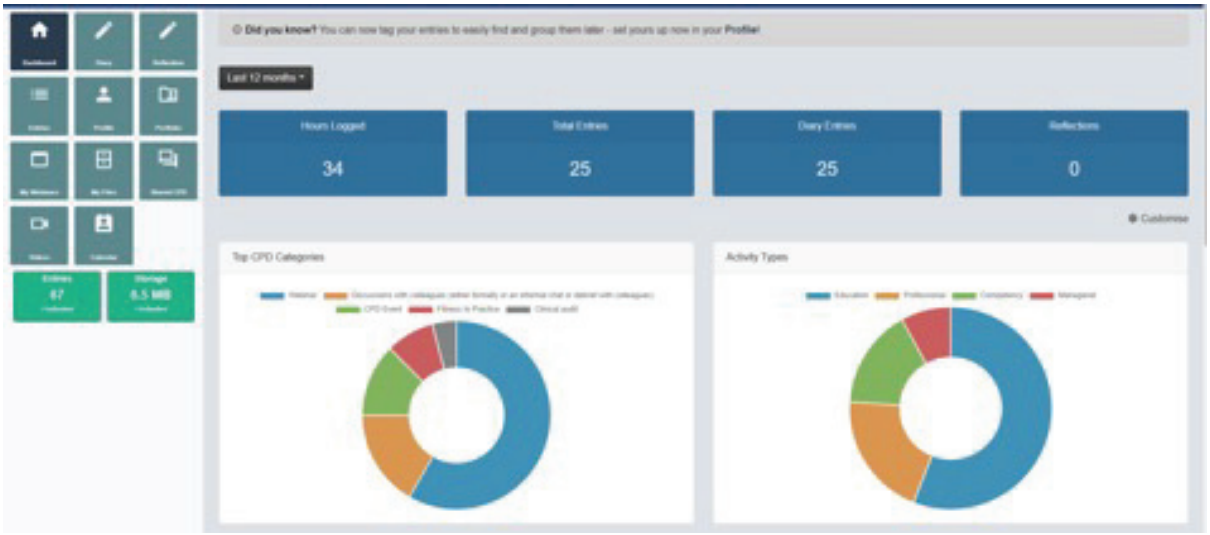
A reminder about BSHI CPD to all members

BSHI CPD is administered externally by CPDMe. You are automatically granted access with your BSHI membership. CPD resources are available on the BSHI website CPD & JBL (bshi.org.uk)

To access your CPD portfolio please login to the CPDMe website www.cpdme.com

Your CPDMe login details are separate to your BSHI login. The details should have been sent to you upon joining but please contact CPDMe via support@cpdme.com if you don't have them.

This is a screenshot of the home dashboard:



It is easy to use CPDme, click on the buttons on the left-hand side to add a diary entry, or create a portfolio to submit to your employer or the Health and Care Professions Council (HCPC). If you do need assistance there is a handy "help" button on the bottom right-hand side of the screen where you can type questions or email support@cpdme.com.

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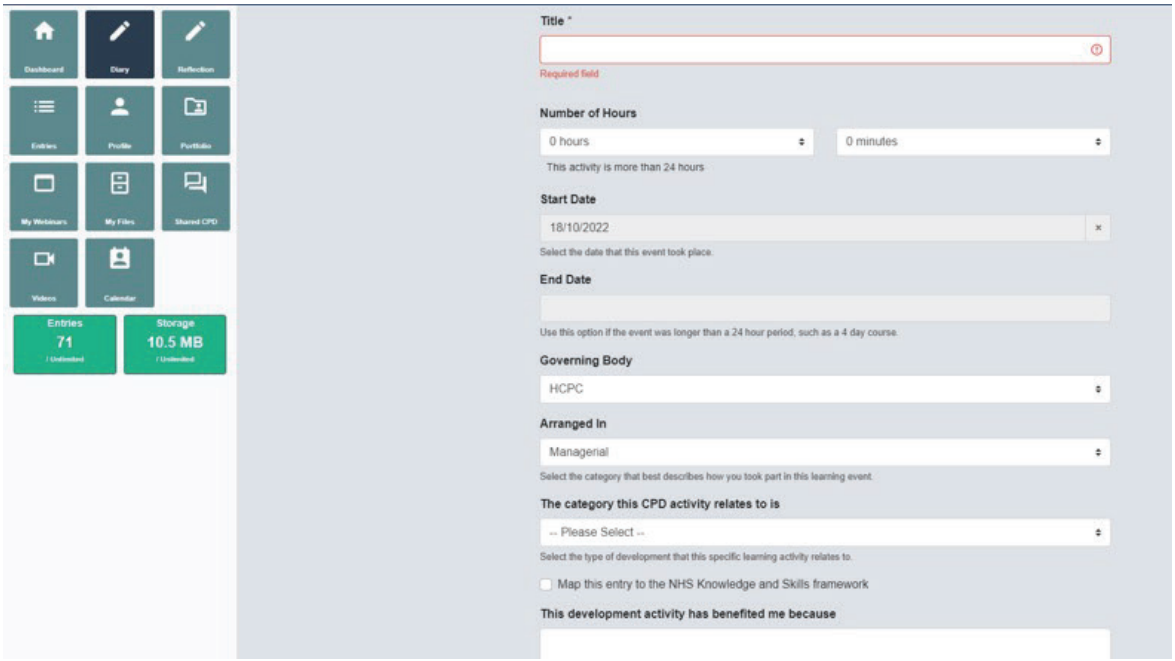
A reminder... continued



When creating a diary entry, select HCPC as the Governing Body and the category of event in the 'Arranged in' field (e.g., Competency, Education, Managerial, Professional). Fill in the remaining fields as appropriate, and then click on 'Save and Close' at the bottom of the screen.

Due to BSHI investing in this electronic CPD product there is no longer a collation or audit of annual returns by BSHI. Individuals are expected to use the CPDme system to build their portfolio in accordance with the mandatory requirements for HCPC registered Healthcare Scientists - Standards of continuing professional development https://www.hcpc-uk.org/standards/standards-of-continuing-professional-development/

If you have any feedback about the CPDme scheme for the BSHI main committee, please email sarah.peacock22@nhs.net (BSHI Education Board Chair).

There are also two YouTube videos which may prove useful.

Build your professional CPD Portfolio (7mins): https://www.youtube.com/watch?v=xoDqE2daGdk&t=73s

Capture CPD using the Mobile App (5 mins):

https://www.youtube.com/watch?v=RnnxszT5BxE&t=2s

End

Sustainability within Transplantation

Mohammad Ali Rafique, VH Bio Ltd.

I was recently given the chance to attend the 50th Anniversary Congress of the British Transplantation Society (BTS) in Belfast. This city was the site of the last in-person BTS meeting in March 2019 and, while much has changed in the 2 and a half years since then, the chairs hoped this meeting provided an opportunity to reflect not only on the last 50 years of the Society but also on the pandemic which necessitated many changes in practice and protocols. My favourite segment of the conference was a session discussing Sustainability in Transplantation, extremely topical given the climate health emergency. Emily Thompson (Newcastle) provided a clinician's overview of the area, which was followed by a lively debate from Brendan Clark (Leeds) and John O'Callaghan (Coventry). I've provided a review of their content and expanded on it to include information pertinent to laboratories; I felt it was important to bring this to the forefront of conversation especially as there are measures that we, as scientists, can take to do our part.

The evidence is clear that, left unchecked, climate change will have catastrophic global health impacts. In 2015, countries committed to limit global warming below 2°C as part of the Paris agreement. However, 5% of all greenhouse gas emissions and over 5 million tonnes of waste come from hospitals worldwide; the annual carbon dioxide emissions arising from the NHS in England are greater than that of all aircraft departing Heathrow Airport, and account for 3% of all UK emissions. These figures have prompted the NHS to pledge to become the first net zero healthcare system in the world by 2040, with interim goals of 51% reduction by 2025 and 80% reduction by 2028. The primary focus is on improving the carbon footprint of the supply chain, increasing the energy efficiency of hospitals, moving to telemedicine, and reducing reliance on anaesthetic gases (which contribute significantly to the greenhouse gas effect as they are 2,500 times worse than an equivalent volume of carbon dioxide). An additional route towards building sustainability comes from new legislation, the Health and Care Act 2022, which highlights that climate change must be considered when making key decisions.

Within the NHS, the most resource-intensive area is surgery; only needed by 5% of patients but accounting for a quarter of emissions from a typical NHS Trust. Surgical theatres use six times more energy than equivalently sized areas of the hospital due to heating, ventilation, and air conditioning requirements; one operating theatre suite was shown to have an annual carbon footprint comparable to over 2,000 homes. Emily used a tool from the Royal Colleges to estimate the carbon footprint of a live donor kidney transplant as approximately 608kg, not including anaesthetic gases. However, I believe laboratories fare little better given our excessive water and energy usage, (fume cupboards, freezers, lab instruments, air conditioning, and IT equipment), dependence on single-use plastics, and the substantial quantities of hazardous and non-hazardous waste generated. Globally, labs are estimated to contribute around 2% of plastic waste, while a single ultra-low temperature freezer can consume as much energy as a house.

However, transplantation is a unique surgical specialty as, by its very nature, it is the most carbon-intensive. During 2021/22, retrieval teams were dispatched to 1,633 potential organ donors, over half of which required cardiothoracic and abdominal teams travelling separately. A high proportion of these involved retrieval team travel times of over 3 hours. 26% of these donors didn't proceed but, for those that did, an average of 3 organs were retrieved requiring separate ambulances for transport. Despite this, transplantation remains a green endeavour represented best by considering renal dialysis which has a large environmental impact; one year of kidney dialysis is equivalent to seven return flights between London and New York. Kidney transplantation is a far more sustainable proposition providing roughly 15 years of kidney-function, reducing overall environmental impacts by 95.7% compared to haemodialysis (HD) and 90.9% compared to peritoneal dialysis (PD). Together, HD and PD also account for 30% of all clinical waste in the UK.

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Sustainability... continued

AGAINST: John argued that there are many other areas of transplantation which could be optimised to reduce carbon footprint, even going so far as to compare the three available ambulances currently used for organ transport (the carbon footprint of which varied significantly); changing these to electric or hybrid vehicles would drastically reduce the amount of carbon dioxide generated during routine transport. He also discussed equity of access provided by a national allocation scheme.

FOR: Brendan presented data provided by the Collaborative Transplant Study (CTS) comparing hazard ratios for an increasing number of HLA-ABDR mismatches (MMs). He found there was no statistically significant increase in risk between 3 versus 4-5 MMs, and that risk was not reduced to an appreciable extent between 3 and 1-2 MMs *(Figure 1)*. In the context of climate change, it is therefore difficult to make an argument for out-of-region shipping except to enable (0 MM) or avoid (6 MM) transplantation at the extremes.

Brendan also made the point that we, as a community, need to re-examine nomenclature in terms of biological significance through a worked example of an HLA-A mismatched donor-recipient pair; epitope-based analysis showed all epitopes found on the HLA-A mismatch were represented within the recipient HLA type thus not seen as foreign.

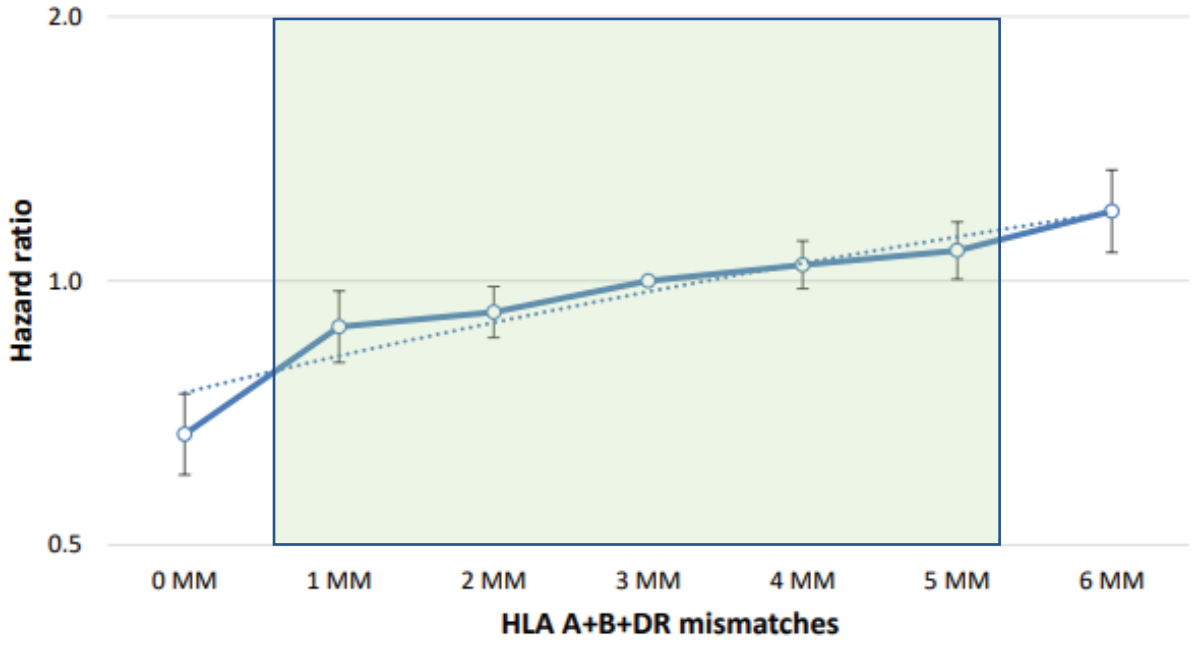

Figure 1. Influence of HLA-ABDR mismatches on death-censored graft survival after first post-transplant year (CTS, personal communication, 2022). The statistical significance of graft mismatches within the box is negligible.

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Sustainability... continued

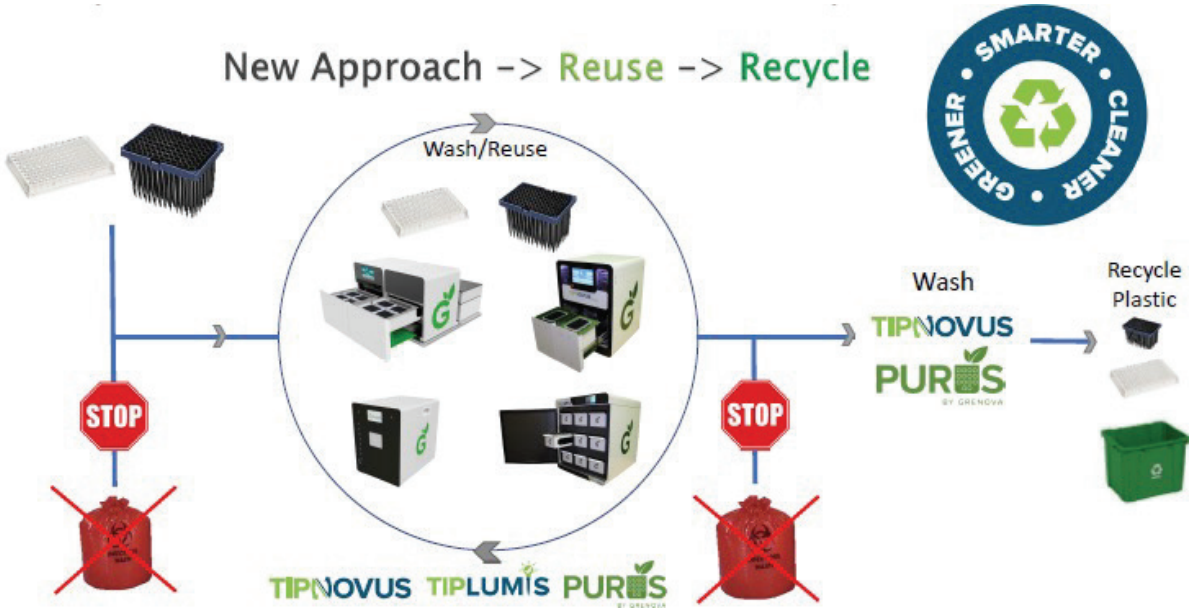

Figure 2. Lab plastic life-cycle (Grenova, 2022).

Coming back to the BTS session, the motion raised was that 'organ allocation should be redirected locally to minimise the carbon footprint of transplantation.'

While this was an extremely divisive and emotive topic, it frames the types of conversations that need to happen to reach a net-zero healthcare system. Looking closer to home, we can take several actions to promote this agenda. Clinical labs may benefit from adopting Laboratory Efficiency Assessment Framework (LEAF) certification or participation in the My Green Lab programme as a framework for promoting sustainability practices. These systems provide information on how to save water and energy, reduce plastic waste, and source sustainable consumables and equipment. There are several companies ready to address the growing requirement for sustainability, such as Grenova who have designed an automated pipette tip washer; this reduces reliance on single-use plastics as tips may be re-used a number of times with no drop in performance or carryover; a final wash also enables tips to be disposed of as non-hazardous waste. Other companies can provide newer, more efficient freezers to replace older end-of-life models; laboratories could also explore 'chilling up' ultra-low temperature freezers from -80°C to -70°C as this can save roughly 30% of energy.

Ultimately, bringing sustainability into routine practice through green endeavours may represent whole-life cost-savings to the NHS but will benefit everyone by reducing global environmental impact.

End

Spotlight on…. Leeds!

Katherine Mounsey and Adrienne Seitz, Leeds

As recent grateful beneficiaries of a BSHI bursary (for the purpose of attending the annual conference) Adrienne and I have been requested to provide a 'virtual lab tour' of the Leeds Transplant Immunology Laboratory, based at St James's Hospital. Having originally been developed under the auspices of the Leeds National Blood Service, based at Seacroft Hospital, the Transplant Immunology Lab moved to St James's (aka Jimmy's), about a mile outside of the main city centre, in 1994, to be closer to the clinical services for which it was providing support. The laboratory was relocated into 'temporary' accommodation on the ninth floor of one of the main hospital wings, Gledhow. Fast forward a quarter of a century and the space afforded to the lab has been expanded and improved upon but remains in temporary residence on Level 9! One of the first thing that visitors to the lab comment on is the perhaps unique view across Leeds with some of its back-to-back terraces and a large mosque, providing distraction during sample incubations, and a brilliant view of the fireworks at New Year!

Some members of the lab team

Having worked on Level 9 for twenty years (scary but true!), I feel that I am fairly well placed to provide an overview of the lab. However, I am not the longest serving member of the lab team by quite a number of years; this accolade belongs to Neil Marsden, who is one of the original team of fourteen who moved from Seacroft, closely followed by Brendan Clark.

We are now a UKAS and EFI accredited laboratory, with a team of some 22 individuals, consisting of Biomedical Support Workers, Biomedical Scientists, Clinical Scientists, clinician scientist, and administration support workers. The core work is a regional service, related to renal transplantation (167 transplants in 2021) and HSCT (a local record of 84 transplants in 2021), but has also grown to include disease association and adverse drug reactions, liver transplantation, and hand/upper limb transplantation (the latter evidenced by the excellent sessions delivered at BSHI 2022). The transplantation work which we support is ever increasing in both numbers and complexity of the cases, with some of the more complicated kidney transplantation cases being facilitated by the national living donor kidney sharing scheme (17 transplants in 2021). In regards to the deceased donor kidney transplantation programme, as a lab Leeds have embraced the challenge of contributing to streamlining this pathway and minimising cold ischaemic time, and we have now achieved a virtual crossmatch rate of 77% (based on either recipient most recent sample or rapid time of offer SAB analysis).

A lot has changed in twenty years…… when I started in 2002, serological HLA typing was one of our main routine methods and DNA extraction was carried out by an extended in-house salting out method that took the best part of two days to complete. Nowadays, routine non-urgent HLA typing is mostly Luminex RSSO and NGS based, with commercial PCR-SSP as back-up. We have just obtained our own MiSeq sequencing platform and our second QuantStudio real-time PCR instrument will be on the bench soon, (fingers crossed!) for rapid HLA typing (using Linkseq methodology) to support the national deceased donor typing contract work.

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In terms of antibody screening/ identification, and crossmatching we are now fully flow based, using Luminex and flow cytometry technology. This work includes post-transplant DSA monitoring work in defined circumstances for renal transplantation. We have a LabXpress robotic platform attached to one of our Luminex analysers, and we are the only laboratory in the UK that uses the LabXpress for both typing and antibody detection.

One of the main strengths of the Leeds H&I service is its strong links with the clinical teams and programmes which we support. We are embedded within the multidisciplinary teams of each of the transplantation services and are truly a patient -focussed service. One of the issues discussed at BSHI 2022 was the post-analytical time often spent in reviewing the complex data that can surround one case, in order to contribute to and facilitate a plan to maximise the chance or opportunities for transplantation, whilst ensuring the best possible outcomes. I will now hand over to Adrienne, to describe our latest approach to managing renal recipients and a taster of our research initiatives.

Over the last few years, we have developed a risk stratified approach to managing our complex renal patients. Based on the active wait time and level of sensitisation, patients are moved through different tiers of increasing immunological risk and delisting strategies in order to facilitate a transplant. Brendan, our lab director, has called this the Transplant Assessment and Relative Opportunity Tool, as he enjoys the thought of providing patients with tarot readings. It was really exciting to see the TAROT scheme win the Medipex NHS Innovation award (Improved process and systems) - thank you Pamela Hughes, our section lead for immunogenetics, for all of your work on this.

The Leeds lab has been a longstanding contributor to national and international meetings, including the organisation of the BSHI annual conference on two occasions. We have an active research programme through our strong links with the renal and immunology clinical teams. We have several members of staff working on research projects that will contribute to higher degrees. Areas of research interests include: regulatory B cells and role in allograft outcomes, the role of HLA antibody binding and subsequent tissue remodelling, and cell free DNA as a biomarker of renal allograft outcomes. We have also investigated T cell memory responses following vaccination in the CKD and renal transplant population.

At the time of writing, here in Leeds we are on the brink of a busy and challenging time ahead, with the planned introduction of a new LIMS and a move into new facilities on the horizon, both scheduled for some time in 2023!

LABXpress with LABScan 3D at rear

Room with a view - pre-PCR laboratory

End

Imlifidase: The solution (…and a problem?)

Adrienne Seitz & Brendan Clark, Leeds

An exciting new therapeutic agent, Imlifidase, has recently been approved by NICE as a desensitisation treatment for highly sensitised adults awaiting renal transplantation. Derived from *Streptococcus pyogenes* (colloquially known as the flesh-eating bacterium), Imlifidase is an enzyme capable of cleaving IgG antibodies into F(ab')2 and Fc. The substrate specificity is confidently stated in a number of transplant-related publications as being exclusively limited to the hinge region of IgG after Gly 236. However, other publications, including those concerned with the biology of *Streptococcus pyogenes,* make the less certain statement that no other substrate than IgG is known. It is unclear from the literature how far efforts have extended in trying to explore the substrate range of the enzyme beyond IgG, but the apparent exquisite specificity has been possibly attributed to a second binding site interacting with the Fc part of IgG. In the present context it is however notable that where articles concern the biological function of IDeS (from which Imlifidase is derived) as a virulence factor of *Streptococcus pyogenes,* there is some differential reactivity reported with IgG2 being stated to be less efficiently degraded.

Under the new NICE guidance, the process where antibodies are delisted from a patient record is subject to decision making at a local level. Similarly, post-treatment laboratory work-up is entirely at the discretion of the treating centre. It is expected that following Imlifidase treatment, all HLA antibodies will be cleaved and therefore lost from the patient profile.

A liberal viewpoint would be that the available evidence for the efficacy of Imlifidase is so great that following an infusion, all HLA antibodies will be cleaved, and the patient can progress to transplant post treatment without the need for further histocompatibility testing. This bold approach possibly risks performing a transplant blinded to persistence of a DSA in a treated patient. In this regard up to 50% of Imlifidase treated patients were reported to have significant levels of DSA 2 hours post treatment, and just over 20% had MFIs>3000 after 6 hours.[1] Cleaving the DSA pre-transplant opens a window of opportunity for transplantation, however the story does not end there. A rebound in DSAs post-transplant is expected, and up to 40% of patients will develop early AMR.[1]

At the more conservative end of things an argument can be made that a more judicious approach to delisting based on antibody levels, behaviours, locus specificity etc should be taken and that time-of-offer testing should involve any of a number of tests including total IgG measurement, wet crossmatching and an assessment of complement binding. This precautionary approach creates complexity in data analysis that risks denial of a transplant opportunity on insubstantial grounds given the clinical circumstance of the patient and their already accepted immunological high-risk status.

A recent discussion following presentations made at the BTS congress agreed that the use of Imlifidase would only be justified in a centre with considerable HLAi transplant experience.

As participants in the Imlifidase post-authorisation trial Leeds have developed a structured, stepwise approach to antibody delisting which seeks to balance increase in immunological risk with increasing donor access with aim to achieve donor N=100/10,000 within the national sharing scheme. This number has been locally shown to be the threshold at which donor offers begin to be received for patients who previously had none.

At time of writing a UK Imlifidase Expert Group has been convened under auspices of NHSE/NHSBT with remit to provide expert guidance on safe implementation of Imlifidase in the kidney transplant pathway. This guidance will be ratified through BTS/BSHI and is expected to be delivered in early 2023.

When interpreting laboratory tests consideration needs to be given to the potential confounding influences of Imlifidase on results. These were partly explored in the recent BSHI Newsletter article from Amy De'Ath. Further possibilities are now raised that may need to be considered by laboratories supporting units employing Imlifidase treatment.

Whilst positive to negative crossmatch conversions and donor specific antibody reductions are widely and confidently reported in the clinical literature there are some theoretical concerns that these may partly reflect changes in the assay systems themselves rather than abrogation of donor alloreactivity in the patient. Whilst acknowledging the claimed specificity of the modality, such changes would relate to antigen cleavage/ denaturation, or inactivation of immunoglobulins used in the detection phase of the assay. Similarly, there are concerns that post-treatment positivity

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may be due to detection of bound antibody fragments rather than intact, biologically functional molecules. Returning to the matter of the relative sparing of IgG2- Imlifidase treatment could lead to comparatively increased concentrations of non-complement-fixing IgG2 resulting in competitive inhibition of binding of other subtypes and risk for erroneous interpretation. Similarly, because Imlifidase does not cleave IgM, the same issue may pertain in patients with HLA-IgM antibodies.

Some limited data are now emerging in respect of these concerns:

The presence of an intermediate Imlifidase digestion product termed single cleaved (scIgG) in treated patient samples has been reported to produce a positive signal in the LABScreen SAB test[2]. Reactivity caused has been reported as significant with results considerably higher than background even with serum samples containing only trace amounts of scIgG. The same authors report that this binding was undetected in the C1q assay variant, but elsewhere in the same paper identify that C1q reactivity was detected with single cleaved rituximab targeting CD20 expressing Daudi cells and with single cleaved HLA IgG using a polyclonal anti-C1q antibody but not with the OL kit reagent. Clarity is therefore lacking in this regard and confidence in the assay system as a means of determining efficacy of treatment and informing clinical decision making requires local determination.

Both CDC and flow crossmatch tests are also compromised, with CDC reactivity being reported as reduced but not entirely lost with serum preparations containing scIgG and flow crossmatch tests stated to remain positive. The authors emphasise that their results reflect suboptimal treatment designed to serve the purposes of their investigation. However, a caution is raised in regard to data interpretation in a clinical context.

Away from these published observations, conversations with various colleagues have indicated that issues with assay performance are sometimes being encountered in situations with samples from patients treated with Imlifidase. Anecdotally, Imlifidase can sometimes increase the SAB negative control signal, affecting assay sensitivity. Others have stated that assays systems are not compromised.

Clearly these two positions do not quite square with each other however this impact is to some extent mitigated for by manufacturer defined limits of acceptability for the negative control signal.

We understand that, at time of writing, One Lambda are currently conducting their own investigations into potential assay interferences.

As a new treatment modality and until a body of evidence has accumulated it is perhaps wise for us to behave with some caution in respect to potential assay interferences and to conduct revalidation of our assay systems as appropriate.

We are presently involved in revalidation of laboratory assays and hope to be able to share our experience with colleagues in due course.

References

1. *Jordan SC, Legendre C, Desai NM, et al. Imlifidase Desensitization in Crossmatch-positive, Highly Sensitized Kidney Transplant Recipients: Results of an International Phase 2 Trial (Highdes). Transplantation. 2021;105(8):1808-1817. doi:10.1097/TP.0000000000003496.*
2. *Bockerman R, Jarnum S, Runstrom A, Lorant T, et al. Imlifidase-generated Single-cleaved IgG: Implications for Transplantation. Transplantation 2022 Jul; 106(7): 1485–1496 doi 10.1097/TP.0000000000004031.*

End

Meetings diary

BSHI Annual General Meeting (AGM)

7th December 2022

Online

EFI 36th Conference

24th April 2023 – 29th April 2023

Nantes, France

ESOT 40th Conference 2023

17th September 2023 – 20th September 2023

Athens, Greece

ASHI Annual Meeting

15th October 2023 – 20th October 2023

San Antonio, USA

BSHI On-line Journal Access

BSHI provides members with full-text access to the following journals:

American Journal of Transplantation
Current Opinion in Organ Transplantation
International Journal of Immunogenetics
Transplantation

Instructions on how to access these journals is on the Members' Section of the BSHI website:
www.bshi.org.uk/

BSHI Continuing Professional Development

Journal Based Learning

The CPD JBL questions can be found on the BSHI website, and you must now submit your answers electronically via the website.

CPD Points

The question/answer page will be marked and scored by an assessor appointed by the Research Executive.
Points will be awarded on the basis of:
0-10 answers correct – 0 points, 11-14 correct – 1 point, 15 – 19 correct – 2 points, all 20 correct – 3 points.

How to participate

If you are registered on the BSHI CPD scheme, then you are eligible to participate in the Journal Based Learning scheme. All you need to do is read the reference article given at the top of the answer card, and then answer the question statements by choosing true or false for each of the 20 statements relating to the article.
Go to *https://bshi.org.uk/training-and-development/current-jbl/*

Then fill in your name, contact address, e-mail address and BSHI membership number.
Simply click on your choice.
Any answers that are not clear, or are ambiguous, will not score.

If you have any comments or suggestions about the Journal Based Learning series and the topics/articles then please get in touch via: *Amy.De'ath@wales.nhs.uk*

The submission deadline for this cycle is: 14th January 2023.

Your answers will be assessed and returned to you with the number of CPD points earned, for inclusion in your BSHI CPD folder. Any members not currently registered on the CPD scheme, but interested in joining should contact the BSHI CPD Co-ordinator; details in the Newsletter.

Continued on next page

Journal Based Learning Cycle 83

Paper title & reference:
Imlifidase-generated Single-cleaved IgG: Implications for Transplantation.
Robert Bockermann , Sofia Järnum , Anna Runström , Tomas Lorant , Lena Winstedt , Niklas Palmqvist , Christian Kjellman.
Transplantation. 2022 Jul 1;106(7):1485-1496.
http://doi.org/10.1097/TP.0000000000004031

JBL submissions to be made via the BSHI Website - https://bshi.org.uk/training-and-development/current-jbl/
Deadline for submission of completed answers: **14th January 2023**
All journals are available through the BSHI access or are open access journals.

1.	Imlifidase is an IgG-degrading enzyme of Streptococcus pyogenes.	**True**	**False**
2.	Imlifidase is a 35-kDa serine protease and can cleave all 4 subclasses of human IgG.	**True**	**False**
3.	Imlifidase cleaves the heavy chains of IgG in two separate reaction steps to generate a F(ab')2 and a homodimeric Fc fragment.	**True**	**False**
4.	Single-cleaved IgG (scIgG) is generated as a final cleavage product.	**True**	**False**
5.	The Human lymphoma cells lines Raji and Daudi, and a human monocytic leukemia cell line THP-1 were used in this study.	**True**	**False**
6.	A 0.12mg/Kg dose of imlifidase from a patient study was shown to be sufficient for the complete removal of circulating IgG.	**True**	**False**
7.	In eAIHA experiments, nine-week-old female BALB/c mice were injected with 0.25mg preparations of intact IgG, scIgG or F(ab')2 generated from rabbit anti-mouse thrombocyte serum.	**True**	**False**
8.	SDS-PAGE analysis and Western blots showed that one hour after imlifidase treatment of serum from an HLA-sensitized patient, all intact IgG was cleaved to scIgG which was further converted to F(ab')2 and Fc fragments after six hours.	**True**	**False**
9.	Pre-treatment serum generated strong signals in both LABScreen and C1qScreen assays, with median MFI values <20,000.	**True**	**False**
10.	Despite the total elimination of intact IgG 1hr after imlifidase treatment, LABScreen signals from anti-HLA scIgG were only slightly reduced in comparison with pre-dose signals.	**True**	**False**
11.	Low levels of scIgG were still present two days after treatment initiation and were weakly detected by Fc-specific Western blot but gave a median MFI signal of 2000-3000 with the LABScreen assay.	**True**	**False**
12.	In this study, the complement fixing capacity of HLA-reactive scIgG was investigated using cytotoxic human serum.	**True**	**False**
13.	Serum fractions containing mainly F(ab')2 fragments with either small or trace amounts of scIgG were negative against donor T and B cells in the panel of five blood donor cells tested.	**True**	**False**
14.	HLA-binding scIgG were not well recognised by the Fc-specific detection antibody used in the LABScreen assay.	**True**	**False**
15.	ADCP stands for Antibody Dependent Cellular Phagocytosis	**True**	**False**
16.	Cytotoxicity was detectable with intact rituximab, single-cleaved and fully cleaved rituximab at 10ug/ml.	**True**	**False**
17.	Anti-erythrocyte scIgG retained about 40% of the ADCC lysing activity at 5 ug/ml.	**True**	**False**
18.	scIgG reduced the number of erythrocytes in eAIHA and reduced platelet count in eITP.	**True**	**False**
19.	AHG-amplified CDCXM relies on anti-IgG and FCXM relies on anti-Fc antibodies in their detection steps.	**True**	**False**
20.	Both FCXM and anti-HLA SAB assays were able to discriminate between intact IgG and scIgG.	**True**	**False**

Scoring
CPD points will be awarded as follows:
0-10 correct 0 points | 11 – 14 correct 1 point | 15 – 19 correct 2 points | 20 correct 3 points

Journal Based Learning Cycle 82 answers

Human Leucocyte Antigen Sensitisation and Its Impact on Transfusion Practice
Christof Weinstock and Martina Schnaidt. Transfus Med Hemother 2019 Oct; 46(5):356-369.
https://pubmed.ncbi.nlm.nih.gov/31832061/

JBL submissions to be made via the BSHI Website - https://bshi.org.uk/training-and-development/current-jbl/

1.	Platelets have a lifespan of 8-12 days *in vivo*	**True**
2.	Cells of the cytotrophoblast express HLA-A and HLA-B	**False**
3.	High titres of maternal anti-D can cause severe haemolytic disease of the newborn	**True**
4.	HLA sensitisation decreases with increasing number of pregnancies	**False**
5.	Red cells are the major source of transfused HLA	**False**
6.	Irradiation can inactivate HLA-bearing cells	**True**
7.	Leucocyte filtration has eliminated HLA sensitisation	**False**
8.	IgM, IgG1 and IgG3 can activate complement	**True**
9.	MAIPA can be used to perform a crossmatch	**True**
10.	Clinical conditions that decrease consumption of platelets include bleeding and fever	**False**
11.	The post transfusion increments following platelet transfusion are similar for donors selected using epitope matching and HLA-A and –B matching	**True**
12.	HLA expression on red cells is decreased during infections	**False**
13.	Bennett-Goodspeed antigen Bga is correlated with the presence of HLA-B7	**True**
14.	Pyrogenic cytokines mediate a fever in febrile non-haemolytic transfusion reactions	**True**
15.	TRALI develops within 2 hours post transfusion	**False**
16.	TRALI is mostly caused by donor-derived antibodies	**True**
17.	Male donors are more likely to cause TRALI	**False**
18.	Transfusion associated GvHD can develop in immunocompromised and immunocompetent patients	**True**
19.	Acid treatment removes HLA from platelets	**True**
20.	Measures to mitigate transfusion reactions include HLA matched products, careful selection of plasma donors and irradiation	**True**

Scoring

CPD points will be awarded as follows:

0-10 correct 0 points | 11 – 14 correct 1 point | 15 – 19 correct 2 points | 20 correct 3 points

Call for Case Studies

This notice is an update on the process for submission of case studies for publication in the Newsletter.

The purpose of publishing case studies in the Newsletter is to highlight interesting cases from individual H&I laboratories that the community as a whole would benefit from in terms of training and education or to generate discussion. We all stand to learn from each others' experiences.

There is no template for the submission. As a guide, it should be approximately 1000 words in length and at least at the level appropriate for inclusion in a portfolio for the Association of Clinical Scientists. Cases should include only a brief description of laboratory tests and focus primarily on the interpretation of results in the clinical context and their impact on patient management. Essentially, the more unusual and informative it is the better. Key learning points should be identified in order to highlight the educational value of the case.

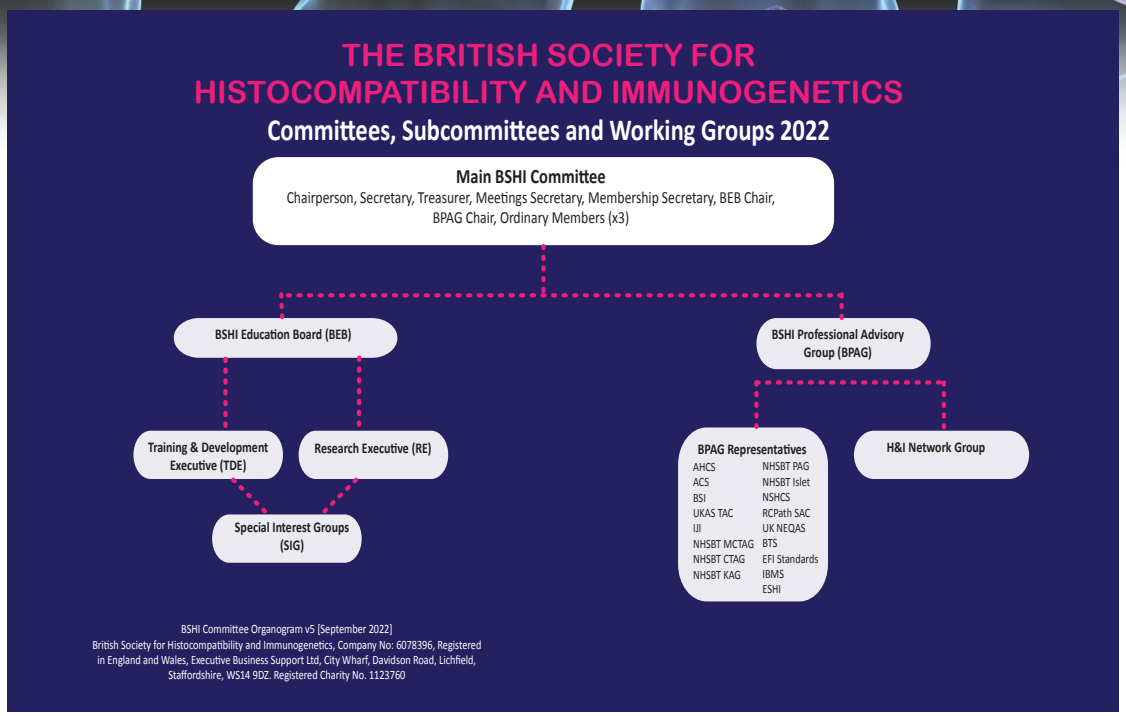
Cases equals prizes!

As a replacement for the CPD prizes previously awarded for achievements in Journal Based Learning, the BSHI Education Board will now award a £25 book token for each case selected for publication in the Newsletter.

Submission process

Please send your submission to the BSHI Secretary, Carla Rosser (secretary@bshi.org.uk). Cases will then be reviewed by at least two members of the Education Board to assess suitability for publication. No more than one case study will be published in each Newsletter but if there is more than one suitable case submitted for one edition then cases may be held in reserve for publication in subsequent editions.

Chair, BSHI Education Board



BSHI Education Board

Name	Role	Until	Contact details
Sarah Peacock	Chairperson	AGM 2024 (2nd term)	Sarah.peacock@addenbrookes.nhs.uk
Carla Rosser	BSHI Secretary	AGM 2024	carla.rosser@nhsbt.nhs.uk
Paul Wright	Chairperson of TDE	2025	Paul.A.Wright@mft.nhs.uk
Anthony Poles	Chairperson of Research Executive	2023	Anthony.Poles@nhsbt.nhs.uk
Amy De ‘Ath	Research Executive Secretary	Aug 2025 (2nd term)	Amy.De’ath@wales.nhs.uk.
Tracey Rees	Chairperson of RCPath panel of examiners in H & I	As required	Tracey.Rees2@wales.nhs.uk
Olivia Shaw	BSHI representative to ACS	As required	Olivia.Shaw@viapath.co.uk
Liam Oates	BSHI representative to IBMS	Mar 2024	Liam.Oates@wales.nhs.uk
Deborah Sage	Co-opted member: UK member of EFI Education Committee	As required	Deborah.Sage@nhsbt.nhs.uk

BSHI Training and Development Executive update 2022

Position	Name	Until	Email
Chairperson	Paul Wright	Sep-24	paul.a.wright@mft.nhs.uk
Secretary	Anna Barker	Nov-22	Anna.barker@mft.nhs.uk
BSHI Diploma Co-ordinator	Fiona Powell	Sep-24	fiona.powell3@nhs.net
STP Co-ordinator	Sandra Lloyd	Nov-22	Sandra.LLoyd4@wales.nhs.uk
CPD Co-ordinator	Katharine Keyworth	Mar-22	Katharine.Keyworth@mft.nhs.uk
RCPath Trainee Representative	Felicity May	Jul-23	Felicity.May@wales.nhs.uk
Meetings Secretary H&I Specialist	Kirti Mepani	Nov-23	Kirti.Mepani@nhsbt.nhs.uk
Meetings Secretary Higher Training	Amy De’Ath	Aug-24	Amy.De'ath@wales.nhs.uk
Academic Liaison	Natalia Diaz Burlinson	TBC	Natalia.DiazBurlinson@mft.nhs.uk
Trainee Representative	Victoria Wood	Apr-22	victoria.wood8@nhs.net
BSHI Certificate of Competence Co-ordinator	Charlene Hoad	Apr-23	Charlene.Hoad@viapath.co.uk
IBMS representative	Liam Oates	Mar-24	Liam.Oates@wales.nhs.uk
Ordinary Member	Jennifer Lord	Dec-23	Jennifer.Lord@mft.nhs.uk
Ordinary Member	Sharon Vivers	Sep-24	Sharon.Vivers@anthonynolan.org

BSHI Research Executive

	Position	Name	Start	End	Contact details	Comment
1	Chairperson (Officer)	**Anthony Poles,** NHSBT Filton	AGM 2020	AGM 2023	Anthony.Poles@nhsbt.nhs.uk	First term
2	Secretary (Officer)	**Amy De'ath,** Welsh Blood Service, Cardiff	AGM 2019	AGM 2022	Amy.De'ath@wales.nhs.uk	First term
1	Ordinary Member	**Olivia Shaw,** Guy's Hospital, London	AGM 2019	AGM 2022	Olivia.Shaw@viapath.co.uk	Staying on for another term – cannot be reappointed in 2022
2	Ordinary Member	**Winnie Chong,** National H&I Service Development, NHS BT Colindale	AGM 2020	AGM 2023	winnie.chong@nhsbt.nhs.uk	Staying on for another term – cannot be reappointed in 2023
3	Ordinary Member	**Stephen Weston,** Leicester General Hospital	AGM 2019	AGM 2022	stephen.weston@uhl-tr.nhs.uk	First term
4	Ordinary Member	**Emma White** Barts	AGM 2020	AGM 2023	emma.white36@nhs.net	First term
5	Ordinary member	**Thomas Turner** Anthony Nolan	AGM 2020	AGM 2023	Thomas.Turner@anthonynolan.org	First term
6	Ordinary Member	**Sarinder Day** Southmead Bristol	AGM 2020	AGM 2023	Sarinder.Day@nbt.nhs.uk	First term
7	Ordinary Member	**Paul Wright,** Manchester	AGM 2021	AGM 2024	Paul.A.Wright@mft.nhs.uk	First term
8	Ordinary Member	**Ying Lee,** NHSBT	AGM 2021	AGM 2024	Ying.Li@nhsbt.nhs.uk	First term

The two officers of the RE are the Chairperson and RE Secretary, there are also a maximum of 8 ordinary members. The tenure of RE committee members is three years. However all members are eligible for immediate reappointment subject to maximum tenure of six years after which time the member will step down.

BSHI representatives to other professional societies/organisations, updated May 2021

Organisation	Member's Name	Term of office	Ends	Tel No./Email
Academy for Healthcare Science Professional Bodies Group	Deborah Sage	As required	N/A	Deborah.Sage@nhsbt.nhs.uk
Association of Clinical Scientists	Olivia Shaw	As required	N/A	olivia.shaw@viapath.co.uk
British Society for Immunology BSHI Affinity Group	Amy De'Ath	3 years	2022	amy.de-Ath@wales.nhs.uk
British Transplantation Society	Arthi Anand	3 years	2025	arthi.anand@nhs.net
European Board of Transplant Immunology (ESHI Diploma)	David Turner	8 years	2025	david.turner@nhs.scot
European Federation for Immunogenetics Standards Committee	Katy Latham	As required	N/A	Katy.Latham@nhsbt.nhs.uk
Institute of Biomedical Sciences	Liam Oates	As required	Mar 2024	Liam.Oates@wales.nhs.uk
International Journal of Immunogenetics	Amy De'Ath	3 years	2022	amy.de-Ath@wales.nhs.uk
NHSBT Cardiothoracic Advisory Group	Delordson Kallon	3 years	2024	dkallon1@nhs.net
NHSBT Kidney Advisory Group	Richard Battle	3 years	Jun 2025	Richard.battle@nhs.scot
NHSBT Multivisceral and Composite Tissue Advisory Group	Sarah Peacock	3 years	Feb 2022	Sarah.peacock@addenbrookes.nhs.uk
NHSBT Pancreas Advisory Group	Arthi Anand	3 years	Aug 2022	arthi.anand@nhs.net
NHSBT Pancreas Advisory Group – Islet steering group	David Turner	3 years	Aug 2022	david.turner@nhs.scot
NSHCS Life Sciences Themed Board	Sarah Peacock	As required	N/A	Sarah.peacock@addenbrookes.nhs.uk
Royal College of Pathologists H&I Speciality Advisory Committee	Richard Battle (BSHI rep) David Turner (Chair)	Sept 2024 3 years	N/A Oct 2024	Richard.battle@nhs.scot david.turner@nhs.scot
UKAS Med Lab TAC (Previously Clinical Pathology Accreditation (UK) Ltd)	Fotini Partheniou	3 years	Jun 24	Fotini.Partheniou@liverpoolft.nhs.uk
UK NEQAS Quality Assurance Advisory Panel in Immunology	Elizabeth Wroe	3 years	March 2022	Elizabeth.Wroe@nhsbt.nhs.uk