European Federation For Immunogenetics

NEWSLETTER

September 2019 - Issue 89

.....from the EFI President

Dear colleagues and friends,

I hope everyone enjoyed the summer and used the holiday time to refill your batteries and start the new season with energy, health and motivation. Autumn and spring are always busy times of the year when it comes to conferences and therefore I hope to see many of you in the upcoming important events like the ASHI meeting, the Eurotransplant meeting as well as various national and regional events in Europe.

It's been several months since we had our annual EFI conference in Lisbon. I am sure that all of you who participated will agree with me that Antonio Martinho and his team did an excellent job. The conference was successful, scientifically, socially and financially. On behalf of the entire EFI Executive committee I would like to cordially thank Antonio Martinho, his local organising committee and their PCO for all the work they put and the efforts they made for this major scientific EFI event. We will definitely remember Lisbon as one of the most successful EFI annual conferences! Also I would like to thank the companies who continuously support our annual meetings. Without their help it would not have been possible to organise these successful conferences which are not only important in terms of continuous education of our members but also in terms of interaction and networking. Much of the scientific collaborations which result to published papers are initiated and planned through contacts made at our annual meetings. Lastly, I would also like to thank the EFI committees involved in the organisation of this event and in particular Katharina Fleischhauer, David Turner and the Scientific and Education Committee, respectively.
In Lisbon we announced the results of the EFI elections which were carried out some months earlier. At the end of the general assembly some of the EC members rotated off and were replaced by new members. I would like to thank Teresa Kauke, Valeria Mioti and Fatma Oguz, our outgoing Councillors for the three years they have dedicated to EFI. At the same time, I would like to cordially welcome our new Councillors: Marco Andreani from Rome, Katarzyna Bogunia-Kubik from Wroclaw and Katerina Tarassi from Athens. I very much look forward to working with all three!

Another highlight in the months since the last EFI newsletter was the International Summer School (ISS) on H&I, which this year was organised and carried out by our ASHI colleagues in Montreal. Once again, this event was extremely successful. It gave the opportunity to a limited number of young scientists not only to widen their spectrum of knowledge in H&I by listening to the presentations given by the Faculty Members, but also to present their own work and discuss about it with the Faculty and with the other students. This year's ISS was the first time where a new H&I society joined and contributed with students and faculty members: The Arabic Society of H&I (ARSHI) is the new member in the club of H&I societies organising the ISS. Each society contributed with two faculty members - EFI was represented by James Robinson/London and me. We would like to thank our ASHI colleagues for giving us the great opportunity to participate in this event and for organising everything so well. The ISS is going to be carried out next year and this time it will be EFI's turn again. The venue and the city have been already selected - it will be beautiful Prague. We thank Tony Slavcev who volunteered to organise next year's ISS and I would personally like to encourage the young students to take the opportunity and apply for a participation in this highly educative event. In 2021 the ISS will then be carried out by ARSHI in a Middle East venue before APHIA takes the turn in 2022.

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....FROM THE EDITOR'S DESK

Hopefully, you have had a great summer and got the opportunity to relax and enjoy some time off. First of all, I would like to congratulate Antonio Martinho and the rest of the organising team of the EFI meeting in Lisbon for the excellent event they put together. I am sure all the EFI members enjoyed the beautiful meeting location, the excellent scientific program, the great gala dinner with dancing, and of course the beautiful fado.

From this place, I would also like to congratulate the winners of the several awards that were presented during the last EFI meeting, including the Ceppellini Lecture (Pamela Bjorkman), the Julia Bodmer Award (Asbjørn Christophersen), the Jon van Rood Award (Marco Carvalho-Oliveira), as well as the three poster award winners (Francesca Lorentino, Ben Matern and Iñaki Ortiz de Landazuri).

This edition of the newsletter contains the report of the general assembly held in Lisbon, information on upcoming elections, several committee reports and reports from the bursary receipients. In addition, some information regarding the upcoming HLA and Immunogenetics Workshop is included in this issue.

Finally, I am very happy to announce that the HLA journal, the official journal of EFI, has seen an increase in its impact factor from 2.558 to 2.785, which is expected to rise with more and more publications from the EFI community. As per usual, the highlights of the HLA journal can be found at the end of this newsletter.

As always, I hope that you enjoy reading the EFI newsletter and I very much look forward to your contributions for the next edition.

Sebastiaan Heidt

Deadline for contributions to EFI newsletter 90 is November 18, 2019
Please send your contributions by e-mail to s.heidt@lumc.nl

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The heterogeneity in Europe, the different languages, the different cultures and the different needs of training and support in H&I issues, including accreditation has lead early in the creation of the EFI Regions. The regions eventually developed own activities and initiatives in the H&I work and so we have now next to the regional accreditation commissioners, region specific EPTs, and region specific educational events some of which over the time became tradition. This year's Balkan (Region 9) educational event will be carried out in Erivan/Armenia. We hope that this will be a great opportunity for the neighbouring countries, which have not been really active within EFI so far (Georgia, Azerbaijan, Iran, Ukraine, Russia), to take the opportunity and join all the colleagues from the region as well as the invited speakers. Another regional conference that is now tradition is the East-West H&I conference (EWIC) which will follow some months later. This time it will be carried out in Budapest. Also here, another opportunity for interaction with neighbouring, H&I less exposed countries is given. We wish Frieda Jordan (Erivan) and Aniko Szilvasi (Budapest) great success for their regional events.

One of the projects that has been going on for a while now is the creation of the new EFI Homepage. This construction site seems now to come to completion and we very much look forward to the new EFI site that is going to be launched in the next couple of weeks. We hope that the new functionalities, and the new look will be appreciated by our members. I'd like to thank Sandra in the EFI Office as well as Eric Spierings and Dave Roelen for spending much of their time on this important project.

Joint EFI-ISO15189 inspections with the national accreditation bodies (NABs) have been a topic of discussion for many years. Indeed, there is a Memorandum of Understanding between EFI and the EA, the umbrella organisation for all NABs in Europe. In Germany, joint inspections between the German NAB (DAkkS) and EFI have been carried out successfully for a number of years. There was no formal agreement so far to cover this cooperation. Ed Petershofen and the German H&I society (DGI) along with DAkkS are currently drafting such an agreement between EFI and the DAkkS, which hopefully can lead to a more formal cooperation between the two organisations and can act as a pattern for similar cooperation agreements between EFI and other NABs.

Finally, I would like to end with a sad message: as you may have heard, one of the pioneer HLA researchers, Prof. John A. Hansen, passed away last August after a long period of illness. Professor Hansen was a member and past President of the International HLA & Immunogenetics Workshop Council. He was well known for his personal and professional integrity. We'll keep John in our hearts and our minds as a methodical scientist with persistence, creativity and steady manner who achieved numerous advances in the fields of Immunology, Histocompatibility and Transplantation.

Joannis Mytilineos

EFI-President

MEMBERSHIP UPDATE

Since the last issue of the EFI Newsletter we received a lot of applications forms from new members. Hereby we would like to welcome the following new EFI members:

D. Kaya, Istanbul, Turkey
K. Kichula, Aurora, USA
J. Neupauerová, Prague, Czech Republic
E. Borotti, Piacenza, Italy
N. Nemat-Gorgani, Stanford, USA
S. Frater, London, UK
A. Basire, Marseille, France
K.T. Nguyen, Besancon, France
A.M. Caragea, Bucharest, Romania
S. Nicola, Glasgow, UK
A.L. Cismaru, Bern, Switzerland
M. Horn, Bern, Switzerland
E. Mancebo Sierra, Madrid, Spain
W.G. Vázquez, Mexico City, Mexico
S. Jarjoura, Brussels, Belgium
T. Hannah, Cambridge, UK
T. Chatzistamatiou, Athens, Greece
G. Dormarkaite, Dublin, Ireland
N. Ivanova, St. Petersburg, Russia
M. Berrino, Venaria, Italy
M. Cargou, Bordeaux Cedex, France
A. Christophersen, Oslo, Norway
T. Milojevic, Rijeka, Croatia
C. Jungbauer, Vienna, Austria
G. Dieplinger, Cologne, Germany
L.M. Viola Solano, Cali, Colombia
J.N. Henao Pelaez, Cali, Colombia
E. Ortiz Lasso, Cali, Colombia
D.R. Makanga, Nantes, France
A. Ospina, Cali, Colombia
C. Silva, Aveiro, Portugal
M. Lilic, Zagreb, Croatia
S. Paul, Decines, France
I. Favre Victoire, Decines, France
R. Ba, Nantes, France
M. Alù, Modena, Italy
A. Gothot, Liege, Belgium
G. Theilliere, Saint-Etienne, France
F. Alpaslan Pinarli, Ankara, Turkey
L. Dubreuil, Nantes, France
G. Ferri, Modena, Italy
C. Vichier, La Tronche Cedex, France
A.A. van Beek, Leiden, the Netherlands
C. Ranzijn, Amsterdam, the Netherlands
A. Kathke, Bern, Switzerland
M. Guarene, Alba, Italy
A. Barker, Manchester, UK

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European Federation for Immunogenetics - Executive Committee Elections

Elections to take up post during the General Assembly at the EFI Conference, 2020

All EFI members are invited to nominate candidates to fill the following vacancies that will arise on the EFI Executive Committee:

- President-elect
- Deputy Treasurer
- Three Councillors

The President-elect is to be elected in 2020 before taking up the office of President in 2021 and serve as President-elect during this period. The President is elected for a period of three years and shall not be eligible for re-election to the same office.

The Deputy Secretary may serve a three year term with the possibility of re-election for another three years. As the accounts for EFI are registered in France, it is desirable that the Deputy Treasurer is also based in France.

The Councillors serve three years and can be re-elected for a second term, but only after one year interval. The present EFI Executive Committee members and their end-of-terms are shown below:

All nominated individuals must complete the 'Nomination Form', which requires seconding by ten paid-up EFI members from at least two countries.

Members of the Executive Committee are requested to participate only in the nominations made by the Executive Committee which will take place during the autumn meeting.

Completed Nomination Forms, accompanied by the candidates brief biography (200 words maximum, excess words will be deleted), including their proposed contribution to the Executive Committee and an electronic photograph suitable for publication should be received by Sandra van Hensbergen at the EFI Central Office (ajvanhensbergen@lumc.nl) by the morning of Tuesday 1st October 2019.

An election will be held if multiple nominations are received for any of the

vacancies. The election will take place electronically. Please ensure that your email address is up-to-date by checking your membership account on www.efi-web.org. The elected candidates are to take up post during the next General Assembly at the EFI 2020 Conference in Glasgow, Scotland.

Position	Name	From	End of term
President	Joannis Mytilineos	Germany	2021
Secretary	Mats Bengtsson	Sweden	2022 (2nd term)
Deputy Secretary	Dave Roelen	the Netherlands	2022 (2nd term)
Treasurer	Gwendaline Guidicelli	France	2019 (2nd term)
Deputy Treasurer	Katia Gagne	France	2022 (2nd term)
Councillor	Pierre-Antoine Gourraud	France	2020 (1st term)
Councillor	Katarzyna Bogunia-Kubik	Poland	2022 (1st term)
Councillor	Neema Mayor	UK	2020 (1st term)
Councillor	Marco Andreani	Italy	2022 (1st term)
Councillor	Katerina Tarassi	Greece	2022 (1st term)
Councillor	Jean Villard	Switzerland	2020 (1st term)

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Report on the EFI General Assembly held on May 10th 2019, during the 33rd Annual meeting in Lisbon, Portugal

Report prepared by Mats Bengtsson, EFI Secretary and Dave Roelen, Deputy Secretary

1) Opening

The EFI president Joannis Mytilineos opened the General Assembly meeting and welcomed all EFI members present. There were approximately 110 members present.

2) Minutes of the General Assembly 11th May 2018 Venice

The minutes of the General Assembly, held on May 11th, 2018 in Venice which were published in the EFI newsletter October 2018, issue 86 were approved.

3) Report of the EFI President

Legal advice

The EFI President reported that EFI is in the process of contracting a lawyer in order to have better legal advice in various aspects of EFI's activities such as contracts with PCOs. Three different offices were contacted and asked for a bid for their services. The idea is to have a trial period for one year. The final selection will be made before summer.

Corporate PCO

The President then continued with describing the process to have an agreement with a Corporate Professional Congress Organiser. The idea is to have one PCO that organizes future meetings together with local organizers. This is something that especially the commercial partners have been asking for. Several PCO companies applied and a meeting with the best three applicants was carried out in Leiden. A decision has been made for the best applicant and a contract has been drafted and is waiting for review by the lawyers. From 2022 all EFI annual meetings will be carried out through this new PCO.

Collaboration with National Societies and other Scientific Organisations

Since last GA the list of agreements about collaboration with National societies has been extended with the newly added agreements with the Bulgarian Association for Clinical Immunology (BAC) and the Japanese Society for Histocompatibility and Immunogenetics (JSHI).

During the last year a number of activities related to existing agreements with other scientific societies have been organised. EFI participated in the EFIS meeting in Amsterdam last September and there was an EFIS symposium with basic science at the EFI meeting in Lisbon. EFI also participated and sponsored a meeting with ISHI in India last year and there are plans for a joint session at the next EBMT meeting in Madrid. For our next annual meeting in Glasgow there are plans for a joint session with ESOT but a MoU needs to be in place for this.

This year's International Summer School (ISS) will be in Montreal 14-17th July. The faculty from EFI are James Robinson and Joannis Mytilineos. Next year it will be hosted by EFI and in Prague with Tony Slavcev as organizer. EFI has together with ASHI also agreed to sponsor a basic Science symposium organised by TTS, AST and ESOT.

Activities of the EFI Committees

The President then gave a brief overview of the activities of the different committees that will be described in more detail later in this report. The accreditation program is continuing to be very successful and we see an increasing number of applying laboratories outside of Europe. The fact that the logbook for the ETHIQ diploma will complement the ESHI diploma is also a huge achievement this last year. He also reported that the new IT & Bioinformatics Committee is working on several projects and the development of the new website is just one such project.

All EFI committees have also been asked to submit a SWOT analyses and the board will review them and make one overall EFI SWOT that will allow us to eliminate the "unaffordable" risks and to focus on areas with opportunities especially since our finances are going well. The outcome will be communicated in the Newsletter and also at next GA.

Honorary membership

The president proposed to grant our Past President Professor Elissaveta Naumova the status of a Honorary member. This was approved by the membership.

4) Report of the EFI Secretary, Mats Bengtsson

Executive Committee Elections

At this year's nominations, EFI sought for vacancies for three councillors, as well as a Treasurer, Deputy Treasurer, Secretary and Deputy Secretary. Since no other nominations were received for the position as Officers than those currently active, there were no elections for those positions. For the three positions as Councillors 5 nominations were received. In the electronic voting 413 members participated, 51,7% of eligible votes. The three people elected were Marco Andreani, Rome, Katerina Tarassi, Athens and Katarzyna Bogunia-Kubik from Wroclaw. The GA approved all the candidates.

Next year there will be new elections since we have vacancy for President Elect and our present Deputy Treasurer has announced that she will step down next year. There will also be vacancies for three Councillors as Neema Mayor, P-A Gourraud and Jean Villard have served their 1st term next year.

The deadline for nominations from the members of the GA is October 1st. The procedure on how to nominate is published on our website. Elections will be held during spring 2020. More information can be found in this newsletter as well.

Two questions were received from the GA, Falko Heinemann asked if the Treasurer needs to be from France. The President responded that for practical reasons this is highly recommended. Steven Marsh followed up with the question if this is described in the Constitution and Mats responded

that it is not, but it is believed that in a French society either the Treasurer or President needs to be from France. EFI is also registered in Strasbourg and there are local laws in Alsace-Moselle for societies that are different from the rest of France. This matter will be further investigated with the help of legal expertise.

Future EFI Conferences
Next years annual meeting will be in Glasgow followed by the joint Workshop meeting in Amsterdam 2021 and then we will be in Nantes 2022 and in Madrid 2023.

5) Report of the EFI Treasurer Gwendaline Guidicelli

The EFI Treasurer presented a combined overview of the of the annual budget for the EFI Office and Accreditation over 2018. Both accounts in Leiden and France had a positive result with a final net result of €74.004. The Venice conference had a net result of €74.645: Many thanks to Valeria Miotti and Carlo Carcassi. The forecast budget for 2019 is a balanced budget with a net result of €6178. The budget was approved by the GA.

Past, present and future projects
The Treasurer continued with describing past, present and future projects. In 2018 we spent €81.000 for the new website, in 2019 the release of the new EFI accreditation website will cost €20.000. The future projects will be the EFI-CME-CPD scheme, the ETHIQ diploma and costs related to launching of e-learning.

Bursaries and support
We have different kinds of bursaries, there are Personal bursaries with four different application periods (described on the webpage). The budget for 2018 and also for 2019 is €3000. The Education and Scientific bursaries also have four periods and the budget both in 2018 and in this year is €6000. The budget for bursaries for the annual meeting was decreased from €9570 in 2018 to €7500 in 2019, and finally we have the budget for the Summer School bursaries that this year will be €4000. In 2018, 2 personal bursaries were awarded, 6 for educational activities and 11 for the annual conference. This year, 10 bursaries for the annual meeting were awarded. During 2018, support was given to the 12th East West Immunogenetics Meeting in Prague, to the Annual EFI region 8 and Balkan EPT meeting, to the ISHI meeting in Mumbai and also to the IMGT HLA database.

6) Report of the EFI committees

a/ Report from the EFI accreditation Committee Chair, Andrea Harmer

Accredited laboratories
The number of accredited laboratories reached a new record with 268 accredited laboratories in 40 different countries. In 2018, 103 inspections were performed in 24 different countries
The number of accredited laboratories has reached a new highest number and is now 268. In 2018, a total number of 103 EFI inspections were performed in 24 different countries, with an increase especially in Latin America. Katharina Fleischhauer asked if there are no laboratories that are closing and Andrea Harmer responded that there are but there are more entering the program then leaving.

Accreditation fee
In 2018 the annual fee for Accreditation was increased to cover also the travel expenses for the inspections. There have been no adverse comments received and all the expenses for 2018 were covered by the fees, There will be no increase in fees for 2019.

Educational activities
In October 2018 there was an Inspector Training Workshop in Leiden where 10 new inspectors were trained. There was also an presentation about the EFI Accreditation program in November 2018 at the ISHI conference in Mumbai, India.
Andrea ended by thanking all the laboratories participating, the Commissioners, Inspectors and Sonja Geelhoed for all their work and dedication.

b/ Report from the Standard Committee Chair, Juha Perasaari

Committee members
The committee has three new members, P. Koefoed-Nilsen from Denmark, T. Lukanov from Bulgaria and A. Walencik from France.

EFI standards
The next EFI Standards version 8.0 has been finished and is planned to be effective from 1 January 2020. This new version includes standards for mismatched and haploidentical-HSCT, real time PCR, functions performed in core facilities and an update on Director qualifications. The work for version 8.1 has started and the plan is to have that version finalized in 2021 so it could be effective from 2022. This version will include revision of section E4, methods for CDC, antibody testing and crossmatching. New items will also be standards for common PCR facilities.

Collaboration with ASHI QAS
The EFI and ASHI Standards Committees continue to work closely together with teleconferences and participation in each annual meetings.

c/ Report of the External proficiency testing committee chair, Falko Heinemann

Committee membership
An overview of the members was presented. S. Ferrari-Lacraz from Switzerland has been newly appointed for region 6 and 11.

Update of standards for laboratories and providers
There will be modifications of the registration documents for providers. It is planned to publish data on providers on our website and the information will also display the number of participants in different schemes.
Since there have been some inconsistencies identified in the standards for laboratories they will be working on an updated version. There is some confusion regarding the minimal number of samples for techniques contra categories.

Education
Also this year a "Meet the Expert" session was arranged that also celebrated 25 years of EPT in H&I.

d/ Report from the Education Committee Chair, David Turner
Committee Membership
An overview of the members was presented. New members are B. Mazzi, Italy, M. Lindemann, Germany and M. Muro, Spain.

ESHI Diploma
During the autumn meeting 2018 there were no candidates for the exam but for the meeting in Lisbon 4 applications were received and all were accepted for examination. In total there have been 20 applicants from 13 different countries so far. There is a need for training for future candidates and there is ongoing discussion with the EBTI about especially e-learning.

ETHIQ Diploma
The training manual for the EFI Technical H&I Qualification for Technical staff working in EFI accredited laboratories has been finalised and approved by the EC. A pilot scheme will be launched.

EFI CPD-CME Scheme
There was a pilot undertaken in 2018 with 31 participants, the outcome is still being assessed but the scheme will be implemented for all members in 2020. There are still some details that need to be worked out.

Teaching sessions, ISS and Regional meetings
The Committee worked with the LOC to organize the Teaching Sessions in Lisbon and are in the process of formulating the Teaching Session for next year's meeting in Glasgow. The guidelines for the teaching sessions have also been updated. Guidelines for organizing the International Summer school have also been developed and the Committee is working with the organization of next year's ISS in Prague together with Tony Slavcev. More than ten regional meetings/workshops have also been approved during last years.

d/ Report from the Scientific Committee chair, Katharina Fleischhauer
Committee membership
An overview of committee membership was presented and the new structure with advisory members. Both J Trowsdale and L Sollid will serve as advisory members for three years. R Blasczyk will rotate off so there will be one vacancy that will be posted in the EFI newsletter.

EFI Conferences
For the Lisbon meeting 319 abstracts were received and scored (72 orals and 247 posters). New for this meeting was also the joint EFI-EFIS session and the PhD students meet the Experts meetings. New were also the Digital Posters that needs further evaluation. The planning for next year's meeting in Glasgow is well in progress. There will be five plenary sessions but also a joint EFI-ESOT session. Next year's Ceppellini Lecturer will be Prof Jacques Neefjes (Leiden, the Netherlands). Next year ethical permission will be mandatory for abstract submissions.

Julia Bodmer Award
This year 6 excellent applications from 5 different countries were received for the Julia Bodmer award. Any EFI member may suggest candidates for 2020.

e/ Report from the IT & Bioinformatics chair, Eric Spierings
Committee membership
At present there are only two members of this new Committee, the Chair and J. Robinson, UK. The committee will welcome applications from the membership but have also some active recruitment ongoing.

Website update
The aim of the committee is to support EFI and its committees with IT and bioinformatics related issues. The committee is now working with updating our website to the latest CMS standards and to create a better user experience. It will be built using existing modules and plugins instead of customized scripts. There will huge improvements in the module for online payment of the annual fee via various payment methods and also the option to automatic annual payments. The plan is to go live at end of July.

Digital data standards
Eric Spierings talked about all the various digital standards that exists, such as GL, hml, HK7, FHIR, MAC codes etc. The Committee monitors the development of these standards and may advise if necessary.

7) Next EFI Conference
The next EFI meeting will be in Glasgow, UK April 26-29, 2020.

8) EFI medal
The EFI medal is awarded annually by the EFI Executive Committee to recognize the achievements of individuals who during the course of their career, have made a significant contribution to EFI. This year the EFI medal was awarded to Marcel Tilanus. Frans Claas presented the medal to Marcel and elegantly described various aspects of his career. The award is described elsewhere in the newsletter.

9) Installation of new EC members:
The President thanked V. Miotti, T. Kauke and F. Oguz for their role as Councillors and welcomed M. Andreani, K. Tarassi and K. Bogunia-Kubik to the EFI EC.

The General Assembly was closed at approx. 19.15.

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Update from the EFI Education Committee September 2019

European Specialisation in H&I (ESHI) Diploma

The application requirements for the ESHI Diploma oral examination are detailed in the 'Portfolio' document available on the UEMS website (http://www.uemssurg.org/divisions/transplantation/transplant-immunology2). Applicants must demonstrate a period of training (3 years for medics and 5 for scientists) within H&I, undertaken in an EFI accredited laboratory under supervision. Since June 2014 a total of 19 candidates have submitted portfolios for consideration to sit the ESHI Diploma exam; 17 candidates have been examined with 14 candidates passing. No candidates applied to sit the examination at the Autumn EFI business meeting in 2019.

The next oral examination will be held at the Glasgow 2020 EFI Conference on Saturday 25th April with a deadline for applications to be received of 25th January 2020. Applications for the examination must be made via the Section of Surgery/Transplantation/Transplant Immunology page of the UEMS website (http://www.uemssurg.org/divisions/transplantation/transplant-immunology2). Note that payment for the exams can be performed via Paypal upon application.

Discussions on the creation of learning resources for individuals wishing to take the ESHI Diploma examination are ongoing. It is hoped that a package of e-learning materials will be made available to EFI members in the future that will provide some structure for covering the knowledge requirements of the ESHI Diploma portfolio. Some resources are already available, such as the Massive Open Online Course (MOOC) on kidney, pancreas and islet transplantation, provided by Leiden University Medical Center (LUMC) in collaboration with the Leiden University's Centre for Innovation. Details on this are already on the EFI website and future links to courses will be added to the Education resources area of the new website.

EFI Continued Medical Education (CME) / Continued Professional Development (CPD)

As previously outlined in the Newsletter, the EFI Education Committee established a simple, pilot EFI CME-CPD scheme in 2018 to allow members to record professional activities. All participants in this pilot have been asked to return their summaries of activities to the EFI Office. It is still the aim of the Education Committee to review this pilot EFI CME-CPD scheme and to launch a scheme for all members in 2020.

The new EFI scheme will be available for members who have no other formal mechanism for recording CME/CPD events. **For those members who hold the ESHI Diploma (either Honorary or by examination) providing evidence of ongoing CME/CPD, either from a local recognised scheme or via this new EFI scheme, will be a mandatory requirement in the future to retain certification.** Also, the recording of training and development events in this EFI scheme will be accepted for EFI Accreditation purposes.

European Technical H&I Qualification (ETHIQ)

A pilot scheme of the ETHIQ logbook has now been launched and is being undertaken by participants in France and the Netherlands. The in lab training scheme is for technical staff working at the bench in EFI accredited laboratories, with supervision given by senior staff in their own labs. The aim is to create a qualification that gives a measure of technician's knowledge and technical competence in the H&I lab. Some of the individuals undertaking the pilot hope to complete the logbook and associated work by August 2020 (the logbook can be completed between 1-3 years after registration), so it is anticipated that the ETHIQ logbook could be made more widely available for EFI members after that date.

EFI Education and Scientific Bursaries

Applications for Education and Scientific Bursaries to promote training in the field of H&I by enabling visits to other laboratories, are now being received four times each year. Details of the closing dates, the process and the application form are available on the EFI website bursaries page http://www.efi-web.org/bursaries.html.

ASHI/APHIA/EFI/ARSHI Summer School

The joint EFI, ASHI, APHIA and ARSHI International Summer School (ISS) provides a short, focused course on many aspects of theoretical and applied H&I. The course is limited to a small group (30-40) and participants are invited to present their own research. It represents a great opportunity for those studying towards higher H&I specific qualifications as well as a chance to meet others working in the field in different parts of the world.

In June 2019 the ISS was held in Quebec, Canada and the next course will be in September 2020 in the beautiful Lindner Hotel Castle, Prague, Czech Republic. Further information on registration will be available via the website and email updates soon.

New Advisory Members to the EFI Scientific Committee

The EFI Executive Committee (EC) has approved the instauration of a new role of up to two Advisory Members (AM) in the EFI Scientific Committee (SC). The AM have the same duties as the other 8 Regular Members (RM). AM are elected for a 3-year term which is potentially renewable beyond the usual 9-year limit, to ensure a certain degree of continuity. AM are suggested and appointed by majority voting within the SC, subject to specific approval by the EC.
The SC welcomes Professor Ludvig Sollid (Oslo) and Professor John Trowsdale (Cambridge) as newly appointed AM for the 3-year term 2019-2022. We thank both of them for their willingness to continue serving in the committee.
Katharina Fleischhauer (on behalf of the EFI SC)

Photo: *The EFI Scientific Committee after their Meeting in Lisbon 2019. From left to right: James Traherne, Silvia Gregori, Katharina Fleischhauer, John Trowsdale holding a mobile phone with Ludvig Sollid connected via Facetime, Sebastiaan Heidt, James Robinson, Lotte Wieten, Luca Vago (Rainer Blasczyk was unable to attend the meeting).*

Jon van Rood Award 2019

The Jon van Rood Award (JvRA) was initiated in 2011 in honor of the late Jon van Rood (1926 - 2017), founding father of EFI and discoverer of the HLA system. The JvRA winner and two runners-up are selected amongst the 8 presenters at the Best Abstract Session by a jury composed of the attending Past EFI Presidents.

The JvRA winner 2019 was **Marco Carvalho-Oliveira** from the Hannover Medical School, Germany for his presentation "Generation of immunologically invisible transgenic porcine pancreatic islet cell clusters after single cell engineering and post-transduction islet reassembling to support xenograft survival".

The two runners-up were **Cynthia Kramer** from the Leiden University Medical Center, The Netherlands for her presentation "Generation of human monoclonal antibodies for definition of actual HLA class II antibody epitopes", and **Esteban Arrieta-Bolaños** from the University of Essen, Germany, for his presentation "HLA-DM-mediated peptide editing impacts T cell receptor diversity against permissive HLA-DPB1 mismatches".

Photo: *Marco Carvalho-Oliveira receiving the Jon van Rood Award 2019.*

Ceppellini Lecturer 2019 - Professor Pamela Bjorkman

Each year at the annual EFI Conference, a scientist who has made substantial contributions to the field of Immunogenetics is honored by the Society and invited to present their work in the form of the Ceppellini Lecture. The Lecture is named in honor of Ruggero Ceppellini (1917-1988), the Italian geneticist who greatly influenced the HLA field. The first Ceppellini Lecture was delivered in 1988 by the late founder of EFI, Jon van Rood. Over the past five years, it has been held by Lorenzo Moretta (2018), John Kappler (2017), Effie Petersdorf (2016), Frans Claas (2015), and Marco Colonna (2014). A complete list of Ceppellini Lecture Awardees can be found on the EFI website.

This year's Ceppellini Lecture was delivered by **Pamela Bjorkman**, Professor for Biology at the California Institute of Technology (Caltech) and a Howard Hughes Medical Institute (HHMI) investigator, at the Annual EFI Conference in Lisbon on May 8, 2019. Pamela's work is well-known to everybody in the H&I field, given the fundamental importance of the crystal structure of peptide-MHC molecules she solved back in 1987. Pamela obtained her PhD in Biochemistry from Harvard Medical School in 1984, working in the lab of Don Wiley where she remained as a postdoc to complete her seminal work on the HLA-A2 crystallography, and then moved on to Marc Davis' lab in Stanford to study the structure and function of T cell receptors recognizing HLA molecules. Since 1989, she has been Faculty member at Caltech, first as Associate and since 1998 as tenured Full Professor, and was additionally appointed HHMI investigator in 1999.

Building on her experience in structural biology and X-ray crystallography gained in her early MHC work, Pamela has since then studied different proteins involved in immune recognition, including MHC-related proteins such as the human homeostatic iron regulator protein HFE and its interactions with the transferrin receptor for iron uptake. More recently, she has used her expertise to make seminal contributions to the development of improved antibodies for the neutralization of viral agents including HIV. She is author of 211 peer-reviewed publications with a Scopus h-index of 73 and over 24.000 citations, and received numerous Awards including the Gairdner Foundation International Award in 1994, the Max Planck Research Award in 2002 and the Rose Payne Distinguished Scientist Award from the American Society for Histocompatibility and Immunogenetics in 2004.

In her Ceppellini Lecture, Pamela started by recalling her early work on solving the HLA-A2 crystal structure. She took the audience through the journey of initial uncertainty and concern about the meaning of the dense structure that co-crystallized inevitably in her experiments, and that turned out to be the peptide in the HLA antigen binding groove, now commonly ascertained knowledge to be found in all immunology textbooks. Pamela then beautifully made the bridge to her subsequent work on the structurally related HFE protein and on antiviral antibodies, illustrating similarities and differences with the MHC that could be exploited to gain new insights into functional properties. She impressively reminded us of the open-mindedness, courage and hard work it takes to make truly new discoveries, and of the vision required to build on previous achievements for breaking new ground in related fields. Pamela Bjorkman's Ceppellini Lecture was an excitingly instructive treat not only for the younger generation, but for the H&I Community at large.

Katharina Fleischhauer - on behalf of the EFI Scientific Committee

Photo: *Pamela Bjorkman receiving the Ceppellini Award 2019.*

Announcement

The 2020 joint EFI/ASHI/APHIA/ARSHI Summer School meeting will be held in hotel Lindner Prague Castle in Prague, Czech Republic from 30 August – 2 September 2020. The concept of the Summer School is that it provides a focused course on all aspects of theoretical and applied Immunogenetics and Histocompatibility. To encourage discussion the course is limited to a small group of participants. It represents a great opportunity for those studying towards higher H&I specific qualifications as well as a chance to meet others working in the field in different parts of the world. Information on applying for the course will be available soon on the EFI website. EFI will be providing bursaries for participation to this event.

Hotel Lindner Prague Castle
Prague, Czech Republic
30 August – 2 September 2020

www.efi-web.org

Julia Bodmer Award 2019 - Dr. Asbjørn Christophersen

The first Scientific Lecture at the Opening Ceremony of the annual EFI Conference is given by a young scientist winner of the Julia Bodmer Award (JBA). This Award was created in memory of Lady Julia Bodmer (1934-2001), one of the founders of H&I and a mentor to EFI, which she served as President from 1996 to 1998. Julia was well aware of the importance of young scientists for the future of our field, and was known for her encouragement and support to younger generations. The JBA winner is selected by majority voting within the EFI Scientific Committee, in a competitive review process between the applications filed. The first JBA Lecture was delivered in 2002 by Benedicte Lee. Over the last five years, it has been held by Maxime Rotival (2018), James Lee (2017), Hannah Siddle (2016), Céline René (2015), and Clemens Hermann (2014). A complete list of JBA winners can be found on the EFI website (http://www.efiweb.eu/awards/the-julia-bodmer-award.html)
This year, among six excellent applications from five different countries, the selected JBA winner was **Asbjørn Christophersen**, an MD PhD from the Celiac Disease Center in Oslo.

Asbjørn obtained his MD from the University of Tübingen in Germany, and then moved back to his home country Norway to complete his clinical training in internal medicine. In 2010, he joined the group of Prof. Ludvig Sollid at the University of Oslo, for a PhD on the Immunology of Celiac Disease, which he completed with honors in 2015. During this time, he developed a novel diagnostic test for celiac disease, using HLA-DQ tetramers to detect gluten-specific T cells even under gluten-free diet, thereby eliminating the need for gluten challenge until then necessary for diagnosis. Moreover, he was able to trace the T cell receptors of gluten-specific T cells in patients, showing that these contain public clonotypes shared between patients and persist for years after diagnosis.
Under Funding from the Fulbright Foundation, Asbjørn then moved for a year as postdoctoral fellow to Mark Davis' laboratory in Stanford. There he combined the gluten-specific tetramer technique with mass cytometry and RNA sequencing to identify a new phenotype of T cells endowed with autoimmune capacities, which is not specific for celiac disease but is present also in other autoimmune disorders. These data have obvious potential clinical relevance and were recently published in *Nature Medicine*.

Asbjørn is a clinician scientist who combines his knowledge in the functional principles of H&I with cutting edge technologies, to make groundbreaking discoveries with direct clinical translation. In his JBA presentation, he brilliantly conveyed his findings to the EFI community. We look forward to see more of his contributions in years to come.

Katharina Fleischhauer - on behalf of the EFI Scientific Committee

Photo: *Asbjørn Christophersen receiving the Julia Bodmer Award 2019.*

Call for applications to the Scientific Committee

Following the announcement at the EFI General Assembly in Lisbon, we are pleased to call for applications regarding an opening for a Regular Member in the EFI Scientific Committee (SC). Any EFI member with a strong scientific background and ongoing activities in scientific research, as evidenced by her/his CV and publication record, is invited to send in her/his application. Applications should consist of

- The completed relevant application form, to be downloaded from the EFI website at https://www.efi-web.org/fileadmin/user_upload/Website_documenten/EFI_Committees/2016-09-16_Committee_Application_Form_v3.pdf
- A short CV with complete publication record (only peer-reviewed publications, published or in press)
- A short letter of presentation stating the motivation for the applicant´s interest in serving the EFI-SC

Applications should be sent directly via email to the chair of the Scientific Committee, Prof. Katharina Fleischhauer (katharina.fleischhauer@uk-essen.de), and/or to the EFI Secretary Dr. Mats Bengtsson (mats.bengtsson@igp.uu.se), no later than Friday October 18, 2019. Applications submitted after this deadline will not be considered.

EFI medal laureate: Marcel Tilanus

The EFI medal is awarded annually by the EFI Executive Committee to recognize the achievements of individuals, who during the course of their career, have made a significant contribution to EFI. During the EFI meeting in Lisbon, it was announced that this year's recipient of the EFI medal is Marcel Tilanus from Maastricht, the Netherlands.

Marcel started his career as a Ph.D. student in the laboratory of Jon van Rood, where he introduced molecular assays for the characterization of the polymorphisms of the HLA molecules. Until that time HLA typing was only performed with serological methods. His research in Leiden resulted in a thesis entitled: "DNA analysis of the HLA system". In the following years Marcel played a pivotal role in the development and introduction of molecular typing methods in the HLA field. He was the chairman of the SBT component of the 12th, 13th, 14th and 15th International Histocompatibility Workshop and guided several PhD students. The results of his research were published in more than 200 papers in peer reviewed journals.

After his initial research in Leiden, he continued his work in Wageningen and Utrecht, the Netherlands and was finally appointed as a full professor at the University of Maastricht. Furthermore, he received an honorary professorship at the blood center of the Shenzhen University in China.

His major contributions to EFI are reflected by his membership of the EFI Council (2003-2004) and his role as a Secretary of the EFI Executive Committee (2004-2010). Marcel was also the local organizer and chairman of the EFI meeting in 2013, which took place in Maastricht.

For all these reasons, the EFI medal handed over to Marcel during the General Assemble in Lisbon was a well-deserved honour!

Best Poster Awards 2019

Amongst the Abstracts presented as Posters at the Annual EFI Conference, 3 receive a Best Poster Award selected by a Poster Review Panel nominated by the Local Organizing Committee, based on the quality of their presentation during the Poster Wine & Cheese session on the second day of the Conference.

The Best Poster Award winners 2019 in alphabetical order were **Francesca Lorentino** from the San Raffaele Scientific Institute Milan, Italy for her poster entitled "Comparative evaluation of HLA-DPB1 mismatch models in HCT identifies association of TCE4 permissiveness with survival", **Ben Matern** from the Maastricht University Medical Center, The Netherlands for his poster entitled "Multiple lineages of DRB1*13-DRB3-DQB1 haplotypes identified by HLA-DRA polymorphism" and **Iñaki Ortiz de Landazuri** from the Hospital Clinic de Barcelona, Spain for his poster "The study of alloantibody reactivity patterns against HLA-DP shows frequent sensitization targets in DPA1 and DPB1".

Standards Committee Report

The EFI Standards v8.0 have been approved by the EFI Executive Committee on August, 2019. Standards and tracking document, which notes all the changes from version 7.0, are available on the EFI website. The revised version follows the same format as current version 7.0. We have introduced changes to standards concerning hematopoietic stem cell transplantation, in order to adapt current developments with mismatched and haploidentical HSCT. For the methodological standards, we have created standards for real time PCR and for capillary electrophoresis. Another area that is included in the next version, are standards for functions performed in core laboratories, as use of core laboratories has become more common. We have also introduced some changes to the qualification of the Director, to consider laboratories seeking accreditation only to categories where H&I training is not present, such as chimerism testing. The terminology used regarding HLA antibody testing has been clarified.

We have started to plan the next version of the standards and suggestions and comments regarding the development of the EFI standards are welcomed.
During our annual meeting in Lisbon two new members were elected: Tsvetelin Lukanov from Bulgaria and Alexandre Walencik from France.

Juha Peräsaari (Helsinki, Finland)
Chair of the EFI Standards and Quality Assurance Committee

EFI Education and Scientific Bursary Report - MUMC / PathWest Collaboration

Benedict Matern

Any EFI member would agree that international collaboration is vital to research into HLA and immunology. With the Education and Scientific bursary provided by EFI, I was able to advance a collaboration between the Maastricht University Medical Center(MUMC): Transplantation Immunology laboratory in Maastricht, the Netherlands and the PathWest Clinical Immunology laboratory at Fiona Stanley Hospital in Perth, Australia.

I am working closely with Dianne De Santis and Linh Truong at PathWest, as well as Marcel Tilanus and Mathijs Groeneweg at MUMC, on several research projects. My focus on using bioinformatics to analyze HLA polymorphism and gene organization, combined with the PathWest expertise on high-throughput next-generation and third-generation sequencing provide an excellent collaboration. I travelled to the PathWest laboratory in June-July 2019, with the objective of further developing our project: "Promotor-focused full-length HLA-DP sequencing."

HLA-DP is generally not considered for transplantation matching, but matching for TCE groups at this locus has been shown to reduce graft-versus-host disease. Close analysis of the overlapping 5' promoter sequence between the two genes allows a method of defining DP haplotypes and an approach to clustering highly-linked DPA1 and DPB1 sequence. This analysis helps to understand the polymorphism and function of HLA-DP, potentially leading to a new nomenclature based on haplotypes or clusters of polymorphism.

A panel of samples possessing a variety of DPB1 alleles from the PathWest and MUMC labs were sequenced and clustered based on promoter sequence. For analysis, I developed a program to generate a consensus sequence from the MinION and NGS data from the three overlapping PCR amplicons. The consensus sequences and sample genotypes were used in further analysis to determine general haplotype patterns, and to determine linkage disequilibrium estimates between the DPA, DPB, and Promoter loci. Results from this research will be reported in a forthcoming joint publication. (Truong, Matern, et. al)

The HLA-DP project is planned to be further extended as a component at the 18th International HLA and Immunogenetics Workshop in Amsterdam, May 2021. During the lab visit, we drafted a workshop component proposal, to be led by Dianne De Santis, Marcel Tilanus, and Effie Petersdorf. This component will allow laboratories to participate in the HLA-DP project by contributing full-length HLA-DP sequencing data from a variety of samples from a wider range of populations.

In addition to the HLA-DP sequencing project and subsequent workshop component, the laboratory visits allowed some beneficial knowledge exchange. The PathWest lab provided me valuable exposure to high-throughput HLA typing and the use of robotics and automation, and I was able to share some of my experience in bioinformatics and HLA polymorphism in PathWest laboratory presentations, attended by lab members and physicians, which I hope provided a relevant and useful perspective.

A heartfelt thank you to the EFI Committee, and especially Sandra van Hensbergen for organizing and providing this Education and Scientific Bursary, and thanks to Dianne and Linh for hosting and helping to organize the visit. It has provided an opportunity for a research collaboration that might not have been possible otherwise, and is helping to strengthen the international HLA & Immunogenetics community.

Time for sequencing action

Full length HLA gene sequences are required as references for appropriate allele assignment. In our International HLA and Immunogenetics Workshop project (components: immunogenetics: hemizygous Sanger sequencing: project name: Extension of incomplete HLA allele sequences in the IPD-IMGT/HLA database) we encourage everyone to participate, who has cells/DNA of alleles of which the full length sequence is not yet fully determined. See for a full description and timeline of the project: https://www.ihiw18.org/component-ngs-for-hla/project-full-length-hemizygous-sanger-sequencing/

NGS and hemizygous Sanger SBT, as performed in the 17th IHIWS (Voorter et al, 2018, Human Immunology 79: 763-772), will be included. Questionable phasing issues of NGS will be addressed by single molecule sequencing and SSBT. DNA must therefore be available.

Today we start with an inventory of samples that can be included. Sequencing will start with HLA class I alleles. If you have cells/DNA of which allele sequences are not fully covered in the IMGT/HLA database subscribe to this workshop project and mail the information about the cells/DNA that you want to include to C.Voorter@mumc.nl.

Looking forward to a fruitful workshop collaboration.

Christien Voorter, Marcel GJ Tilanus, Mathijs Groeneweg

Announcement and Call to Action from the HLA Dictionary Project of the 18th IHIWS

Dear Colleagues,
The HLA Dictionary Project of the 18th IHIWS is being organized with the goal of providing a more comprehensive serological equivalent list for HLA Class I and II alleles. In the era of NGS-based typing, the previous HLA Dictionary report from 2008 is showing its age.

We are writing to let you know what steps we are taking in the next couple of years and invite all interested laboratories to participate in this project. In the upcoming year, we will begin compiling a list of HLA alleles (Class I and II) for which serological equivalents have not been identified. We are also seeking results from previous serologic testing of HLA alleles that were characterized at high resolution by DNA-based methods but not listed in the 2008 Dictionary. Subsequently, we will prioritize common and well documented alleles within global populations for actual serological typing of untested alleles.

This is going to be an ambitious project, to say the least! If you or your laboratory is interested in participating, please navigate to the HLA Dictionary project under the Antigenicity and Immunogenicity component at the IHIW18 website (https://www.ihiw18.org) and fill out the form. The more participants we have, the more complete our databases will be and the more patients will ultimately benefit!

EFI 2020

FROM RESEARCH TO CLINICAL REALITY

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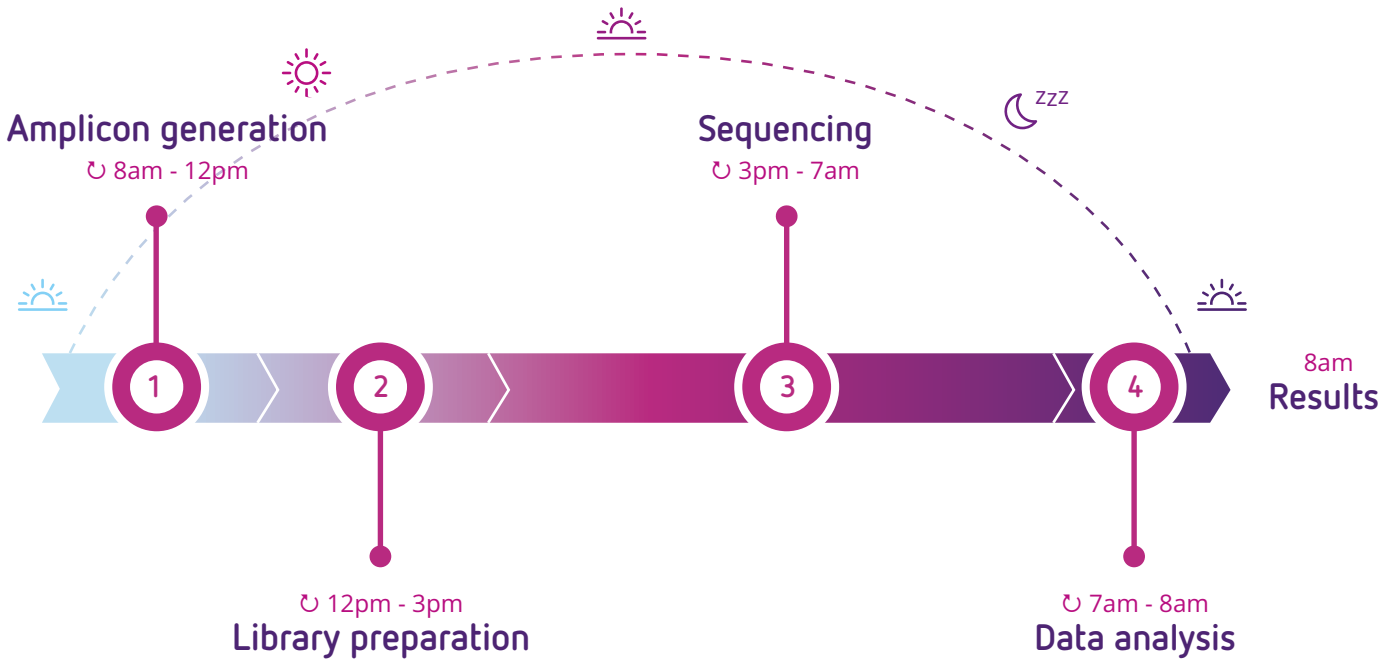

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Bursary reports from the 33rd EFI annual meeting 2019, Lisbon

EFI offers a wide range of bursaries and among those are the bursaries for attending the annual meeting. There is no age restriction but applicants must be an EFI members for at least one year at the time of application. In 2019 we received 27 applications from our members. Bursaries are preferentially given to participants with presentations at the conference. All recipients of a bursary were grateful to EFI for receiving the support, which enabled them to attend the meeting. For the meeting in Lisbon, 10 bursaries were given and here are their reports.

Marion Alvares, Abu Dhabi, UAE

The Centro Cultural de Belem in Lisbon was recently abuzz with scholars, speakers, academicians, researchers, students and company representatives from across the globe attending the 33rd European Immunogenetics and Histocompatibility Conference. It was an event that brought the scientific community together to learn, discuss, deliberate and build meaningful connections in this outstanding field.

From this year's Ceppellini lecture delivered by Prof. Pamela Björkman, who first presented the crystal structure of the HLA-A2 way back in 1987, to the nostalgic closing lecture by Prof. Antonio Coutinho; there were exciting exceptional educational sessions surpassing my expectations.

The prestigious HLA Award 2019 was won by T.R. Turner et al. for the original article published in HLA titled "Single molecule real-time DNA sequencing of HLA genes at ultra-high resolution from 126 International HLA and Immunogenetics Workshop cell lines". The characterization of B-lymphoblastoid cell lines by Single Molecule Real-Time (SMRT) DNA sequencing would indeed be very useful as a resource in Next Generation Sequencing.

The Plenary sessions over the next three days were on Hematopoietic Stem Cell Transplantation, Cancer Immunogenetics, Solid Organ Transplantation, Infection and Regenerative Medicine. These were diverse areas of histocompatibility and immunogenetics chaired by stalwarts like Carlo Carcassi, Pierre-Antoine, Frans Claas, Ana Fernandes and Luca Vago to name a few.

An interesting lecture in the first plenary session was on Microbiota presented by Marcel Van den Brink. He vividly spoke about the role of gut flora in patients with GVHD and developing strategies to address microbiota injury in HSCT. The "One Study" introduced by Birgit Sawitzki was designed to test safety and partial efficacy of regulatory cell therapy in kidney transplantation. It involved the standardization of leukocyte profiling by flow cytometry between eight transplantation centers located in Europe and the USA. Prof. Gunnar Tufveson form Uppsala University gave a wonderful talk on Immunosuppressive protocols, donor specific antibodies and the effects of IdeS in the third Plenary session.

While the teaching session on HLA HPA and HNA included case presentations and algorithms for molecular investigations; the population genetics session introduced us to useful tools for handling data as in HLA-Net and HLA Matchmaker. Prof Ann-Margaret spoke affluently on Population diversity and emphasized the importance of submitting population and allele data to existing databases.

The 18th International Histocompatibility Workshop Report reiterated the extensive international collaboration involved for its success. Within the 18th IHIWS, HLA epitopes will take center stage with research projects involving immunogenic and non-immunogenic epitopes.

An innovative way of presenting ePosters was on eyecatching LCD screens, providing a convenient and environmental friendly way to view and learn. Enthusiastic participants proudly presented their work during the wine and cheese reception. Oral presentations were the highlight of all the days reflecting high levels of research activities in a plethora of topics.

Summing it all up was the Gala Dinner held at the beautiful botanical Estufa Fria that came alive with music and dance. As I bid farewell to this magnificent cultural city of Lisbon I knew that over a thousand other minds would have been as enriched and happy as mine.

Anush Martirosyan, Yerevan, Armenia

I am a first year EFI member and currently taking first steps in exploring this field so it was a big opportunity for me to participate in EFI2019. The conference delivered cutting edge science along with excellent networking opportunities. The EFI annual meeting is one of the most highly-regarded international conferences in the field. EFI2019 brought together researchers from around the world. The meeting attracted more than 1,000 delegates from 56 countries and offered the highest standards in terms of both scientific and social programs. It repre-

sented the best opportunity for young specialists to present their research in front of a relevant, international audience while also provided the learning opportunities.
I had the invaluable opportunity to attend many exciting and inspiring talks across the full range of the EFI2019 program. Several of the sessions which I attended were very informative and insightful on their particular subjects. This allowed me to explore new areas of immunological research and to gain new skills and insights which will have a direct benefit on the quality of my final PhD research.

Prof. Caetano Reis e Sousa opened the plenary session 2 (Cancer Immunogenetics | Cellular and Molecular Mechanism of Immune Evasion in Cancer) with an interesting talk about the unique abilities of a specific DC subset. Once recruited into cancer microenvironment they enhance local cytotoxic T cell function as well attracts additional immune cells to the site. Modulation of DC activity may represent a promising new strategy to improve the response to cancer immunotherapy. In the second talk, Prof. Annette Paschen discussed resistance mechanisms that develop with melanoma progression and highlighted the potential of combination therapies for tumor elimination. The session closed with the exciting talk from Prof. Soldano Ferrone about MHC Class I abnormalities in malignancies and their underlying molecular mechanisms. Relevance of defective HLA class I antigen processing machinery (APM) component expression in tumors cannot be overestimated. Driven mainly by epigenetic mechanisms, HLA class I APM abnormalities are of the main mechanisms used by cancer cells to evade immune surveillance. This is highlighted by the much higher frequency of HLA class I APM component abnormalities in metastatic cells than those found in primary tumor cells.
I am still impressed with the plenary session 3 (Solid Organ Transplantation/Advances in Monitoring and Maintenance of Solid Organ Grafts) with the specific focus on renal transplantation. Topics discussed in presentations summarized the modern knowledge and challenges of the fast-moving field of kidney transplantation. The first speaker of the session was Prof. Birgit Sawitzki. Her research related to cell-based tolerance-promoting therapies. In elegant experiment interplay between Mregs, Tregs, DCregs and Mregs dependent conversion of allogeneic CD4 T cells with subsequent inhibition of dendritic cells was demonstrated. Results have important implications for clinical practice and suggested allergenic Mreg based treatment to prevent allograft rejection. The second presentation by Prof. Olivier Thaunat outlined the pathophysiology of DSA-mediated allograft failure. Specific focus was done on risk stratification for the development of donor-specific antibodies in recipients of kidney transplants, their pathogenicity and the strategies for prevention of DSA generation. The final talk of the session was given by Prof. Gunnar Tufveson who presented promising strategy to prevent rejection among HLA-sensitized renal-transplant recipients. Efficient elimination of DSA in patients sensitized to HLA is still an unresolved issue. Administration of IgG-degrading enzyme derived from *Streptococcus pyogenes* (IdeS) was shown to reduce DSA to the levels that allowed successful transplantation.
On May 9th I presented the results of our recent experiment, abstract entitled: “Anti-domain 1 β2-glycoprotein I antibodies induce activation of monocytes and NK cells, and provoke prothrombotic settings” In our research we only recently have started to focusing on NK cells so then my attention was drawn to the oral session 7 “NK and Miscellaneous” which offered a wonderful opportunity to share ideas, discuss challenges and opportunities. Not surprisingly KIR was the subject of investigation in all presented abstracts. The

killer-cell immunoglobulin-like receptors (KIR) recognize HLA molecules and involved in regulation of NK cell activity. KIR variation are thought to be implicated in susceptibility to immune mediated diseases including autoimmunity, may influence hematopoietic stem cell transplantation (HSCT) outcome and along with HLA variations supposed to interfere with the risk of developing cancer. Plenty of reports devoted to KIR genes allelic diversity, which may influence the function of the receptors, well reflected the importance of the topic.
Also, I wish to note how convenient and enjoyable it was to use E-Poster viewing LCD Screens, as they made it possible to go through any posters at any time.
Summarizing, I should state that attendance at the EFI2019 has provided me with valuable experience of an international conference. I would like to express my sincere gratitude and thanks to EFI for generous support that made my attendance possible. Warm thanks for the great organization and welcome and looking forward to Joint Meeting of EFI Region 8 & Balkan EPT /3rd HLA Educational Workshop to be held in my hometown (Yerevan, Armenia, October 25-27, 2019).

Nana Talvard-Balland, Paris, France

I had the chance to present my work and discuss my data about the lack of alloreactive potential of human Mucosal-Associated Invariant T (MAIT) cells that recognize and are activated by microbial-derived precursor riboflavin derivatives presented by the nonclassical MHC class I-related molecule MR1. We have shown that MAIT cells do not respond to allogeneic stimulation and do not participate in GVHD induction in respectively *in vitro* and *in vivo* models as well as in patients who received geno-identical or HLA-matched unrelated transplantation. These results prompt us to use MAIT cells from healthy donors as a novel source for adoptive immunotherapy in an allogeneic setting.
During the meeting, I had the opportunity to attend to Pr. Marcel van den Brink's lecture from the Memorial Sloan Kettering Cancer Center, USA, who talked about a particular hot topic; Microbiome changes in HSCT. In his talk, he discussed the role of the intestinal microbiome in the risk for Graft versus Host Disease (GVHD) after allogeneic bone marrow transplantation through two topics. First, his team investigated the composition of the gut

microbiota in recipients of allogeneic HSCT from a multicenter study where weekly stools from 4 centers (Japan, Germany and within the US) were collected and the microbiota composition was determined using 16S rRNA gene high throughput sequencing.
They found dramatic changes in the composition of the flora, specifically a significant early loss in microbiota diversity, with a domination of enterococcus bacteria, associated with the occurrence of GVHD. Indeed, high microbiota diversity within the gut predicts overall survival and protection from lethal acute GVHD. Furthermore, in the four centers, they observed a similar pattern at about 14 days after HSCT corresponding to when patients were off of antibiotics, and a loss to a greater extend leads to a greater risk for lethal GVHD. They did not find any apparent clustering of baseline samples by geography diversity deadlines with similar kinetics across centers. They also observed that the damage for gut microbiota was persistent, which leads to a higher risk of GVHD development.

The second topic was about what happened with the domination of the flora with the bacteria enterococcus. They demonstrated that the microbiota of mice that received allogeneic bone marrow + T cells transplantation, and therefore developed acute GVHD, show a blossoming of enterococcus bacteria especially *E. faecium*, in contrast to mice who only received bone marrow transplantation. This domination specifically occurs during GVHD in both mice and humans, and enterococcus in multiple ways seem to aggravate the GVHD. This happens by pushing out all the normal commensal flora that is capable of making short chain fatty acids that are really relevant for the health of the gut, by increasing the risk of infection and finally by activating the allogeneic donor T cells that leads to GVHD. In the mouse model, enterococcus has a very specific need for lactose, so its metabolic pathways are different for those that are used by most of the commensal flora bacteria. The loss of the antimicrobial peptide Reg3G and the digestive enzyme lactase during GVHD may be host factors contributing to the enterococcus bloom. Furthermore, they demonstrated that mice under a lactose-free diet get lower levels of GVHD. Patients who have lactose intolerance have higher incidence of enterococcus dominance. Indeed, lactose-free diet attenuates the enterococcus bloom and ameliorates lethal GVHD. Their results suggested that both the flora and diet are relevant for post-transplant risks for GVHD.

Helena Car, Zagreb, Croatia

In the first plenary session, my attention was caught by Marcel van den Brink's presentation on *Microbiota*. He gave an overview of the key players in the celiac disease pathogenesis, described how HLA class II tetramers can be used to diagnose celiac disease and why gluten-specific CD4+ T cells can be used as target molecules for immunotherapy in celiac disease. Furthermore, he related findings on celiac disease and gut microbiota to transplantation outcome. *PhD students and Research Postdocs meet Experts Session* was a

good opportunity to hear more about his work and his career path.
A very interesting talk *DSA in kidney transplantation: Where to look?* was given by Olivier Thaunat where he gave an excellent and clear overview of studies done on this topic and new findings. As known, T follicular helper cells help naive B cells to differentiate into memory B cells and alloantibody-producing plasma cells within germinal centers and therefore they play a crucial role in humoral alloimmunity. In his talk, the speaker pointed out that blocking T follicular helper cells in immunosuppression therapy is not always efficient. That results with 10-20% of transplant recipients having de novo DSA at 5 years after the transplantation. Further was demonstrated that DSA are sequestrated in the recipient's circulation and explained the DSA access to allogeneic endothelial cells as a step to antibody mediated rejection. Finally, data on serum IgG glycan core composition in inflammatory diseases were presented and concluded that antibody mediated rejection depends on the DSA quality.

In his talk *IgG cleavage for desensitization,* Gunnar Turverson offered the solution for the formed HLA antibodies. Thereby, the speaker introduced the IgG degrading enzyme of Streptococcus pyogenes (IdeS) and its roll in the elimination of anti-HLA antibodies. Good safety profile and small size of IdeS what enables clearance of IgG in all extracellular spaces were highlighted during the presentation. In conclusion, the speaker proposed the use of IdeS in rapid desensitization before transplantation of organs and cells, in ABO incompatible transplantations, treatment of antibody mediated rejection etc.
Since my major interest is in solid organ transplantation, I attended *Epitope matching and prediction of alloantibody production after the transplantation teaching session*. It is well known that in most types of solid organ transplants HLA matching between donor and recipient is beneficial for the transplantation outcome. The teaching session started with an introduction on B cell epitopes by Sebastiaan Heidt who explained that every HLA molecule carries a unique set of epitopes but the individual epitopes are often shared with other HLA alleles. Following this talk, Eric Spierings introduced the T cell epitopes and the Predicted Indirectly Recognizable HLA Epitopes (PIRCHE) computational algorithm. In addition, Jennifer McCaugan elaborated on how structural analysis of HLA molecules enables the prediction of their immunogenicity and identification of highly immunogenic epitope mismatches. As the final speaker of the session, Nils Lachmann explained the correlation of B and T cell epitope mismatches with de novo DSA formation. Thereby, he pointed out that T-cell epitope (PIRCHE-II) and B-cell epitope (HLAMatchmaker) matching independently predicts DSA formation and allograft survival. He introduced linked recognition concept between T and B epitopes as a possible way to predict acceptable mismatches and minimize de novo DSA formation.

Joanna Wielinska, Wroclaw, Poland

During the opening ceremony, Prof. Paulo Rodrigues Santos gave a presentation about the Portuguese Histocompatibility Pioneers. With great Portuguese discoveries in the background, we were continuing the memorable scientific programme with outstanding speakers from all over the world. I would like to mention an excellent speech given by Asbjørn Christophersen, this years's Julia Bodmer Award winner. The presentation was titled "T cells specific to celiac disease and the implications for autoimmunity". The author focused on gluten-specific CD4+ T cells as an attractive target for immunotherapy due to their very distinct phenotype and persistency in patients.
There were plenty of oral and teaching sessions I was interested in, but the one I appreciated the most was Oral Session 2 "Reproduction, Autoimmunity, Infection & Cancer", which covered my own scientific interests. The session was coordinated by Fatma Savran Oguz (Turkey) and Silvia Gregori (Italy).

The first presentation during this session was given by Juliette Krop and titled "Mapping dynamic changes in the maternal immune compartment throughout pregnancy using mass cytometry with a specific focus on regulatory T cells". Cell subsets at the maternal-fetal interface in a healthy pregnancy were presented. The data showed significant heterogeneity in both decidual lymphoid and myeloid cell lineages as well as the kinetics of changes during pregnancy e.g. Treg cell populations with co-expression of ICOS, TIGIT, PD1 and CD39 that are infrequent at the beginning of pregnancy and more detectable with time being. Flow cytometry suggested an increase in activated CD4+CD127+CD25+ T cells complemented by an increase in CD4+CD127-CD25+FOXP3+ Tregs.

A second presenter, Jill A. Hollenbach gave a speech "The Shared Epitope of HLA-DRB1 mediates risk and interacts with smoking history in Parkinson's Disease". She showed that risk and protection in Parkinson's Disease may be explained by the HLA-DRB1 shared epitope (SE) together with position 11. Her team found that a combination of smoking and the presence of protective SE and V11 results in genotype greater protection. On the other hand, no smoking history with the presence of risk SE plus V11 leads to genotype

greater risk. Peptide binding prediction suggests that post-translational modification attributable to smoking enhances binding to protective alleles and diminishes binding to risk alleles.

The third speaker was Mehmet Tevfik Dorak who described longevity-associated HLA Class II Region Variants Map to the B-cell-specific Super-enhancer XL9 in the GTEx project. Dorak et al. revealed that two longevity-associated HLA region SNPs map to super-enhancer XL9 in the HLA class II region. Moreover, the haplotype formed by the two longevity-associated alleles rs28383322-T and rs34831921-A is exclusive to DRB1*13:01/02 and 08:03:02 haplotype. The presence of three non-coding RNA loci within XL9 is intriguing. In their opinion, identification of their functions and targets together with next generation sequencing-based disease association studies should unravel the exact role of XL9 in genome biology.

The next presentation by Stana Tokić was about integrative mRNA/microRNA analysis in T cells of patients with Hashimoto's thyroiditis (HT). They measured mRNA expression levels of several transcription factors (RUNX3, RORC, FOXO1, PLZF) and their regulating microRNAs (hsa-miR-106a-5p, 20a, 301a, let-7a). The analysis showed that the patients with higher RORyt mRNA levels had a greater prevalence of hypothyroidism, showing higher peak TSH level at diagnosis. Also, T cells from aged HT patients accumulate more RUNX3 mRNA. The chronic inflammation in HT may be caused by Th17 and Tc17 cell differentiation influenced by dysregulation of the miR-106/RORyt feedback loop.

The fifth presentation was held by Kazutoyo Osoegawa with a title "High-resolution haplotype analyses of classical HLA genes in families with multiple sclerosis". Interestingly, they identified a risk haplotype for multiple sclerosis, DPA1*01:03:01:02~DPB1*104:01. Additionally, they found that DRB1*01:01:01 which was a highly protective allele and DQB1*03:03 and DPB1*09:01:01 were moderately protective. For class I, A*02:01 :01:01~C*03:04:01:01~B*40:01:02, B*27:05:02 and B*38:01:01 showed moderately protective effects.
Anush Martirosyan gave another interesting lecture demonstrating anti-domain 1 β2-GPI antibodies-mediated substantial activation of NK and T cytotoxic cells and suppression of B cells. They suggested that the cytotoxicity of NK cells along with the shift from a humoral to a cellular immune response in the presence of anti-D1 b2GPI may represent a potential mechanism linking this epitope with the poor obstetric outcome.

The following presenter, Esther Schwich, showed the results of an investigation of HLA-G 3´UTR variants as promising prognostic factors of therapy and disease outcome in locally advanced breast cancer patients. They found that the UTR-4 haplotype was negatively associated with the response towards neoadjuvant chemotherapy and overall survival, whereas UTR-2 haplotype was associated with improved neoadjuvant chemotherapy response and prolonged progression-free survival and overall survival. Furthermore, +3003C, a unique variant in UTR-4 is responsible for a detrimental outcome, while the +3196G variant (unique for UTR-2) is responsible for a protective clinical outcome.

The final speaker of this session Faisal K. Almalki gave an interesting talk about discovering a genetic variation in mouse intelectin genes using an Illumina GWAS sequencing. They found a deletion at the reference mouse genome (C57BL/6n), as well as several deletion events across laboratory strains and within wild populations of mice. Also, early stop codons SNPs in certain intelectin genes that may cause truncation of the resulting protein were revealed.
To summarize, the described session was a valuable as a means of exchanging knowledge and research experience, learn about new technologies and determine new scientific approaches. It was also a great opportunity to interact with international immunogenetics community.

Esther Schwich, Essen, Germany

For the first time, PhD students and Postdocs had the opportunity to meet invited experts during an exclusive session. During the pleasant meeting with the transplantation immunologist Marcel van den Brink, he reported about his experiences in the scientific surroundings, his expectations towards PhD students and Postdocs in order to become a good scientist and his daily lab management. In this familiar setting, we could ask questions as well as ask for advice. I think this session is a good innovation in the frame of the EFI conference and will also be helpful for students in the future.

The oral session "Immunotherapy, Gene Therapy and Cellular Therapy" chaired by Constanca Figueiredo and Lotte Wieten was filled with informative presentations. The first speaker was Constance Figueiredo herself and she presented work on the silencing of MHC expression to prevent allogeneic immune responses after cornea transplantation. She demonstrated that by targeting either the b2-microglobulin or the alpha chain of MHC class II molecules the immune response was alleviated. This could bear great potential to conquer rejection after cornea trans-

plantation. The next two presentations were given by Esteban Arrieta-Bolanos who focused on T cell alloreactivity against self-HLA restricted minor histocompatibility antigen (mHAg) peptides. On the one hand, he showed that naïve T cells mediate alloresponses to mHAg, whereas direct alloreactivity is exerted by both, naïve and memory T cells. On the other hand, he reported that the non-classical HLA-molecule HLA-DM which defines the peptide repertoire could be a crucial factor for the balance between graft-versus-leukemia effect and induction of graft-versus-host disease. The session continued with a presentation given by Fang Zhao about the combined HLA I and HLA II haplotype loss in melanoma cells which efficiently evades anti-tumor immunity. Further, this loss was associated with resistance to immune checkpoint blockade which introduces HLA gene loss as a potential novel parameter in the prognosis of melanoma patients. Femke Ehlers demonstrated in the next presentation that glucose levels in bone marrow of multiple myeloma patients were lower compared to that of healthy controls. Additionally, Femke Ehlers showed that in contrast to T cells, NK cells do not rely on glucose availability and can exert their anti-tumor effects in a low glucose environment. In the next presentation Monika Lindemann presented a novel predictor for patient survival after selective internal radiotherapy with the beta-emitter yttrium-90. Combining chronic renal insufficiency, response to therapy and the response rate to recall antigens one week after therapy significantly predicted patient survival.

Casimir de Rahm presented his work on human induced pluripotent stem cells and their derivates, neurospheres and mature dopaminergic neurons, cellular therapy for Parkinson disease. He analyzed the expression of classical HLA-I and -II, HLA-G and HLA-E molecules in dependence of IFNγ treatment and showed that the different cell types differently express these molecules and that neurospheres treated with IFNγ as well as treated and untreated mature dopaminergic neurons were partially protected against allogeneic NK cells. Christina Bade-Doeding closed the session with her presentation about the impact of the HLA-G genotype on the outcome of decidual NK cell development. The genotype HLA-G*01:04 was shown to be a strong catalyst of decidual NK cell proliferation, although a rather innate character of the interacting partner for HLA-G was suggested. The session gave a comprehensive overview of the new insight in the field of immunogenetics current results on Immunotherapy and was filled with excellent scientific findings.
As a whole, this year's EFI meeting was, again, a stimulating and informative conference offering the great opportunity to discuss current research with great experts in the field.

Cynthia Kramer, Leiden, The Netherlands

The program was very diverse with excellent scientific talks covering this year's theme 'Functional Immunogenetics: the historical challenge'. I was intrigued by the presentation of Marcel van den Brink in plenary session 1 on microbiota in hematopoietic stem cell transplantation. Intestinal bacteria play an important role in health. After hematopoietic stem cell transplantation, the composition of intestinal microbiota changes and certain group of gut bacteria were identified that were associated with improved survival. Indicating that improving intestinal bacteria will contribute to patient's health.

My main interest is in transplantation immunology and the speakers of the solid organ transplantation plenary session gave very diverse and interesting talks. Birgit Sawitzki gave an excellent talk about the One Study and showed the changes of immune cell subsets in blood that were monitored after kidney transplantation as part of the study. Next, Olivier Thaunat gave a talk about HLA donor-specific antibodies in kidney transplantation. To pro-

duce these antibodies, B cells require help from T follicular helper cells and it is suggested that immunosuppressive drugs do not always efficiently block these cells.

This supports the findings that still a significant group of patients develop donor-specific antibodies after transplantation that is associated with inferior graft survival. Prof. Thaunat further showed that while C3d binding antibodies are predictors of risk, the activation of complement by donor-specific antibodies is dependent on quantity. Further, he showed that the highly variable sialylation status of donor-specific antibodies had not impact on rejection outcomes. This session was closed by Gunnar Tufveson, who provided insight into the use of IdeS an agent to cleave human IgG to desensitize patients before transplantation.

My research focus on B cell epitopes on HLA and I was therefore happy to see the large number of people attending the epitope teaching session. During this session, Sebastiaan Heidt gave a nice introduction on B cell epitopes and the presentation of Jennifer McCaughan fitted in well with that as she provided more insight on identifying highly immunogenic epitope mismatches. She showed the identification of immunogenic epitope, 45EV and $45GE_3$, found in DQA1*05 with DQB1*02 or DQB1*03:01. Beside B cell epitopes, T cell epitopes are also involved in the induction of HLA antibodies. Erik Spierings taught us more about T cell epitopes and Nils Lachmann showed the correlation between B and T cell epitope mismatches with *de novo* donor-specific antibody formation. Thus, various aspects of epitopes are studied, which will contribute to implement epitope matching and prediction of alloantibody response after transplantation.
Overall, this meeting was very informative, and I was able to catch up with colleagues from other laboratories as well as meeting new people. Obrigada!

Estelle Geffard, Nantes, France

The European immunogenetics and histocompatibility conference covers an interesting diversity of topics. One topic that caught my attention this year is the new approaches to improve the clinical outcome in transplantation. I was able to attend several presentations on this theme, from donor selection based on antigen recognition sites (ARS, Dianne De Santis) to the prediction of rejection with the study of the microbiota (Marcel R. M. van den Brink), as well as the development of new strategies for the experimental study of epitopic crossmatch to reduce the risk of Donor-specific antibodies (DSA, Cynthia Kramer and Loren Gragert).

Marcel R. M. van den Brink (Sloan Kettering Institute) is a hematologist studying bone marrow transplantation immunology with a particular focus on intestinal microbiota. He presented his work on microbiome changes in allogeneic HSCT (Hematopoietic stem cell transplantation). He stated that a microbiota composition signature could predicts mortality after allo-HSCT, thus could inform the development of strategies to improve outcomes of allo-HSCT. Indeed, high diversity improves overall survival and protection from lethal acute GVHD (graft versus host diseases). From a multicenter study, they collected weekly stool samples from 4 centers, the flora composition changed over time. Intestinal microbiota diversity declines after HSCT transplants with an increase of specific bacterial domination. Particularly, he showed that enterococcus bacterial domination is associated to GVHD. The gut microbiota plays an important role for patients with hematological malignancies undergoing HSCT: antibiotics/drugs, diet (lactose plays a role on enterococcus bacterial increase after GVHD) as well as conditioning regimens can affect flora changes. In addition, he concluded that auto FMT (Autologous Fecal Microbiota Transplantation) restores pre-HSCT microbiota in mice model.
Dianne De Santis is a senior medical scientist-in-charge at the Department of Clinical Immunology at PathWest, Royal Perth Hospital and works as the Marrow Match Manager for the Western Australian Donor Search program. She works on the development and implementation of Next Generation Sequencing (NGS) technology for immunogenetic applications such as HLA genotyping. In this context she demonstrated that super high-resolution HLA matching by NGS improves the clinical outcomes of HSCT. HLA matching between donor and a recipient in HSCT is crucial for the clinical outcome. Matching the antigen recognition sites (ARS) or HLA-A, -B, -C and -DRB1 2-field typing between donor and recipient are associated with improved survival. She investigated if matching outside of the ARS or matching for additional HLA genes further improved HSCT outcome. HLA six loci long-range PCR combined with NGS were performed on transplant pairs with available clinical data. HLA matching was determined at either 2-field, 3-field (class II) or 4-field (class I) resolutions. She concluded her data suggest that out-of-ARS polymorphisms may be markers of specific haplotypes and matching for these polymorphisms could improve HSCT clinical outcome.
DSA produced during transplantation are triggered by immunogenic epitopes on incompatible HLA alleles of the donor. The number of mismatches between donor/recipient HLA class II epitopes is correlated with the development of DSA. However, not all mis-

matches lead to DSA apparition. This may be explained by the fact that HLA epitopes are predicted, there is a lack of experimental validation because the number of available HLA class II monoclonal antibodies is limited. To fill this gap Cynthia Kramer (Department of Immunohematology and Blood Transfusion, Leiden University Medical Centre) focuses on the definition of HLA class II immunogenic epitopes, and the impact of HLA matching on sensitization in kidney transplantation. During the best abstract session, she presented an innovative project. She and her team work on the engineering of human monoclonal antibodies to better define HLA class II antibody epitopes. Human recombinant HLA class II specific monoclonal antibodies can be generated from single memory B cells. These monoclonal antibodies can be used to identify possible immunogenic HLA class II epitopes and also functional studies on the effect of HLA antibodies in transplantation. In parallel of these wet lab technology, computer-generated crossmatches are being developed. Loren Gragert (assistant Professor at Tulane Cancer) and his team developed a computer based tool for direct interpretation of molecular HLA typing data in organ allocation systems. His Virtual Crossmatch tool compares transplant candidate's HLA antibody assay results to donor's HLA typing to evaluate potential incompatibility. The VIrtual CrossmaTch for mOleculaR HLA typing (VICTOR) tool computes the probability of each potential conflicting specificity.
Overall, these diverse presentations from different background exemplified all the new perspectives currently studied and developed with innovative strategies, technologies and bioinformatics. The common goal is toward improvement of clinical outcomes in transplantation.

Aleksandar Senev, Mechelen, Belgium

Although the EFI conference 2019 covered many quality lectures on a variety of topics, on my EFI report I would like to focus on the "hot topic" in organ transplantation: Epitope matching and prediction of alloantibody production after transplant. Sebastiaan Heidt from the Netherlands opened this teaching session with interesting lecture on B cell epitopes. The epitope concept, defining each HLA molecule as a unique set of specific epitopes and which some of them are shared with other HLA alleles, could better explain the sera reactivity in anti-HLA immunized patients than the traditional HLA antigen concept. Thus, counting the number of HLA epitope mismatches instead of HLA antigen mismatches between the transplant pair could provide better insights on HLA compatibility between the transplant pairs and better prediction of the allograft outcome. One of the algorithm to identify crucial amino acids determinants on the surface of HLA molecules (HLA eplets) responsible for antibody formation is HLAMatchmaker. The speaker explained the main principals of this algorithm to quantify eplet mismatches between the transplant pair but also emphasized that for anti-HLA antibody formation and antigen-antibody binding other amino acid differences in the surrounding area of the HLA molecule are crucial and those are not part of the eplets defined by HLAMatchmaker.

The next speaker, Eric Spierings also from the Netherlands, introduced the concept of T cell epitopes and PIRCHE II (Predicted Indirectly ReCognizable HLA Epitopes) computational algorithm, which can predict indirectly recognizable HLA-derived donor peptides by recipient HLA class II that are likely to induce the production of donor-specific anti-HLA antibodies. He explained in detail the T cell dependent antibody response which require T-cell help in order to activate naïve B cells against specific antigen. He also provided information on how PIRCHE II algorithm predicts T cell epitope recognition and how the production of anti-HLA antibodies after transplantation depends on HLA-DRB1 alleles from the recipient.

Jennifer McCaughan from the United Kingdom in her talk clearly emphasized the need of identifying highly immunogenic epitopes mismatches for obtaining optimal epitope matching in organ transplantation. Immunogenic epitopes are the most important ones for *de novo* antibody formation and for prediction of whether antigen-antibody binding will occur in immunized patients when exposed to certain HLA antigen. She also explained the main differences between eplet and epitope and the main characteristics that make them immunogenic. Finally, she elaborated more on DQ epitopes, as DQ antibodies are the most frequently detected ones after solid organ transplantation.
The last speaker of this teaching session, Nils Lachmann from Germany gave talk about "Correlation of B and T cell epitope mismatches with *de novo* DSA formation". He explained in detail the epitope determinants recognized by B and T helper cells in T cell dependent antibody responses and provided extensive overview of the currently published literature on PIRCHE-II and HLAMachmaker algorithms in solid organ transplantation. Concluding that the both algorithms independently can predict *de novo* DSA formation after solid organ transplantation and can provide better risk stratification of the kidney transplant recipients than the traditional antigen mismatch approach.

Marco Carvalho Oliviera, Hannover, Germany

I would like to focus my report on the Oral Session 1: Solid Organ Transplantation. Constança Figueiredo (Germany) opened the session showing the feasibility to reduce

the immunogenicity of porcine lung endothelium by silencing SLA-I and SLA-II expression using a lentiviral vector encoding for shRNAs targeting beta2-microglobulin and CIITA, respectively. She demonstrated a downregulation of SLA class I expression by up to 72% and SLA class II by up to 62%, leading to a significant decrease of pro-inflammatory cytokines release as well as a delayed de novo donor-specific antibodies formation in the silenced lungs, prolonging the survival of the graft. The second presentation was hold by Caroline Wehmeier (the Netherlands). She focused on the contribution of the memory B-cell compartment to alloimmune responses.

Caroline was able to demonstrate the potential of her new method to predict antibody-mediated rejection (ABMR) by analyzing the profile of memory B cell-derived HLA antibodies. The third presentation was given by Navchetan Kaur (United States of America). He developed informatics tools capable to automate the translation of HLA data between antigen-based and molecular nomenclature systems in order to assess the virtual crossmatch in the short time available to accept organ offers, improving the specificity for potential conflicts at antigen level. The fourth presentation was given by Marica Grskovic (United States of America), who demonstrated the utility of assessing donor-derived cell-free DNA (dd-cfDNA) in order to assess allograft rejection and injury by correlating dd-cfDNA with biopsy-defined T-cell mediated rejection or antibody-mediated rejection (ABMR). The fifth presentation given by Matteo Togninalli (Switzerland) was related to the dynamics of allo-immune responses directed at HLA antigens in patients on the kidney transplant waiting list. Matteo showed that the time between single antigen bead assay (SAB) does not appear to have an influence in MFI (Mean Fluorescence Intensity) changes towards individual HLA antigen in patients on waiting list.

Aleksander Senev (Belgium) gave the following presentation on the importance of a high-resolution (HR) HLA typing for determination of the compatibility between the donor and the host in solid organ transplantation despite the associated costs. He performed a study where HR HLA and Low Resolution (LR) HLA typing was compared and was able to conclude that HR extended HLA typing is needed in order to decrease the DSA (Donor Specific Antibody) misclassification that occurred in LR-HLA typing. The seventh presentation, by Petya Yankova (Bulgaria), illustrated the importance of monitoring the immunosuppressive therapies (IST) effects after kidney transplant. She showed the dynamic changes in T, B and NK cells as well as the humoral immune responses (levels of immunoglobulins, complement C3 and C4, and HLA antibodies). These findings demonstrate the importance of using a combination of immunological and molecular biomarkers in order to monitoring and decrease biological effects of IST and to personalize drug dosing. The last presentation was given by Ingrid Faé (Austria). She focused on HLA molecules mismatch, more specifically HLA-DP, wondering if high or low expression levels would have an impact in donor specific antibodies production after organ transplantation (variant A of rs9277534 predicts low expression, the G variant predicts high expression). She showed 86 DP mismatch in 103 patients, 20 of them demonstrated DSA. Thirty-one donors showed low expression levels but only three were DSA positive. Fifty-five donors possessed high expressed alleles and found DSA in 17 of them. With this, she demonstrated a tendency of higher incidence of DSA in the group of donors with high expressing DP molecules but further studies are required.

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Report on an educational visit to Ljubljana

Ines Šimac Sušanj, BSc.med.lab.diagn.
Clinical Hospital Center Rijeka, Clinical Institution of Transfusion Medicine
Tissue Typing Laboratory Rijeka - Croatia

First of all, I would like to thank the EFI Education Committee for the bursary which has enabled me to visit the Tissue Typing Centre, Ljubljana, Slovenia for a period of two weeks in May 2019. Also, expressing my great gratitude to dr. Blanka Vidan-Jeras and her team for the warm hospitality and time devoted to my education.

The aim of my educational visit to the host Laboratory was to expand my theoretical and practical knowledge on detection of HLA antibodies by Complement Dependent Cytotoxicity (CDC) and Luminex techniques. I focused particularly on evaluating the impact of this two techniques on antibody screening policies in transplant setting. In the Rijeka Tissue Typing Laboratory HLA antibody detection and specificity determination has been performed by the CDC technique for many years. The more sensitive, Luminex assay was introduced in 2012 as an additional method to the CDC test. This implementation gave us new insights in interpretation of results and clinical decisions made with respect to the detection of pretransplant HLA sensitization.

The training program started in participating with HLA antibody screening by CDC assay. Beside observing the preparation of panel cells for the test, I patricipated in the plate reading noticing some elements that can affect (improve) the viability of lypmhocytes. My mentor, Natalija Pišec demostrated utilization of Lambda Cell Trays (One Lambda, Thermo Fischer, Canoga Park, USA) as an additional reagent for PRA and HLA antibody screening by CDC that can be combined with larger cell panels. She introduced me into the program that can help in result interpretation which I found to be very useful. Related to the panel cells typing on molecular level and the new studies about the allele distribution in our population, I discussed with Natalija about the optimal lypmhocyte panel composition. The final conclusions on antibody specificity is performed based on CDC and Luminex assay results. I gained a new knowledge and experience about the interpretation and the clinical relevance of the HLA antibodies. We exchanged opinions and experience in the management of higly sensitised patients through several cases.

The visit in Ljubljana was very fruitful and inspiring. I was pleased with the opportunity to visit such an excellent and hospitable laboratory. My deep gratitude goes especially towards dr. Blanka Vidan-Jeras and Natalija Pišec for hosting me and arranging my training program, their enthusiasm and patience with answering my numerous questions and also for sharing their theoretical and practical knowledge. Further, I would like to express my gratitude to all members of the laboratory as they were generous and benevolent, offering me full professional and personal support. Although the weather conditions were not favorable, I enjoyed staying in Ljubljana.

Finally, I'm pleased to becoming a member of EFI community which enabled me to meet wonderful people from the Tissue Typing Centre, Ljubljana with whom our laboratory successfully cooperates for many years.

Photo: *Natalija Pišec, Ines Šimac Sušanj*

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Antonij Slavcev, Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic
Gottfried Fischer, Medical University of Vienna, Vienna, Austria

The East-West Immunogenetics Conferences, since the first one organized in Prague in 2006, became an important meeting for professionals from the immunogenetics field not only from the Central European region. The motto of the first EWIC "Transfer of Knowledge" was upheld throughout all the following meetings and the blend of exciting new scientific insights and future perspectives in this field on one hand, and practical, routine information and discussion on the other, has proven to be a winning combination for a successful conference. After Prague, Pilsen, Olomouc, Vienna, Ljubljana and Wroclaw, the honour of hosting the EWIC 2019 was given to Zagreb, the capital of Croatia, which represents both the historic and political threshold between East and West. The attendance numbers confirmed this choice, with 181 participants from 25 countries, making the EWIC 2019 the biggest EWIC thus far.

The main intention of EWIC is to bring together professionals in order to share different ideas and approaches in achieving the same high quality of patient care, and this was reflected in the conference motto "Building Bridges". A plethora of eminent experts from the HLA field gave insightful and inspiring plenary lectures, covering all four main areas of interest: solid organ transplantation, hematopoietic stem cell transplantation, population genetics and HLA associated diseases.

The EWIC 2019 opening ceremony started with the addresses from Renata Zunec, who welcomed all the attendants, and Antonij Slavcev who gave a brief overview of the past EWIC conferences. The ceremony was made special by the presence of the professor Andrija Kaštelan, the founder of the immunogenetics and HLA in Croatia. The ceremony itself was rounded by a choir performance of the Croatian folk songs. The conference was launched with lectures given by Croatia's national transplantation coordinator, Mirela Bušić, and the University Hospital Center Zagreb transplantation coordinator, Jasna Brezak, presenting the highly successful transplantation program in Croatia. Their talks were followed by an exciting lecture given by Francesca Poli about the history of HLA, during which attendants were once again reminded why the HLA complex is such a remarkable and fascinating subject of investigation.

The highlights of the hematopoietic stem cell transplantation section were an outstanding lecture given by Steven Marsh about the impact of third generation HLA sequencing on haematopoietic stem cell transplant outcomes in a UK cohort, as well as an exceptional talk about the role of HLA antibodies in HSCT which was concisely and clearly presented by Ann-Margaret Little. The section included several more excellent lectures, with topics ranging from haploidentical stem cell transplantation experience presented by Milena

Vrana, immunological predictors of GVHD and GVL in allogeneic HSCT discussed by Frantisek Mrazek and utilisation of the NGS data addressed by Daniel Mathow; to presentation of the Croatian HSCT programme given by Radovan Vrhovac and 25th anniversary of the "Slovenia donor" presented by Blanka Vidan Jeras.

The solid organ transplantation section also consisted out of several excellent talks, foremost a remarkable review of the novel methods to detect HLA-specific B cell memory given by Sebastiaan Heidt, followed by the presentation of Caner Susal who gave an overview of the exceptional work done for the CTS with the recent data on post-transplant monitoring. The section also included two presentations given by Croatian leading clinicians in the field of kidney transplantation: Tvrtko Hudolin who addressed the non-immunological problems in kidney transplantation; and Mladen Knotek who discussed the clinical decision making in highly sensitised patients. Finally, Robert Liwski provided information about their Halifax/Halifaster protocols for flow crossmatch assay, Sabine Wenda gave an overview of the role of laboratory in kidney paired exchange and Aniko Syilvasi presented the kidney transplantation programme in Hungary.

The population genetics section started with an excellent review of the application of HLA polymorphism data in gaining knowledge about the evolution of populations given by Alicia Sanchez-Mazas, followed by interesting lectures about the distribution of HLA alleles and haplotypes in two populations. The first lecture was given by Zorana Grubić and presented the data about the Croatian population, while Irina Pavlova provided information for the Russian population.

The HLA and disease section consisted out of three lectures giving both an overview of the current state as well as the future perspectives about the role of HLA in various diseases etiology. The section commenced with an excellent talk by Brigitte Flesch who discussed TRALI and leukocyte antibodies, followed by Luca Mascaretti who gave a concise and useful information about the role of HLA typing in rheumatic diseases. The final lecture presented by Martin Petrek focused on HLA in sarcoidosis.

In addition to the plenary lecture sections, EWIC 2019 programme also included oral and poster presentations. The scientific committee evaluated 36 abstracts out of which 13 were chosen for oral presentation and 23 for poster presentation. The award for the best oral presentation was given to Helena Car for the study describing the detection of IgA HLA antibodies using a bead-based Luminex screening assay, while the best poster presentation award went to Katarzyna Bogunia-Kubik for the study investigating single nucleotide polymorphisms within the TERT gene in various malignancies.

A special EFI affairs section gave the attendants plentiful information about the EFI accreditation, with Blanka Vidan Jeras, Ingrid Fae, Luca Mascaretti and Ann-Margaret Little as EFI commissioners providing an up-to-date status for their respective regions. Their reports were followed by the external proficiency testing reports for 2018 which were given by Gottfried Fischer for the CET- EPT, Katarzyna Bogunia-Kubik for the HLA proficiency testing for Central and East Europe, Milena Vrana for the EPT for detection of HLA alleles associated with diseases and Hana Cechova for the EPT for cell chimerism analysis.

The task of organizing such an important event as EWIC, albeit a little overwhelming in the beginning, has in the end proven to be an immensely valuable experience. The 13th EWIC was organized under the auspices of EFI and I would like to take this opportunity to thank EFI for the kind support. I would also like to acknowledge the help and support in organizing this conference provided by the Croatian Ministry of health and the Croatian Society for Nephrology, Dialysis and Transplantation.

In the end, our main intention in organizing EWIC 2019 was to give the participants a well-balanced amount of new scientific insights and future avenues in the histocompatibility and immunogenetics field, but at the same time provide the opportunity to present everyday routine work of various laboratories. Also, we hope that the conference schedule gave the attendants plenty of time for socializing and discussing new projects resulting in new contacts and collaborations as the best outcome of a successful scientific conference.

Highlights from the HLA journal

By Luca Vago, Section Editor HLA journal

High-resolution analysis of the HLA-A, -B, -C and -DRB1 alleles and national and regional haplotype frequencies based on 120926 volunteers from the Italian Bone Marrow Donor Registry

Sacchi N, Castagnetta M, Miotti V, Garbarino L, Gallina A.
HLA. 2019 Sep;94(3):285-295. doi: 10.1111/tan.13613.

National unrelated HSC donor registries not only represent the solution to offer transplantation to patients that lack a suitable family donor, but are also a valuable research tool to analyze the HLA asset of a given population. In the present study, N. Sacchi and coworkers used data collected from more than 120'000 Italian unrelated HSC donors enrolled in the national registry (IBMDR) and typed them with a high-resolution (HR) method for the HLA-A, -B, -C and -DRB1 alleles to calculate allele and haplotype frequencies and correlate them with the donor region of origin. The allele and haplotype frequencies obtained in this study are useful for a number of purposes including: (a) to determine which alleles should be defined by HR techniques because of the higher heterogeneity; (b) to assign the most likely types in the donors recruited in the past and typed at lower resolution; (c) to categorise a patient's haplotype at the beginning of the unrelated donor search as either common or uncommon in the national donor population, giving an important predictive estimation of the probability of finding a matched unrelated donor; (d)

to better understand donor availability in each region, and implement better recruitment strategies where needed.

Towards uniformity in the definition of acceptable mismatches for highly sensitized patients

Chen M, Zoet Y, Roelen D, Martorell J, Middleton D, Slavcev A, Iniotaki A, Claas F, Fuggle S.
HLA. 2019 Aug;94(2):147-153. doi: 10.1111/tan.13607.

The presence of donor-specific HLA antibodies, especially when detectable in complement-dependent cytotoxicity tests, is considered a contra-indication to kidney transplantation. As a consequence, to avoid the risk of leaving highly sensitized patients in the waiting list for inacceptable time, consensus should be reached on the definition of mismatches that are considered acceptable for these patients. EUROSTAM is a project funded by the European Commission to analyse the feasibility and requirements for a Europe-wide acceptable mismatch program to enhance transplantation of patients with rare HLA phenotypes in their own population. In particular, this study was designed to assess the differences in the practices of HLA antibody definition and risk stratification for transplant amongst the project partners. Following the exchange of a panel of 18 sera, the study highlighted a high level of variability in Luminex results and their interpretation. Moreover, variation in the definition of acceptable mismatches appeared to be due not only due to differences in laboratory procedures, but also the interpretation of the same results still lead to discrepancies, suggesting that to ensure fairness and maintain consistencies of organ exchange among partner transplant centres, a centralized facility would better uniform definition of acceptable mismatches.

HLA-G, HLA-E, and IDO overexpression predicts a worse survival of Tunisian patients with vulvar squamous cell carcinoma

Boujelbene N, Ben Yahia H, Babay W, Gadria S, Zemni I, Azaiez H, Dhouioui S, Zidi N, Mchiri R, Mrad K, Ouzari HI, Charfi L, Zidi I.
HLA. 2019 Jul;94(1):11-24. doi: 10.1111/tan.13536.

Non-classical HLA class I molecules and the tryptophan catabolic enzyme Indoleamine 2,3-dioxygenase (IDO) have shown by several studies to be critically involved in promoting tumor immune evasion, but never investigated in detail in vulvar squamous cell carcinoma (VSCC). In this interesting study, Boujelbene and coworkers analyzed by immunohistochemestry expression of HLA-E, -G and IDO in 61 VSCC samples collected at disease diagnosis, and correlated results with patient outcome. The three molecules of interest were highly represented in tumoral tissues vs healthy matched vulvar tissues ($P = 0.0001$). At 5 years, survival was significantly lower for patient with high expression of HLA-G or IDO, and even worse for patients whose tumor coexpressed all three molecules. These data hints to an important involvement of loss of immunesurveillance in the pathogenesis of VSCC, providing at the same time new prognostic markers and potential therapeutic targets.

Regulation of p38MAPK-mediated dendritic cell functions by the deubiquitylase otubain 1

Xuan NT, Trung DM, Minh NN, Nghia VX, Giang NV, Canh NX, Toan NL, Cam TD, Nga NT, Tien TV, Hoang NH.
HLA. 2019 Jun;93(6):462-470. doi: 10.1111/tan.13534.

Dendritic cells (DCs) represent the most efficient professional antigen presenting cells in our organism, and act as a crucial link between innate and adaptive immune responses. In this study, Xuan and coworkers dissect a novel pathway of regulation of their function though the deubiquitylase otubain 1 (OTUB1). By transfection of mature DCs with OTUB1 siRNA, they demonstrate that absence of this deubiquitylase leads to prolonged activation of p38MAPK, with acquisition of a proinflammatory phenotype characterized by increased CD54 expression, IL-6 release and induction of IFN-γ-producing CD4 cells in mixed lymphocyte cultures. All the effects were completely abolished when the cells were exposed with p38MAPK inhibitor SB203580. These data highlight a new layer of regulation of DC function, demonstrating that OTUB1 prevents the prolonged activation of p38MAPK, which in turn compromises DC functions.

Finally we would like to point the attention of the EFI newsletter readership to a number of comprehensive reviews published during the last few months in *HLA*, focused on the link between *HLA* and hypersesitivity to antiepileptic drugs (June issue), on the possibilities offered by virtual crossmatch for kidney transplants (July issue), on the results obtained by the PROfiling Consortium in studying the immunobiology of kidney transplantation (August issue), and on how genetic variability in immune genes shapes the development and course of human disease (September issue). Moreover, recent issues of *HLA* collected the abstracts from the 33rd EFI Conference (Lisbon, Portugal, May 8-11, 2019; Volume 93, Issue 5, published in May), from the 2018 KIR Workshop (Camogli, Italy, October 25-27 2018; Volume 94 Issue 2, published in August), and from the 27th Annual Conference of the German Society for Immunogenetics (Cottbus, Germany, September 4-6, 2019; Volume 94 S1, published in September).

The 18th International HLA & Immunogenetics Workshop: HLA epitopes take center stage

As was the case for previous workshops, the 18th IHIWS contains many different projects, covering the breadth of work performed in the H&I field. These projects have been categorized in the components Antigenicity & Immunogenicity, Immunogenetics, and Bioinformatics. A major focus of the 18th workshop is on HLA epitopes, which is part of the Antigenicity & Immunogenicity component. The main aim is to lay the foundation for an extensive database that can be used for HLA epitope research in the current workshop and beyond. By making use of the power of international collaboration, HLA matching on the structural level should gradually become a clinical reality in different populations of the world.

Many clinicians have become aware of the promise of 'HLA epitope matching' for patients and are eager to start using this in the clinical setting. However, while on the population level the degree of molecular mismatch can identify risk for adverse events, such as donor specific antibody (DSA) formation, rejection and graft failure [1-4], many issues need to be resolved before epitope knowledge can reliably be used for the individual patient.
The first challenge is already in the definition of what an epitope actually is. Several terms are used interchangeably that not necessarily mean the same [5]. First of all, an epitope can refer either to a B cell/antibody epitope, or a T cell epitope. An antibody epitope is defined as 'the part of an antigen molecule to which an antibody attaches itself.' So by definition, an HLA antibody epitope describes the amino acids that are involved in binding of a DSA (antigenicity), and has also been called a structural epitope [6]. An immunogenic epitope describes a polymorphism (which could be a single amino acid) that triggers an antibody response (immunogenicity). This is not the same as an eplet (also known as a functional epitope), which describes the amino acids configuration responsible for antibody formation. Eplets are short discontinuous sequences of amino acid residues within an HLA epitope [7]. On the other hand, T cell epitopes that are involved in DSA formation are peptides of the allogeneic HLA that can be presented in self HLA class II molecules [8]. It is clear from the above that the definition of an epitope and usage of the correct terminology is actually rather problematic. The difficulty to harmonize these definitions was already addressed during the concluding meeting of the 17th IHIWS in Palo Alto, where a long discussion on this subject was held. In line with this was the discussion on the actual nomenclature of HLA epitopes. The International HLA epitope registry that was initiated during the 16th workshop contains information on all theoretical and antibody-verified eplets [9], but it remains to be seen whether the nomenclature used is the most pragmatic one. Since no clear consensus on these subjects was reached during the 17th workshop, the discussion will continue during the 18th workshop. For simplicity, in the remainder of this article, we will refer to epitopes in the context of immunogenicity.

There are several ways to study the degree of molecular mismatch between patient and donor [10]. This can be done by using eplets (HLAMatchmaker)[11], amino acid mismatches (Cambridge [12] and Leiden algorithms (manuscript in preparation), physiochemical properties of amino acid mismatches (EMS-2D and EMS-3D scores) [12,13], as well as indirectly recognizable T cell epitopes (PIRCHE) [14]. Up till now, for eplets, amino acid mismatches and EMS-2D, it has been shown that these algorithms give a similar predictive value for DSA formation [15]. On the other hand, while both eplets and PIRCHE are representative of the level of amino acid mismatches, these values do seem to provide different information, which is biologically explainable [16]. For the 18th workshop, we aim to further study molecular mismatches by all these approaches, and we therefore have included principle investigators that are experts on all the above-mentioned algorithms.

In November 2018, a meeting was held in Leiden, the Netherlands including Peter Nickerson (Canada), Vasilis Kosmoliaptsis (Cambridge), Anat Tambur (USA), Frans Claas, Cynthia Kramer, Sebastiaan Heidt and Eric Spierings (the Netherlands). René Duquesnoy (USA) was invited but unfortunately could not join. During this meeting the strategy for the epitope component of the 18th workshop was further specified. It became clear that, while on the population level eplet, amino acid mismatches, physiochemical properties of amino acid mismatches or PIRCHE are predictive of the chance of DSA formation, for an individual patient, a high or low molecular mismatch score is not definitive proof of high or low risk. One of the reasons is the fact that not all epitopes are equally immunogenic. Obviously, whether an epitope is immunogenic for an individual patient is dictated by the HLA phenotype of the patient itself, but also by the physiochemical characteristics of the amino acid substitution that gave rise to the epitope. Importantly, since immunogenicity is partly dictated by the HLA phenotype of the patient, immunogenicity will be dependent on the population studied [10]. Finally, an antibody epitope needs to be accompanied by a T cell epitope to give rise to an IgG DSA. Therefore, algorithms on antibody epitopes, the properties of the amino

acids involved and T cell epitopes will have to be combined to reflect the biology of an antibody response.

During the meeting, two main projects (led by Eric Spierings and Sebastiaan Heidt) were identified to get more insight into the relative immunogenicity of epitope mismatches. The first project involves gathering data of non-immunized patients at time of transplantation who either became immunized by the transplant, or remained DSA-free for at least 5 years. From these patients we require HLA typing data (preferably second field resolution) of both patient and donor, and the raw single antigen bead data pre-transplant and at time of DSA detection, or at 5 years in case of no DSA detection. With a large dataset, we will be able to identify those epitope mismatches that very often result in DSA formation. The second project aims to define non-immunogenic epitopes. For this project, we require data from highly sensitized patients (defined as cPRA of 95% and above). From these patients, we require HLA typing data (second field resolution) and the raw data file of the single antigen bead assay. With this information, we can identify epitopes that never or very rarely result in antibody formation. For details on the data required for both projects, please visit the official IHIWS website (www.IHIWS.org).

Besides these two projects, two other epitope projects have been included, one which is focussed on HLA-DQ immunogenicity (headed by Anat Tambur and Lloyd D'Orsogna). It is known that HLA-DQ mismatches are particularly immunogenic due to the polymorphic alpha and beta chain [17,18], which warrants further detailed analysis on HLA-DQ immunogenicity. The fourth project aims at defining an algorithm for individual risk assessment based on molecular mismatches, combined with other relevant data (such as immunosuppressive regimen and compliance), led by Peter Nickerson [19].

We invite all laboratories who have an interest in HLA epitopes to join the projects described above. Since our current knowledge on HLA is mainly based on studies on Caucasian populations, we especially welcome laboratories from non-Western countries to participate, in order to bring the field forward for patients worldwide. We welcome all (high quality) data, from single cases up to large datasets to build the database required for the large-scale analyses we aim to perform. Applying for projects can be done through the IHIWS website.

Sebastiaan Heidt and Eric Spierings

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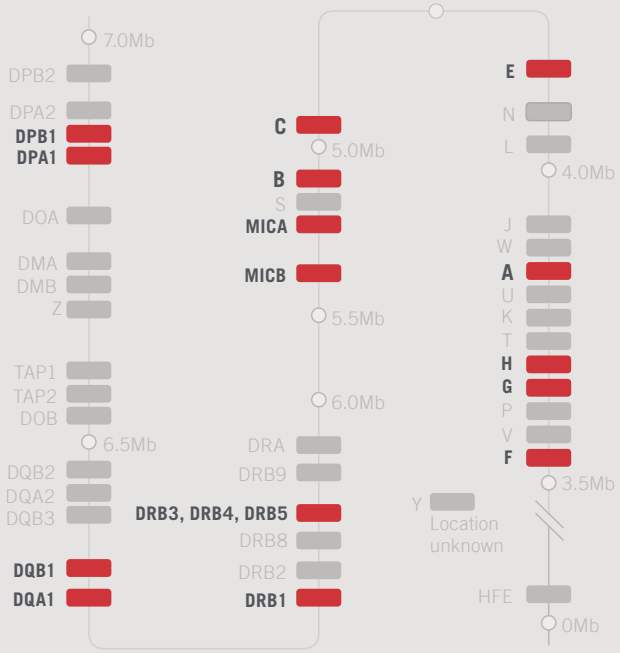

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