**EUROPEAN FEDERATION** 

# NEWSLETTER



## For Immunogenetics

#### DECEMBER 2019- ISSUE 90

# .....FROM THE EFI PRESIDENT\_

## DEAR COLLEAGUES AND FRIENDS,

The busy autumn time with all the conferences and events comes to an end and by the time you will have received this EFI Newsletter it will already be Christmas. So I hope that you all have left a successful conference period behind you and that you are ready to enjoy the Festive Season and also spend a peaceful and relaxing time with your families over Christmas and New Year's holidays.

Unfortunately, last October we lost another great personality and a great colleague in the H&I field, one of our previous EFIpresidents, Professor Jacques Hors. Jacques was our fourth EFI president and served from 1992-1994. He was one of the pioneers in the field of immunogenetics and transplantation immunology in France and in Europe. As a member of the Experts Committee on Histocompatibility of the Council of Europe he was decisively involved in the creation of our society and was in fact one of its founding members. Under the auspices of the Council of Europe, he also launched the first call to recruit EFI Inspectors, and also became the first Chairman of the EFI Accreditation Committee. We are deeply saddened about the loss of Prof. Hors and will keep him in our minds and hearts as a great scientist and colleague! Our condolences go to his family and his closest friends and colleagues.

In the next couple of weeks and definitely by the time you will be reading this article we will also have launched our new EFI website. This has been a project that lasted longer than we initially anticipated, but we are proud that it is now completed and ready to be used by our members. Many thanks to Sandra van Hensbergen, our EFI administrative secretary, and to Eric Spierings, the Chair of our newly constituted IT and Bioinformatics Committee, for all the work they have put in the creation of the new homepage. We hope that you will find our new website useful, functional and well designed. Please contact Sandra if you experience any mal-functionalities. We have tried to eliminate any errors, but as I am sure you all know it takes a while until all the bugs have been completely identified.

In the weekend of October 11-13 EFI has had its annual business meeting in Leiden, where several committees, including the Executive Committee, met and discussed outstanding issues as well as planned ahead for the future. A lot of decisions were made at this meeting and I am happy to share with our members some of the important points which will probably be decisive for the next couple of years. First of all I am happy to announce that EFI has selected a new Professional Congress Organiser (PCO) who will be in charge of organising our annual conferences for three consecutive years, starting with the 2022 conference in Nantes. We had announced this opening some time ago and several PCO companies applied. After a number of selection rounds and discussions within the EC we decided to accept the bid from "Guarant", a PCO from Prague, who had already organised an EFI annual meeting before as well as several East-West H&I regional events. The contract with Guarant has been finalised and will have been signed by the time you'll have this EFI newsletters issue in your hands. Guarant will also be involved in the organisation of the 2020 Summer School in Prague. We look forward to a successful and hopefully long lasting cooperation with Guarant! I'd like to thank particularly Dave Roelen, our deputy secretary, as well as Jean Villard, our Councillor from Switzerland, who both were extremely instrumental and motivated to bring this project to an end!



Basically, starting with the above mentioned PCO project, the EC decided to systematically seek legal advice whenever contracts and agreements are involved, but also for the review of our core documents, like our constitution, in order to see whether these are still state of the art as far as legal requirements and current practices in France and Europe are concerned. We have approached various legal agencies and asked for offers. Eventually, we decided to go with a French law agency when it comes to issues that affect our French "nature" (finances, taxes, constitution, data protection etc), and a German law firm for advise in international affairs (e.g. the PCO contract and possibly other contracts to come).



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EFI website www.efi-web.org Editor-in-chief Sebastiaan Heidt

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## ....FROM THE EDITOR'S DESK

Before you lies the 90<sup>th</sup> edition of the EFI Newsletter, which has been printed somewhat earlier than usual due to the fact that the EFI Conference in Glasgow is already in April. The motto of this upcoming 34<sup>th</sup> EFI meeting is 'From research to clinical reality'. This very tangible motto has been incorporated throughout the program and promises to give us an extremely interesting meeting.

The time to vote has come again, and in this Newsletter the candidates for the vacant positions in the EFI Executive Committee are presented to you. Please use your right as EFI member to vote on your favourite candidates.

This newsletter contains multiple reports on the very successful International Summer School on Immunogenetics held in Montreal, Canada in July 2019. Next year's Summer School will be organised by EFI in Prague, under leadership of Antonij Slavcev.

As always, I hope that you enjoy reading this newsletter and I am looking forward to your contribution to the next edition.

#### Sebastiaan Heidt

Deadline for contributions to EFI Newsletter 91 is Februari 17, 2020. Please send your contributions by e-mail to s.heidt@lumc.nl



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## .....FROM THE EFI PRESIDENT (CONTINUED)

We feel relieved that we were able to come forward with this project and look forward to the cooperation with the selected law firms.

Another decision which was taken at the autumn meetings in Leiden to be connected more frequently and try to follow up on decisions taken on a timelier manner. Therefore, we have decided to carry out bimonthly teleconferences. This will help all EC members to stay updated on running projects and also hopefully help us all be more efficient as a society.

Within 2020 we will have quite some changes in some of our committees. New chair persons will be in charge and there will be a hand full of new committee members. Details will be most probably announced at the next EFI Newsletter and all the changes will be effective from after the annual EFI meeting in Glasgow.

A lot of the discussions during the EFI business meeting in Leiden concerned e-Learning opportuni-ties. EFI is committed to promote e-learning and offer to its members platforms that will allow continuous education to be carried out electronically. Furthermore, EFI has discussed with its sister societies and works with them on joint e-learning projects. Several options were discussed and we are currently investigating and prioritising projects. Ideally, we would have as a starting point our new website from which members and users will be linked to the various e-learning modules that will eventually be set up. As a first project Marco Andreani and David Turner, the UEMS-EBTI and EFI Education Committee Chairs, managed to secure funds for the creation of an e-learning platform which will provide learning opportunities for ESHI diploma applicants. The e-learning technology vendor has been identified and contracts signed. So we expect the first visible results in the next couple of months. Further e-learning opportunities for EFI members will also follow soon. We'd like to thank Marco Andreani, David Turner and Eric Spierings for all the efforts they have put in order to make the first steps of EFI in the e-learning technology.

In 2020 the EFI members will have again the opportunity to elect new members in the EC. This time we will have to elect three new Councillors again, but also our new President-Elect. The newly elected members will become active EC members right after our annual meeting in Glasgow and the new President-Elect will take over the EFI lead right after the Annual Meeting in Amsterdam in 2021. It is important that we have as many members participating in the elections as possible! More details on the election will be sent by blast e-mail on time and there is a section in this issue of the EFI Newsletters where the candidates are introduced. Please take a minute to read the details about the candidates and make sure that you will give your e-vote whenever this will be announced in the beginning of 2020.

Finally, I would like to remind you all to start planning for our next annual meeting which will be carried out in Glasgow/ Scotland/UK in the time between April 26 and 29, 2020. The Scientific and Educational program have been already settled and preparations are going on at a max speed. Make sure that you will have taken advantage of the early registration fee and most importantly, that you have submitted your abstract until the 10<sup>th</sup> of January where the portal for submitting abstracts will be closing.

I would like to close by wishing a peaceful and relaxing Christmas Season and a prosperous, successful and healthy New Year to you, your families, your colleagues and co-workers!

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:

R. Pavolsky Gutman, Ramat Gan, Israel

- E. Matteucci, Bologna, Italy
- D. Pisapia, Bologna, Italy
- A. Pallotti, Bologna, Italy
- S. Capelli, Bologna, Italy
- R. Masi, Bologna, Italy
- A. Villegas, Cali, Colombia
- S. Norrbom, Stockholm, Sweden
- N. Lundin, Stockholm, Sweden
- L. Istanbullu, Stockholm, Sweden
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- Y. Bolon, Minneapolis, United States
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# **REPORT OF THE EFI EXECUTIVE COMMITTEE AUTUMN** MEETING IN LEIDEN OCTOBER 13<sup>TH</sup> 2019

The EFI Executive Committee (EC) meets two times every year. There is always one meeting scheduled at the annual conference but there is the additional autumn meeting with the possibility to also meet all the chairs from the different committees.

This year an extra half day was scheduled to go through all the SWOT analyses that the different committees had submitted. A summary of this will be reported separately at another occasion.

#### E-learning and the web

An important theme for this meeting, which was also clearly communicated during the SWOT analysis, is the need for e-learning, and a special working group will be established to continue to work on this. This working group will have representation from the IT and Bioinformatics committee, the Accreditation, Education and Scientific committees and from the EC. The group will define the areas for which e-learning should be prioritized, the technical platforms, budget and timeline. One thing that we can expect to see in rather short time is e-learning for members that will apply for the ESHI diploma: Marco Andreani has done a fantastic job together with EBTI and secured funding from the Italian charity organization the Berloni Foundation. There will be 10 recordings of 30 minutes each about the major topics from the EBTI syllabus. Our President has also discussed with our sister societies on how we can collaborate and share resources in this field.

Hopefully when you receive this newsletter the EFI new website has gone live. It has been a lot of work for Sandra at the office to test all functionality and to move all content. EFI has also decided to create dedicated space for future annual conferences to be hosted within the EFI site. When this is finished the users will have the same experience every year and we can also develop our own tools for an EFI app that can sync and download content. So I think that we can look forward to some very exciting new things the next few years.

#### Mats Bengtsson EFI secretary.

#### International collaboration

Collaboration has always been one of the main topics for EFI, both within Europe and internationally. We have recently also started to work with other societies such as EFIS, EBMT and ESOT. In Glasgow there will be a joint symposium with ESOT and in Amsterdam with EBMT. This collaboration will increase the visibility of EFI as a scientific society. We have also been invited to participate in a joint session at the European Congress of Immunology in Belgrade next year. It will be EFI that organizes the International summer school next year and the planning is going well.

#### **Corporate PCO**

We have had legal advice on the contract with a PCO and we also had a chance to again discuss with representative from the company, and all concerns raised by the EFI board and the lawyers were sorted out so after final adjustment the contract will be signed. This means that EFI will work with the same PCO for at least three years starting in Nantes 2022.

#### **EFI Conferences**

Antonio Martinho reported from the very successful Lisbon meeting. There were 1061 registered participants coming from 56 different countries. The revenues from the conference are much better than predicted and keeping the expenses low was one of the key factors. Next year's meeting will be in Glasgow and Ann-Margaret Little gave us an update on the meeting. Everything is going as scheduled. The joint conference and International Workshop in Amsterdam 2021 were presented by Eric Spierings. The elegant design of the branding was presented that links science to old Dutch artwork. Finally, Pierre-Antoine Gourraud gave a preview of the meeting in Nantes in 2022. We have some really exciting meetings to look forward to!

#### **EFI elections**

At the General Assembly the vacant positions were announced and we have candidates for all positions that are presented elsewhere in this newsletter. There will be an election next year and it will use electronic voting and all members are urged to check that their contact details are up to date. If you do not receive the announcement of this newsletter by e-mail then your details need to be updated!

#### Scientific Summer School

The Scientific committee has proposed to organize a scientific summer school the year after the ISS is organized in Europe. The EC approved this idea and have asked the committee to come up with a plan for program, budget, organization and target group.

#### EFI budget

The EFI budget seems to be in balance and there was a very good benefit from the Lisbon meeting. It was decided that next year we will give 4 Education and Scientific bursaries of max  $\leq 1500$ each and for the annual conference 10 bursaries of  $\leq 750$  each. For all bursary recipients a report on the meeting will be required.

Finally, the EC also discussed and decided the nominations for the Ceppellini lecture and the EFI medal to be awarded during the Glasgow meeting. Overall, it was a busy but very fruitful meeting.



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# THE JULIA BODMER AWARD \_\_\_\_

Applications are invited for the prestigious Julia Bodmer Award, to be delivered on Sunday April 26, 2020 during the Opening Session at the 34<sup>th</sup> EFI conference in Glasgow, UK. The Julia Bodmer Award is given to a young scientist in recognition of their outstanding work within the Immunogenetics field. The Award also acknowledges the laboratory in which the scientist has performed their research.

Any member of EFI can propose a candidate for the Julia Bodmer Award. The application must include the candidate's CV with a list of publications and a letter of support from the head of the candidate's laboratory. Candidates must be an EFI member (or become a member at the time of application) and be no more than 10 years past completion of their doctoral thesis if applicable; candidates who have not undertaken or completed a doctoral thesis are also eligible.

All applications will be reviewed by the Scientific Committee who will make the final decision on who will receive the Award. In addition to the presentation at the Opening Ceremony of the EFI Conference, the Award winner will also be invited to contribute a dedicated "Julia Bodmer Review" to HLA, the official journal of EFI. He/she will receive €1000 in addition to the expenses for registration, travel and lodging for attending the EFI Conference.

Applications must be sent in writing to the EFI Secretary via Sandra van Hensbergen at the EFI Central Office, (ajvanhensbergen@lumc.nl) before February 15, 2020.

# EFI ANNUAL CONFERENCE BURSARIES \_\_\_\_

EFI Personal Bursaries are available for the annual EFI Conference to be held in Glasgow, UK 26-29 April 2020. Full details on how to apply for EFI personal bursaries are given on the EFI website in the document entitled "EFI Personal Bursaries". The application form for the EFI Personal Bursaries is also available on the EFI website.

In addition to the general deadlines for personal bursary applications, a deadline of February 7<sup>th</sup> 2020 has been set for applications for bursaries specifically to support attendance at the annual EFI conference in Glasgow. Preference for these applications will be given to members who have been selected to present an abstract at the EFI conference (either oral or poster presentation). Only one bursary per laboratory will be awarded.

All bursaries are awarded on the strict condition that the recipient submits a report of  $\sim$ 1 page on any scientific session of the conference, which will be published in the EFI newsletter, following the conference.

For all bursary applications, the following are required: completed "EFI Personal Bursary Application Form"; CV of applicant; letter of support from Lab Director; submitted abstract where appropriate, and confirmation of selection for oral or poster presentation as soon as this is available.

These must be sent before February 7<sup>th</sup> 2020 to the EFI Secretary via Sandra van Hensbergen at the EFI Central Office, (ajvanhensbergen@lumc.nl).

## BURSARY DEADLINES 2020

It is our pleasure inform you about the upcoming deadlines for application for the EFI Personal Bursary, the EFI Education and Scientific Bursary and the support for EFI 'International Affairs'.

The bursary deadlines for 2020 are set as per below:

	Deadline 1	Deadline 2	Deadline 3	Deadline 4
EFI Personal Bursary	1 February 2020	1 May 2020	1 August 2020	1 November 2020
EFI Education and Scientific Bursary	1 February 2020	1 May 2020	1 August 2020	1 November 2020
Support for EFI 'International Affairs'	1 February 2020	1 May 2020	1 August 2020	1 November 2020

Next to the above, please note an Annual Conference Bursary is made available to attend the 34th European Immunogenetics and Histocompatibility Conference and more information is to be found elsewhere in this Newsletter. Also a Bursary is allocated to support EFI Members to attend the 2020 International Summer School and more information will be provided at a later time. Reminders of upcoming Bursary deadlines and information about the application procedure will provided to you by the EFI Office by email. More information on the respective Bursaries is to be found in the Bursaries page on our website www.efi-web.org.

# News from the EFI Committee for External Proficiency Testing

The present EPT Standards for Laboratories (Version 7.0) claiming ten samples as the minimum number of EPT samples for every HLA typing method led to inconsistent interpretation: Some laboratories used ten samples for every technique (SSP, SSO, etc.), but others used only ten samples for every category (e.g. low resolution typing) and therefore split the samples (e.g. five for SSP low, res, and five for SSO low, res, if both assays were established in the lab). In addition, the minimum numbers of EPT samples for supplemental typing techniques, for example only applied for resolving ambiguities after SBT, were not clearly defined in the present EPT Standards.

# The EFI community is kindly asked to note the following changes:

The EFI Committee for External Proficiency Testing (EPTC) announces new EPT Standards in chapter D of the next EFI Standards (Version 8.0, effective from January 1<sup>st</sup> 2020).

For the implementation of external proficiency procedures (EPT) laboratories must now prospectively define <u>core</u> and <u>supplemental</u> techniques according to their Accreditation Application. They are defined as follows: <u>core</u> techniques are used individually or in combination to produce a final result whereas <u>supplemental</u> techniques are used only occasionally for rare cases in combination with core techniques to refine the final result.

Example 1: SSP and SSO are used in a laboratory to produce final results for low resolution typing (e.g. SSO in daily routine and SSP as additional technique also for 24/7 organ donation duty service). Both techniques are thought to be defined as core techniques.

Example 2: SBT is used as a core technique in a laboratory, but SSP is also used to resolve ambiguities. Depending on the frequency of use of SSP by the laboratory, it may be defined as a core technique (frequent, routine use) or a supplemental technique (occasional use for rare situations). Laboratories are expected to justify the basis for defining techniques as supplemental and regularly review this to ensure it remains accurate.

D1.2	The laboratory must prospectively define core and supplemental techniques according to the Accreditation Application.
D1.2.1	Core techniques are used individually or in combination to produce a final result
D1.2.2	Supplemental techniques are used occasionally for rare cases in combination with core techniques to refine final results
D1.3	The laboratory must
D1.3.1	Prospectively document the relevant EPT schemes or workshops on an annual basis
D1.3.2	Have a predetermined policy for testing EPT samples and must document this prior to the annual commencement of the EPT cycle
D1.3.3	Have a predetermined policy if they select individual shipments or samples for EPT
D1.3.4	Have a predetermined policy for the selection of samples or shipments for supplemental techniques

It is essential that each laboratory prospectively documents all relevant EPT schemes or workshops on an annual basis. Moreover, there must be a predetermined policy defined for testing EPT samples, which must be documented prior to the annual commencement of the EPT cycle. The policy must also include information relating to the selection of individual shipments and how samples are <u>selected</u> for <u>supplemental</u> techniques (if relevant).

## Impact of change on minimum EPT sample requirements:

The minimum numbers of samples for EPT per year (as defined in D1.5) now only applies to all core techniques used to produce a final result. For supplemental techniques the number of EPT samples tested must be in accordance with the laboratory's predetermined policies. establish a documented procedure for interlaboratory comparisons (i.e. EPT) that includes defined responsibilities, instructions for participation, and any performance criteria that differ from the criteria used in the interlaboratory comparison programmes. However, minimal sample numbers for specific diagnostic assays are generally not defined for interlaboratory comparisons.

The EFI EPTC has tried to obtain relevant information about national regulations within the various EFI regions regarding samples numbers for interlaboratory comparison in medical diagnostic laboratories. A small survey revealed that there are no specific numbers defined in most European countries that were checked (F, I, UK, DK, ES, P, NL), instead it is referred to by monitoring authorities (e.g. EFI) in specific regulations. Only a few countries have national

D1.5	Minimum number of samples for EPT per year
D1.5.1	The minimum number of samples applies to all core techniques used to produce a final result:
D1.5.1.1	Serological typing: 10 samples
D1.5.1.2	Each low resolution DNA-based typing technique: 10 samples
D1.5.1.3	Each high resolution DNA-based typing technique: 10 samples
D1.5.1.4	Each allelic resolution DNA-based typing technique: 10 samples
D.1.5.2	For supplemental techniques the number of EPT samples tested must be in accordance to the predetermined policies described in D1.2 and D1.3.

# How can the EPT for supplemental techniques be implemented in routine practice?

According to ISO and good laboratory practice each laboratory must regulations specifying numbers of samples and when defined, the numbers varied for each country (CH: four/year, D: two/year, BG: variable from one/ year to five/year).

## How many EPT samples must be tested for supplemental techniques?

Due to the national and international regulations mentioned above it is the responsibility of the laboratory to determine how many EPT samples should be processed for supplemental techniques. However, to enable useful result evaluation, the EFI EPT Committee recommends analysing at least two samples per year for every supplemental technique.

It is expected that supplemental techniques are used in addition to the core technique(s) for the selected EPT samples. According to the EFI EPT Standards the same samples can be used for more than one technique or category, but the results must be analysed independently and must be available for inspection.

Example: SBT is used as a core technique. In some cases it is necessary to resolve ambiguities which is done with SSP as a supplemental technique. For SBT a minimum of ten samples must be tested in EPT, and it is recommended that for at least two of these samples, SSP testing is also performed.

In case of any questions please contact the EFI EPTC chairpersons or your regional representative within the EPTC.

Falko Heinemann and Yvonne Zoet (chair and co-chair of the EFI EPTC)

# UPDATE FROM THE EFI EDUCATION COMMITTEE NOVEMBER 2019

#### European Specialisation in H&I (ESHI) Diploma

The next examination will be held at the Glasgow 2020 EFI Conference on Saturday 25<sup>th</sup> of April with a deadline for applications to be received the 25<sup>th</sup> of 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/trans-plantation/-transplant--immunology2). Payment for the exams is performed via Paypal upon application.

Discussions took place at the Autumn 2019 EFI Business meetings on the creation of on line e-learning resources for individuals wishing to take the ESHI Diploma examination. It was agreed to take forward a plan to develop ten 30 minute on line lectures, facilitated by an Italian company (ACCMED) in the first instance. It is hoped these will available early in 2020 via the Education Committee pages of the EFI website. Also, please note that many other on line 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) and the Basic and Advanced on line courses provided by WMDA. In addition, members can access pdfs of slides from conference Teaching sessions and Summer Schools via the members area of the website.

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

Discussions are ongoing regarding the best way to provide the new EFI CME/ CPD scheme for recording of individual's training and ongoing education. It is still hoped that a scheme can be provided to 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)

The pilot scheme of the ETHIQ logbook is now being undertaken by participants in France, the Netherlands, Italy and Sweden. As described before, the scheme is for technical staff working at the bench in EFI accredited laboratories, with supervision given by senior staff in their own lab. 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 Training Bursaries

Applications for Education and Training 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 (~50) and participants are invited to present their own research or clinical cases. It represents an opportunity for those studying towards higher H&I specific qualifications as well as a chance to meet others working in the field from different parts of the world.

The next ISS 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.



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# UPDATE FROM THE IT AND BIOINFORMATICS COMMITTEE – NOVEMBER 2019

#### The Committee

The IT and Bioinformatics Committee takes questions from EFI regarding IT, suggests solutions and advises, solicited and unsolicited. The committee actively monitors developments in the field and communicates with their findings EFI. These developments also include data exchange formats and analysis software. Currently, the committee consists of three members: Jose M Nunes (Geneva), James Robinson (London), and Eric Spierings (Utrecht, chair).

#### Achievements 2019

The IT and Bioinformatics Committee has addressed the use of more standard tools for abstract submission for conferences. These efforts are in coordination with the Scientific Committee and the Educational Committee. The proposal to switch to the EasyChair software has been approved by EFI. Transition to this abstract submission and conference management software package will start with the upcoming Summer School. If successful at this small scale, the EasyChair software will used for the annual EFI conference 2021 as well.

Various committees expressed their need for e-learning. The IT andBioinformatics Committee has explored the technical option for e-learning and advised to use Moodle for that. This e-learning environment will further be discussed with all committee chairs. Currently, the IT and Bioinformat-

ics Committee is working on an integrated Federation & Conference app. Today's technology allow us to combine various sources into one single mobile application. This would mean that all digital resources within the EFI domain may become available within one single application.

#### Challenges

If you feel challenged by our activities and plans, please apply for a position as a member of our committee. Since we prefer a committee size of 4-5 active members, there is still room for 2 additional members. Check the webpage for the application form: (https:// www.efi-web.org/efi-committees.html).

#### **Eric Spierings**

Chair of the IT and Bioinformatics Committee

# Nominations for the EFI Executive Committee vancancies and the electronic election process \_\_\_\_\_

Nominations were sought for the positions of President-Elect, Deputy Secretary as well as three Councillors. One nominations has been received for the position of President-Elect as well as for the position of Deputy Treasurer. The nominated candidate for both positions are presented here. Since no other nominations for this positions were received, there will no voting for these positions; the nominations are subject to approval by the EFI General Assembly in Glasgow, Scotland.

We received four nominations for the postion of three Councilors and the nominated candidates are presented below. As a result, elections will be organised early 2020 for the three Councillor positions. The elections will be held electronically as we have had the last three times.

All active EFI members (having paid their membership fees for 2019) will receive notification by email regarding the election procedure. We urge members to check and ensure that the email address EFI holds is up to date. If you for some reason do not want to participate in the electronic election but would like to vote on paper, please notify Sandra van Hensbergen at the EFI Central Office and we will arrange for you to receive a postal application.

#### **Nomination for President -Elect**

One nomination has been received for the position of President-Elect. No other nominations for this position were received so there will be no voting for this position and the nomination is subject to approval by the EFI General Assembly in Glasgow, Scotland.

#### Ann-Margaret Little

I am delighted to be nominated as a candidate for President-Elect. I became a member of EFI in 1998 and have participated on the Education Committee, the Executive Committee as Councillor, Deputy Secretary and Secretary and I am currently serving on the Accreditation Committee as an EFI Commissioner. I am employed as the Laboratory Director for H&I in Glasgow,



where we are hosting the EFI 2020 conference. My activities in EFI have had a positive impact on my development as an H&I scientist and the clinical services delivered by my laboratory.

EFI's strengths include the provision of educational assets that promote professional development in research and diagnostic laboratories. Delivering diagnostic excellence for patient care is additionally supported by our Standards, approved EPT schemes, and regular audit by EFI trained inspectors. If elected, I will advocate and guide the EFI Committees to develop their successful activities and to resolve challenges that arise.

Also, if elected, I will continue with the developments initiated with other organisations. This is pivotal for the exchange and development of knowledge and also for the recognition of EFI and our immunogenetics expertise by the wider scientific and medical community.

I welcome the opportunity to further serve EFI.

#### Nomination for Deputy Treasurer

One nomination has been received for the position of Deputy Treasurer. No other nominations for this position were received so there will be no voting for this position and the nomination is subject to approval by the EFI General Assembly in Glasgow, Scotland.

#### Paul Rouzaire

Passionate about Immunology, I am Pharmacist by training. I graduated in 2009 and got a specialization in Immunology in Lyon, where I defended my PhD thesis in 2011 at the Ecole Normale Supérieure, on immunobiology of NK cells. In 2012, as medical biologist, I was appointed deputy director of the EFI-accredited H&I lab in Clermont-Ferrand, France. For the past 2 years I have been leading the lab and its partial re-organisation.

I currently dedicate my time to diagnostic and clinical research. As an associate professor at the University, leading the Immunology department of the Pharmacy School, e-learning and teach-



ing modern immunology combining basics, technology and informatics are very important to me, these must be addressed at the trans-national level.

As an EFI member and professional practitioner in H&I, I would like to bring my motivation to the community. The European dimension of our activities is crucial for the recognition of the field. As a deputy-treasurer applicant, I will commit to dedicate my time to serve EFI, I am high motivated by the optimal use of society funds to improve scientific knowledge, promotion of the high level of professional standards and a sense of community between members, clinical and research laboratories. Nominations for Councillor

For the three positions as Councillor four nominations have been received and the candidates are presented here. The information will also be available electronically during the voting process.

#### **Esteban Arrieta-Bolaños**



I finished my training in Microbiology and Clinical Chemistry (i.e. Clinical Pathology) at the University of Costa Rica in 2006. After this, I combined professional practice with postgraduate studies with a focus on Histocompatibility and Immunogenetics, which I completed in 2010. During this time, I also worked as lecturer and researcher at the University of Costa Rica, and was able to undergo further training in H&I at Anthony Nolan in London. I later returned to the UK and in 2014 was awarded a PhD in Haematology from University College London after working in non-HLA immunogenetics of haematopoietic cell transplantation.

After that, I moved to Germany and have been working in Prof. Katharina Fleischhauer's group combining translational research in T cell alloreactivity and clinically-focused HLA population genetics. I have been a member of EFI since 2010 and have actively participated at its scientific meetings ever since, many times receiving support from EFI. As a Councillor I would strive to enhance our society's interaction with other professional societies, especially those where H&I plays a central clinical and scientific role. Moreover, I look forward to contributing to the education and development opportunities for our members, especially those at the start of their careers.

#### António Martinho

In 1987, I graduated in Biochemistry at the Faculty of Sciences, Coimbra University, in Portugal. After 2 years working in enzymology, I became head of Molecular Genetics Laboratory at the Center of Histocompatibility of the Centre (Lusotransplante). I took the first steps in HLA typing by molecular biology techniques applied to solid organ and HSC transplantation. Since that time, I am committed to H&I training, education, research and development programs. I was member of the Administration Council of the institution (1999 - 2012) and Head of Laboratory. My presence in H&I conferences started in 1990 in Strasbourg followed by the participation in the International HLA & Immunogenetics Workshops, beginning in Yokohama in 1991. Our first EFI Accreditation was in 1998 and I became an EFI inspector in 1999 and member of the EFI Educational Committee from 2010 to 2013. I had the privilege of hosting, as conference chair, the 33rd EFI Conference, Lisbon 2019. As an EFI councillor, I hope that, with my experience, knowledge and nature,



I will be able to support the EFI annual activities plan development, to promote collaboration and knowledge among EFI members and local societies, and to expand the EFI family to Portuguesespeaking countries.

#### **Kay Poulton**



I joined the H&I community in 1989 when I enrolled as a PhD student in Manchester University while working in the Transplantation Laboratory in Manchester Royal Infirmary. I spent my early postdoctoral years working in an academic H&I laboratory at Manchester University, before moving back into the clinical setting as Head of the Immunogenetics team in 1998. I have been a Consultant Clinical Scientist since 2000 when I became a Fellow of the Royal College of Pathologists in H&I, and this was also the point when my EFI career started as I became a member of the Standards Committee. I became Chair of the Standards Committee in 2008, until 2014 when I began my first term on the EFI Executive Committee as a Councillor and supported the Accreditation Committee as an EFI inspector.

I have been Chair of the British Society for H&I, and Chair of the H&I Subcommittee of the Royal College of Pathologists in the UK, both of which focussed my attention on the education of our next generation scientists in H&I. I believe that the key to progress is to share our experiences and ideas worldwide and that "Together we are stronger" as our Manchester phrase tells us. As an EFI Councillor, I would use my experience to promote collaborations between EFI members, and to actively promote membership of the society.

#### Marie Schaffer

In 1980 I started as a technologist in the H&I laboratory at Karolinska University Hospital, Huddinge, Sweden. Karolinska is a centre for both solid organ transplantation and HSCT. I studied molecular biology 1988-89. Back at the lab, I joined Olle Olerups group during the development of PCR-SSP. In 2006 I obtained my PhD from Karolinska Institutet on KIR and HLA in HSCT. Since 2008 I am Co-director of the lab and received my Honorary ESHI diploma in 2015.



I am an EFI member since 1997 and have participated at EFI conferences and IHIWs from 1983 and onwards. In 2014 I co-chaired the EFI Meeting in Stockholm. I have been a member of the Educational committee 2011-2019. Recently we have worked on the development of the diploma for the technical staff in H&I (ETHIQ) that soon will be launched. For me with a background as a technologist, I think it's very important for young people to get the possibility to receive further training and deeper knowledge in the field of H&I This is lacking in several countries especially the smaller, where there is no national H&I society. If elected I hope that my long experience in our field will be useful for EFI.



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#### Ziyaad Valley-Omar - Groote Schuur Hospital, Observatory, Cape Town, South Africa

I am a new director-in-training with limited histocompatibility and immunogenetics experience. All past academic and pathology-related experience have focussed on infectious disease (predominantly viral) molecular biology, etiology and epidemiology. The 14<sup>th</sup> International Summer School on Histocompatibility and Immunogenetics hosted by ASHI, EFI, APHIA and ARSHI in Old Montreal, Canada therefore served as an ideal introductory course into this field for me. While the 3 day course included an in-depth coverage of the theoretical and practical aspects of histocompatibility and immunogenetics, I was specifically drawn to the basic principles and research findings that underpin the relevance of the HLA-system during solid organ and hematopoietic stem cell transplant. The meeting was well-paced and all topics were comprehensively covered. At times lecture topics seemed slightly disjointed as similar material was covered by more than one presenter and similar threads were not necessarily covered consecutively. This was though a minor issue in an otherwise excellently run meeting.

The informal-relaxed nature of the meeting allowed me the valuable opportunity to network freely with members of faculty and other Summer School attendees both during sessions and while visiting many of Old Montreal's beautiful sites and evening dinners at neighbouring restaurants. The hotel setting was perfectly placed close to tourist sites, which enabled visits to the Old Port, the many Cathedrals along cobblestone roads, Mount Royale, the science centre and also view the International fireworks competition. The overall experience has been positive and I would like to express my gratitude to the organisers for accepting my application and to EFI for granting me a scholarship to attend the meeting.

Owing to my role as a molecular scientist employed in a state tissue typing laboratory, my interests did not extend to advanced clinical aspects of the meeting, which are therefore not covered in this report. What follows is a summary of the content covered that interested me the most.

#### **HLA molecular typing**

Numerous in-house and commercial NGS-based HLA typing reagent kits and data analysis platforms are available. Publically available analysis platforms include ATHLATES/ ATHLON, GATK HLA Typer, HLA-caller, HLAVBseq. While commercial platforms have been developed by GenDX, Omixon, CareDX and Thermofisher.

#### Non-HLA histocompatibility systems

ABO incompatibility: was problematic for transplants but more recently with advanced treatment regimens, it is no longer a problem. Non-classical (Class I and II molecules): large number of alleles, functionally relevant, some involved in antigen-presenting processes. Minor histocompatibility antigens (MiHA): diverse peptides ~9-12 amino acids in length on the cellular surface of organs that can give an immunological response in some organ transplants when bound to both the MHC class I and II proteins. Peptide sequences can differ among individuals and these differences arise from SNPs in the coding region of genes, gene deletions, frameshift mutations, or insertions. They cause rejection less frequently than MHC antigens. NK cells, Killercell immunoglobulin-like receptors (KIRs): family of type I transmembrane glycoproteins expressed on the plasma membrane of NK cells and a minority of T cells. Regulate NK cell killing function by interacting with MHC I molecules. KIR receptors can distinguish between MHC class I allelic variants, which allows them to detect virally infected cells or transformed cells. As a result of KIR's role in killing unhealthy self-cells and not killing healthy self-cells, KIRs are involved in protection against and propensity to viral infection, autoimmune disease and cancer.

#### Antibody Mediated Rejection (AMR) and Impact of HLA Donor Specific Antibodies (DSA)

Improvements in HLA antibody detection and identification together with more effective immunosuppression have changed the phenotypes of AMR over the past 50 years. Strong donor specific antibody and reduced immunosuppression have lower graft survival, whereas weaker antibodies with carefully targeted immunosuppression and monitoring can have acceptable outcomes. *De novo* antibody has emerged as a major cause of premature graft loss and reflects under immunosuppression for the degree of HLA mismatching.

Hyperacute antibody-mediated rejection is due to preformed DSA where antibody activates complement and adhesion of platelets and promotes coagulation. Complement activation leads to endothelial cell injury, which in turn could lead to irreversible graft loss. This type of rejection does not respond to intervention. Acute antibody-mediated rejection is due to preformed DSA and a memory response and results in acute graft dysfunction. This type of rejection mostly responds to intervention + DSA may disappear. Non-HLA antibodies may explain early graft loss in HLA identical or HLA antibody/DSA negative and late injury HLA antibody negative. This type of rejection is not well characterized, no distinct pathological character features seen consistently. Reported antigens include: MICA, AECA, AT1R.

#### Alternatives to traditional HLA matching

EPLETS = HLA matchmaker: EPLETs defined as the functional component of an HLA antigen (antibody binding region/ paratope). Consist of configurations of amino acids in 3 angstrom radius of a polymorphic amino acid when observing the three-dimensional structure of the molecule. HLA Match-Maker = theoretical algorithm that predicts the epitopes/ EPLETs. Amino acid and electrostatic mismatch analyses: The number of mismatched amino acids and/or physiochemical properties of mismatched amino acids shown to predict HLA antibody development in repeat renal transplant recipients. PIRCHE-II: Predicted Indirectly Recognizable HLA Epitopes. The PIRCHE-II algorithm predicts and scores mismatched donor-derived HLA epitopes that can be presented by recipient HLA class II surface proteins, shown to correlate with HLA mismatch and HLA Matchmaker EPLET mismatch; predict overall survival in 9/10 mismatched hematopoietic cell transplants and predict HLA DSA production and graft survival.

#### Post-Transplant testing- DSA, Biomarkers of rejection

Histologic: DSA, C4d, gene transcript analyses. Urinary proteins: CXCL9 increases associated with preceded rejection up to 30 days and CXCL10 increase also associated with rejection. Donor derived cell free DNA (Dd-cfDNA) analysis: detection of donor DNA in blood samples of the recipient after transplant. SNPs unique to the donor vs recipient can be detected and quantitated to assess degree of damage. Can also be done by QPCR or NGS. (Promega and GenDX kits available) Dd-cfDNA levels above established cut-off values shown to be associated with rejection. Levels tend to be higher in AMR than TCMR. Detection of increased amounts of donor DNA = failure of engraftment and not rejection. Blood Molecular signatures: kSORT = microarray based test performed on peripheral blood. Identified genes involved with leukocyte trafficking, activation, adhesion, cytolysis. Predicts rejection with high sensitivity. Molecular microscope: molecular signatures-Biopsy = microarray-based gene expression assay to detect/differentiate TCMR and ABMR.

#### HSCT workup and donor selection considerations

Donor considerations: HLA type, Age, gender, CMV status, ABO blood group, Cell dose (cord blood), donor availability, donor willingness, DSA, other genes (KIR, MICA etc) and cost. Several matching schemes exist. NMDP HLA matching: 6/8 allele level (A, B, C, DRB1), adult donor but recommend 8/8, 4/6 antigen level for A, B and allele level for DRB1, cord blood unit. EBMT HLA matching: all at high resolution,



10/10 (A, B, C, DRB1, DQB1) for adult unrelated donors, 8/8 (A, B, C, DRB1) for cord blood units. Consider DPB1 allele or epitope matching. Anthony Nolan registry HLA matching: A, B, C, DRB1, DRB3, DRB4, DRB5, DQB1, DPB1 essential for optimal typing, high res typing and matching for all recommended genes.

The Current best practice for HLA matching assessment: HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1, -DQB1, -DPB1 allele typing of patient and donor. Fully assess matching/mis-matching; will assist with haplotype assignment; clinicians are then fully informed when selecting the donor. Confirmatory HLA typing of patient and donor. Antibody screening and identification – essential if looking at any mismatched donor (unrelated or family donor). Repeat antibody screening if patient transfused.

#### HLA and disease association

Past studies linking HLA to disease have shown inconsistent associations because of small study numbers, poorlymatched controls and insufficient coverage of all ethnic groups. Suggested that the inconsistencies may occur because HLA-disease associations could result from specific haplotypes or non-HLA genes only present in specific ethnic groups. Furthermore, HLA disease associations could be linked to different viral or bacterial strains that are unique to different geographic locations. Generally disease results from multiple factors in combination with certain HLA types including other MHC genes (KIR on NK cells, leukocyte immunoglobulin-like receptors on myeloid/monocyte cell lineages, cytokines), non-MHC genes, viral/bacterial infections, environmental factors, and the health of the individual. HLA typing cannot therefore solely be used for diagnosis of certain diseases but can assist in diagnosis (e.g. Coeliac disease, Narcolepsy) and serve as a risk indicator of some severe adverse drug reactions.

#### Gia-Gia Toni Ho - Hannover, Germany

It was a great pleasure to participate the International Summer School on Immunogenetics in the beautiful city of Montreal, Canada, on July 14 – 18, 2019. The 14<sup>th</sup> International Summer School on Immunogenetics was organized by ASHI, EFI, APHIA and ARSHI. The meeting place was set at Marriott Springhill Suites Old Montreal which was a great location for hosting this event. The faculty board including Patricia Campbell (ASHI), John Schmitz (ASHI), Medhat Askar (ASHI), Lyanne Weston (APHIA), Heather Dunkley (APHIA), Fadi Al Zayer (ARSHI), Joannis Mytilineos (EFI) and James Robinson (EFI) provided a wonderful setting and presented high quality lectures.

At the first evening all participants gathered for welcome dinner and drinks. The welcome dinner offered a warm and friendly atmosphere to get to know the other participants of the summer school and for a first contact with the faculty. The very interesting and informative scientific program included lectures from the faculty members and presentations from the participants during abstract sessions. The abstract session gave participants the opportunity to present their research and to receive feedback for the presentation from the faculty and the students.

James Robinson started the scientific program with a remarkable introduction of the HLA history, nomenclature



and polymorphism. Fadi Al Zayar continued the session with an impressive overview about HLA typing methodologies. The first session was closed by a very instructive description of the immunogenetic databases by James Robinson. Coffee breaks and delicious lunch between the sessions offered more opportunities for interesting discussions about various topics with focus on HLA. In the second session Joannis Mytilineos, Medhat Askar and Lyanne Weston gave a formidable insight into the role of non-HLA molecules, KIR, NK cells and the role of HLA testing in transfusion.

In the next lecturer session Heather Dunkley, Lyanne Weston and Patricia Campbell focused their most informative presentation on the role of HLA molecules in disease association, transplant immunology and immunosuppressive medication and mechanisms. In the following tutorial sessions John Schmitz, Patricia Campbell and Fadi Al Zayer gave fascinating overviews on the field of solid organ transplantation from pretransplant risk assessment (AB testing basics, crossmatching and virtual crossmatching) to posttransplant testing (DSA, biomarkers of rejection and tolerance). The last session was about the highly interesting topic of donor selection and compatibility in hematopoietic stem cell transplantation. The scientific program covered comprehensively all aspects of HLA and their relevance in disease, transplantation and transfusion medicine.

Besides the scientific program the social program gave us a lot of opportunities to interact with all participants and the scientific faculty. A guided bus tour around Montreal showed us the highlights of the city and a walk to the Mont Royal gave us a fantastic view over the whole city. Overall, the summer school provided a stimulating environment for intellectual discussions and created a warm and friendly atmosphere that facilitated the informal exchange of ideas with renowned experts in the field.

In my opinion the summer school was a big success and I would like to express my deepest gratitude to the EFI educational committee for the bursary that provided me with the opportunity to participate in this year's Summer School. What impressed me most was the chance to meet the experts in the field of immunogenetics and I would like to thank all tutors for their kindness and their helpful advises. Furthermore, I would also like to thank all participants for the nice and familiar atmosphere during the summer school. I will keep the experience of the summer school in good memory.

#### Hannah Turnbull - Tissue typing laboratory, Addenbrookes hospital, Cambridge, UK

ASHI hosted the 14<sup>th</sup> International Summer School on Immunogenetics, at the Marriot Springhill Suites in Montreal, Canada. This summer school was a by joint collaboration from ASHI, EFI, APHIA and ARSHI societies who facilitated and organised teaching from experts within the field of Histocompatibility and Immunogenetics. The programme covered key elements associated with transplantation, including genetics of the HLA system, non-HLA and HLA in transfusion, HLA and disease, solid organ and haematopoietic stem cell transplantation. Following teaching sessions in the morning and afternoon, each delegates selected to attend the summer school presented a short talk on an abstract of their research.

The evening before the first day of teaching and presentations, attendees from all around the world arrived to Montreal in Quebec, Canada. Delegates attended a welcome dinner organised by ASHI at Auberge Saint-Gabriel, a 16<sup>th</sup> century building full of Quebec's history. The welcome dinner provided a great opportunity to meet and socialise with fellow delegates attending summer school. Before dinner was served, former ASHI president John Schmitz delivered a welcome toast to introduce the event.

The first morning of presentations was covered by James Robinson, a bioinformatician from the Anthony Nolan institute. James gave two talks; the first talk was on MHC, HLA gene and nomenclature, and a second on HLA databases. These talks gave the background and history of HLA and its polymorphisms and discussed why having a standardised nomenclature is so critical in the field of HLA. Fadi Al Zayer, a HLA laboratory supervisor from ARSHI society gave an intro-

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ductory talk on HLA typing, both serological and molecular. His talk focused on how technologies have advanced to high resolution molecular typing over the past decade from serological techniques. Following each presentation session, a group of delegates gave their short presentations on their abstracts. Each delegate spent time preparing and practicing their presentations to give an informative and interesting talk to the rest of the group.

The afternoon session moved onto non-HLA and HLA in transfusion. Joannis Mytilineos from Ulm University gave a talk on ABO, MICA and minor antigens, demonstrating the importance of non-HLA proteins and the roles they play on transplant outcomes. Medhat Eskar from Baylor University in Dallas gave a talk on NK cells and KIRs involvement in the immune system and transplantation. To end the first day of lectures, Lyanne Weston from the Australian Red Cross gave a presentation on HLA testing in transfusion and discussed the benefits of matching platelets at the epitope level.

After the first day of presentations finished we went on a city excursion around Montreal. ASHI society organised a personal tour bus to take us around the city to learn about the city's history and culture. The tour bus tour took us to Mont-Royal, which had a fantastic view over Montreal and gave us a good photo opportunity to get a group summer school photo. Following the tour of the city we went out for dinner and socialising with the new friends we had made.

The morning session of the second day started with lectures on HLA and disease. Heather Dunckley from New Zealand blood service gave a talk on HLA involvement in disease, autoimmunity, infection and drug hypersensitivity. The talk focused on the possible mechanisms of disease susceptibility involving HLA, such as molecular mimicry and lack of peptide presentation. Lyanne Weston presented the second morning talk on transplant immunology, covering allorecognition and T cell receptor signalling. To end the morning session, ASHI president Patricia Campbell gave a talk on immunosuppression its mechanisms and the development of immunosuppression protocols worldwide over the years. Patricia included case studies to her presentation which included differences in these protocols depending on the clinical situation of the patient, and strategies on how to treat these patients if they show signs of antibody mediated rejection.

The afternoon session concentrated on solid organ transplantation. John Schmitz gave a talk on pre-transplant risk assessments, reflecting on how to analyse antibody results and the challenges we face with interpreting solid phase assays. John spoke about crossmatching techniques and the move towards virtual crossmatching due to the induction of Luminex technologies in H&I laboratories. John's second talk was on HLA epitopes and systems that can be used to assess immunogenicity of HLA, such as HLA Matchmaker and PIRCHE. These programmes can be used to assess compatibility of donor and recipient HLA types based on amino acid mismatches, physical positions and electrostatic charge differences within the HLA molecules. Lastly, Patricia Campbell gave a talk on organ allocation and tied together the similarities and differences in allocation schemes across the world but ultimately how the focus is on utility and equity of organs for transplantation. Following more delegates presentations we headed out for a well-deserved dinner and drink to socialise and engage with the other delegates.

The final day of summer school consisted of more interesting talks following on from the previous session on solid organ transplantation. We had another talk from Patricia Campbell on antibody mediated rejection and the impact of HLA donor specific antibodies and non-HLA antibodies on transplant outcome. Fadi Zayer then gave a talk on strategies to transplant highly sensitised patients, such as desensitisation protocols, paired donation schemes and HLAi transplants. John Schmiz carried on with the theme of antibodies and delivered a talk on post-transplant testing, biomarkers of rejection and tolerance to end the morning session.

The afternoon session focused on haematopoietic stem cell transplantation. Heather Dunckley gave the first talk on stem cell workup, donor selection. She discussed the considerations that need to be made to find a suitable donor such as HLA, CMV and age of the donor and their effects on transplant outcomes. Reem Ameen from Kuwait University followed on from the stem cell transplant theme with post-transplant monitoring by chimerism and different methods in which this can be achieved. To end the session Joannis Mytilneous gave a talk on compatibility in stem cell transplantation, graft vs host disease and relapse.



Three delegates were awarded best abstract presentations following the three days at summer school. Congratulations to presentation winners; Gia-Gia Toni Ho from Hannover Medical School, Germany for her PhD presentation on 'The HLA-F redistricted immune-peptidome represents an exceptional proteomic footprint'. Nina Svetlicky from Sheba Medical Centre, USA for her presentation on 'The central role of graft resident memory T cells in pathogenesis of GvHD after intestinal transplantation'. Finally, Matthew Najor from Georgetown University hospital, USA for his presentation on 'Mitigating background in solid phase antibody assays'. Well done to all the other delegates for their hard work and interesting presentations.

I would like to thank EFI for awarding me a bursary to attend the 14th international Summer School on Immunogenetics. This summer school was a valuable learning experience which has development my knowledge and understanding as a trainee in the field of H&I. The next summer school will be hosted by EFI in Prague, Czech Republic in 2020.



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# JOINT MEETING OF EFI REGION 8 BALKAN EPT AND 3<sup>RD</sup> HISTOCOMPATIBILITY WORKSHOP IN ARMENIA

The joint EFI Educational Meeting and Workshop / Region 8 and Balkan EPT Meeting, hosted by the Armenian Bone Marrow Donor Registry (ABMDR), took place in Yerevan, from October 25 to 27, 2019.

The highly-anticipated conference functioned as a regional forum for sharing the latest advances in the fields of immunogenetics, histocompatibility, transplantation on the one hand, and provided advanced training and education to participants on the other. By doing so, the conference helped expand the knowledge base and increase the professional capabilities of participants, and promoted continued international medical collaboration, specially among new and emerging national bone marrow registries and transplantation laboratories.



Featuring an outstanding roster of speakers, the joint conference was part of events dedicated to the 20th anniversary of the founding of ABMDR. The close to 200 participants of the conference included scientists, physicians, representatives of national bone marrow transplant centers and registries, and medical students from the Caucasus, the Middle East, the United States, Eastern Europe, Russia, Kazakhstan, and Cyprus. Overall, 30 countries were represented.

The conference was kicked off on October 25 with a festive reception, during which opening remarks were delivered by ABMDR Executive Director and Conference Chair Dr. Sevak Avagyan as well as EFI President Dr. Joannis Mytilineos (Germany). In his address, Dr. Avagyan emphasized the importance of hosting the EFI conference in Yerevan, given the fact that Armenia has become a regional hub, functioning as a bridge between EFI and countries in the region.

On his part, Dr. Mytilineos underscored EFI's instrumental role in educating its members, bringing all member countries together to ensure the quality of lab work in the fields of transplantation and immunogenetics, and, ultimately, in increasing the chances of survival for patients across the world. The conference kicked off on October 26 with an opening ceremony, during which ABMDR President Dr. Frieda Jordan and EFI President Dr. Joannis Mytilineos addressed the participants with welcome remarks.

"Twenty years ago, many of you who are here today helped us establish the Armenian Bone Marrow Donor Registry," Dr. Jordan said in her remarks and continued, "We owe you so much and are so very grateful for your help. I can't wait to show you how far we have come, how much we have accomplished, and how we, in turn, have been paying back and helping new registries form. As the first registry in the Caucasus region, ABMDR is recognized today as a model to emulate. From Africa to Jamaica to Sri Lanka, we advise groups ready to start their own registries, foster and guide them, give them a road map and whatever support we can, and celebrate their successes — just like you did with us."

The first session of the conference, moderated by Dr. Mihran Nazaretyan (Armenia) and Dr. Paul Costeas (Cyprus), was dedicated to the most recent developments in the fields of histocompatibility and bone marrow and organ transplantation; and the criteria for selecting matched bone marrow stem cell donors. In a highly-educational introduction to the subject, Dr. Joannis Mytilineos made a presentation on the genetics, structure, and functions of the human MHS. Dr. Matti Korhonen (Finland) detailed the role of HLA in hematopoietic stem cell transplantation, and presented a comprehensive overview of factors in donor selection. Dr. Frieda Jordan made a presentation on the launch of the Armenian Bone Marrow Donor Registry 20 years ago. She focused on the various aspects of the organization's growth and the challenges it has faced, as well as its positive impact on Armenia's medical establishment. For a broad evolutionary perspective on the subject, Dr. Ileana Constantinescu (Romania) spoke about the past, present, and future of HLA laboratory assays. The presentation made by Dr. Ilias Doxiadis (Germany) was dedicated to the new approach to immunogenetics in renal grafting and its great promise. And a lecture on HLA and disease association, presented by Dr. Chryssa Papasteriades (Greece), was of particular interest to rheumatologists and pediatricians. The presentations were followed by a lively Q&A session.

The second session was moderated by Dr. Chryssa Papasteriades and Dr. Lyudmila Bubnova (Russia). In the session's first presentation, Dr. Paul Costeas spoke on the subject of genetic testing available for a diagnosis of leukemia. In their respective presentations, Dr. Elissaveta Naumova (Bulgaria) and Dr. Katerina Tarassi (Greece) focused on the new EFI standards and the EFI accreditation program.

Subsequently short presentations were made on the subject of recent histocompatibility and BMT activities in regional countries including Iran, Armenia, Russia, Israel and Kazakhstan. The presentations were made by Dr. Mohammadreza Ostadali, Dr. Samvel Danelyan, and Dmitry Klyuchnikov, Dr. Moshe Israeli and Azhar Shakenova.





# 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

On the evening of October 26, a gala dinner-dance was held to celebrate the success of the EFI Educational Meeting and Workshop.



The second day of the conference encompassed presentations on the diverse activities of Region 8 labs, as well as the EFI membership and accreditation processes, including external proficiency testing (EPT) protocols. The session was moderated by Dr. Elissaveta Naumova and Dr. Katerina Tarassi. Participants were encouraged to become members of EFI in order to be able to optimally connect with registries and transplant centers throughout the world, while representatives of non-EFI-accredited labs were provided with comprehensive information on how to obtain EFI accreditation. Two EFI Commissioners, Dr. Amal Bishara (Israel) and Dr. Milena Ivanova (Bulgaria), provided a comprehensive overview of the Region 8 accreditation process. Subsequently Dr. Anastasiya Mihaylova (Bulgaria) presented a report on the subject of 2019 schemes for HLA antibodies, crossmatching, HLA-B27 testing and BEPT report on HLA typing. Conference participants received certification from the European Accreditation Council for Continuing Medical Education.

In addition to the Gala on October 26, conference participants enjoyed various social events organized by ABMDR, including a Speakers' Dinner on October 25. Participants also enjoyed their stay in Yerevan, as they had the chance to visit the famed landmarks, sights and sounds, as well as culinary and entertainment hot spots of the capital.

"We warmly thank all of our conference speakers for their excellent and thought-provoking presentations, all of which have led to stimulating exchanges between participants," stated Dr. Frieda Jordan. "I think the joint 2019 EFI conference in Yerevan has been a highly-productive and enriching experience for participating scientists, physicians, representatives of bone marrow donor registries and labs, and students alike. Finally, I'd like to convey our gratitude to our conference sponsors and working partners, including Immucor, One Lambda, Histogenetics, CareDx, Parseq Lab, and Alliance Global."

# REPORT ON THE EFI REGION 8 & BALKAN EPT/ 3<sup>RD</sup> HLA EDUCATIONAL WORKSHOP, YEREVAN, ARMENIA

The second EFI Workshop and third EPT Conference I participated took place in Armenia on October 25-27 in Yerevan. I was very impressed by the report of Ilias Doxiadis on HLA epitopes. I found his report was very interesting, clear and extensive. Besides, I have to tell that Ilias is a great presenter. Moreover, I would like to highlight the report made by Chryssa Papasteriades about disease association. It was very interesting to get to know how HLA and disease association can be explained, about analysis in association studies, drug hypersensitivity associated with HLA and the differences in associations in different populations. I met interesting people and I got many good things to know and teach from them.

I presented a short report on HLA-A, -B, -DRB1 frequencies in five Tatar populations from different regions of Russia. We found some significant differences in A\*02, A\*23, B\*27, B\*38, B\*40, B\*44, B\*58, DRB1\*07, DRB1\*11, Dmitry Klyuchnikov, Samara, Russia



DRB1\*14 frequencies. We will try to improve these data to make it even more interesting. It really was a beneficial event for me and a great pleasure to be there. It left me with many things to think about and possibly implement in our lab in Samara. You know every conference you participate inspire you I would like to thank the organizers of this great meeting for the hospitality and I congratulate the Armenian Bone Marrow Registry with their 20<sup>th</sup> anniversary. I thank Sandra van Hensbergen and the Educational Committee for this opportunity and their support. It is a great pleasure to feel part of the EFI society.

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Scheme	Scheme Title		
1A	HLA Phenotyping		
1B	HLA-B27 Testing		
2A	Cytotoxic Crossmatching		
2B	Crossmatching by Flow Cytometry		
3	HLA Antibody Specificity Analysis		
4A1/ 4A1i	HLA DNA Typing at 1 <sup>st</sup> Field Resolution Interpretive HLA Genotype		
4A2	HLA DNA Typing to 2 <sup>nd</sup> or 3 <sup>rd</sup> Field Resolution		
5A	HFE Typing		
5B	Interpretative: HFE Genotype and Hereditary Haemochromatosis		
6	HLA Antibody Detection		
7	HLA-B*57:01 Typing for Drug Hypersensitivity		
8	HLA genotyping for Coeliac and other HLA associated diseases		
9	KIR Genotyping		
10	HPA Genotyping		
11	HPA Antibody detection/Specification		
ED	Educational Scheme - HLA typing Samples		
iED	Interpretive Educational Scenarios Solid Organ transplant HSCT Platelet/transfusion Immunology		
EDXM	Educational Scheme Samples for combined HLA typing/antibody analysis/crossmatching		
Chimerism	Post-Stem Cell Transplant Chimerism Monitoring (http://www.ukneqasli.co.uk/)		

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#### **Educational Schemes**

The free educational schemes include rare/novel HLA alleles and interpretive educational clinical scenarios which are not assessed. The scenarios include patient cases with laboratory results which enable users to practice clinical and scientific interpretative skills. Samples are also offered for an educational crossmatching scheme whereby HLA typing/antibody analysis and crossmatching can be performed mimicking routine clinical kidney transplant testing.

#### EFI Conference 2020

UK NEQAS for H&I are excited to be supporting the EFI 2020 Conference in Glasgow. Come and visit our stand to find out more about our external quality assessment services, including demonstrations of our new online Participant's Portal system for full EQA participation management.

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Full information on all our schemes and service can be found in the UK NEQAS for H&I Participant Manual on our website www.ukneqashandi.org.uk or contact ukneqashandi@wales.nhs.uk.

# HIGHLIGHTS FROM THE HLA JOURNAL

#### Soluble HLA-G levels in seminal plasma are associated with HLA-G 3'UTR genotypes and haplotypes.

Craenmehr MHC, Haasnoot GW, Drabbels JJM, Spruyt-Gerritse MJ, Cao M, van der Keur C, Kapsenberg JM, Uyar-Mercankaya M, van Beelen E, Meuleman T, van der Hoorn MP, Heidt S, Claas FHJ, Eikmans M.

HLA. 2019 Oct;94(4):339-346. doi: 10.1111/tan.13628.

HLA-G is a crucial regulator of fetomaternal tolerance, expressed in soluble and membrane-bound form by many of the cell types that are involved in this complex and fascinating process. Whereas several studies have investigated the association between a common genetic polymorphism in HLA-G 3'UTR and the concentration of the soluble molecule in the blood, it was to date unknown whether the same variants could also impact the levels of HLA-G in seminal plasma. In the present study, the Authors analyzed the genotype and seminal plasma levels of HLA-G in 156 healthy individuals, describing significant associations for a number of polymorphisms (including the 14 base pair insertion/deletion) and haplotypes. They also analyzed the potential correlation between the levels of soluble HLA-G in the seminal plasma of these individuals and medical history of recurrent miscarriages in the partner, but found no significant interaction, suggesting the need to investigate this issue in larger studies and integrating also other variables that are already known to play a role in miscarriage and other pregnancy complications.

#### Recombinant human monoclonal HLA antibodies of different IgG subclasses recognising the same epitope: Excellent tools to study differential effects of donor-specific antibodies.

Kramer CSM, Franke-van Dijk MEI, Priddey AJ, Pongrácz T, Gnudi E, Car H, Karahan GE, van Beelen E, Zilvold-van den Oever CCC, Rademaker HJ, de Haan N, Wuhrer M, Kosmoliaptsis V, Parren PWHI, Mulder A, Roelen DL, Claas FHJ, Heidt S.

HLA. 2019 Nov;94(5):415-424. doi: 10.1111/tan.13664.

#### By Loca Vago, section editor HLA journal

The pathogenicity of antibodies against donor HLAs in organ transplantation is determined not only by the specificity and affinity of the antibody for the HLA epitope recognized by the Fab part, but also by the effector function of the antibody, defined by the Fc part. Whereas in many patients a mixture of different IgG subclasses can be detected, the relative contribution of each subtype to allograft rejection remains poorly understood. In this work the Authors employed recombinant DNA technology to generate a panel of antibodies sharing the same anti HLA-Fab, but belonging to all four different IgG subclasses. They showed that the newly generated Abs retained the same affinity and specificity for HLA class I and class II molecules, but differed for their ability to induce complement-mediated cytotoxicity: whereas in fact the IgG1 and IgG3 isotypes were capable of binding complement component 3d (C3d) and elicit cell lysis, the IgG2 and IgG4 subclasses were not able to induce cytotoxicity. This elegant model represents a novel and highly informative tool to dissect antibody-mediated reactions in a controlled fashion.

#### MiR-199a-3p modulates the function of dendritic cells involved in transplantation tolerance by targeting CD86.

Xiong A, Wang J, Mao XL, Jiang Y, Fan Y. HLA. 2019 Dec;94(6):493-503. doi: 10.1111/tan.13677.

Dendritic cells (DCs) are key players in physiological and pathological immune responses, coupling antigen presentation to stimuli that can activate or tolerize T cells. However, the fine mechanisms by which this balance is regulated are not fully elucidated. In this interesting study, the Authors dissected the role of one micro RNA (miR-199a-3p) in regulating the levels of expression of the costimulatory molecule CD86. They showed that miR-199a-3p levels correlate with DC maturation, secreted cytokine profile, and activity of the PI3K/AKT/NF-KB signaling pathway. Moreover they demonstrated that by targeting the 3'-UTR of CD86, miR-199a-3p can promote its degradation, ultimately prolonging allograft survival in a mouse model of heart transplantation. By this study, the Authors provide new translationally-relevant evidence about the central role of epigenetic mechanisms, and miRNAs in particular, in tuning the interplay between antigen presenting cells and T lymphocytes.

Finally we would like to point the attention of the EFI newsletter readership to two excellent reviews published during the last months in HLA, focused on the role of follicular helper T cells in organ transplantation (November issue) and on the pros and cons of physical versus virtual crossmatching (December issue). Moreover, we bring to the attention of our readers the obituary that Paul J. Martin and Effie W. Petersdorf dedicated to the memory of John A. Hansen, reminding his seminal contributions to the field of hematopoietic stem cell transplantation and in particular on laying the foundations of volunteer donor registries.





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