



NEWSLETTER

DECEMBER 2022 - ISSUE 99

.....FROM THE EFI PRESIDENT

DEAR EFI FRIENDS



October was a busy time for the EFI committees. We had our first face to face committee meetings in Leiden since 2019. It was a very full and useful long weekend. The Executive Committee met firstly with the chairs of the various EFI committees. This was a productive interaction as it gave everyone a clear oversight of the activities that have been taking place and of the plans for future developments. You can read the full updates from the individual EFI committees elsewhere in this newsletter.

Briefly, I will comment on some of the work that is ongoing. The Education Committee, with Deb Sage as chair, has progressed the European Technical Histocompatibility and Immunogenetics Qualification (ETHIQ) which will open very soon. This training scheme, which was successfully piloted in France with four candidates, is aimed at all technologists working in our field particularly those that do not have their own national training scheme. The members of the Education Committee (present and past) have put much effort into the development of this qualification, so I hope to see technologists register and benefit from the training that will soon be available for applicants. As described during our General Assembly in Amsterdam earlier this year, the Accreditation Committee, with chair Blanka Vidan-Jeras, is pursuing recognition as an ISO recognised certification body. This is a huge task, but the team are extremely focused and have already made progress in this endeavour. The EPT committee, under chair Helle Bruunsgaard, continues to improve the standards for EPT providers and will soon publish the most recent update of these standards. Eric Spierings, chair of

the IT and Bioinformatics committee, presented us with their exciting challenge for facilitating conformity of HLA data to enable data sharing without loss of information. This development will impact on the work of the Standards Committee and hopefully we will see 'data standards' in the next full EFI Standards revision. In the meantime the Standards Committee has finalised version 8.1 which will be available to review shortly. Unfortunately Luca Vega, chair of the Scientific Committee was unable to make the meeting due to a professional commitment. This committee has been seeking new members and having received nominations, will soon be back to full quorum.

The Executive Committee had their own meeting where we made progress with our activities including the ongoing review of our statutes (in response to legal advice received several years ago). We finally think we have finished this task and the minor amendments to be made will be published online and in this newsletter prior to the next meeting of the General Assembly in Nantes. As you will read elsewhere in this newsletter, I was pleased to learn that we have received nominations for the vacancies that will arise on the Executive Committee at the next General Assembly and I encourage all members to participate in the elections.

An area that required much discussion at our Executive Committee meeting is the EFI budget. As expected our expenditure is currently exceeding income due to the absence of profitable conferences during the pandemic. However, we were all delighted to hear that the excellent conference held in Amsterdam made an overall profit despite being more costly to prepare due to the hybrid format. So congratulations to Eric and Sebastiaan and their local teams for this successful outcome. As the EFI bank accounts have savings, we can at present continue to meet our financial commitments, but we also need to have very careful forward planning in place due to the uncertain financial times ahead.

Overall, the Executive Committee members are making progress with the various ongoing projects. Our new members have really picked up the baton from the departing members and have made an immediate contribution. I am grateful to all the officers and councillors for their contributions.

Following a review of the workload undertaken by the EFI Central and Accreditation Offices in Leiden, the Executive Committee approved expenditure to cover an extra day of

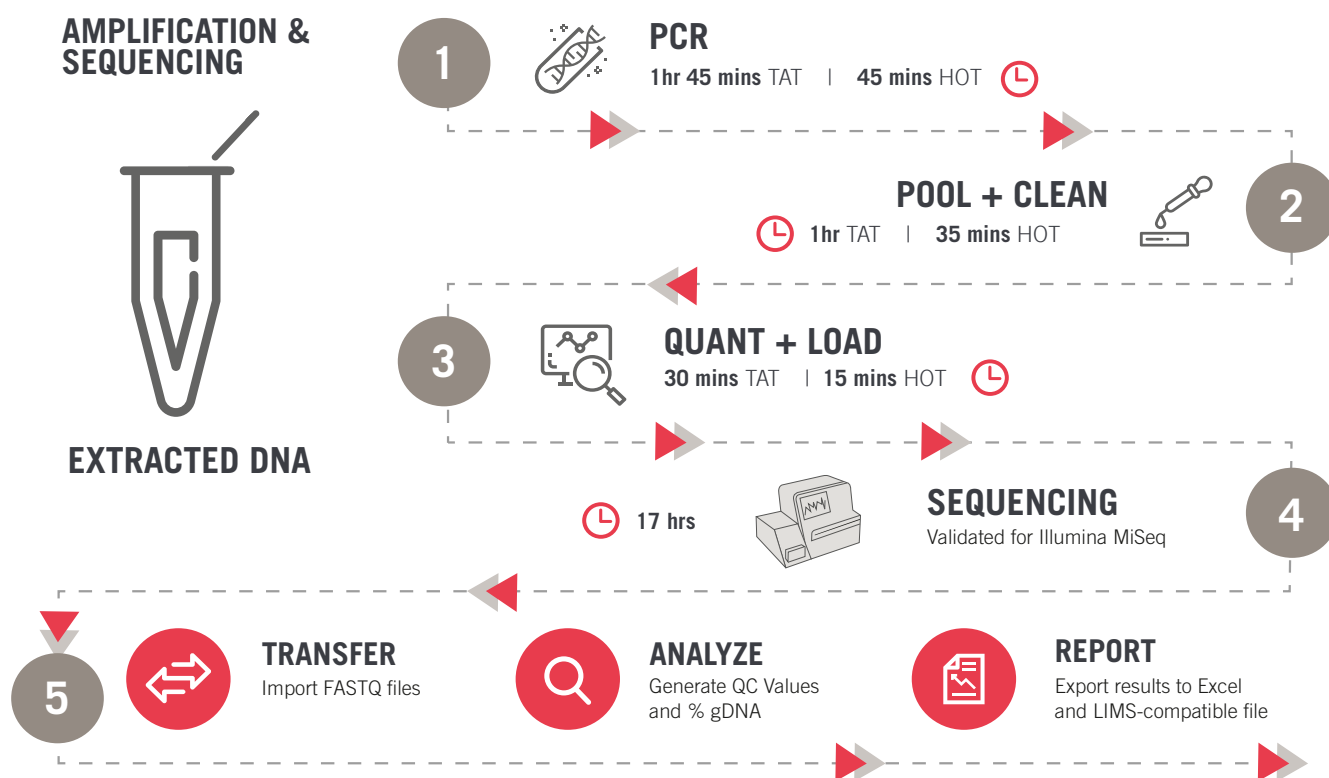
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www.efi-web.org

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....FROM THE EDITOR'S DESK

Before you lies EFI Newsletter edition 99. During the general assembly of the Amsterdam EFI meeting, it was announced that the EFI newsletter would not be distributed in printed version anymore. This decision has since been discussed and the final format of the Newsletter has still to be decided upon. Until this final decision, the Newsletter will be printed and distributed as normal.

This newsletter contains the report of the autumn meeting of the Executive Committee, which was the first 'live' autumn meeting in years. Additionally, there are some reports of our committees, as well as the presentation of the nominees for councillor.

Finally, there is a vacancy listed for a new Editor-in-Chief of the EFI Newsletter. I have had the pleasure to serve as Editor since 2016, but after six years I feel it is time for me to pass on the pen to a new Editor. The Executive Committee is looking for someone who is proficient in the English language and who has good ideas on what the Newsletter should be in the future.

As always, I hope you enjoy reading this Newsletter. I wish you a Merry Christmas with friends and family, and a great start of 2023.

Sebastiaan Heidt

Deadlines for contributions to EFI Newsletter 100 is February 20, 2023. This will be a festive edition, so any contributions on (the history of) EFI, including pictures, are welcome!

Please send your contributions by e-mail to s.heidt@lumc.nl



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

administrative duties. It is my pleasure to welcome Ingrid Abelman back to the EFI office. Ingrid worked with EFI several years ago supporting the secretariat. She is now predominantly supporting the work of the Education Committee.

Last month, I attended the American Society for Histocompatibility and Immunogenetics (ASHI) conference. This was my first ASHI conference in many years and it was wonderful to meet and chat with ASHI members that I had not seen for a long time and to meet new members. I had a lunch meeting with the ASHI President, Annette Jackson, the ASHI President Elect (now President) Rob Liwski, and the APHIA President, Heather Dunckley. Unfortunately Dada Ashraf, President of ARSHI, could not make the meeting but hopefully we will see him in Nantes. We had a very informative discussion and all agreed to remain committed to supporting each other's activities, particularly the "International Summerschool", which this year is hosted by ARSHI in Egypt. I look forward to reading the reports from the attendees of the Summerschool in a future edition of this newsletter. The EFI faculty for this meeting will be David Turner and Luca Vago – thank you both for committing your time to this meeting.

During the ASHI conference, it was fantastic to see presentations being made by several EFI members including Sandra Tafulo, from Porto, Portugal whose abstract "Identification of a Novel 43Q Eplet by Studying Sera from a Highly Sensitized Patient with a Pan-HLA-A Reactive Antibody" was selected for

presentation in the International Scholar session. Congratulations to Sandra.

So now our focus is on our next conference in Nantes, France, April 26-29 2023. The website is open (efi-conference.org) and the abstract submission deadline is imminent, and will probably have passed by the time you are reading this letter. Don't miss the early registration deadline date of 25th February 2023. Pierre-Antoine Gourraud and colleagues have put together an interesting programme with the theme: "Big Data In Immunogenetics At The Crossroad Of Care, Tools, And Research". We wish them well with their final arrangements.

As we approach the end of 2022, we can look back and reflect on the previous year. I am thankful to all the EFI members that have supported to our successful conference in Amsterdam, to all the committee chairs and their teams for their continued contributions, and to Sonja and Sandra for the running of the EFI accreditation and central office. We have benefited from the hugely successful SARs-Cov-2 vaccination programmes allowing us to enjoy the "back to normal" professional interactions. However, I am acutely aware that this year has not been joyous for all; my thoughts are with everyone as I wish you, your families and friends a healthy, successful and especially a peaceful 2023.

Ann-Margaret Little



REMINDER
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VACANCY FOR EDITOR-IN-CHIEF OF THE EFI NEWSLETTER

The EFI Newsletter is the most important source of information for the EFI community. The Newsletter is issued three times a year and contains information on the activity of the EFI committees, reports from bursary awardees, the program of the annual EFI conference, amongst others.

With the 100th edition of the Newsletter to be published next year, the EFI Executive Committee is looking for a new Edi-

tor-in-Chief who would like to take the Newsletter forward. Any EFI member with affinity for English language and writing is encouraged to apply. The work involves redirecting submitted pieces, interaction with sponsors on advertisements, and selecting appropriate photographs for printing. The Editor-in-Chief is a central position within the EFI community, being the first to know all details of what is happening within EFI, and having direct contact with the EFI

President and Secretary, as well as the chairs of the EFI Committees.

The Editor-in-Chief is assisted by the EFI office, who make sure that those who need to submit content will stick to deadlines and communicate with the companies and the Newsletter printer. Anyone interested is encouraged to contact our current Editor-in-Chief via the EFI Office (efioffice@lumc.nl) for further information.

REPORT OF THE EFI SCIENTIFIC COMMITTEE

Following the opening of two positions as Regular members in the Committee, we received a number of excellent applications, that were carefully examined and scored by the members of

the Committee, and the selection was approved by the Executive Committee. We thus welcome as new Regular members Dr. Raphael Carapito (University of Strasbourg, France) and Dr. Pietro

Crivello (University of Essen, Germany). We are sure that they take on their new role with enthusiasm, and bring their high-level expertise to further advance the science of our Society.

UPDATE FROM THE EFI STANDARDS COMMITTEE

The Standards Committee had a face to face meeting in Leiden during the October meetings. Although the committee has met virtually, being together to work through particular aspects of the standards is a valuable mechanism to ensure each revision is understandable, meets the Laboratories' needs, and the requirement of ensuring EFI's standards.

We agreed on the changes for version 8.1 during the Amsterdam meeting and took the time in Leiden to work through inconsistencies that were highlighted when reviewed. We will now be working with the EFI office for publication of the tracked change version for comment from the membership prior to acceptance from the Board. Moving

onto version 9 of the standards, we have agreed working groups within the committee to focus on particular areas which are:

- Overall structure of the standards
- Clinical practise with a focus on the Solid Organ standards
- DNA sequencing including NGS and future technologies

The working groups shared their initial thoughts and the committee agreed next steps, we intend to meet as working groups remotely to bring our progress to the next face to face meeting in Nantes. We've also been asked by the ECC to include Data Standards, working in collaboration with the IT committee.





EFI 2023

36TH EUROPEAN IMMUNOGENETICS AND HISTOCOMPATIBILITY CONFERENCE

April 26–29, 2023, Nantes, France, www.efi-conference.org

Important Dates

November 11, 2022	Abstract submission open
November 16, 2022	Registration open
December 7, 2022	Abstract submission deadline
February 15, 2023	Early registration fee deadline
April 15, 2023	Regular registration fee deadline
April 26–29, 2023	36 th EFI Conference



REPORT OF THE EFI EXECUTIVE COMMITTEE AUTUMN MEETING 2022

As per usual, the EFI Executive Committee (EC) had its second annual meeting in Leiden in October. This is the meeting where members of the EC have the best opportunity to discuss EFI business. The EFI EC, including the new councillors Dave Turner, Tony Slavcev and Neema Mayor (Luca Vago was absent) also met during the annual conference, but the time available for thorough discussion is more limited. Additionally, the EC meets with all the chairs of the various EFI committees the day before the EC meeting. This year, the “new” chairs Deborah Sage (Education), Katy Latham (Standards), Helle Bruunsgaard (EPT), Blanka Vidan-Jeras (Accreditation) attended our joint meeting for the first time. With this arrangement, a lot of proposals and ideas were considered and decisions made during the EC meeting afterwards.

The EC discussed various items in detail including a proper description of the various procedures which we use, such as the annual meeting manual, membership procedure, election procedure and reimbursement procedure. These are being finalized and will soon be available on our website. Also the roles of the EFI office, EFI secretaries and EFI treasurers have been put on paper (although currently they are still in draft form).

EFI elections

Since a number of members of the EC have served their period of office, there will be vacancies next year and elections will be held. The nominations are presented elsewhere in this newsletter. We will again use electronic voting and 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 please check on the website to see whether your details need to be updated!

EFI Finances

Our treasurer, Jean Villard, summarised income and expenditure for the year to date. The expenditure is currently exceeding revenue this year and there are outstanding costs to be covered. The 2022 Conference had a net result of approximately €17,000 after deposits were returned. There are reserves

to cover this loss in anticipated funds, but longer term, EFI must find ways to increase income or reduce expenditure. Discussions were held about potential ways to regain financial stability.

We also have some major investments to make in the future. During the meeting with the chairs of EFI committees, the request for e-learning and increased educational activities on the website was raised multiple times

EFI newsletter

The cost of producing and shipping the EFI Newsletter has steadily increased. It is possible to keep the weight <200g which would reduce postage costs significantly and would be within the existing budget. The distribution should be limited to fee paying members only. There is an option to convert the Newsletter to a Digital version, but this will require additional work for the Editor. There will be a festive themed Newsletter for the 100th edition. The EC would like to thank Sebastiaan Heidt who has been the Newsletter Editor for 6 years as he will step down after the 100th edition.

EFI annual conferences

We look back on a very successful meeting which was held in Amsterdam and was organised by Eric Spierings and Sebastiaan Heidt in conjunction with the Dutch HLA Working Group. The upcoming meetings in Nantes (April 2023) and Jerusalem (May 2024) have been discussed in the presence of representatives of the local organisers and that of Guarant. EFI has an agreement with Guarant to act as the Professional Conference Organiser for our EFI annual meetings for the next 4 years. The options for the location of the conference in 2025 were discussed, and a final decision will be made soon..

EFI bursaries

EFI Personal Bursaries are available for the annual EFI Conference to be held in Nantes, France on 26-29 April 2023. Full details on how to apply for EFI personal bursaries are given on the EFI website on the Membership page in the document entitled “EFI Personal Bursaries”. In addition to the deadlines given for personal bursary applications,

a deadline of February 20th 2023 has been set for applications for bursaries specifically to support attendance at the annual EFI conference in Nantes. 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 ~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 to the EFI Secretary via efioffice@lumc.nl.

The EC also discussed and agreed upon the nominations received for the EFI medal.

Overall, the EC had a very productive and interactive weekend. The members of the EC and all the committees would collectively like to thank Sonja Geelhoed for the excellent organization of the meeting.

*Kay Poulton and Dave Roelen,
EFI Secretaries*



REPORT FROM THE EFI EXTERNAL PROFICIENCY TESTING COMMITTEE (EPTC)

Meetings in the EPTC: We have had three virtual meeting and one hybrid meeting in 2022.

EFI standards for providers: the committee has presented suggestions for minor changes of standards for providers to the Executive Committee. We will very soon be ready to ask for the final approval. During our meetings the EPTC has evaluated the potential need for adjustments of consensus limits in Luminex single antigen assessments. The EFI standard is now that a 75% consensus for all serologically-based EPT should be used. However, current EPT schemes have different consensus limits in Luminex Single antigen bead assessments in different regions. On the EPTC meeting on June 7th simulations for different consensus limits were presented from different

schemes. The schemes with most participants showed that the percentage of concordance increased with increasing consensus percentage. Therefore, the conclusion was that there is no need to change the consensus limit now.

Website and procedure Manual: We will soon be ready to introduce updates including documents with lists of Providers, EPT schemes, and EFI EPT regions.

EPT standards for laboratories: We do not find any need for updates at the moment but we have discussed if there is a need for the introduction of a new category for EPT in disease associations. The background for this is that HLA typings of samples in the accreditation category "Disease associations"

include often other techniques and procedures than used for full HLA typings and some providers do already run schemes for HLA-B27, HLA-B*57:01, and specific HLA class II alleles. This suggestion has been approved by the Executive Committee and we will therefore start the working process during the winter.

Interactions with other parts of EFI: The EPTC will try to be represented in future EFI conferences so conference participants can book meeting with individual EPT coordinators.

*On behalf of the EFI EPT Committee,
Helle Bruunsgaard
Chair EFI External Proficiency Testing
Committee*

NOMINATIONS FOR THE EFI EXECUTIVE COMMITTEE VANCANCIES AND THE ELECTRONIC ELECTION PROCESS

Nominations were sought for the positions of, Deputy Treasurer as well as two Councillors. One nominations has been received for the position of Deputy Treasurer, which is presented here. Since no other nominations for this position were received, there will no voting for this position and the nomination is subject to approval by the EFI General Assembly in Nantes, France.

We received three nominations for the position of two Councilors and the nominated candidates are presented below. As a result, elections will be organised early 2023 for the two Councillor positions.

All active EFI members (having paid their membership fees for 2022) 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 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 Nantes, France.

Nicolas Vince

I am a research scientist with 10-year experience in HLA genetic associations with diseases. During my PhD, I explored the complex disorder common variable immune deficiency (CVID) both on genetic and immunologic sides. Then I did my postdoc in Mary Carrington lab where I studied HLA more deeply including disease association with HIV as well as HLA-C expression regulation. In 2016, I joined the CR2TI



as a researcher to develop new HLA approaches. In our group, we have developed and are still developing several bioinformatic tools to help the scientific community (clinicians and researchers) accelerate their research and clinical projects. Easy-HLA (hla.univ-nantes.fr) is a website gathering several modules; including HLAUpgrade, which statistically improves HLA typing resolution, and EasyMatch-R,

which predicts the expected number of HSCT donors for a given patient. We also created the SNP-HLA Reference Consortium (SHLARC) which aims to develop gold-standards in HLA imputation from SNP (GWAS genotyping) data. To be deputy treasurer of the EFI would be a new exciting experience for me. While I am convinced I will learn a lot, I shall bring a rigorous look on the future development of EFI financial assets. I am looking forward to exchange with other members of the EFI executive committee.

Nominations for Councillor

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

Sebastiaan Heidt



I am Director of the Eurotransplant Reference Laboratory and Associate Professor / group leader at the Department of Immunology at the LUMC, Leiden the Netherlands. After obtaining my PhD on the role of B cells in transplantation in the laboratory of Frans Claas, I worked as a postdoc in the laboratory of Kathryn Wood in Oxford, focusing on immunomonitoring of kidney transplant recipients. After my return to the LUMC, I continued my research with Frans Claas, focusing on the humoral alloimmune response in organ transplantation. My main research interests are HLA epitope matching, the formation and detection of HLA-specific B cell memory, definition of acceptable HLA mismatches and novel treatment

options for sensitized patients. I am the current president of the International HLA and Immunogenetics Workshop. Furthermore, I am actively involved in EFI, where I am member of the Scientific Committee, serve as Editor-in-Chief for the EFI Newsletter, and am Section Editor for Solid Organ Transplantation of the HLA journal. In addition, I co-chaired the 2022 EFI conference in Amsterdam. As a Councillor I would like to work on future communication strategies for the EFI membership, and would like to help optimize the process of organizing the EFI annual meeting.

Falko Heinemann

I started in molecular biology at the University of Bielefeld, Germany, before joining the transplantation immunology field in 1998 as PhD student under the direction of Hans Grosse-Wilde at the Institute of Immunology in Essen, Germany. My work focused on the analysis of factors affecting the outcome of hematopoietic stem cell and solid organ transplantation. After being appointed as head of the Essen HLA lab in 2001, my duties expanded to local clinical H&I diagnostics and quality control issues in national and international organizations like the German Society for Immunogenetics (DGI) and EFI. In the following years, I was further involved in research in transplantation immunology and in teaching for the Medical Faculty of the University of Essen. Since the year 2021 I am elected president of the DGI. I have been an active member of EFI's Committee for External Proficiency Testing for more than ten years and I was



appointed as Chair of the EPTC from 2012 to 2021. During these years, I was able to gain insights into EFI structures and procedures and I would be grateful to get the opportunity to further contribute to the EFI community as Councillor of the Executive Committee.

Katerina Tarassi



I was born and educated in Greece. After graduating from the Medical School (1984), I completed my specialization in Medical Biopathology (1990) and my PhD Thesis (1997). My interest in H & I dates back to 1990 when I started working as Registrar in Immunology-Histocompatibility Dept of "Evangelismos" Hospital in Athens where I still work as Director since 2010. Additionally, I reinforced my knowledge in molecular techniques, trained in ARC Epidemiology Research Unit, Manchester-UK (1995 & 1996), in Immunology Laboratory-Hospital "Virgen de Rocio", Seville-Spain (1998) and in H & I and Disease profiling Laboratory-Stanford Medical School-USA (2015). I was also involved in research through publications, research projects and active participation in IHIWs since 1991. I was entitled to Honorary ESHI Diploma since July 2014. I have been an EFI member since 1991 and EFI Inspector since 2009. I would be happy to serve as EFI Councillor and I will try to do my best in order to promote collaboration between different countries and to support young scientists. I believe that the experience gained from my involvement as Member of the Executive Board of the Hellenic Society of Immunology (currently Vice-President) for many years will help me to accomplish this goal.



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EFI EDUCATION AND TRAINING BURSARY REPORT

Recently, I had the great pleasure to stay at GENYO – Centre for Genomics and Oncological Research in Grenada, Spain under the supervision of Dr. Juan Sainz. During my training, I was guided by professional bioinformatician, Maria Luisa Canadas Garre. I had the opportunity to participate in the analyses of genome-wide association studies (GWAS) data. The hosting laboratory commissions an external institute to carry out the GWAS assays. Later on, the massive set of generated data have to be analysed employing a wide range of informatics and biostatistical tools. The GWAS approach results in the identification of several genetic abnormalities in patient samples as well as multiple susceptibility loci. Thus, studying GWAS data potentially leads to pointing out new markers of disease susceptibility and prognostic treatment outcomes. In this study, all the analyses were performed using PLINK. Plots and some statistical analyses were conducted in R software.

The first step of bioinformatical analysis is a quality control assessment, in case checking every SNP (single nucleotide polymorphism) manually would be impossible. During this step samples and SNPs are removed to avoid spurious associations, which is critical for the success of a case-control study and necessary before statistical association testing. We distinguished samples to be removed by testing discordant sex information, missing genotyping rates or outlying heterozygosity rate, and selection of duplicated or related individuals, as well as, we identified all SNP markers with an excessive missing data rate and selected them by Hardy-Weinberg Equilibrium (HWE) and Minor Allele Frequency (MAF). After every operation PLINK creates a .log file which details the completing commands, the number of cases and controls in the input files, any excluded data and the genotyping rate in the remaining data. In the end, we got clean data set without bad SNPs and samples from the raw dataset. The next step was to perform an association analysis. This approach incorporated several statistical analyses:

selection of disease models, selection of single SNP tests of association using logistic regression, the test of associations assuming multivariable models and including covariates using logistic or linear regression, visualization and interpretation, adjustment for multiple testing, population stratification and replication. I also performed population stratification analysis (PCA) calculation for association analysis. I tried a different number of covariates to find out how many PCA I needed by compression of a genomic control parameter. The last operation I performed was data imputation. Firstly, VCF files needed to be prepared, checked and created using Will Rayner Tool, and then the Michigan Imputation Server working online was employed. In the following step, data were moved to the Alhambra cluster. After the imputation of the clean data set and quality control, the association analysis had to be repeated.

Additionally, during my stay I assisted in DNA isolation from swabs using a commercial kit, and prepared equal dilutions of all samples, measuring DNA concentrations on a NanoDrop spectrophotometer. I also learnt the basic rules of KASPar genotyping assay design.

In conclusion, my stay at GENYO allowed me to learn the approach of GWAS in silico analysis. This training also tightened collaboration between my laboratory in Wrocław, Poland, and the team in Granada, and helped to foster our future cooperation. I would like to thank the European Federation of Immunogenetics for awarding me EFI Education and Training Bursary which allows me to travel to Granada and accommodate there for the training period. I also would like to thank Dr. Juan Sainz and his research group for hosting me in the laboratory and for their warm welcome.

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By Luca Vago, section editor HLA journal

Higher risk for chronic graft-versus-host disease (GvHD) in HLA-G mismatched transplants following allogeneic hematopoietic stem cell transplantation: A retrospective study.

Neuchel C, Gowdavally S, Tsamadou C, Platzbecker U, Sala E, Wagner-Drouet E, Valerius T, Kröger N, Wulf G, Einsele H, Thurner L, Schaefer-Eckart K, Freitag S, Casper J, Dürholt M, Kaufmann M, Hertenstein B, Klein S, Ringhoffer M, Frank S, Amann EM, Rode I, Schrezenmeier H, Mytilineos J, Fürst D. HLA. 2022 Oct;100(4):349-360. doi: 10.1111/tan.14733.

HLA-G is a non-classical HLA class I molecules that, both in soluble and membrane-bound form, has been extensively shown to represent a key tolerogenic mediator in many immune-related interactions, including pregnancy, antitumor responses and transplantation. HLA-G display a relatively limited allelic polymorphism, but is characterized by a remarkable level of alternative splicing of the primary transcript and polymorphisms in the 3' UTR and the promoter region greatly influence the HLA-G expression profile. In this study, the Authors explored the impact of HLA-G mismatching in 2.083 10/10 matched high resolution HLA-typed allo-HSCT transplants. Almost all transplant pairs were HLA-G matched with 91.8% HLA-G matched versus 8.2% HLA-G mismatched cases, respectively. They found that HLA-G mismatching does not affect survival, but (when present in the graft-versus-host, GvH vector) is significantly associated to higher risk of chronic graft-versus-host disease. One possible explanation is that the immune regulatory function of HLA-G may be adversely affected in a HLA-G mismatched allo-HSCT setting either because of suboptimal interaction between the mismatched HLA-G of the recipient with the inhibitory receptors of the donor immune cells or direct allorecognition by the latter of the host cells carrying the mismatched HLA-G. Beside prompting investigation on the biological bases of these observations, if confirmed, the results from this study would have direct clinical implications, suggesting to avoid the selection of HLA-G incompatible donors.

Mobilisation of HLA-F on the surface of bronchial epithelial cells and platelets in asthmatic patients.

Fiouane S, Chebbo M, Beley S, Paganini J, Picard C, D'Journo XB, Thomas PA, Chiaroni J, Chanez P, Gras D, Di Cristofaro J.

HLA. 2022 Nov;100(5):491-499. doi: 10.1111/tan.14782.

HLA-F is classified as a non-classical HLA class I molecule because of its structure, low genetic diversity and restricted expression pattern. The least studied of the non-classical HLA class I molecules so far, HLA-F, is reported to be retained in the cytoplasm and mobilized on the cell surface upon activation of different cell types such as B and T lymphocytes, NK cells, monocytes, and bladder, skin, and liver cell lines. HLA-F has the same structure, but a shorter cytoplasmic tail, compared to HLA-A, HLA-B or HLA-E, and has been reported to bind to the KIR3DS1-activating NK cell receptor. In this interesting paper, the Authors explored the expression of HLA-F transcript and protein in peripheral blood mononuclear cells and in human bronchial epithelial cells (HBEC), either in basal condition or upon chemical activation, and both in healthy individuals and in asthmatic patients. They showed that in physiological conditions HLA-F is expressed and retained in cytoplasm by HBEC and platelet, and that in both cell types, the HLA-F protein reaches the surface in the inflammatory asthma context. Overall, results from the study suggest that HLA-F surface expression is a ubiquitous post-transcriptional process in activated cells, and that this molecule might represent an interesting therapeutic target in controlling lung inflammation.

Cumulative mean fluorescent intensities of HLA specific antibodies predict antibody mediated rejections after kidney transplantation.

Heinemann FM, Lindemann M, Keles D, Witzke O, Kribben A, Baba HA, Becker JU, Heinold A, Horn PA, Eisenberger U. HLA. 2022 Dec;100(6):553-562. doi: 10.1111/tan.14790.

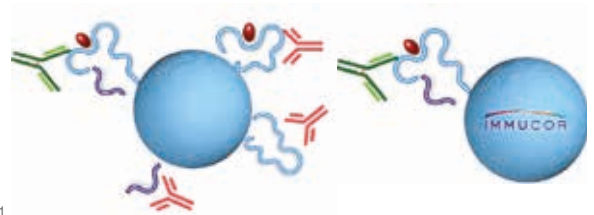
The detrimental effect of HLA-Donor Specific Antibodies (DSA) in kidney

transplantation is now widely recognized, but it is still not fully resolved whether the strength of pretransplant HLA-DSA, determined as cumulative mean fluorescence intensities (MFI) against multiple HLA specificities, have a predictive value for allograft function. In this study, the Authors analyzed preformed HLA antibodies by Luminex™ Single Antigen Bead (SAB) assay, including C1q addition, in relation to rejection and clinical outcome in 255 cross match negative kidney allograft recipients. Only 13% of the patients showed early antibody-mediated rejection (AMR) during the first year posttransplant, but in patients with pre-transplant DSA the rate was increased to 38%. Three year graft survival was significantly shorter in patients with histological signs of AMR compared with patients without AMR or with no biopsy. In patients with HLA-DSA, a cumulative MFI value of all HLA antibodies of more than 103.000 indicated the highest risk for AMR post-transplant ($p = 0.01$). Putting together these observations, in patients with HLA-DSA, the cumulative MFI value may help to further stratify the risk of AMR after kidney transplantation.

In addition, we would like to suggest to the EFI newsletter readership the excellent review published in the November issue of *HLA* regarding the clinical utility of serial serum dilutions for HLA antibody interpretation and a less conventional one, published in the October issue and authored by Eric Reits and Jacques Neefjes, explaining the role of HLA molecules in transplantation, autoimmunity and infection control by the use of fun and clever comic book vignettes. Finally, we would like to mention here that the impact factor of *HLA* for the year 2021 further rose to 9.2: we would like to congratulate our Editor-in-Chief Steven Marsh and the entire editorial team for this great achievement, but also thank the Authors for their excellent contributions and the readership for their interest and reference to *HLA* papers in their works.



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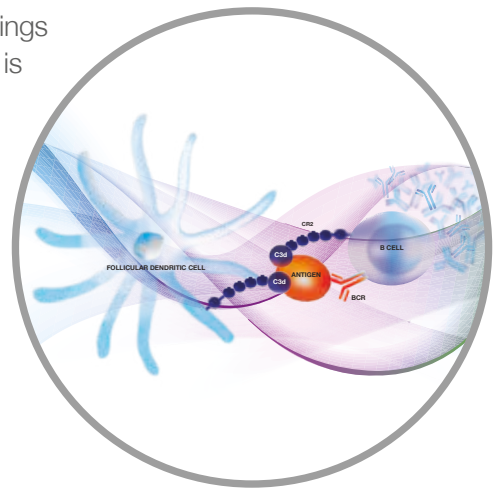


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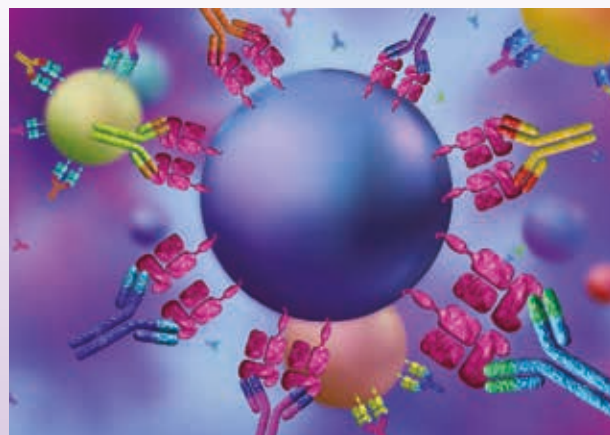
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¹ Ravindranath M.H., et al. Monitoring native HLA-I trimer specific antibodies in Luminex multiplex single antigen bead assay: Evaluation of beadsets from different manufacturers, J. Immunol Methods (2017) 450:73-80.

² Sicard, A. et al. Detection of C3d binding Donor Specific Anti-HLA Ab at diagnosis of Humoral Rejection Predicts Renal Graft Loss. JASN (2014) October, Vol 26.

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