EUROPEAN FEDERATION FOR IMMUNOGENETICS

NEWSLETTER

SEPTEMBER 2017 - ISSUE 83

.....FROM THE EFI PRESIDENT

DEAR EFI MEMBERS,

I hope you have enjoyed summer holidays with your family and friends.

Time is flying fast and we are moving soon into the busy months of autumn.

Writing this current issue of the newsletter I was very saddened to learn that our deeply respected Prof. Jon van Rood passed away on July 21 at the age of 91. I met him for the first time during my training in Leiden. As my mentor and teacher he inspired me to dedicate my future career to immunogenetics and its clinical application. Jon's remarkable and long scientific life was mainly focused on the field of histocompatibility, immunogenetics and transplantation immunology. Moreover, he has made very important contributions to the global cooperation in both organ and HSC transplantation by being a founder and co-founder of many organizations like Eurotransplant, BMDW, WMDA, Europdonor, EBMT, EFI, etc. For his outstanding scientific and humanitarian achievements Prof. van Rood was honored and awarded many times. We lost a great personality, brilliant scientist, inspiring teacher and dear friend.

And now let me go to the EFI activities and share with you the events that highlighted its spring-summer season.

First of all, it's the extremely successful EFI annual meeting being held in Manheim/Heidelberg, Germany that attracted more than 1200 participants from about 50 countries. The elegant and exceptionally well composed Opening Ceremony combined with jazz music in harmony with the latest scientific achievements was followed by the well designed scientific and educational programs keeping the participants in the halls. The social program was selected in a way allowing the participants to touch the Heidelberg's antique atmosphere and have fun too. Last but not least, the excellent organization made it possible for the busy schedule of the meeting to run smoothly without excessive strain and overloading in a pleasant and relaxing atmosphere. So, we are very grateful to the local organizers, the team of Caner Süsal for their excellent job organizing this EFI meeting. As usual the EFI Committee meetings were held before and during the conference. Later on, during the General Assembly the enormous and extremely important activities of these committees for EFI were presented and subjected to discussion and assessment by the attendees. Thank you all for your time and support.

Secondly, the usual meeting with the current ASHI President, this time with Michael Gautreaux, was held in Mannheim and the main point discussed was the international collaboration in H&I. Renowned experts in H&I were invited to participate in the discussion and many of them, including Steven Marsh, Dominique Charron, Marcelo Fernandez-Viña, Frans Claas and Gottfried Fisher, attended the meeting. We all agreed that there is a desire and a motivation for a more efficient and structural collaboration between APHIA/ASHI/EFI and IHIWS. Furthermore, there is a need for continuity and continuation in the work from one IHIW to the next. In relation to this it would be useful to have representatives from each of the three HLA associations acting as liaisons with the organizers of the future IHIW. These liaisons should be appointed for the full period until the next workshop. Additionally, it was discussed that if the IHIW is scheduled to take place in a continent where APHIA/ASHI/EFI operate, the respective association should organize a joint conference with the IHIW meeting. All these points were subjected to further discussion along with the IHIW councilors in Asilomar. I would like thank all participants in the meeting for the constructive discussion and the interesting ideas, as well as and their support to the international collaboration in the exciting field of immunogenetics.

Thirdly, the 13th International Summer School on Immunogenetics was held in Dublin, 23-26 July, 2017 and was organized by EFI. There was a huge interest in this year's summer school from the members of each of the three associations, and it was really difficult to select 48 participants from all over the world. The organizers had selected a very suitable venue for the school - Trinity College, one of the seven ancient universities of Ireland and Britain, which

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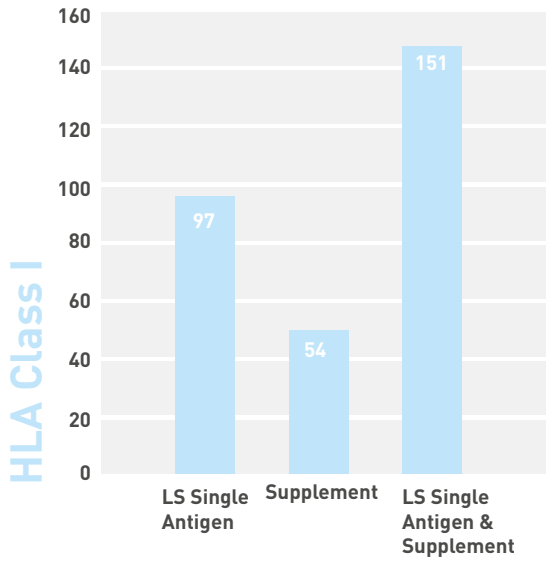

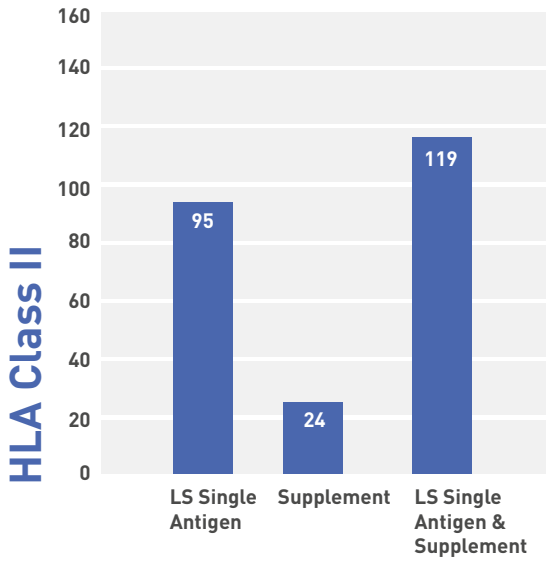

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....FROM THE EDITOR'S DESK

After a summer break, which hopefully all of you thoroughly enjoyed, it is time for a new edition of the EFI Newsletter. First and foremost is the sad news that Jon van Rood passed away this summer, while on holiday in Friesland, the Netherlands. We all know Jon as an incredibly inspiring scientist with a very warm personality. He remained very active in the laboratory in Leiden, where he was a regular at our scientific meetings, always giving valuable advice, or even sometimes a history lesson on immunology. He will be thoroughly missed by all of us. This newsletter contains an obituary on Jon, highlighting some of his major contributions to the field.
Furthermore, this newsletter contains several reports of the bursary recipients on the excellent joint DGI and EFI meeting that was held in Mannheim/Heidelberg this year. Caner Süsal and his colleagues organised a great meeting with an excellent scientific program and social program to match.
New in this edition of the Newsletter is an overview of the highlights of articles recently published in HLA, the official journal of EFI. This will be a recurring overview in the EFI Newsletters to come and will give you an impression of the excellent science published in our house journal.
As always, I hope that you enjoy reading the Newsletter and I very much look forward to you contributions for the next edition.

Sebastiaan Heidt

Deadline for contributions to EFI Newsletter 84 is December 15, 2017.
Please send your contributions by e-mail to s.heidt@lumc.nl

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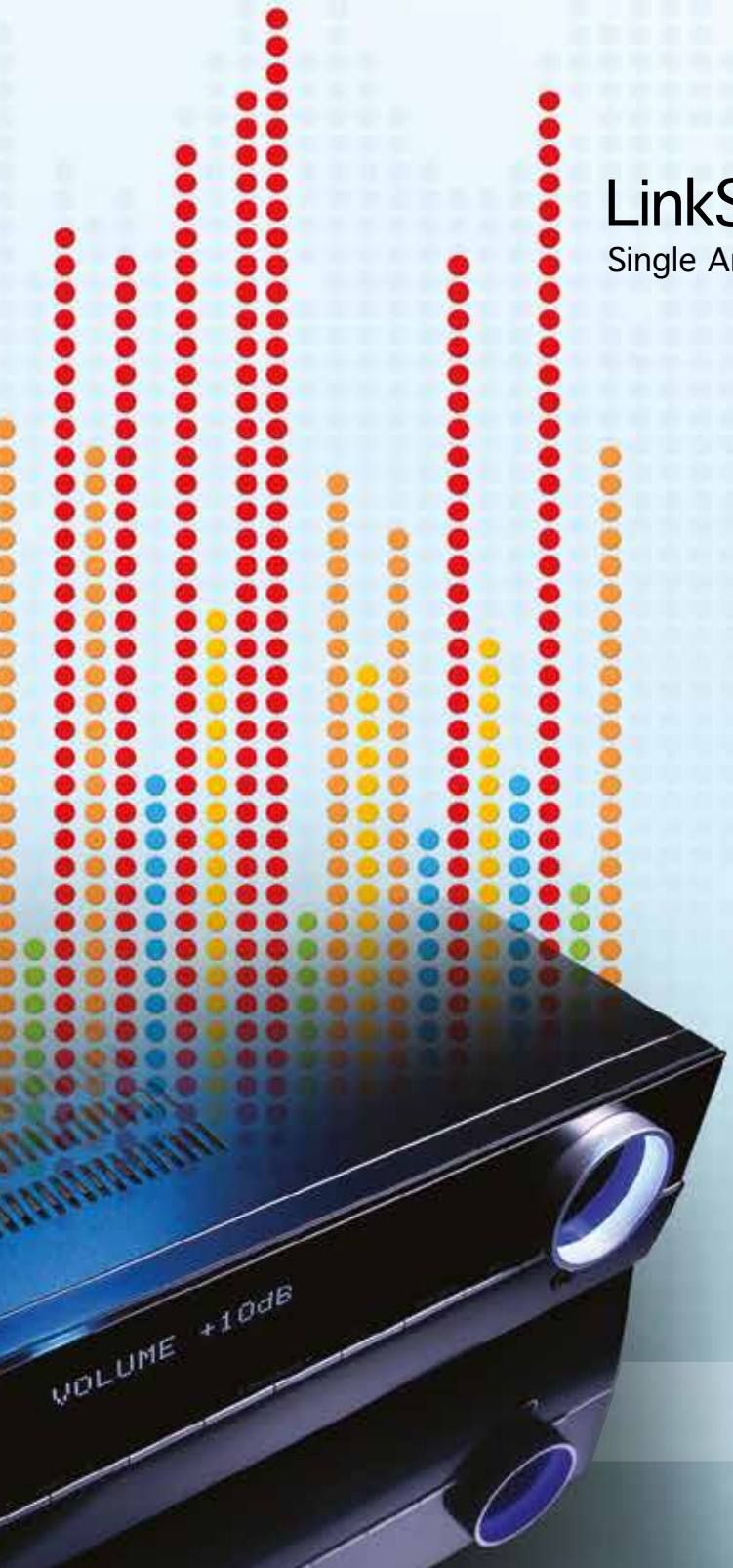

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created a unique academic atmosphere for the participants and the lecturers. The program was well prepared and the lectures were presented by well-known eminent immunogeneticists as the faculty. The participants were invited to briefly present their own research, and the discussions were held in an informal atmosphere even with a glass of the famous Irish beer, Guinness. I greatly thank Richard Hagan and David Turner as well as Sandra van Hensbergen for their wonderful job contributing to the great success of the Dublin summer school.

Fourthly, as you know over the last year a Memorandum of Understanding (MoU) was signed between EFI and the Polish Society for Immunogenetics. A first step in implementing this collaboration was the conference held in Warsaw in April this year dedicated to: "Current approaches in immunogenetics in modern transplantation". During the first session the participants were provided with detailed information on EFI accreditation, External Proficiency Testing and the Education programs which were excellently presented by the chairs of the respective EFI Committees. Then a very important discussion followed between the Polish representatives who are authorized for legalization, coordination and accreditation of the HLA Laboratories in Poland and those from EFI, including the directors and staff of more than twenty HLA Laboratories. Undoubtedly, this joint meeting has contributed to a better integration of the Polish laboratories into the EFI family and will encourage them to apply for EFI accreditation.

And finally, how are our relations with our European sister associations progressing? In March we signed a MoU with the European Society for Blood and Marrow Transplantation (EBMT) and recently with the European Federation of Immunological Societies (EFIS). One of the possible ways of collaboration is setting up working groups involving representatives from each of the two organizations on a given topic as well as organizing joint sessions at meetings, etc. For example, given that the number of publications for the significance of the non-HLA-genes (KIR, MICA, mHLA etc.) is constantly increasing in the field of HSCT, one possible topic which could be considered by this collaborative group could be to assess the influence of various genetic systems outside the HLA region on HSCT outcome, and to propose a consensus whether to include them in the algorithm for selection. Of course, this should be subjected to a further discussion both within EFI and with EBMT as well. With respect to this, representatives from the EFI Committees should be selected so that they can coordinate each of those collaborative activities related to science, education, accreditation and promotion. Any suggestions and desire to work in this direction are welcome.

Dear Colleagues, I'm convinced that expanding the European and the International collaboration will lead to both a greater promotion and recognition of EFI's work on the one hand, and on the other hand, will help the achievements in H&I and transplantation reach every corner of the world.

Elissaveta Naumova

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:

E. Masson Frenet, New York, USA
C. Hirschauer, Papeete, French Polynesia
I. van Hoogstraten, Amsterdam, the Netherlands
E. Dijke, Edmonton, Canada
C. Lenehan, Dublin, Ireland
M. Jain, New Delhi, India
L. Walsh, Dublin, Ireland
J. Bonneau, Saint-Etienne, France
K. Lund, Copenhagen, Denmark
J. Kerkhofs, Mechelen, Belgium
L. Nicol, Edinburgh, UK
G. Simper, Hannover, Germany
C. Rosser, London, UK
S. Singh, Columbus, USA
M. Sholan, Khamis Mushayt, Saudi Arabia
S. van Wageningen, Utrecht, the Netherlands
S. Gabriellini, Pisa, Italy
S. Weston, Leicester, UK
M. Kasar, Adana, Turkey
E. Carter, Manchester, UK
D. Cook, Manchester, UK
M. Simonenko, Saint-Petersburg, Russia
B. Stefan, Ilfou, Romania
L. del Giudice, Camposampiero, Italy
T. Gallucio, Rome, Italy
C.M. Alvarez, Medellin, Colombia
S. Jaman, Split, Croatia
A. Zare, Tehran, Iran
A. Ali, Budapest, Hungary
L. Kasperidus, Essen, Germany
R. Tomoya Michita, Essen, Germany
R. Özdemir, Balikesir, Turkey
D.A. Mytilineos, Ulm, Germany
R. Landgraf, Leipzig, Germany
S. Shahmohammad Farid, Fabriz, Iran
L. Yu, Paris, France
Q. Pan, Nanjing, China
X. Wang, Shanghai Shi, China
C. Lingzhen, Guangzhou, China

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Obituary: Prof dr. Johannes Joseph (Jon) van Rood (1926-2017)

Prof. dr. Jon J. van Rood, a distinguished member of our scientific community, passed away on 21 July at 91 years of age. In light of his scientific legacy, we wish to commemorate some of his most significant achievements and contributions.

A few historical aspects

Jon was born on 7 April 1926 in Scheveningen, a town situated on the coast of the Netherlands. At the end of the second World War, he began his medical studies at Leiden University. After finishing these, Jon was active as a 'house doctor', and visited many of his patients in the country areas. He considered this one of the best medical learning experiences of his early career, as he was confronted with so many different illnesses. Jon could also tell amazing stories about touring on his motor bike in bad Dutch weather in the rural countryside. Apparently he was a poor driver, and ended up parking his motorbike at least six times in a canal.

He moved temporarily to New York in 1950, and under the guidance of Dr. R.F. Loeb (Presbyterian hospital, New York), he became intrigued by Internal Medicine. Upon returning to Leiden, Jon began his training with Prof. dr. J. Mulder in order to specialise in the field. In 1957, he was certified as a specialist in Internal Medicine (equivalent to US board certification), and was appointed as head of the Leiden Blood Bank. To quote Jon: 'The board thought that a young, inexperienced doctor could do the least harm in such an unimportant place'. Those were the days just after open-heart surgery had been introduced, and unprecedented amounts of blood were required. Jon began to organise things, recruiting large numbers of donors, and improving the supply pipeline. All of this demonstrated his talent for organisation, and the young doctor soon proved to be a highly capable manager.

At its inception, the entire Blood Bank team comprised just a handful of staff members and technicians. One of them was George Eernisse, an MD, who could isolate, radio-label, and perform in vivo studies of red blood cells and platelets; the other was Aad van Leeuwen, who had a pair of golden hands and was an eminent serologist. The combination of Jon's, George's, and Aad's talents created the basis for a forceful team, ready to embark on great discoveries, as Jon was able to think well out of the box. He was at his best when trying to comprehend something in order to answer a question, and was prepared to conduct things in an unconventional manner while squeezing out the answer that would finally satisfy his curiosity. For instance, the male staff members of the Blood Bank exchanged skin grafts and platelet transfusions to study the relationship between transfusion and transplant immunity. It soon became clear that the young doctor was destined to become a zealous medical investigator, who expected of his employees the same high level of dedication and commitment, although this aspect of his character was not always easy for everybody to accept.

The early days of HLA

Science often begins with a key observation. One of Jon's male patients had to receive a blood transfusion on a monthly basis, simply to stay alive. After each of these events, he developed a severe transfusion reaction. No adverse reactions occurred when the white blood cells were removed from the blood transfusion, demonstrating that leukocytes had been responsible for the previous transfusion reactions. Jon always credited the collaboration with Prof. dr. J.J. van Loghem for sharing the isolation technique. The second Eureka moment soon followed in 1958. A woman who had given birth to twins – followed by a fluxus post-partum – experienced a severe transfusion reaction. Her medical record showed no previous blood transfusions, and she assured Jon that she had never been transfused. A subsequent series of elegant tests indeed demonstrated that the woman possessed antibodies directed to the white blood cells of the transfusion donor and her husband. This set of key observations became the very basis of the discovery of the HLA system. Independently, and in the same timeframe, the groups led by Jean Dausset (Paris, France) and Rose Payne (Stanford, USA) made similar

observations using slightly different approaches. Jon van Rood published his discovery in the scientific journal Nature, and graduated in 1962 cum laude as a Doctor in Medicine (PhD). His thesis entitled 'Leucocyte grouping: a method and its application' was reprinted on several occasions, and probably ranks among articles most cited. An American publisher offered to bring the thesis on the market in the form of a book. Jon bluntly refused, and to quote him: 'I was rather leftish, and could not allow publishers to earn money on the backs of my patients'. In fact he was one of the first bioinformaticians using computers to determine the reactivities of different anti-HLA sera. His stories about the large size of the room and those enormous old-fashioned computers with limited calculating power are legendary.

Unearthing HLA complexity and workshops

During a conference involving an additional laboratory work session organised by Dr. Bernard D. Amos in Washington DC in 1964, it was realised that the different HLA markers discovered by independent research teams showed no or poorly understood relationships. Hence, a ground-breaking and novel set-up was needed, and the exchange of sera was promoted. The first official Histocompatibility Testing workshop was organised in 1965 in Leiden. Bernard Amos was acting President and Jon was the Secretary General. This approach turned out to be a success, and the first light was shed on the allelic complexity of the HLA system. The tradition of organising workshops is

still a strong one. He foresaw that the growing number of HLA alleles would sooner or later impact HLA-matching protocols in the context of organ donor selection. He also realised that given the polymorphism of HLA, the optimal combination of donor and recipient might benefit from a large number of donors across geographic borders. In 1967, he founded Eurotransplant, the first international organisation to promote allocating a donor organ to the best matched recipient. Since then, many similar organisations have been created around the globe. In 1968, Jon was involved in the first successful allogeneic bone marrow transplantation in the Netherlands, and one of the three first transplants conducted worldwide. The story was told at several international meetings over the years, and always caused quite a thrill. In 1969, the Leiden University appointed him as full professor. Some of the old-timers refer not only to the high standards of Dutch science but also to the fantastic after-parties.

In 1985, he was one of the founding fathers of the European Federation for Immunogenetics (EFI), and he was the acting President from 1985 until 1988. In the first chapter of Article 3 (aims) of the EFI, it reads: 'to support the development of Immunogenetics in Europe as a discipline of medicine and promote research and training in this field'. This simple statement breathes in every detail the input of Jon van Rood. In 1988, he was also heavily involved in setting up a registry of bone marrow donors – Bone Marrow Donors World Wide (BMWD) – and he founded the Europdonor Foundation, now called Matchis, the Dutch centre for stem cell donors.

Retirement, thus not

In 1991, Jon van Rood turned 65, and had reached the age of retirement. It was generally considered that one then begins to enjoy life's other fine aspects. Although Dutch law did not allow exemptions to the rule, Jon saw it slightly differently. He said he 'was forced to retire, and that was more than scandalous and a waste of resources'. A respected Dutch newspaper published an exciting two-page interview regarding his successful career, and looking back at his accomplishments. The reporter's last question translates as follows: *'What are you going to do after your retirement?'* Jon answered: *'Spend a lot of time on my hobby'*. The reporter walked straight into the open trap, and asked: *'What is your hobby?'* Jon replied in only two words: *'My work'*.

He found scientific refuge within his old department, and to secure his future, Frans Claas kindly offered him a PhD position. For quite some time, Jon told anybody who wanted to hear it – proudly and with a big smile on his face – that he had just started to work on his new thesis. He 'found' a room with a view at the Europdonor Foundation, and simply kept busy with what he had been doing previously. From 2011, he and Anneke Brand shared an office, reuniting transfusion and transplantation immunology. Remarkably – but wisely – he rarely interfered with the new management of his former department. Instead, his energy was channelled into promoting his new 'scientific babies', such as the NIMA (Non-Inherited Maternal Antigens) concept and the impact of breast-feeding on a child's immune system. We have always been astonished by and in awe of Jon's own scientific curiosity, but also by the way in which he strove to support and stimulate young researchers in the field. The three of us had contact with him on a very regular basis. On the one hand, he would phone or contact one or all of us at the most unexpected moments when he wished to discuss some of his novel ideas. On the other hand, he would use any given moment – suitable or otherwise – to hammer home an old message that he felt was worth pursuing. Long after his retirement, he continued to attend EFI, ASHI, and various transplantation meetings, as well as PhD, research and clinical meetings. Over time, however, his impaired mobility interfered with the possibility of travelling and attending international meetings. He hated that fact, and it took him some time to come to terms with it. But this did not mean that he gave up. In fact, he never missed any interesting meeting that was within range of his bike or his car.

The Jon van Rood school

When Jon retired in 1991, the Department of Immunohematology and Blood Bank had an impressive number of almost 200 employees, all of them dedicated to the central theme of HLA research. He always stressed that a strong relationship between research and the clinic is the basis for success, and he advocated that MDs and researchers in other life science disciplines should work closely together. Jon's legacy is immense. He acted as a promotor of more than 60 PhD defences. Many of his former PhD students have become professors themselves. They are spread all over the world, and continue to work along the threads of the web Jon originally started weaving. A famous member of our scientific community stated once that Jon must be proud being the father to a fantastic pedigree of well-known scientists. The Grand Master himself published more than 400 scientific papers, and the last one was published in a reputable peer-reviewed journal about three weeks before he passed away.

International prizes and recognition

Jon served on the boards of many journals, either as an editorial board member or as an editor-in-chief, and received many prizes for his work. The list is too long to present in full, but a few noteworthy ones are: the Karl Landsteiner Memorial Award and recipient of the Robert Koch medal (both in 1977); The Wolf Prize in Israel (together with Jean Dausset and George Snell) in 1978; The Stella Artois-Baillet Latour prize (Belgium, 1985); The Heineken Prize Amsterdam (1990); and the Peter Medawar Prize (together with Jean Dausset and Paul Terasaki) in 1996. He delivered the Ceppelini lecture (EFI, 1988) and the Niels Jerne lecture (1990), and received the Rose Payne award (ASHI, 1991). In 1978, he was appointed as a member of the highly prestigious Royal Academy of Sciences of the Netherlands (KNAW). He also became a member of the likewise prestigious National Academy of Sciences of the United States of America. On top of that, his achievements were awarded in the form of honorary doctorates from eight international universities. He was so proud when Queen Beatrix promoted him to the high-ranking status of Commander in the Knighthood Order of Oranje Nassau. Whenever Jon received a prize, he celebrated the event with the whole department, as he regarded any award as a team achievement. Jon had a warm personality, and the celebration often meant a fantastic dinner followed by a big party with dancing and drinks. And he sure loved to dance.
If the prize involved a sum of money, the funds were always re-routed directly into his lines of research.

A few concluding remarks

Jon was a visionary medical scientist and a pioneer in immunology, but he was also a caring doctor who invariably approached things from the perspective of the patient. He made tremendous contributions to the progress in medical science, and was one of those rare dinosaurs that actually made a difference. Jon's life, however, was not only about work; for instance, he loved to go hiking and skiing, though sailing was really his big thing. He regarded his boat, de Zeehond (the Seal), as an extra set of lungs. We knew that the time to say farewell would come, and in fact he reminded us on a regular basis that it was getting closer and closer. When we said goodbye to each other after a meeting or a dinner, he would use the phrase 'Deo valente' increasingly often.

Yet when the moment did arrive, it was unexpected and far too soon. We have lost not only an exceptional tutor but most of all a dear and respected friend. We miss him already in this capacity, and will be forever grateful for all the lessons, the wisdom, the support, and the precious time that was spent together. We will always cherish these memories. Above all, we will strive to continue weaving on the wonderful web that Jon van Rood started, and to carefully guard his scientific testimony and thoughts.

Jon was married to Sacha, and he fathered three children, Yanda, Peter, and Tinka. We wish them strength in this time of their loss.

Ronald Bontrop[1], Anneke Brand[2], and Frans Claas[3]

[1] Biomedical Primate Research Centre Rijswijk, Rijswijk the Netherlands
[2] Jon van Rood National Center for Clinical Transfusion Science, Leiden the Netherlands
[3] Department of Immunohematology, LUMC, Leiden the Netherlands

The same text will be published in Immunogenetics, HLA and Human Immunology

EFI EDUCATION AND TRAINING BURSARIES

To promote training in the field of Immunogenetics and Histocompatibility, the EFI Executive Committee has allocated a fixed number of bursaries for EFI members wishing to visit another laboratory to learn new techniques and to develop research collaborations.
There are four deadlines in each year for receipt of applications: February 1st, May 1st, August 1st and November 1st. Applications must be submitted at least six weeks prior to the start of the planned education and training visit. EFI members will be informed of the upcoming Application submission deadlines in the EFI Newsletter; moreover, the deadlines will also be announced by blast mail six weeks ahead according to the following table:

Month of visit	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Application submission deadline date	November 1st			February 1st			May 1st			August 1st		
EFI Newsletter announcement	September issue			September and January issue			January issue			January issue		
Announcement by blast mail	September 15th			December 15th			March 15th			June 15th		

CALL FOR APPLICATIONS TO THE SCIENTIFIC COMMITTEE

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

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

Applications should be sent directly via email to the chair of the Scientific Committee, Prof. Katharina Fleischhauer (katharina.fleischhauer@uk-essen.de), and/or to the EFI Secretary Dr. Mats Bengtsson (mats.bengtsson@igp.uu.se), no later than **Friday October 13, 2017**. Applications submitted after this deadline will not be considered.

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Report on the EFI General Assembly held June 1st, during the 31st annual meeting in Mannheim, Germany

Report prepared by Mats Bengtsson, EFI Secretary and Dave Roelen, deputy secretary

1) Opening

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

2) Minutes of the General Assembly May 13th 2016 Kos

The minutes published in the EFI newsletter September 2016, issue 80 were accepted.

3) Report of the EFI President

EFI Office

The President reported that the EFI office has a new location since September 2016. The office is still close to the LUMC. The EFI office administrator Ingrid Abelman has recently left her position and is replaced by Sandra van Hensbergen since May 16th. The SLA with LUMC for support of the EFI office has been updated to reflect those changes.

Collaboration with National Societies

To strengthen the work on education, accreditation and other activities, EFI has for a number of years worked to formalize the relationship with national societies for histocompatibility and immunogenetics. Since last presentation at the General Assembly in Kos we now also have signed relationships with the Polish Society - PSI, the German Society - DGI, The Dutch working group - HLA - WN and the Spanish society - SEI, besides the previously signed agreements with Italy - AIBT and the British Society - BSHI. Agreements with France and Portugal are underway. As a consequence of the agreement, EFI also actively participated in a meeting held in Warsaw between April 19-20th. The meeting was highly successful and we look forward to have many more laboratories in Poland applying for EFI accreditation

Relationship with other societies

At the beginning of 2017, the Presidents of EFI and EBMT signed an agreement to cooperate on scientific, and educational matters in the field of histocompatibility and transplantation. The agreement also covers cooperation in promotion of activities of both societies, guidelines for joint sessions and development of working groups for development of various projects. A similar agreement has been made also with EFIS - European Federation of Immunological Societies. Together with ASHI and APHIA, our society has published a joint resolution on how to cooperate in scientific, educational and accreditation matters.

Request for reduced fee for retired members

The Executive Committee has reviewed a proposal from the former Treasurer Mogens Thomsen to consider suggesting to the General assembly to have a reduced membership fee for members that are retired. The EC discussed this during the recent meeting. The present structure of the website that handles payment does not permit this kind of changes. The whole website and the paying module are however under reconstruction and the request will then be considered again. This was supported by the membership.

Editor in Chief EFI newsletter

The EFI President then expressed her sincere gratitude to Frans Claas for his work as Editor in Chief for the newsletter for so many years. A small gift was presented as a token of appreciation.

4) Report of the EFI Secretary, Mats Bengtsson

Executive Committee Elections

Three councillors are stepping down, Kay Poulton, Jaume Martorell and Paul Costeas. For those three vacancies six nominations were received. As our President will step down in 2018 there was also an election for President elect. For this position two nominations were received. This was the second time with electronic voting. To minimize problems with the voting the EFI office sent out a preparatory mail a few days before the actual voting mail was sent. Members were informed that they should receive the e-mail and if not contact the EFI office. Still some problems were encounted where emails could not be delivered because of outdated addresses. In total 339 votes were received. For the position of President elect, Joannis Mytilineos received the highest number of votes and for Councillors, Neema Mayor, Jean Villard and Pierre-Antoine Gourrad received the highest number of votes. These candidates were accepted by the General Assembly.

Bursaries.

Personal bursaries were awarded to 13 EFI members and three education and training bursaries. After a suggestion from the Educational and Scientific Committees the procedure for the Education and Training bursaries will be changed so there will be four instead of three application periods.

Future EFI Conference

The conference locations and organizations for our annual meetings have been decided up to 2020, we are now looking for people interested in organizing the EFI Conference in 2021. Applications must be received by September 2017, more details were published in the April issue of the newsletter and on the website.

5) Report of the EFI Treasurer Gwendaline Guidicelli

The EFI treasurer presented a combined overview of the of the final budget for the EFI Office and Accreditation over 2016. This year was the first time the budget for the EFI office, with the bank accounts in France and for the Accreditation, with the bank accounts in the Netherlands, were presented together. The positive net result for 2016 was € 96.026, mostly because of the profit from the Kos meeting. This must however be balanced against the fact that the net result from 2015 was € 36.350. The provisional budget for 2017 was presented with a substantial increase in the amount of money dedicated for education and training purposes

(from € 8055 in 2016 to € 39.459 in 2017). The budget proposal was approved by the membership. The decision to increase the membership fee last year for most members, in order to decrease the fee for new members, has so far not changed the number of paying members.

6) Report of the EFI committees

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

Accredited laboratories and Commissioners

The number of accredited laboratories has reached a plateau and is now 264. In 2016 a total number of 78 EFI inspections were performed in 28 different countries.
The Chair and Co-chair have been reappointed for a further term. Carlo Carcassi will leave the committee in October 2017 and will be replaced by Franco Papola.

Inspectors workshop

An Inspectors workshop was organized on May 29th with a focus on common findings such as deficiencies in wipe tests, test validation and continuous test monitoring.

Joint inspections with ISO accrediting bodies

The cooperation with DAKKS in Germany is now well established but the progress to establish a common joint inspection scheme is prevented by the lack of uniformity between the different National Accreditation Bodies. The work will continue with individual countries were there is interest.

Inspection travel costs

A recent review identified a wide variation in charges to laboratories and this variation is not region specific, except region 99. To make the costs for laboratories more predictable, a flat fee will be introduced for 2018. The costs for laboratories will then be the same every time. The Accreditation Committee will propose the flat fee rate to the Executive Committee for approval during the Autumn meeting. The laboratories will then be informed accordingly. Region 99-outside of Europe will not be included in the flat fee rate and continue to be charged for full costs.

b/ Report from the Education Committee Chair, David Turner (with additional report from the EBTI)

Committee Membership

An overview of the members was presented. Recently appointed members are Maria Spyropoulou-Vlachou, Deborah Sage and Michel Eikmans.

Teaching Sessions

The planning for next year's meeting in Venice is underway. At present all the teaching sessions are scored by the participants, how to use this information in the best way will be reviewed. All teaching material can be found on the membership section of the EFI website

Summer school

EFI organized the 13th International Summer School on Immunogenetics which will be in Dublin, Ireland from 24th-26th July 2017. The summer school was held at Trinity College and the local organizer was Richard Hagan. There were 46 students registered for the course.

ETHIQ for technical staff

The work with the European Technical Histocompatibility and Immunogenetics Qualification has not progressed as planned but the committee plans to move on and hopefully deliver something during 2018.

ESHI Diploma

All applications for the Honorary Diploma have been assessed and for the exam there have been nine applicants. Next exam will be in October 2017. The syllabus has been updated and the major changes are that trainees are now required to register for the program and there will be a requirement for CPD/CME collections from 2018. This will apply not only to trainees but also to those who already have the exam.

EBTI Executive Committee members

There has been some changes to the EBTI Executive Committee. The new chair is Marco Andreani and new co-chair Tony Slavcev. David Turner has been appointed Senior secretary and Eduard Palou is the new Junior Secretary. Valerie Dubois replaced M. Drouet in December 2016.

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

Committee membership

Due to the fact that Region 5- Central Europe is large and rather heterogeneous, it has been decided to appoint Katarzyna Kubic from Wroclac as extra representation besides Martin Petrek.

Registration of EPT providers

There has been an update in the registration documents and the overview is available on the EFI website.

Update of standards for laboratories and providers

The standards for laboratories have been updated to the new version 7, which contains clarifications of sample selection rules and on how to report results, and also now includes KIR/MICA requirements. The KIR/MICA have also been added to the standards for providers. The committee has also finished the work with a manual for inter-laboratory exchange. This will allow laboratories to test performance when access to official EPT programs is missing.

Education.

A "Meet the Expert" session was arranged this year about evaluation of patient based clinical scenarios with a lot of interesting discussions.

d/ Report from the Scientific Committee chair, Katharina Fleischhauer

Committee members

Luca Vago is a new member of the Scientific Committee and there will be a new vacancy since Jean-Marie Tiercy will be leaving the committee.

EFI Conferences

For the Mannheim meeting 320 abstracts were scored (96 orals and 224 posters). The organization for next years conference in Venice is well in progress. There will be 5 plenaries and one special session with WMDA.

Julia Bodmer Award

This year 5 outstanding applications were received from 5 different countries. Any EFI member may suggest candidates for 2018 and laboratory directors are asked to encourage PhD students to apply.

EFI- SC Population Genetics Working Group (PGWG)

This group started its work in 2014 and has recently completed the work with an EFI catalogue of CWD alleles. The work was published in the HLA journal. The data come from AFND, HLA-net and also from DKMS. It comprises almost 4 million individuals from up to 121 data sets. It also includes 7-loci to the 2nd field level. Compared to the ASHI data there are substantial differences between the data with 48.9% of EFI CWD missing in the ASHI dataset and 48.1% of ASHI CWD missing in the EFI dataset.

A new project for the PGWG will be to construct a European Haplotype map with data from family segregation. Interested laboratories should contact either Katharina Fleischhauer or Alicia Sanchez-Mazas.

e/ Report from the Standard Committee Chair, Juha Perasaari

Committee members

The committee has two new members, Jennifer Schellekens from the Netherlands and Sara Maxfield from the UK, as Christiene Voorter and Susan Fuggle have left the committee after serving for nine years.

EFI standards

The committee has been working with the new version 7.0 of the EFI standards. They are completely reorganized to reduce redundancy and make the different sections more logical both for laboratories and inspectors. The new version will have separated the bead array standards from flow cytometric standards, as well as separation of Sanger sequencing from NGS. New standards for KIR/MICA typing are introduced. The new format will also allow more flexibility to introduce new methods or clinical applications. The new version will be sent for approval during the autumn with a plan to be effective from beginning of 2018.

Collaboration with ASHI QAS

The EFI and ASHI standards committees continue to work close together. During the ASHI meeting in 2016 in St. Louis, EFI was represented by Moshe Israeli, and Cindy Raven from ASHI attended the EFI meeting this year. The challenges for EFI and ASHI are similar but the regulatory environment is very different.

7) Next EFI Conference

The next EFI meeting will be in Venice, Italy from May 9th to May 12th 2018.

8) EFI medal

The EFI medal is awarded annually by the EFI Executive Committee to recognise the achievements of individuals who during the course of their career, have made a significant contribution to EFI. This year the EFI medal was awarded to Constanze Schöneman and Pascale Perrier. Joannis Mytilineos presented the medal to Constance Schöneman and Anne Cesbon to Pascale Perrier. The award is described elsewhere in the newsletter.

9) Installation of new EC members

The President thanked Kay Poulton, Jaume Martorell and Paul Costeas as Councillors and welcomed Joannis Mytilineos, Neema Mayor, P-A Gourraud and Jean Villard to the EFI EC.

The General Assembly was closed at approx. 19:25 hrs.

Standards Committee Report

Comments from several EFI members were received to proposed Standards v7.0 and they were addressed at the Standards committee meeting during the annual EFI conference in Mannheim. Some changes to the proposed standards were done based on the comments. The revised version waiting for approval can be found on the EFI website as a pdf file (http://www.efiweb.eu/efi-committees/standards-committee.html). A tracking document, which notes the changes from version 6.3 as well as the standard numbering according to both versions 6.3 and 7.0 is available on the EFI website as well.
The revised version is prepared in a new format reorganizing the standards in a new way. With the new format we have separated methods from clinical applications e.g. methodological standards concerning Chimaerism Monitoring from Haematopoietic Stem Cell Transplantation. Also standards for individual methods has been separated from each other e.g. Sanger sequencing and next generation sequencing. In addition to changes in standards format, also new standards have been introduced. For Haematopoietic Stem Cell Transplantation, standards describing which party takes responsibility of the histocompatibility component of the transplant have been introduced. Also standards for other immunogenetics markers e.g. KIR have been introduced. With the new format we aimed flexibility to introduce new methods and clinical applications to the EFI Standards as well as user friendliness to Inspectors and Laboratory Directors in their daily routine. I hope we have reached these goals with Standard v7.0.
During our meeting in Mannheim we have elected two new members: Jennifer Schellekens from the Netherlands and Sarah Maxfield from the UK.

Juha Peräsaari (Helsinki, Finland)
juha.perasaari@bloodservice.fi
Chair of the EFI Standards and Quality Assurance Committee

Ceppellini Lecturer 2017 – Professor John Kappler

Each year at the annual EFI Conference, a scientist who has made substantial contributions to the field of Immunogenetics is honored by the Society and invited to present their work in the form of the Ceppellini Lecture. The Lecture is named in honor of Ruggero Ceppellini (1917-1988), the Italian geneticist who greatly influenced the HLA field. The first Ceppellini Lecture was delivered in 1988 by the late founder of EFI, Jon van Rood. Over the past five years, it has been held by Effie Petersdorf (2016), Frans Claas (2015), Marco Colonna (2014), James McCluskey (2013) and Gerhard Opelz (2012). A complete list of Ceppellini Lecture Awardees can be found on the EFI website (http://www.efiweb.eu/awards/the-ceppellini-lecture.html).

This year's Ceppellini Lecture was delivered by John Kappler, Professor in the Department of Integrated Immunology at National Jewish Health in Denver, Colorado and appointed Investigator of the Howard Hughes Medical Institute, at the Annual EFI Conference in Mannheim on May 30, 2017. John Kappler is famous for discovering the T cell receptor (TCR), together with his wife Philippa Marrack, back in 1983, and for subsequently unravelling the basic principles of MHC-restricted antigen recognition and self-nonself discrimination by the TCR. He obtained a PhD in biochemistry from Brandeis University and joined Richard Dutton's laboratory at the University of San Diego as a postdoc in 1969, to pursue in vitro studies of the immune system. Since 1979, he has been in Denver with a double appointment at National Jewish Health and the University of Colorado Health Sciences Center. Among the impressive list of John's 498 PubMed publications since 1970 are countless papers published in Cell, Nature and Science, in addition to many other prestigious journals including PNAS and Journal of Experimental Medicine. These report his groundbreaking observations regarding the structure and function of the TCR in earlier years, and elegant experiments using MHC-linked peptide libraries to unravel peptides relevant for the pathogenesis of autoimmune diseases and metal hypersensitivity later.

In his Award Lecture entitled "Proinsulin-derived neo-epitopes in Type 1 Diabetes", John presented some of his newest work on how post-translational modifications including transpeptidation and reverse proteolysis can give rise to insulin-derived neo-epitopes recognized by autoreactive TCR, with obvious implications for the pathogenesis of type I diabetes.

John's important contributions to our understanding of T cell immunology and their implications in Medical Science have received numerous Awards, among which the William B. Coley Award from the Cancer Research Institute (1993), the Louisa Gross Horwitz Prize for Biology or Biochemistry from Columbia University (1994) and the Wolf Prize in Medicine (2015). EFI is proud to include the Ruggero Ceppellini Award 2017 in this distinguished list, to honor one of the most eminent scientists of our field.

Katharina Fleischhauer – on behalf of the EFI Scientific Committee

EFI medal recipient: Dr. Pascale Perrier

All members of the French HLA laboratories know Pascale and many of the people within the EFI community know her too, since she has been an active EFI Inspector during 16 years and an EFI French Commissioner during 9 years (which is the maximum term).

Pascale has retired now but she has been in charge of the HLA laboratory in Nancy for 34 years (from 1981 to 2015), which means that she was present at the very beginning as soon as she became a medical biologist in 1980. Her laboratory was accredited from 1998 onwards. Pascale is expert in CDC, but she also introduced molecular biology in her lab at a very early stage (1989 with RFLP), and she was also interested in human platelet antigens, human neutrophil antigens, as well as KIR. She has published about 50 papers, first in immunohematology, and then in H&I field. Pascale also

actively participated to teaching at the University, amongst others. Moreover, many students spent time in her lab in order to prepare their medical thesis or any scientific report

Everybody knows Pascale's perfect knowledge of A, B and C Packets for EFI Accreditation as well as EFI Standards: when she was reviewing an EFI Packet, she always had many questions, new documents to ask and during Inspection, no deficiency could escape her. For sure, she was giving a lot of advice too. As French Commissioners, we have worked together for 5-6 years and we have organized one day meetings for French Inspectors. Pascale has attended many scientific meetings in relation with H&I where she often presented her work as poster or oral communication. She went to 13 French educational meetings where she often participated in teaching sessions, 4 international Workshops (Vienna , New York, Yokohama and Paris) and 23 EFI conferences.

To summarize, we can say that HLA was an important part of Pascale's life and we thank you for all the time you have spent and for everything you have done for EFI and the H&I field.

Pascale now has many other topics of interest: she likes to travel, to practice skiing and to go for long walks in the snow.

Anne Cesbron-Gautier

EFI MEDAL RECIPIENT: DR. CONSTANZE SCHÖNEMANN

Dr. Constanze Schönemann studied Biology at the University of Leipzig and received specific training in the field of animal physiology and Immunology. This was where she first discovered her "love and affection" for immunological processes. Inevitably, this lead to further involvement in the area – so her Diploma thesis dealt with the implementation of a "leucocyte adhesion inhibition test". Later on she wrote her PhD-thesis about the effect of CMV prophylaxis in stem cell transplantation. HLA and Transplantation was the "credo" of Constanze's professional life from the very beginning. She was employed already from 1976 in the Transplantation Immunology and Histocompatibility laboratory in East Berlin and from 1984 on she was working in the Immunology laboratory of the Friedrichshain hospital in Berlin under the "legendary" Dr. Leverenz. I vividly remember when Dr. Leverenz introduced me to Constanze sometime in the early nineties, soon after the reunification of Germany – it was at a Eurotransplant meeting in Leiden in the Gorlaeus laboratory-building.

Constanze's involvement in the HLA field was not only scientific, but also "political". She has been increasingly and very effectively involved in the regulatory and representational work of our field, particularly within Germany. She was for many years the chair of the DGI-committee for Organ Transplantation as well as of the committee for Transplantation Immunology within the German Transplantation Society. She represented Germany successfully for at least as many years in the Eurotransplant Tissue Typing Advisory committee and finally became President of the Germany Society for Histocompatibility and Immunogenetics (DGI). Constanze was also very efficient in representing the field of Transplantation Immunology within the commission for Organ Transplantation of the German Board of Physicians, probably the organisation that mostly influenced the political and regulatory development of solid organ transplantation within Germany in the last twenty years.

Constanze was also an EFI inspector since 2006 and almost "permanently" booked as an active contributor for various educational activities covering the field of HLA-antibodies in solid organ transplantation. Constanze has been a listening and integrative "officer" and scientist. She has been one of the most pleasant colleagues and collaborators – always calm, objective, friendly, factual and fair, but still and always enduring, visionary and mostly efficient.
As Constanze went into retirement from the beginning of 2017, and because of her merits as a scientist in the field of Histocompatibility and immunogenetics in Europe, EFI recognizes her for the services she provided to the HLA community and honours her with the prestigious and well deserved "EFI-medal". It was a great pleasure and honour for me to be selected to give the laudation for her - a great colleague and friend - at the Mannheim EFI-conference.

Joannis Mytilineous

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Julia Bodmer Award 2017 – Dr. James Lee

The first Scientific Lecture at the Opening Ceremony of the annual EFI Conference is given by a young scientist winner of the Julia Bodmer Award (JBA). This Award was created in memory of Lady Julia Bodmer (1934-2001), one of the founding mothers of H&I and a mentor to EFI, whom she served as President from 1996 to 1998. Julia was well aware of the importance of young scientists for the future of our field, and was known for her encouragement and support to younger generations. The JBA winner is selected by majority voting within the EFI Scientific Committee, in a competitive review process between the applications filed. The first JBA Lecture was delivered in 2002 by Benedicte Lee. Over the last five years, it has been held by Hannah Siddle (2016), Céline René (2015), Clemens Hermann (2014), Daniele Focosi (2013), and Pierre-Antoine Gourraud (2012). A complete list of JBA winners can be found on the EFI website (http://www.efiweb.eu/awards/the-julia-bodmer-award.html)

This year, among five applications from five different countries, the selected JBA winner was James Lee, currently affiliated with two different Universities, Harvard and Cambridge. James is a true physician scientist, whose career reflects the power of translational science. He graduated with multiple honors from Medical School in Oxford in the UK in 2004, and became a member of the Royal College of Physicians in 2007. He then decided to enroll into a Wellcome Trust Clinical PhD program in the laboratory of Professor Ken Smith in Cambridge, where he worked on the genomics of inflammatory bowel disease. This led to the discovery of a novel expression biomarker in CD8+ T cells that predicts outcome in patients with Crohn's disease and ulcerative colitis, a finding that became the basis for a prospective clinical trial led by James of patient stratification and treatment.

After his PhD, James pursued both his research and his clinical activities in Cambridge, specializing in Gastroenterology in 2014. In 2013, he published a milestone Cell paper describing the novel inflammatory pathway FOXO3 which is modulated by a single genomic SNP and is associated with the outcome of, amongst others, Crohn's disease. Taking the lead from this discovery, James recently further unraveled the complex genomic architecture of Crohn's disease, in which susceptibility and outcome are modulated by functionally distinct SNP. This observation, published recently in Nature Genetics, has obvious important implications for the treatment of patients and for drug development.

In his JBA lecture entitled "The genetics of prognosis in Crohn's disease", James brilliantly presented his findings, managing to make complex data seem simple, and to eloquently underline the translational implications of his work. His presentation reminded us of the scientific and clinical potential of our field, and as such was very motivating to the entire audience of the 2017 EFI Conference.

Katharina Fleischhauer – on behalf of the EFI Scientific Committee

Jon van Rood Award 2017

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

The JRA winner 2017 was, University of Essen, Germany, for his presentation "HLA-DM mediates permissiveness of T-cell alloreactivity to HLA-DPB1". The two runner-ups were Alexander Celik, Hannover Medical School, Germany for his presentation "HLA-G mediated immune regulation is impaired by a single amino acid exchange at residue 110", and Niken Mahaweni, Maastricht University Medical School, The Netherlands, for her presentation "Clinically approved monoclonal antibodies and PM21 particle-stimulated ex vivo-expanded alloreactive natural killer cells: a potent combination against cancer cells".

Best Poster Awards 2017

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

The three Best Poster Award winners 2017 in random order were Daniel Fürst with his poster entitled: impact of MICA polymorphisms on HSCT outcome, Sara C. Lobo-Alves with her poster entitled: lncRNA polymorphisms and pemphigus foliaceus susceptibility, and Elisa Lahtela with her poster entitled: MHC SNP variants in sarcoidosis.

Thanks from Mannheim

Dear Colleagues

It was a great honour, also on behalf of the DGI, to host the EFI community from May 29 to June 2, 2017 in Mannheim and Heidelberg. With excellent speakers chosen by the EFI scientific committee, good weather and more than 1,000 participants from as many as 57 countries, we had a great scientific meeting with a good financial result. Thank you very much for your trust!

I hope you enjoyed the Opening Ceremony with great talks by the Julia Bodmer Awardee James Lee and the Ceppellini Lecturer John W. Kappler and performances of young artists from our Rhine-Neckar region.

Despite good weather, the scientific sessions were extremely well attended and I think it was worth staying with us until the Closing Ceremony; the talks at the very last day of the Conference, including those of the Best Abstract Session and the plenary session on Novel Technologies and the Closing Lecture by Ralf Bartenschlager on the 'Cure of HCV' will remain as unforgettable highlights in our memory.

Besides the other plenaries and meet the experts and teaching sessions, I am sure you also enjoyed the debates on MFI and NGS. Under the motto 'Translational Immunogenetics' 96 abstracts had been accepted as oral presentation. However, also among the contributions accepted as posters there was excellent science which we regrettably could not consider for the abstract sessions due to limited space.

Also with the help of good weather, the Gala Dinner at the Heidelberg Castle was, at least for us, a once-in-a-lifetime event.

All this, of course, would not have been possible without our PCO m:con and the generous support of the 12 sponsoring (efi2017.org/industry/sponsors) and 26 exhibiting companies. I would also like to thank my colleagues Volker Daniel, Michael Müller-Steinhardt, Sabine Scherer and Hien Tran and our secretary Michael Döntgen for their great help.

Now, our colleagues from Italy are preparing the next meeting. Please support this conference as well and book your hotel as soon as possible because I cannot wait to meet you all again in Venice!

Yours sincerely,

Caner Süsal
President of the EFI/DGI Joint Meeting 2017

Bursary reports from the EFI annual meeting in Mannheim

EFI offers a wide range of bursaries and among those are the bursaries for attending the annual meeting. There is no age restriction but applicants must be EFI members for at least one year at the time of application. Bursaries are preferentially given to participants with presentations at the conference. All recipients of a bursary were grateful to EFI for receiving the support, which enabled them to attend the meeting. In 2017, eight bursaries were given and here are their reports.

Petroula Gerasimou, Nicosia, Cyprus

The EFI conference was hosted in the small city of Mannheim. Mannheim is a city in the northwest corner of the state of Baden-Württemberg in Germany, at the confluence of the Rhine and Neckar rivers and as other German cities the amount of green scenery gives a great first impression. Notably impressive was that the Rosengarten, the conference hall of reddish brick where the speeches were held, had as a view the iconic Water tower. One of the most famous icons of the Arte-Nouveau style in Germany, the water tower (and small park surrounding it) was a great place to sit during breaks and lunch times.

The attendees at the conference had the opportunity to obtain knowledge from experts in the field of Histocompatibility and Immunogenetics as the conference offered speeches and lectures on a variety of topics including organ transplantation and diagnosis, immunotherapy, HLA population genetics, HLA in autoimmune disease etc.

My attention was drawn to the 'Meet the Experts' sessions as it was a great opportunity to exchange ideas and knowledge with key individuals in the H&I community. More specifically, on May 31st a 'Meet the Experts 2' session was held in the Gustav Mahler Hall 3 of the Rosengarten center were the HLA frequencies and their clinical applications were discussed. The session commenced with the talk by C. Müller (Ulm, Germany) on the 'Theory and challenges of HLA frequency estimation'. The population definition, the heterogeneity of samples, the sample size and precision were listed as the current challenges in frequency estimation. This was followed by an interesting speech by H. Eberhard (Ulm, Germany) on the 'Application of HLA haplotype frequencies in probabilistic donor matching'. This talk presented the potential of a more probabilistic approach on donor 'hunting' were the patients cultural background is also taken into consideration. Nevertheless, the speaker noted that it can be hard to assign the correct/best population specific haplotype frequencies to individual donors. The speaker concluded that population specific haplotype frequencies have the potential to improve match probabilities, broad haplotype frequencies are not completely wrong but further validation is necessary. The final talk of the session was given by M. Maiers (Minneapolis, USA) on 'How much do we know about HLA frequencies in the Middle East?'. The speaker presented a universal Middle Eastern haplotype showing that Middle Eastern populations have region-specific ancestral haplotypes different from European and North American populations. He concluded that these trends result in a significant need of unrelated donors for HCT in the Middle East, but few to no registries are able to meet the demand. Lastly, the session was chaired by A. Sanchez-Mazas (Geneva, Switzerland), a leading expert on HLA population genetics and her input and discussion remarks on each speech was of a great importance.

Alexander Celik, Hannover, Germany

My report is concerned with the second plenary session that focused on further improvements in hematopoietic stem cell transplantation, where utilization of mismatched donors and KIR matching as well as the need for post-transplant monitoring were discussed.

The first talk given by Dr. Annalisa Ruggeri (Hôpital Saint Antoine, Paris, France) was dealing with the utilization of HLA-mismatched donors. The number of haploidentical stem cell transplantations is constantly increasing (291% since 2005) and haploidentical donors are widely available. Due to selective allodepletion with post-transplant cyclophosphamide (PT-Cy) it is not necessary to select a donor with a minimum HLA mismatch to the recipient. The approach to haploidentical SCT differs between institutions, incorporating either RIC or MAC bone marrow (BM) with PT-Cy (John Hopkins) or mobilized BM with high numbers of immunosuppressive drugs (Chinese / Italian approach). Since the early 2000's BM is used as the primary stem cell source in non-T cell depleted (non TCD) haploidentical SCT, whereas PBSC are more frequently used in single centers. Here UCB has greater tolerance of donor-recipient HLA disparity than other graft sources, however, a total nucleated cell (TNC) threshold of 2-3 x 10^7 / kg is needed for engraftment. Allele level matching does lower NMR risks as well as an 8/8 match. If the minimum number of cells for a single UCBT is not achieved, however, a double UCBT should be considered preferably with an HLA match of 0-1, but no more than 2. Additionally, a class I MM should be preferred to a class II MM and HLA-C typing (avoiding C MM) should be included. Further considerations, if several CBU are available, include cord blood bank accreditation status and location, ABO compatibility, NIMA and KIR status. Double cord blood transplantation lowers the risk of relapse; however, it shows a higher GvHD incidence and is very expensive, nevertheless, in the

final outcome there was no difference to single blood transplants. Pre-formed donor specific antibodies (DSA) directed against CBU have a deleterious impact on transplant outcomes and recipient screening and identification of DSA should be performed using standardized methodology as part of donor selection. Comparing the outcome of UCBT and non TCD-haploidentical SCT, DSA can impact engraftment for both, whereas UCBT shows delayed neutrophil and platelet engraftment, non TCD-haplo on the other hand is comparable to MRD or UD. A low incidence of GvHD with less stringent HLA matching is needed in UCBT. In non TCD-haplo a low incidence of GvHD is achieved with BM and PT-Cy use or ex-vivo TCD. UCBT shows a strong GvL effect with the incidence of relapse being comparable with other stem cell sources; however, there is no possibility for DLI. In non TCD-haplo there is high relapse in some series using BM and RIC regimen. Non relapse mortality in UCBT is high due to graft failure, in non TCD-haplo lower NRM is observed when unmanipulated cells are used in comparison to $CD34^+$ cells. Lastly, overall survival in UCBT and TCD-haplo is comparable to the different stem cell sources in single centers and registries studies.

In the second talk, Prof. Katherine Hsu (Memorial Sloan-Kettering Cancer Centre, New York, USA) discussed the utilization of KIRs for HCT donor selection. The causes of death after unrelated donor HCT within the first 100 days post-transplant is caused to 23% by the primary disease, whereas after 100 days relapse of patients is increased up to 46%. Individuals express different types of KIRs, and inhibitory KIRs can recognize different HLA molecules that are routinely typed. The goal is to utilize anti-leukemic effects in HCT by maximizing activation and minimizing inhibition. NK alloreactivity due to *missing self* is obligated by HLA-mismatched HCT. However, NK alloreactivity due to the missing ligand is dictated by the HLA genotype. For utilizing KIR in HSCT the knowledge which KIR/HLA interactions can achieve the greatest anti-leukemic response in HLA-matched/compatible HCT and whether an intervention based on KIR is possible, needs to be expanded. The highly polymorphic KIR3DL1 occurs in >95% of individuals and in contrast to the activating KIR3DS1 does bind HLA-Bw4. The Bw4 epitope is present on 40% of HLA-B alleles. KIR3DL1 exhibits high, low or null surface expression, whereas the 43% of this allele are highly expressed and were shown to bind to Bw4-I80 with high affinity. Low expressed KIR3DL1 can be detected in 27% of the alleles and binds both I80 and T80 with equivalent affinity while the null expression variant in retained intracellularly. However, the control of NK inhibition is actionable and feasible. In AML patients weak/no interaction between KIR3DL1 and HLA-Bw4 subtypes were associated with lower relapse and higher survival. This effect is separate from and additive to KIR3DS1 effects for relapse and survival. Not only KIR genotyping but KIR allele typing selected donors is supported by the data to maximize leukemic control while minimizing unwanted toxicities. And considering that 100% of the population is 3DL1/S1+, donor selection based on 3DL1-Bw4 combinations is a feasible approach.

The session was closed by Dr. Luca Vago (San Raffaele Scientific Institute, Milan, Italy) who focused on leukemia immune escape. In allogeneic HSCT, relapse is still an unsolved issue. The incidence of relapse has not changed significantly over the last 20 years and currently available treatments for relapsing leukemia are largely ineffective while insights into the biological bases are still lacking. Considering HLA loss as one of the principles of leukemia immune-editing, HLA loss also occurs after unrelated donor HSCT, although frequency and risk factors still have to be assessed in larger cohorts. HLA loss is frequent and in at least 30% of relapses independent of the haploidentical HSCT platform employed and in the case of late relapse and especially in VHR patients with cGvHD HLA loss is to be suspected. Clinically relevant is the documentation of HLA loss where DLIs are inefficacious and isoforms may salvage treatment decisions. Ongoing studies aim to understand the underlying biology by generating a library of xenografts for HLA loss relapses and by trying to understand the role of NK cells in these conditions. Diagnostically, the development of new tools for the detection of HLA loss variants is necessary and in the clinic the investigation of the incidence and risk factors in different HSCT contexts in a large multicenter study needs to be assessed. Here, next generation sequencing will provide the means to detect the HLA loss in patients as well as post-transplant monitoring chimerism analysis. The development of new technologies to detect HLA loss early is also part of the HLALOSS study where its frequency in different transplant settings and identification of risk factors are analyzed.

Müberra Ahci, Essen , Germany

In this report I would like to focus on the hot topic: ***Next Generation Sequencing***. We started with NGS in the opening ceremony, we had abstract sessions, satellite symposiums and poster presentations with NGS, a debate and plenary sessions, that showed the impact of this novel technology. During the Opening ceremony we could already see that its application has a lot of contributions to the development of Immunogenetics. This year the Julia Bodmer Award was presented to Dr. James Lee from Cambridge, UK. His study was the first to characterize the genome wide genetic influences and biological determinants to the prognosis of inflammatory Crohn's disease. This is not only important for disease understanding but has also important implications for drug development.

The HLA award was handed over to Dr. Jamie Duke from Philadelphia, USA for their work on "Determining performance characteristics of an NGS-based HLA typing method for clinical applications". This confirmed the high interest of the audience and showed that this technology is not only used in research but also moving towards the daily clinical diagnostics. Since I am working with NGS for a part of my PhD project this was one of the publications which I enjoyed reading.

In abstract session 4 "New technologies and Antigen presentation" and 8 "Bioinformatics and Miscellaneous" several groups showed their experience and results by using different protocols and platforms for various applications of NGS. But not only research groups are working with this new technology. By the time companies started focusing on this method, as well. During the Satellite Symposium diverse companies showed their commercial kits and software for an easy use of NGS in the laboratories.

After we had a debate on "Exons only or whole gene typing" last year in Kos, Greece, this year the focus was "NGS – Should I wait or not". This already shows that the future is tending towards using this technology. But as it is always with a new evolving method there are a lot of different parameters to take into account which were discussed during this year's debate. Prof. Steven Marsh (London, UK) and Joannis Mytilineos (Ulm, Germany) pointed out the most important challenges we are facing when adapting this new technology to the field of Histocompatibility and Immunogenetics. One of the key arguments of Prof. Marsh, who favoured switching now, was the impact of NGS on the HLA matching of donor recipient pairs and the overall survival after stem cell transplantation. He underlined that by changing the technology and by looking at exon 4 we are able to get rid of the ambiguities, we had learned to live with. He showed a study by Hou et al. from 2017 where they looked at the matching status of class I alleles in unrelated donors and their recipients in 10/10 paired transplants. By comparing NGS to Sanger Sequencing they found 2.4% additional variations inside and/or outside the antigen recognition domain. The idea is implementing this method as soon as possible, to decrease the error rate and to find the perfect match for each patient as Prof. Marsh showed with the example of patient Esme.

Dr. Mytilineos was more focusing on the fact that it is not that easy to switch to a new method which just started evolving in our field. His argument was that it is important to know what we need high resolution for. The reason is that until now there is no scientific proof that inclusion of polymorphic information from other exons or even intronic regions are associated with better outcome in HSCT. He claimed that besides the pros this technology promises one will face challenging considerations when implementing NGS in the routine diagnostics.

Pros can be: maximum resolution with small quantities of DNA possible, less ambiguities for the perfect match, more genetic information on polymorphisms and the most important advantage of NGS, lower costs by high throughput. **But very important questions to consider will be:** the cost-benefit analysis. Do I really have that high throughput? If not; is it better to partner to have a faster turnaround time for the clinical service? Can I afford the costs for reagents and equipment like robotics or IT infrastructure (software and servers)? Which platform do I use? Which protocol will it be? Will it be shotgun, whole gene or exon based analysis? Will it be commercial or in-house? Do I type more genes like KIR or HLA only? Where do I store all the large data volumes? Am I allowed to upload patient data onto a cloud service? How do I manage the workflow and staff training? Do I have bioinformaticians? Do I have a back-up method in case of problems?

The debate was a chance to see that many labs are willing to switch towards NGS typing but have strong concerns about the implementation of this technology. In my opinion the most important task now is to focus on association studies and show that these newly identified polymorphisms and all the newly generated data on the IMGT database have indeed a "translation" into the clinical practice like in autoimmune disease risk, T cell alloreactivity and patient outcome after transplantation. NGS is a powerful technique which will provide us high quality data with complete information and surely it is the future, particularly for the long road to the identification of the ideal donor. But is there any reason to rush? After NGS appeared in 2005 it took a while until it entered the field of transplantation. Now in 2017, a decade later, we can see that we are more and more moving towards personalized medicine. Therefore, I am very curious to see how much we will have achieved with this technology at the upcoming conferences.

Natalija Martinez, Zagreb, Croatia

The meeting program of the congress was excellent with many quality lectures and presentations on a variety of topics. The lectures that impressed me are related to epitope matching in organ transplantation.

HLA matching of donor and recipient is beneficial for the outcome of most types of solid organ transplants. But, the polymorphism of the HLA system makes the selection of an HLA identical unrelated donor very difficult. The identification of crucial amino acids on the HLA molecules (HLA epitopes), which are responsible for the induction and reactivity of HLA

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antibodies, is very important. So, every HLA molecules carries a unique set of antibody epitopes, but the individual epitopes are often shared with other HLA alleles. The number of HLA epitope mismatches between donor and recipient instead of counting the number of HLA mismatches may be a better approach to predicting transplant outcome.

The predicted indirectly recognizable HLA epitopes (PIRCHE) is designed to predict indirectly recognizable HLA-derived donor peptides that are likely to induce the production of donor specific anti-IgG antibodies. High number of PIRCHE, likely to represent a higher number of epitopes that can be presented by HLA class II molecules, correlate with a higher incidence of antibody formation, suggestive that the relevant T cell epitopes are included in this algorithm.

The main conclusion is that moving from HLA matching to HLA epitope matching might be beneficial for more reasons.

The first one is improving the outcome of virtual crossmatching, prediction of acceptable HLA mismatches that will enhance kidney allocation to highly sensitized patients awaiting transplantation, diminish the chance for de novo DSA development and improving graft outcome, minimize the risk of post-transplantation allosensitization, especially in children and young patients who will need re-transplantation in their life.

The final goal should be a reliable prediction of antibody formation for an individual patient as well as post-transplantation immunosuppressive therapy for each patient separately.

Dmitry Klyuchnikov, Samara, Russia

It was the first time I attended the annual EFI conference and it was the biggest conference I ever saw. The program of this conference was so great and highly topical. At the opening ceremony all the participants enjoyed the amazing dance of David Kwiek and fascinating and charming songs of Ron Jerome and Luna & Lewis.

I visited many sessions and got a lot of new information about diagnostics of HLA loss, graft survival analysis and markers for GvHD, HLA crossmatch assay, autoimmunity and immuno-editing. I still remember the reports of Carlheinz Müller, Hans-Peter Eberhard and Martin Maiers in the session about clinical applications of HLA frequencies. Now I can say that I know a thing or two about probabilistic donor matching and match rates. NGS implementation for HLA typing is no more a very big question thanks to warm debates of Joannis Mytilineos and Steven Marsh. As for me I'm on the side of Joannis, and I guess that he was sounding rather convincing. The reports in the session on reproduction and autoimmunity were also very interesting for me. Last year we performed some work on HLA association with recurrent miscarriage and natural sterility, and I think now I know how to finish it.

Also, my colleague Larisa Trusova and I presented a poster about distribution of alleles and haplotypes in Russian and Tatarian populations of Samara region. Moreover, I saw a lot of interesting posters about Nanopore sequencing, HLA association and many others.

I was very happy to meet all our inspectors, our colleagues and friends from the Netherlands, Croatia, Germany, Russia and Kazakhstan. I got a lot of ideas about our work and I guess we have a lot to improve in our lab in Samara. Some new ideas about our population genetics studies, upgrading our laboratory system, implementation of new software for analysis and methods. I was very excited about the meeting, the number of reports and posters, and I will do my best to attend the meeting in Venice next year.

Jessica Catalina Ruiz Munevar, Bogota, Colombia

Report of the presentation "Autoimmunity: Pathogenic CD4 T cells in diabetes"

The speaker, John Kappler, began the presentation by mentioning how proteins could have a lot of polymorphisms and how this fact could influence the immunogenicity in the organism. There are a lot of possible polymorphisms and some can be more immunogenic than others. For this reason, this variety plays an important role in T cell recognition.

Understanding the connection between protein polymorphisms and immunity has been the goal in the past few decades, in order to find the relationship between MHC-mediated antigen presentation and autoimmunity diseases like diabetes, because it would open the door to investigate how the recognition of antigens proceeds in this disease.

A NOD mouse model was used because it has extensively been studied. First, a peptide and two T cell clones were identified that play an important role in diabetes in NOD mouse. They continued studying the role of these elements

and found that there was no recognition between the peptide and these T cell, so the hypothesis was that the peptide had an inhibitory effect on these T cells and by changing an amino acid, the binding of the peptide would change.

They evaluated some amino acid mutations in specific positions and specific insulin-derived peptides. A specific mutation produced a peptide with a stronger binding with TCR in comparison with the other peptides evaluated. This peptide leaded to an increase of affinity with the studied T cells, causing the stimulation of these clones which haven't shown reactivity before towards the original peptide.

By doing this specific mutation, they found an enormous increase in the interaction with the peptide, and binding changes in β-chain of the TCR. They studied additional mutations of different amino acids in this peptide, and found similar results, so it was confirmed that one specific amino acid position served as the clue in the insulin-derived peptide/TCR affinity.

Transpeptidation is the opposite process of proteolysis. In this process two peptides are put together and it occurs in the proteasome. In the case of diabetes, it is believed that the insulin-derived peptide is reformed by binding two peptides that weren't initially together, and this would be the mechanism employed by the cell to obtained the specific mutation that increases the immunogenicity.

The conclusion of this study was that posttranslational modifications would be essential in the autoimmunity in diabetes because they would cause the mutation required to generate the immune response when mutated insulin-derived peptide is presented to T cells, and this behaviour leads to the diabetes.

Katerina Tarassi, Athens, Greece
Teaching Session 3 - Epitope matching in organ transplantation

The teaching session started with an introduction on epitope matching in organ transplantation by Frans Claas (Leiden, the Netherlands). It is well established that HLA matching between donor and recipient is beneficial in most types of solid organ transplantations and especially in kidney transplantation. However, as the polymorphism of HLA system is extremely high (almost 15,000 HLA alleles up to now), the chance to find an HLA identical unrelated donor is very low. On the other hand, structural analysis of HLA molecules enables the prediction of their immunogenicity. It is clear now that every HLA molecule carries a unique set of epitopes but the individual epitopes can also be present on other HLA alleles. As a consequence, the immunogenicity of a specific mismatch is different for individual patients. Furthermore, the number of epitope mismatches predicts the chance that an HLA mismatch will lead to *de novo* antibody formation after kidney transplantation. In an immunized patient, an immunogenic epitope can induce antibody formation but additional amino-acid differences in the vicinity of the immunogenic epitope determine whether antibody binding will occur.

The second speaker, Sebastiaan Heidt (Leiden, the Netherlands) focused on the second application of epitope-matching in virtual crossmatching for patients with already existing antibodies. Only a few amino-acid differences may by the trigger for antibody formation, but the actual antibody may need up to 6 crucial contact sites with the HLA molecule in order to react with the mismatched HLA allele. So, careful analysis of the HLA epitopes recognized by the existing antibodies enables prediction of a positive or negative crossmatch in immunized patients (virtual XM). Additionally, future matching strategies will be based on epitope-matching, as it is less complicated (polymorphism can be explained by about 180-200 crucial epitopes instead of more than 10,000 HLA class I alleles) and prevents antibody formation.

Finally, Eric Spierings (Utrecht, the Netherlands) analyzed the role of PIRCHE (Predicted Indirectly Recognizable HLA Epitopes) computational algorithm, which is designed to predict indirectly recognizable HLA-derived donor peptides that are likely to induce the production of donor-specific anti-HLA IgG antibodies. The most relevant anti-HLA antibodies are of IgG class and $CD4^+$ T helper cells are crucial for such class switching (from IgM to IgG). T cell dependent antibody responses require the activation of B cells by T helper (Th) cells that respond to the same antigen. The exact epitopes recognized by B and Th cells may be different but physically linked (linked recognition). Peptides derived from the HLA molecules of the donor (over 350 HLA-derived peptides have been eluted from HLA) must be presented by class II molecules on the surface of B cells to cognate $CD4^+$ Th cells, which then provide signals and cytokines to these B cells to

undergo activation and differentiation. As a consequence, the type of anti-HLA antibodies produced after transplantation depends on HLA-DRB1 alleles of the recipient. PIRCHE-II can reliably be estimated using serological splits, although PIRCHE-II estimation could be significantly increased in precision if HLA high-resolution typing of the recipient is used. It is concluded that 1) PIRCHE-II algorithm (T-cell epitopes) and Matchmaker score (B-cell epitopes) independently predict *de novo* DSA formation and allograft survival, 2) combined PIRCHE/Eplet score is independent risk factor in order to stratify *de novo* DSA formation and 3) PIRCHE-II can classify kidney transplants in low and high risk. Therefore, risk profiling could be used to anticipate on the PIRCHE probability.

It is clear that epitope matching has more potential that classical HLA matching, especially for the prediction of *de novo* antibody formation after transplantation.

Marja Marchesani, Helsinki, Finland

Abstract Session 5 – Reproduction, Autoimmunity, Infection &Cancer

The first speaker of the session was Julie Di Christino. Her research related to HLA-G polymorphisms and scleroderma. The results indicated that the decreased production of soluble HLA-G observed in scleroderma is not genetically determined, but rather the result of epigenetic mechanisms.

The second presentation by Kirsten Geneugelijk indicated the fact that a previous miscarriage and a previous successful pregnancy have a different impact on HLA antibody formation during a subsequent successful pregnancy. The results indicate that the percentage of immunogenic antigens was significantly lower after a single successful pregnancy that was preceded by single miscarriage compared to a successful pregnancy.

The third presentation by Nina Svetlicky related to anti-neutrophil-cytoplasmic antibody (ANCA)-associated vasculitis. The study concentrated to the ANCA-myeloperoxidase modulated neutrophils activity by immunodominanat epitope identification. This research demonstrated the homology of amino acid sequence of RL-14 peptide to Staphylococcus aureus membrane protein.

The fourth presentation by Silvia Gregori indicated new HLA-G-related biomarkers for staging Type 1 Diabetes(T1D) This was the first demonstration that DC-10 frequency progressively decrease in first-degree relatives according to the risk to develop T1D and the data supported that HLA-G genotype may be associated with T1D.

The fifth presentation by Shiva Dahal-Koirala indicated that 5 Pre-Existing clonotypes dominate the CD4 T cell response to gluten antigen re-exposure in celiac disease The group demonstrated that the T-cell response to gluten is dominated by clonally expanded T cells, and that the majority of expanded clonotypes at peak response were present prior to challenge suggesting a pre-determined T-cell receptor repertoire that does not change upon antigen re-exposure.

The sixth presentation was my presentation. I talked about genetic variations in classes I and III of MHC that associate with acute coronary syndrome (ACS) in Finnish population. We studied 13.580 SNPs and 3594 ACS cases from different parts of Finland. The most significant novel result was the risk haplotype of 3 SNPs from ATP6V1G2-DDX39B-LTA genes with p-value of 2.0E-26(OR=3.42) and r2 values of ≥0.68.Our results indicated that we have identified novel and confirmed previously known ACS risk variants of MHC genes.

The final speaker of the session Umut Özbek gave also the interesting presentation

The group examined correlations between SNPs and common HLA epitopes (Bw4/Bw6; C1/C2) / genetic supertypes (DR52/DR53) in a panel of 95 HLA-typed cell lines using ImmunoChip genotyping and 8,045 SNPs. They found proxy SNPs for each epitope/supertype. The strongest proxy for C1/C2, rs12211087 is the top GWA risk marker for psoriasis (P=5E-723). Four SNPs for example showed strong correlations with DR53 and were among the top GWAS hits for rheumatoid arthritis, ulcerative colitis and sarcoidosis.

The session 5 had very nice scientific atmosphere with several interesting and important questions for the speakers!

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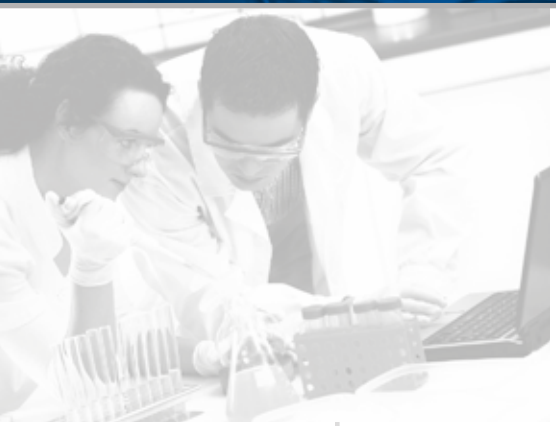

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Highlights from the HLA journal

By Luca Vago, Section Editor HLA journal

Starting from the present issue of the EFI Newsletter, we are introducing a brand new section, to highlight the most exciting and relevant manuscripts published recently in "*HLA*", the official journal of EFI. Please be aware that all EFI members have free access to all of the content from "*HLA*" via the members only area of the EFI website.

Over the last four months, a number of really intriguing works have been published in "*HLA*", and amongst them the ones that we found to be especially relevant to the EFI newsletter audience were:

TypeLoader: A fast and efficient automated workflow for the annotation and submission of novel full-length HLA alleles.

Surendranath V, Albrecht V, Hayhurst JD, Schöne B, Robinson J, Marsh SGE, Schmidt AH, Lange V.
HLA. 2017 Jul;90(1):25-31. doi: 10.1111/tan.13055. Epub 2017 May 14.
Highlights: inevitably, humans have the propensity for error, particularly when facing repetitive tasks, and having to adhere to strict database format specifications. Therefore, it is pivotal to automate such procedures to minimize error and save time. To facilitate the upload of full-length HLA alleles to sequence repositories, the new open-access bioinformatic tool Typeloader has been developed, automatically performing sequence annotation and all the steps involved in preparing the specific formats required for submission, reducing by more than 95% time spent on these procedures as compared to standard manual upload.

Scandiatransplant acceptable mismatch program (STAMP) a bridge to transplanting highly immunized patients.

Koefoed-Nielsen P, Weinreich I, Bengtsson M, Lauronen J, Naper C, Gäbel M, Sørensen SS, Wennberg L, Reisaeter AV, Møller BK; Nordic Kidney group and the Tissue Typing group in Scandiatransplant.
HLA. 2017 Jul;90(1):17-24. doi: 10.1111/tan.13046. Epub 2017 Apr 27.
Highlights: Inspired by the Eurotransplant acceptable mismatch program, the Scandiatransplant acceptable mismatch program (STAMP) was launched in March 2009, to prioritize highly immunized patients. The aim of the program was to increase the likelihood of transplantation in highly immunized patients without increasing the risk of acute antibody-mediated rejections. Between March 2009 and February 2015, 96 highly immunized patients underwent kidney transplantation from deceased donors selected based on acceptable mismatches, resulting in an overall allograft survival at 5 years of 79.1%.

Dual redundant sequencing strategy: Full-length gene characterisation of 1056 novel and confirmatory HLA alleles.

Albrecht V, Zweiniger C, Surendranath V, Lang K, Schöfl G, Dahl A, Winkler S, Lange V, Böhme I, Schmidt AH.
HLA. 2017 Aug;90(2):79-87. doi: 10.1111/tan.13057. Epub 2017 May 25.
Highlights: this paper describes a novel workflow that had been developed for whole-gene sequence characterization in order to submit novel alleles and sequences that are incomplete in the IPD-IMGT/HLA Database. This "dual redundant sequencing strategy", based on the combination of shotgun sequencing on an Illumina MiSeq instrument with single molecule real-time (SMRT) sequencing on a PacBio RS II instrument, allowed the full-length gene characterization of 1056 HLA alleles, more than doubling the number of fully characterized alleles in the IPD-IMGT/HLA Database.

Effects of weak/non-complement-binding HLA antibodies on C1q-binding.

G. Hönger, P. Amico, M.-L. Arnold, B. M. Spriewald and S. Schaub
HLA. 2017 Aug;90(2):88-94. doi: 10.1111/tan.13062. Epub 2017 Jun 5.
Highlights: HLA antibodies in the serum of humans are usually polyclonal in nature and contain mixtures of IgG subclasses. It is unknown under what conditions and to what extent weak/non-complement binding IgG subclasses can block C1q-binding triggered by complement-binding IgG subclasses. Various IgG subclass variants of an HLA class II-specific monoclonal antibody were tested in isolation or in combination in single antigen bead assays for C1q binding. It was found that when targeting the same epitope, an excess of IgG2/4 represses the extent of IgG1/3 triggered C1q-binding in vitro. Since such IgG subclass constellations can be found in about a third of sensitized patients, this may be a relevant finding warranting further research.

Pronase treatment improves flow cytometry crossmatching results.

Apithy MJ, Desoutter J, Gicquel A, Guiheneuf E, Westeel PF, Lesage A, Piot V, Choukroun G, Guillaume N.
HLA. 2017 Sep;90(3):157-164. doi: 10.1111/tan.13073. Epub 2017 Jun 28.
Highlights: The flow cytometry crossmatch technique is the most sensitive cell-based method to detect donor-specific antibodies. Unfortunately, background flow cytometry crossmatch reactivity is elevated in assays using B lymphocytes. This article shows that pre-treating lymphocytes with pronase can drastically reduce the presence of kappa light chains and Fc receptors on B cells, while maintaining acceptable levels of expression of CD19, CD20 and HLA class-I and -II molecules, thus improving the sensitivity and specificity of flow cytometry crossmatching.

In addition we would like to point the attention of the EFI newsletter readership to some excellent reviews from internationally renowned opinion leaders on the topic of transmissible cancers (H.V. Siddle, April issue), hematopoietic stem cell transplantation and cellular therapies (H.J. Kolb, May issue) and epitope matching in renal transplantation (F.H.J. Claas, July issue).

Finally, we would like to remind everybody that the June issue of "*HLA*" was a special issue, collecting all the abstracts from the 31st EFI Annual Conference, held in Mannheim/Heidelberg, Germany between May 30 and June 2, 2017, thus granting the opportunity to the entire EFI community to get a glimpse to all the innovative findings presented at the excellent meeting of our Society.

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