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3-6 October 2012
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UPDATED!
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Call for Participation

Participate in NEMO study
Read more

Do you offer STAT3 mutation detection?
If yes, kindly contact Prof. Dr. Bodo Grimbacher under b.grimbacher@ucl.ac.uk

NEWS @ ESID

President's Corner

Dear Friends,

only two months passed from my last letter and we were able to finalize the program for our next meeting in Florence in October.

The program is very interesting and I am sure that all of you who will attend the meeting will enjoy both the science and the wonderful city of Florence!

I take the opportunity of this short message to wish you all happy holidays and wishes for the New Year which for sure will be very exciting to our society.

Amos
ESID President

Secretary's Corner

Dear ESID members,

The New Year is coming and new ideas and events are being discussed. I would like to give you an update on the ESID initiatives and problems reviewed during the last ESID Board Meeting held in Amsterdam at the end of October. I would like you to pay special attention to the "hot topics" described below and if possible, hear your opinion, criticisms and suggestions. I will summarize issues discussed during that meeting:

- **ESID biennal meeting:** we have finalized the programm of the next ESID biennal meeting (please see the Treasurer' s report)
- **Financial support for ESID activities:** we have thoroughly discussed and decided on the rules concerning ESID financial support for scientific meetings. The ESID board has decided to support four speakers from ESID to attend the next African Society for Immunodeficiency (ASID), that will be held on March 2012 in Hammamet (Tunisia) organized by Prof R. Barbouche. The scientific programme is available on **www.asid.ma**
  and on our ESID web site.
  Moreover, travel grants have been approved for the workshop in Freiburg organized by the ESID Registry Working Party (please refer to Dr Stephan Ehl).
- **ESID Endorsed Meeting:** we have long discussed whether or not the ESID logo can be applied to educational activities that fulfill the scope of ESID's mission and objectives. Finally, we agreed that under specific conditions, ESID can endorse educational/ scientific events. The main points are as follows:

  The candidate should submit the proposal to the ESID Board at least three months in advance to give enough time to the Board members to examine and understand whether the endorsement is appropriate. The application form can be found on the ESID website or directly required by sending an e-mail to my address (**villa.anna@hsr.it**) or to **esid.admin@kenes.com.**

  On the application you should indicate:
  - The details of the meetings (name venue dates organizer)
  - That the organizers are active ESID members
  - The Preliminary Scientific Programme, including invited speakers

  If there is a secondary or follow-up meeting, re-application is mandatory.

  The endorsement does not entail any financial or other obligations/liabilities on the part of ESID. The ESID

Endorsement Guidelines are now available on the ESID website and should be carefully read before submitting any proposal.
This initiative represents a good opportunity to strengthen the awareness of PID around the world and increase the interactions among different European centers. At the same time, we have to maintain the control of the scientific quality proposed. I would be grateful to have your feedback, suggestions and criticisms on this decision taken by the Board. I know that some of you had some concerns about this issue and I would like you to share your opinion and bring your objections to the Board table. Please send me an e-mail, let me know your thoughts.

- **FOCIS Society:** we have been approached by FOCIS, which is now the Federation of Clinical Immunology. Unfortunately, the previous agreement of a reduced membership fee for the FOCIS meeting was not renewed. We are trying to mediate a new agreement.
- **Board Elections:** Every two years we need to elect or renew the terms of office of some of our Executive Board members. The next article of this newsletter will give you the full details on the terms of each position. Please consider that your application and participation are important to improve and bring new ideas to our Society. Please send your applications together with a programme letter to **esid.admin@kenes.com**.
- **Call for Next Biennial meetings:** As Bids for biennial meetings take place four years in advance, we have been calling for applications. As you know, Anne Sediva will organize the next ESID Biennal Meeting 2014 in Prague. Now we can accept applications for the coming years, please send a formal application to my attention or **esid.admin@kenes.com**.

The following information may serve as a guideline for the bidding process:

- The Host must be a full member of ESID
- Include details of the proposed city and venues - including description of facilities, travel connections and clear indications of restrictions for entering the country
- Include availability of hotel rooms in the proposed city
- Propose dates (preferably for October)
- Include suggested programme outline
- Include possible social events
- Provide finances/provisional budget and information on local tax rules

- **Renewal**
  I would like to ask all of you to support our Society by convincing new members to join ESID. I would like to remind you of the benefits of ESID membership:
  - Reduced registration fee to ESID biennial congress
  - Access to a privileged network of PID professionals
  - Eligibility to receive awards: travel grants, fellowships, publications
  - Preference to take part in ESID PID Schools
  - ESID Newsletter (quarterly)
  - Access to ESID website members only area
- Finally, I would like to draw your attention to the new **Osteopetrosis Guidelines** edited by Ansgar Schuz (Ulm) and are reported in Bobby Gaspar's report.

All my best for a peaceful New Year to you and your families.

Anna
villa.anna@hsr.it
Tel +390226435273

Treasurer's Report

Dear all,

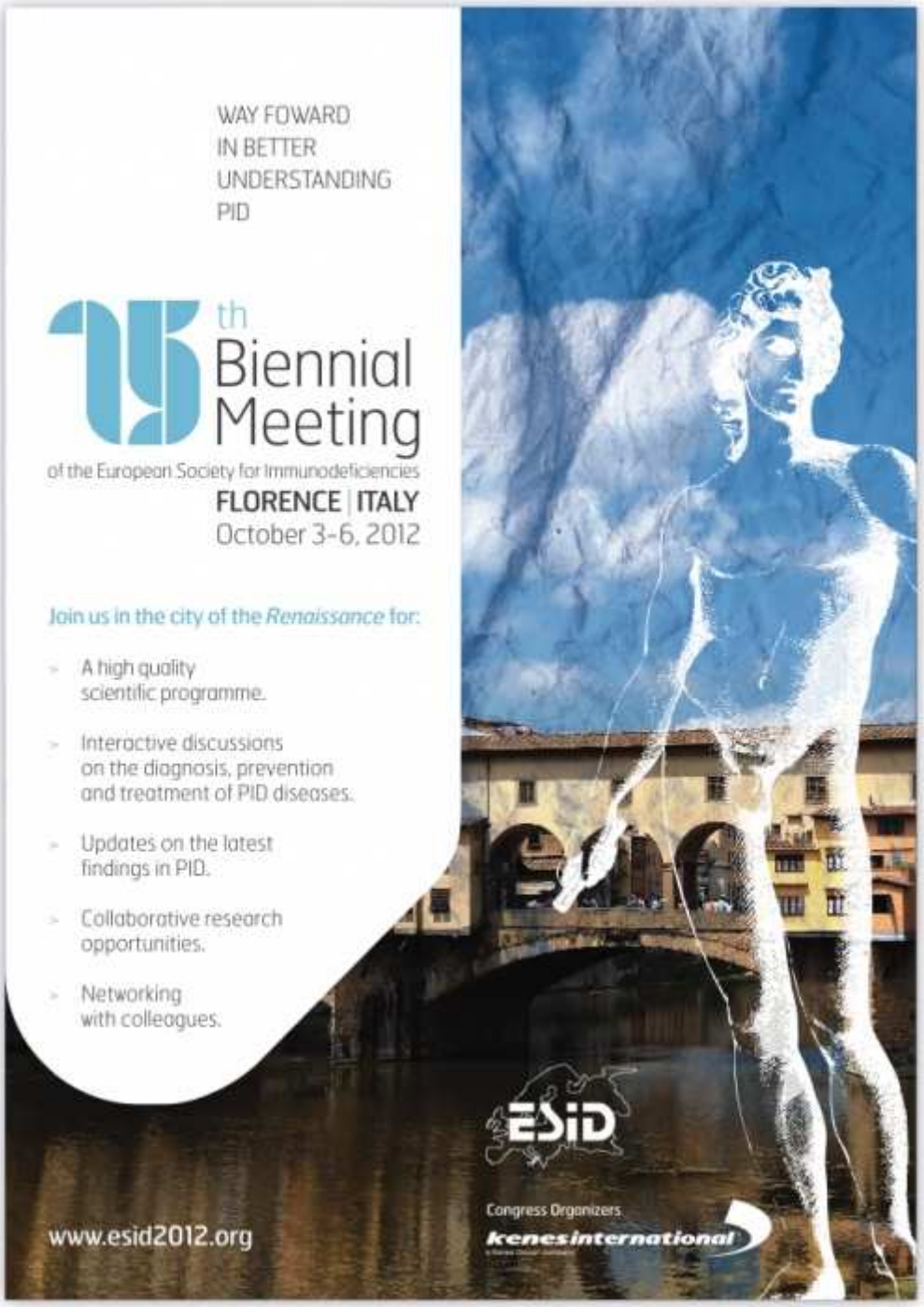
The Holiday Season is approaching and the 2012 will bring a lot of new exciting things!
First of all, the Florence meeting in October! The program is finalized! All the invited speakers have confirmed their participation and mostly the abstract submission process is now open!

NEWS @ ESID

There will be also important news regarding posters and awards, so please keep checking the website and stay tuned!
Official ESID 2012 Website

Happy Holiday Season to you all!

Eleonora Gambineri
ESID Treasurer & 2012 Congress President



News: ESID Working Parties

BMT & Gene Therapy

Dear All

We are all reaching the end of the year and I'm sure you have all had a very busy time. There are a number of important issues that have concerned the BMT and GT WP party over the past year and I will take the opportunity to summarise these:

1) I think we should be very happy with our achievement of producing the Guidelines document. This is something very tangible that our Working Party can generate and offers considerable help for immunodeficiency units worldwide. I again thank all those of you who have contributed and helped put this together. It truly has been a collaborative exercise. I also recognize that the guidelines are an evolving process and I have suggested that we incorporate changes on a yearly basis. However, sometimes we need to make changes quickly and I was informed of an important misunderstanding in the initial document regarding Treosulfan dosing. This has now been rectified and a revised version named 'EBMT_ESID GUIDELINES FOR INBORN ERRORS FINAL 2011' has now been uploaded to both the ESID and EBMT websites. Please use and distribute this revised version.
2) Nizar Malahoui and colleagues at Necker hospital have also worked very hard in generating a new SCETIDE data collection form. This is now being finalized and will also be incorporated into a new data collection system to be held at Necker under the supervision of Paul Landais. The major benefit of this is that it will allow improved mobility of data between SCETIDE and PROMISE (the EBMT database) so that centres will not need to enter data to both databases. I once again thank Nizar, Paul Landais, Alain Fischer and Virginie Courteille for their considerable efforts in putting this together
3) I am also attaching with this letter, the amended guidelines for diagnosis, therapy and follow-up of patients with osteopetrosis. This will also form the basis of a new study to collect data on this patient population. My thanks to Ansgar Schulz, Anna Villa, Despina Moshous and Colin Steward for their hard work on this.
4) I have recently informed you of issues within reorganization of EBMT. There have been proposals to reorganize the working party structure and to merge the Inborn Errors Working Party (which is essentially the EBMT equivalent of the ESID BMT> WP) with a generic Paediatric diseases WP. We have argued strongly that Inborn Errors, which predominantly covers the severe immunodeficiencies, should have a strong identity given the rarity of these conditions and the difficult transplant related issues they raise. Decisions will be made at an EBMT board meeting in January and I will keep you updated of the outcome. Rest assured however, that whatever the outcome, a forum for discussing transplant and other management related issues relating to severe immunodeficiencies will remain and the collaborative spirit of education and research into these conditions will be maintained
5) Finally, my WP highlight of the year is as always our Autumn meeting, organized and hosted this year in Belgrade by Mario Abinun and Srdjan Pasic. Many thanks to both of them for putting together a most enjoyable meeting and we had numerous excellent contributions including a number from the USA. I will let you know more details of the 2012 meeting once they have been finalized

It remains for me only to thank you all for all your contributions to the WP this year. I hope you all have a very enjoyable and restful holiday season and my best wishes to you all for 2012

Bobby

NEWS @ ESID

Clinical

Dear all,

Update on current activities:

- **Development of SOP for diagnostic criteria in PIDD and CVID**:
  The project will be finalized in beginning 2012.
- **Diagnostic workshops**:
  The first Diagnostic workshop for PIDD was held in Freiburg on the 21./22.10.2011. About 60 participants discussed with Stephan Ehl, Philipp Henneke and me the diagnostic work up of combined immunodeficiency, innate immunodeficiency and primary antibody deficiency. The workshop was very well appreciated and I can highly recommend to establish similar activities in your country. If you plan any activity in your country please let us know we are happy to endorse meetings focussing on diagnostics of immunodeficiency and support you with our experience. On the upcoming ESID biennial meeting in Florence we will focus the Workshop of the Clinical Working party on “Diagnostics in combined immunodeficiency”.
- **ESID endorsement is now available for meetings on PID!**
  You are now able to request ESID endorsement for your meeting (logo usage etc. but no financial support) year round. The right to organise ESID-Endorsed Meetings is one of the benefits of ESID membership. Requests should be sent to the ESID Administrative Office by e-mail (esid.admin@kenes.com) at least 3 months prior to the event and are subject to the approval of the ESID Board. For details see: **http://www.esid.org/home-new-esid-endorsed-meeting-application-394**
  The decision on potential financial support by ESID for activities in the field of PID has been postponed and is expected beginning 2012.
- **BCGitis in PIDD**:
  The survey has been closed and the data evaluated and are currently prepared for publication.
- **Splenectomy in CVID**:
  The manuscript was submitted and we are awaiting the reply of the reviewers.
- **NEW! NEMO study**:
  Capucine Picard, Jordan Orange and Jean Laurent Casanova initiated a multi-institutional survey of the CLINICAL and Immunological PHENOTYPE of NEMO-deficient patients. This important call is now open and looks for all centers to contribute NEMO patients.
- **Immunosuppressive treatment in CVID**:
  The survey in four centers is ready for submission. We are currently preparing a proposal for a subregistry in the ESID registry in order to prospectively follow up on the outcome of immunosuppressive treatment in CVID. Similarly, PBSCT has become a treatment option in selected CVID patients. Marta Rizzi et al has just published a manuscript on our experience with the first 4 patients (M. Rizzi et al J Allergy Clin Immunol. 2011 Dec;128(6):1371-1374). In order to collect all cases we also prepare a subregistry for PBSCT in CVID to be announced in late January 2012.

Thanks to all of you who have supported this work. I wish all of you a merry Christmas, a time to reflect the new ways to support our patients so we can start into an exciting New Year 2012.

With best regards,
Klaus

NEWS @

Education

Dear all,

For the November round of ESID Short-term Educational Grants (1 month, €1000), we had 5 applications, from which 2 were selected. Wesal Abbas, a laboratory specialist from Sudan, will go to the Centre for Chronic Immunodeficiency in Freiburg, Germany, to gain knowledge upon laboratory diagnosis of PIDs. Gaspar Markelj, a clinician working with PID patients from Slovenia, will go to Newcastle, UK, to gain further clinical experience in PIDs and its treatments; interestingly, he will be there at the same time a Slovenian patient is being transplanted in the unit.

Best wishes, Esther de Vries, Chair of the Educational Working Party of ESID

Genetics

NEMO study

Dear colleagues,

We would like to initiate a multi-institutional survey of the CLINICAL PHENOTYPE of NEMO-deficient patients. We would like to invite you, as a physician caring for such patients, to take part in this survey.

Our hope is that the combined efforts of multiple institutions will allow us to define the clinical phenotype of this disease in more detail. This study could potentially facilitate the development of treatment guidelines for this heterogeneous genetic disorder.
We intend to publish the results of this survey in a clinical journal focusing on clinical hematology and immunology or pediatrics in the near future, to raise the awareness of clinicians concerning this condition.
NEMO-deficient patients have several features of special interest to us for the purposes of this survey (survey for download below):

1. EDA phenotype
About 90% of the NEMO-deficient patients described to date have EDA, with sparse hair, abnormal teeth (conical teeth, tooth agenesis) and hypohidrosis (a lack of sweating). Could you please provide us with a description of these abnormalities in your patients and their families?

2. Infection

- Please provide clinical data for infections, as follows:
- Invasive bacterial infections (meningitis, sepsis, arthritis, deep inner abscesses)
- Opportunistic infections (pneumocystosis, chronic candidiasis etc.)
- Mycobacterial infections
- Severe viral infections
- Other infections

3. Signs of inflammation

a) Clinical signs
- Some patients develop a disseminated skin eruption, dermatitis, eczema and/or erythema early in life. Please provide a clinical and histological description of these conditions if observed in your patients.
- Colitis is also found in 21% of patients and some patients have intractable diarrhea with failure to thrive. Please indicate whether your patient displayed irritable bowel disease.

b) Biological signs
We would like to determine whether NEMO deficiency is a condition that predisposes the patient to

the development of severe infections in a context of weak inflammation. We would therefore like to ask you, in particular, for:

- The date of onset of infectious episodes, as provided by the patient's parents or guardians, and all dates of the analyses provided.
- Please provide at least three values for the following parameters: temperature, CrP, ESR, total white blood cell count and differential blood count. Please provide the values immediately after admission, the maximum value during the infectious episode and the value immediately before discharge.

4. Immunological status

a) T-cell immunophenotype and T-cell proliferation
The immunological parameters used for diagnosis, such as the numbers of blood phagocytes, B and T lymphocytes, lymphocyte subset distribution (CD4, CD8), T-cell proliferation in response to mitogens and antigens, are generally normal in most patients tested, but some patients have been reported to display weak T-cell proliferation in response to OKT3.

b) Specific antibody deficiency/ deficiency of antibodies against polysaccharides
Please provide information about antibody production (IgG, A, M and specific antibodies).
NEMO patients are unable to mount an adequate response to polysaccharides. Please provide us with information concerning the corresponding vaccinations (dates and vaccine used: 7-valent conjugated, 13-valent conjugated or 23-valent non conjugated?) and the results of serological tests for antibodies against polysaccharides. Please also state whether your patients have allohemagglutinins.

5. Treatment

Please provide as much detail about the treatments administered as possible (e.g. generic names of antibiotics, route of administration and duration of treatment). We would also like to know whether your patients have undergone transplantation and the details of the procedure if they have (conditioning regimens, donor, engraftment and outcome).

We would be delighted if you would agree to participate in this study, by completing the attached questionnaire, paying particular attention to the points of interest outlined above. If you have any further questions, please feel free to contact us under:

Laboratory of Human Genetics of Infectious Diseases
Faculté de Médecine Necker, 156 rue de Vaugirard
75730 Paris Cedex 15, France
Tel 33 1 44 49 50 88, Fax 33 1 42 73 06 40
E.mail capucine.picard@inserm.fr

With kind regards,

Capucine Picard, MD, PhD
Jordan Orange, MD, PhD
Jean-Laurent Casanova, MD, PhD

Download Survey here

Survey - The clinical features of NEMO defects (157k)

NEMO - letter (32k)

NEMO - questionnaire 2 (67k)

NEWS @ ESID

Registry

Report from the Registry Working Party
ESID Registry Workshop, Dec 1-2, 2011

Figure 1: Shaping new ideas - group work

In an endeavour to improve the ESID registry, we have recently re-evaluated data quality and completeness and have decided to introduce some changes to the database. Since this is an important step that should be decided by a broad group of users of the database, we have held a meeting in Freiburg on December 1 and 2, 2011, where we discussed again the goals of the registry and how changes could be implemented. Representatives of many national registries contributing to the ESID registry attended the meeting, as well as members from PPTA, who are important sponsors of the database. Not all countries contributing to the registry have been represented at this kick-off meeting, but will be involved in the process at the next ESID meeting.

The workshop set off with a plenary session where we collected the goals, problems and ideas of each of the represented national registries. Stephan Ehl gave an overview on the current state of the registry. Paul Landais from Paris gave a talk on the SCETIDE registry and how it could be connected to the ESID and EBMT registries. Werner Vach from the Institute of Medical Biometry in Freiburg explained in which ways a patient registry can help to answer scientific questions. Thomas Klopstock from Munich provided a very interesting “look across the fence” by presenting the German mitoNET registry for genetic mitochondrial disorders. Finally, Albert Farrugia presented the PPTA perspective on the registry. During the presentations and discussions we gathered all important issues and at the end of the day, all participants identified the goals and ideas that were most important to them.

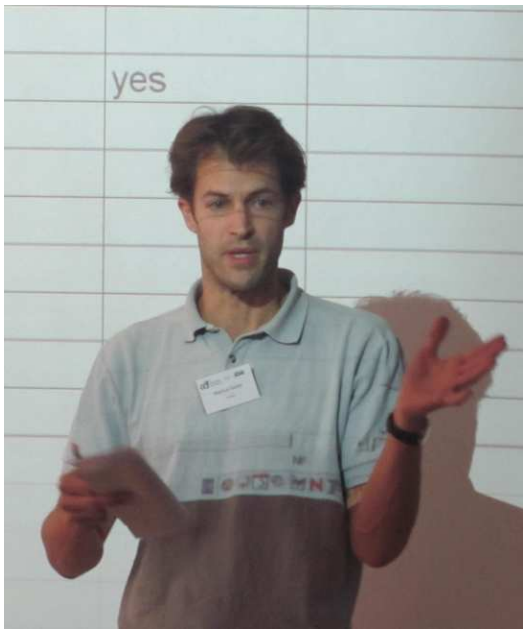


Figure 2 Dr. Markus Seidel from Graz represented the Austrian National Registry

The five most important issues identified were:

(i) Epidemiology
(ii) Treatment and treatment costs
(iii) Prognostic and predictive factors
(iv) Follow-up including self-reporting by patients
(v) Data definitions, monitoring and quality control. These issues were then discussed in five groups and results of the discussions were afterwards presented to the plenum.

As a result of these lively discussions, we agreed on a simple 1 page dataset for a one point registration and a 2 page dataset specific for each of the 8 IUIS categories that provides more specific information on clinical manifestations, lab values and treatment and can be used as a yearly follow-up sheet. The patients shall be motivated to self-report quality of life data using simple evaluated QoL tools. It was decided that the category-specific datasets should be drafted by December and finalized in January. A Registry steering committee (initially with 10 members, to be

reduced after 1 year) has been formed that will include a PPTA and a patient representative. This group will finalize the datasheets at a meeting in February 2012 and decide on the next steps for implementation. The new concept will be presented at the ESID meeting in Florence.

We would like to thank all the participants of the workshop for their contribution to take the Registry project to the next level.

Stephan Ehl
Chairman, ESID Registry Working Party

Figure 3: Prof. Thomas Klopstock gave an insight into the mitoNET registry

Figure 4: Prof. Albert Farrugia presented the PPTA's ideas for the future of the Registry project

Figure 5: Prof. Taco Kuijpers from Amsterdam talked about the National Dutch Registry

Figure 6: Prof. Werner Vach from Freiburg explained the potentials of a patient registry

NEWS @

ESID Juniors

Dear ESID Juniors,

Here we are at the end of very fruitful year for our working party. Looking back, we had a sum of great events and opportunity to improve our knowledge in PID and to network, starting with the Prague Spring meeting hosted by Anna Sediva that this year celebrated his 10th anniversary, the Tampere workshop greatly organized by Crina Samarghitean, and finally our biannual ESID Summer school that was held in Barga, Italy. The ESID organized summer school and the ESID supported events had lots of applicants and very enthusiastic participants (the reports of those events can be read in the previous newsletters), this teaches us that the possibility to meet in international contest, exchange experiences and learn from seniors are essential activities for the Juniors. Therefore, to match the request of our fellows, we need to keep organizing high quality meeting and workshops. In this direction, as I promised last year I organized a workshop in Freiburg 'Methods in primary Immunodeficiency'. The workshop is directed to PhD, postdocs and MD doing their doctoral thesis, to exchange their projects and experiences in basic research in PID. You can already send your application and look at the program clicking on this link: **http://www.uniklinik-freiburg.de/cci/live/events/WorkshopMethodsinPID.html**
Furthermore, Anna Sediva will organize the 11th Prague meeting, more info will come on the ESID web site at the beginning of the year.
And more important, next year will take place in Florence our biannual meeting with a whole educational day planned for Juniors. So, let's connect!

Two more things have been implemented this past year:

- The map of centers, where we can see which institution are available to host Juniors for short, medium or long term fellowship, and what can be done in each center. Some new centers have been added to the list, and I hope this will help the Juniors to develop new ideas on how to deepen their interest in PIDs.
- The Facebook group ESID Juniors. This is an initiative started after the Summer school, we created a closed community **(http://www.facebook.com/groups/esid.juniors/)**, accessible only to members, where we can exchange information, photos of events, ask questions, report on experiences. We are already 22 Juniors in the community, we are waiting for more! Become more active and participate to the group!

At the end of the year I want to thank specially the Juniors that are actively contributing to the advancement of our WP, Imma Brigida and Sara Ciullini for the redaction of our young researcher corner, Ales Janda for the work on the map of center, Ales again and Margje Haverkamp for contributing to the organization of the coming educational day in Florence, Crina Samarghitean for her support as past WP chair and for organizing the Tampere meeting, and finally all the Juniors that with their interest, questions and participation push the Junior WP forward.

I wish you all a happy and relaxing holiday season, a joyful Christmas and a great start in the New Year!

Marta

NEWS @ ESID

Young Researcher Corner

APPLICATION OF HIGH-THROUGHPUT SEQUENCING IN GENOME WIDE ANALYSIS.

One of the major tools of biological research is the knowledge of DNA sequences to apply identification of mutations or vector integration profile in gene corrected cells. Gene expression is a complex trait influenced by cis- and trans-acting genetic and epigenetic variation, and also by environmental factors. The characterization of the human genetic variation that affects gene expression could be studied with different strategies, and next-generation sequencing technologies are generally used for global functional genomics assays. To this aim, high throughput sequencing techniques were developed for quantitative genetic and epigenetic studies in order to deepen insight gene functions. Basic approaches for DNA sequencing started in early 1970s with the use of Sanger's method, based on the separation of DNA bases from different DNA fragments, allowing the determination of only a few hundred nucleotides at a time. The key principle of the Sanger method was the use of single-stranded DNA template, a DNA primer, a DNA polymerase, deoxynucleotidetriphosphates (dNTPs), and modified nucleotides (dideoxyNTPs) that terminate DNA strand elongation, which could be radioactively/fluorescently labeled for detection in automated sequencing machines. Major issues rely on the time used for the separation of different fragments by size, even though allowing the identification of thousands of interspersed genomic features and protein-DNA interactions, and the cloning procedures depending on base composition, length, and interactions with the bacterial host system. To overcome these limitations, alternative sequencing techniques have been developed by different companies, able to outperform the older Sanger-sequencing technologies by a factor of 100-1000 in daily throughput, with a significant reduction of the cost of the analyses per sample, with the final goal to create platforms to share high-throughput sequencing capacities. This facilitates not only the study on molecular and biological issues with higher resolution and efficacy likely the de novo sequencing of unknown genomes, but also the identification of several epigenetic features at genome wide level, like methylated DNA loci and DNase I hypersensitive sites.

Furthermore, they were combined with chromatin immuno-precipitation procedures (ChIP-seq), allowing to high-throughput map a number of protein-DNA interactions and chromatin features like DNA polymerase and transcription factors binding sites as well as histone tails acetylation and methylation in several cell types. Chromatin immunoprecipitation (ChIP) process used massively parallel sequencing, specific DNA sites that interact with transcription factors or other chromatin-associated proteins (non-histone ChIP) and sites that correspond to modified nucleosomes (histone ChIP), in order to enrich the crosslinked proteins or modified nucleosomes of interest using an antibody specific to the protein or the histone modification. The purified DNA is next sequenced using different next-generation platforms, with enzyme-driven extension of all templates in parallel. After each extension, the fluorescent labels that have been incorporated are detected through high-resolution imaging. Pyrosequencing was developed by 454 Life Sciences, and consists in amplification of DNA inside water droplets in an oil solution (emulsion PCR). Each droplet contains a single DNA template attached to a single primer-coated bead that then forms a clonal colony. The sequencing machine contains many picoliter-volume wells each containing a single bead and sequencing enzymes. Pyrosequencing uses luciferase to generate light to detect individual nucleotides added to the nascent DNA, and the combined data are used to generate sequence read-outs. The Illumina (Solexa) sequencing is based on reversible dye-terminators in which DNA molecules are first attached to primers on a slide and amplified in order to form local clonal colonies (bridge amplification). Four types of ddNTPs are added, and non-incorporated nucleotides are washed away. Unlike pyrosequencing, the DNA can only be extended one nucleotide at a time. A camera takes images of the fluorescently labeled nucleotides, then the dye along with the terminal 3' blocker is chemically removed from the DNA, allowing the next cycle. Recent applications of these techniques involved also RNA deep sequencing (RNA-seq) with the full analysis of the transcriptome and exome as well as miRNAs identification and quantification.

Applications of high-throughput sequencing were used in the last years for the study of chromatin

structures in hematopoietic cells, in order to shed light to the genome wide localization of epigenetic marks and their influence on lineage differentiation. DNase I hypersenstive sites (HSS) are short regions of chromatin able to bind transcription factors resulting in the displacements of histone octamers leaving these regions more susceptible to DNase I enzyme cleavage. HSS are considered markers for many different types of genetic regulatory elements, including promoters, enhancers, silencers, insulators, and locus control regions and are primarily associated to transcribed and expressed genes. Nevertheless, the high-throughput genome wide analysis detects a number of HSS in intergenic regions highlighting the presence of long-distance acting enhancer. The application of the CHIP-seq technique to hematopoietic cells was recently described for the identification of several histone modifications, likely methylations of lysine and arginine. This process induces alterations in the charges on the protein surface influencing histone-histone interactions and the strength of their binding to DNA molecules, influencing the nucleosome positioning, the DNA methylation status and the chromatin condensation by the interaction with several regulatory proteins. Some combinations of different histone methylations are associated with euchromatin configurations (H3K4me3 or H3K27me1), which are usually associated with active promoters and transcribed genes, while some others with heterochromatin formation (H3K9me3 and H3K27me3), found more often in inactive/silenced loci.

More recently the high-throughput technique was coupled with DNA bar-coding to track single hematopoietic stem cells during in vivo differentiation in mouse model, allowing the identification of the same integration found in the HSC into the daughter. Moreover the use of bar-coding, although being a process requiring several hours, did not alter HSCs function. Coupling these two methods allows a better characterization of HSCs, in terms of single cell level clonal tracking of both in vitro and in vivo processes for virtually any cell type that can be infected by a lentivirus, thereby separating the behavior of HSCs from that of other progenitors by directly measuring their clonality. This system can be used to simultaneously track the proliferation and development of hundreds of cells in vivo with single-cell precision. High throughput is critical to study rare or stochastic cellular events, revealing novel features in presence of low cell numbers. Moreover the high sensitivity of the barcode tracking system allows a direct examination of the entire hematopoietic process starting with the hematopoietic stem cells themselves. For instance, this barcode tracking system can be applied to cell and gene therapy to follow and quantify the fate and distribution of transplanted cells. The high sensitivity of this technique allows for the analysis of clinical samples with very low cell numbers and for the identification of early-stage malignancy before subsequent expansion or metastasis.

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Immacolata Brigida

PID Care in Development

Prague, December 2, 2011

The activities of ESID PID in Development WP are traditionally targeted at further improvement of awareness on PIDs. In the end of the year WP activities thus interconnected with IPOPI major events.
First, Global leaders meeting took place in London in early November. The meeting attracted leaders in PID field from all over the world, with very active participation of ESID. Recommendations from the event are here **http://www.ipopi.org/uploads/Recommendations%20GLM%202011.pdf**
Second, ESID representatives are going to lecture on the second PID Forum at the European Parliament on the topic of Health Technology Assessments (HTAs) on Tuesday, December 6, organized by IPOPI. This Forum is to respond to the increasing pressures on healthcare budgets through the use of cost containment tools such as HTAs that might have a negative impact on access to appropriate treatment for the PID community. The forum is the policy event that would try to identify threats and opportunities to ensure that restriction do not impact PID patients access to care. This valuable activity is already second occasion to establish the discussion with EU authorities. The first Primary Immunodeficiency Forum was organized earlier this year and focused on newborn screening for SCID. Newborn screening represent unconventional mode of better and earlier diagnosis of PIDs. After the initial pilot studies SCID screening is being encouraged in several European countries. ESID members are leading force behind these activities.
Traditional activity supporting awareness on PIDs in Eastern and Central Europe, J project, is ongoing, with meetings in Macedonia and Slovakia in the end of a year.
I hope that you also noticed that Search Engine Optimization (SEO) tool was applied in order to optimize internet search for ESID and other PID related topics. Google request for immunodeficiencies now returns ESID on the first page, giving a great visibility to the ESID organization.
Finally, PID in Development WP wishes all of you great Christmas time, we are looking forward to the ongoing cooperation in the year 2012.

15th Biennial Meeting - Florence, Italy

Abstract Book

The abstracts of the 15th Biennial Meeting of the ESID are being published in an online supplement of the **Clinical Immunology Journal** published by Springer.
A printed copy of the Abstract Book has been handed out to participants during the meeting.

Travel Grants

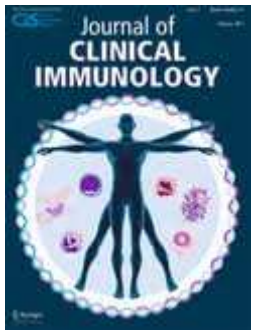
Congratulations to our successful ESID 2012 Travel Grant Awardees!

Zheng Jie
Moncada Marcela
EIFeky Reem
Makatsori Melina
Maggadottir Solrun Melkok
Chinnabhandar Vasant
Abolhassani Hassan
Barbosa Rita

NEWS @ ESID

Kampitak Thatchai Myles Ian

ESID Secretariat



Program
Click here to view the program

Meet the Faculty
Access information and CVs here

Certificates of Attendance & CME Accreditation (20 Credits)
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Oral and Poster Awards
If you have not received your claim form yet or have any questions, kindly contact Susanne Schmitt under esid.admin@kenes.com

Photo Gallery
click here

CME Certificate
Coming Soon

APPLY NOW! ESID Endorsed Meeting Application

ESID Endorsed Meetings

You are now able to request ESID endorsement for your meeting (logo usage etc. but no financial support) year round.
The right to organise ESID-Endorsed Meetings is one of the benefits of ESID membership.
Requests should be sent to the ESID Administrative Office by e-mail (esid.admin@kenes.com) at least 3 months prior to the event and are subject to the approval of the ESID Board.

NEWS @

ESID Endorsement Guidelines

ESID Endorsement Guidelines (85k)

Application Form

ESID Endorsed Meeting Application Form (105k)

Contact

In case of question, please do not hesitate to contact us under:

ESID Administrative Bureau
Email: esid.admin@kenes.com
1-3 rue de Chantepoulet, CH 1211 Geneva 1, Switzerland
Fax: +41 22 732 26 07

ESID Endorsed Meetings in 2013

2nd Workshop on Diagnostics in Immunodeficiencies 2013
June 17-19, 2013
Hotel Fortuna, Kirchzarten Germany

Local Organizer: CCI Freiburg

Contact: Ilka Fuchs, Ilka.fuchs@uniklinik-freiburg.de, +49-761-270-71010
CCI, University Medical Center Freiburg, Breisacher Str. 117, 79106 Freiburg, Germany

Annoucement 2nd Workshop on Diagnostics in Immunodeficiencies 2013 (182k)

III Curs d'Immunodeficiències Primàries per a residents (3rd Meeting on Primary Immunodeficiencies for residents and fellows)
May 2013
Acadèmia de Ciències Mèdiques de Catalunya I Balears, Carrer major de Can Caralleu 1-7, Barcelona, Spain (http://www.acmcb.es/)

Local organizer: PID Group of the Societat Catalana de Pediatria (Catalan Society of Pediatrics, www.scpediatria.cat)

Contact: Pere Soler Palacín, MD, PhD.
Pediatric Infectious Diseases and Immunodeficiencies Unit Hospital Universitari Vall d'Hebron
Assistant Professor. Universitat Autònoma de Barcelona
Passeig de la Vall d'Hebron 119-129
08035 Barcelona, Spain
E-mail: psoler@vhebron.net; 34660psp@comb.cat
Web: www.upiip.com

Scientific Program II Curs (646k)

NEWS @

Updated! EBMT/ESID Guidelines for Haematopoietic Stem Cell Transplantation for PI

A. Introduction

Primary immunodeficiencies are rare heterogeneous disorders. Patients present with a variety of clinical symptoms and a wide range of infections and other complications. Treatment by bone marrow transplantation is increasingly successful (reference: Antoine C, et al. The Lancet 2003;361:553-60; Gennery et al., JACI 2010;126:602-610) and the joint EBMT/ESID Working Party has played a pivotal role designing and developing the guidelines which have led to this success.

The clinical heterogeneity of the patients, together with the fact that outcome data are based on observational studies, means that it is not yet possible to recommend tightly defined clinical protocols for transplanting these conditions. Each case needs to be carefully evaluated in a centre which has significant ongoing experience of performing these procedures. The exact transplant protocol will be devised using these guidelines, but sometimes modified according to the particular variant of the primary immunodeficiency and/or the patient's clinical condition. For all these reasons the Working Party strongly recommends that all patients with primary immunodeficiency are transplanted in a centre that regularly transplants such cases, and also actively participates in the Working Party, as only in this way can optimum results be obtained.

The guidelines are reviewed on an annual basis and sub-groups of Working Party members revise some of the guidelines for specific conditions each year.

B. Conditioning Regimens

Over the years a number of different conditioning regimens have evolved as newer, less toxic conditioning agents have been made available. For these and other reasons, it has been difficult to gather data on the use of a particular conditioning protocol for any one disease such that a strong recommendation can be made. In most cases, groups of primary immunodeficiencies have been transplanted using certain generic protocols often with modifications (e.g Flu/Melph/Campath or ATG). It is also important to note that specific conditioning regimens are not risk factors for survival in the SCETIDE data.

To address these issues and to simplify matters, the IEWP decided that rather than to recommend specific protocols for specific conditions, one approach would be to make a list of protocols available. For disease groups, a recommendation would be made to choose from the protocol list e.g for Wiskott-Aldrich syndrome with a MUD use protocol A, B or D. The aim of this approach is that:

1) By limiting the number of protocols available, there will be less variation between centres
2) If centres use specific protocols as defined, then we will be able to gather data on the success or otherwise of a specific protocol in treating these conditions
3) We also recognise that for smaller or less experienced centres this guidance is important and by making these guidelines available on the EBMT and ESID websites, the information is readily available

We have therefore made a list of four protocols A-D which are outlined and are recommended for the majority of diseases. Specific details/examples of these protocols are made available in the **appendix (see PDF below)**.

Exceptions to these recommendations are SCID, where some transplants can be undertaken without any conditioning and severe immunodeficiencies associated with radiosensitivity which require specialised protocols.

We ask that if protocols are used, then they are adhered to in terms of dosing and schedule as much as possible since only then can meaningful data be accrued over time.

Appendix

EBMT ESID GUIDELINES FOR INBORN ERRORS 2011 Updated (1180k)

OP Guidelines 2011 (326k)

Call for Participation! STAT3, DOCK8, or Tyk2 Genes

Dear ESID colleague,

We do **CPA-certified STAT3 mutation detection** at the Royal Free Hospital in London. If we detect a previously reported genetic change we issue a mutation report. If we identify a previously unreported change we ask for blood of the parents to see whether it is a de novo mutation, and of the patient to perform the IL10-mediated inhibition of TNFa release assay for testing the integrity of the STAT3 signal transmission.

Doing so, we have observed normal results in patients with a clear cut HIES (Jobs) phenotype. Polyphen says probably damaging… So maybe this functional assay leaky?

Who is also doing STAT3 mutation detection in HIES?

What do you do to verify that an observed genetic change in STAT3 is disease causing?

I am also very interested to learn who does Dock8 or Tyk2 testing in ESID-world.

Please drop me a ping

b.grimbacher@ucl.ac.uk

Thanks!
Yours, Bodo