ESID NEWSLETTER

2009 - Issue 3

www.esid.org

ESID Editorial Office

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ESID members are invited to publish in this newsletter

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Dear ESID members,

As I write this, it is dark, cold and rainy outside, but inside lights and colours still cherish Christmas. Tomorrow, the year will end, as will my editorship of the ESID Newsletter. I have really enjoyed the task, and want to thank everyone who has taken the trouble to send in their contributions, to read the Newsletters, and to send me their comments by e-mail now and then.

In this issue you will find the well-known sections: contributions by Board members, by Chairmen of Working Parties, and as always by organisers of J-Project meetings.

I hope to see many of you in Istanbul in October, and wish Eleonora Gambineri success with her new task as chief editor of the ESID Newsletter from now on!

Best wishes,

Esther de VRIES,
Editor

INSIDE THIS ISSUE

XVI th ESID
ISTANBUL
A city of the Four Elements

October 6-9, 2010

www.esid2010.org

A Note from the President

Dear All,

Please let me take this opportunity to wish you a happy new year! Obviously, 2010 is of special importance for the ESID, because of the up-coming meeting in Istanbul. I therefore invite you all to communicate intensively about this meeting, and to convince as many colleagues as possible to attend. As you know, Necil Kutukculer and his team are doing a fantastic job and they are all willing to provide you with whatever information or media you may need to advertise the meeting (slides, posters, etc.). Please don't hesitate to liaise with them. We have great expectations, so let's make this Istanbul meeting a great success!

Again, let me wish you all a happy new year!

Jean-Laurent CASANOVA
ESID President

Secretary's Report

I will need to resign as ESID secretary in Istanbul and I would like to thank all ESID members for their support and help during the last years. However, I would like to continue with my activities to serve our Society.

As Head of the ESID registry Working Party from 2002 to 2006 I have initiated with all your help the new online-based patient registry. Many other specialties, especially from the field of rare diseases, admire what we have created, so ESID can be very proud of this achievement.

During my time as ESID secretary 2006-2010 I was asked by the ESID board to facilitate the transition to a professionalized organization management and a Professional Congress Organizer (PCO). We have picked Kenes following the General Assembly in Holland and at least the board feels that our work has since become much more organized and professional. This starts with the planning of board meetings, the preparing of the minutes, the follow-up of commitments, and goes all the way to the layout of the ESID newsletter and the ESID website. I can assure my successor that with Kenes at his or her side it is much, much less work to guide our society as a secretary.

ESID Board meetings

The ESID Board met in Berlin on September 15, 2009 during the ECI congress. This brief meeting gathered only a few members of our ESID Board and was aimed at solely discussing topics related to the next 2010 ESID biennial congress – Istanbul 6-9 October 2010.

Although the next ESID Board meeting will only take place in March 2010, we have decided to implement regular conference calls not only to cover topics that need urgent approval and decision making, but also to shorten the time between board meetings.

Secretary's Report — Continuing

Finances

During 2009 ESID awarded four travel grants to Junior members and one short-term fellowship. The society will continue to support and promote the involvement and contribution of young physicians and researchers in the advance of PID, by enabling them to attend special events or undertaking fellowships.

ESID was able to attract financial support from different sponsors in Europe for some of their Junior activities. Any surplus of these funds will be strictly used to finance other Junior educational activities.

The year ahead is also looking very promising with the upcoming congress in Istanbul. The event expects to gather a high number of participants and if our forecast is correct this will have a positive impact on the Society's finances.

Short term & Long term Fellowship 2010

Fellowships and Publication Awards

Each year the Society awards a short-term and a long-term fellowship of Euros 1,000 and Euros 10,000 respectively. Therefore, we invite applications from all those who are interested. Details on how to apply can be found on our website under the Juniors and Education Working Parties sections (www.esid.org).

The ESID Publication Award will be re-opened in 2010. We invite all ESID members working with the ESID database to submit their papers for selection. The award will only be given to papers using data from the ESID Registry and citing the ESID registry e.g. in the acknowledgements. Details on how to apply can be found under the report of our Registries Working Party in this newsletter issue.

New activities

Eleonora Gambineri has launched a new ESID initiative – the Junior Workshop. These kinds of workshops are aimed to provide a continuing learning platform to PID students encouraging interactions and discussions between participants and Faculty. Although shorter than the already well-established ESID Summer Schools, workshops focus on very specific and current topics of primary immunodeficiency diseases.

The first workshop took place in Florence on January 11 and 12, 2010 and it was a success!

Secretary's Report — Continuing

2010 Online Board Elections

As it happens every two years we need to elect or renew the term of some of the members of our Executive Board. The online voting will take place during September, one month prior to our biennial congress which will take place in Istanbul from the 6-9 October 2010.

As you know each term of office is 2 years for the President, Secretary and chairpersons of all Working Parties, renewable at the next Biennial meeting, but limited to 2 terms (4 years) only.

As our new Treasurer, Eleonora Gambineri, is entitled to serve for eight years and our President-elect, **Amos Etzioni** has already been identified and I now hereby ask you to send me (B.G.) applications for the following positions:

- Secretary
- Educational Working Party Chairman
- Genetics Working Party Chairman
- PID Care in Development Chairman

JOIN THE BOARD !

Applications are open for Elections 2010!

Please submit your applications to b.grimbacher@ucl.ac.uk by 15 March 2010!

They will be published in the ESID newsletter and on the ESID website.

Search for an ESID meeting venue in 2014

With effect from 2012, Kenes International will undertake the responsibility for the core organisation of ESID Biennial Meeting in close collaboration with the local steering committee. The scientific content of the meeting is proposed by the appointed scientific committee but decided by the ESID board.

As bids for ESID Biennial Meeting take place four years in advance, **we would like to ask for nominations regarding the 2014 Biennial meeting**! The President and the location for the 2014 Biennial Meeting will then be decided by electronic voting after a presentation of the bid at the ESID General Assembly in Istanbul.

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;
- proposed dates
- include suggested programme outline
- include possible social events
- provide finances/provisional budget and information on local tax rules

Please submit your applications to esid.admin@kenes.com by 1st of August 2010

Secretary's Report — Continuing

Membership

It is time to renew your ESID membership and take advantage of all the benefits that our Society has to offer you. Please do not forget that this is a congress year, so as members you are offered a reduced registration fee!

Our Society has been growing in membership over the past six years and we are expecting this trend to continue. We want to develop our network of PID professionals and bring our mission higher with your help!

Here are some figures on our membership development:

Membership Growth from 2004 to 2009

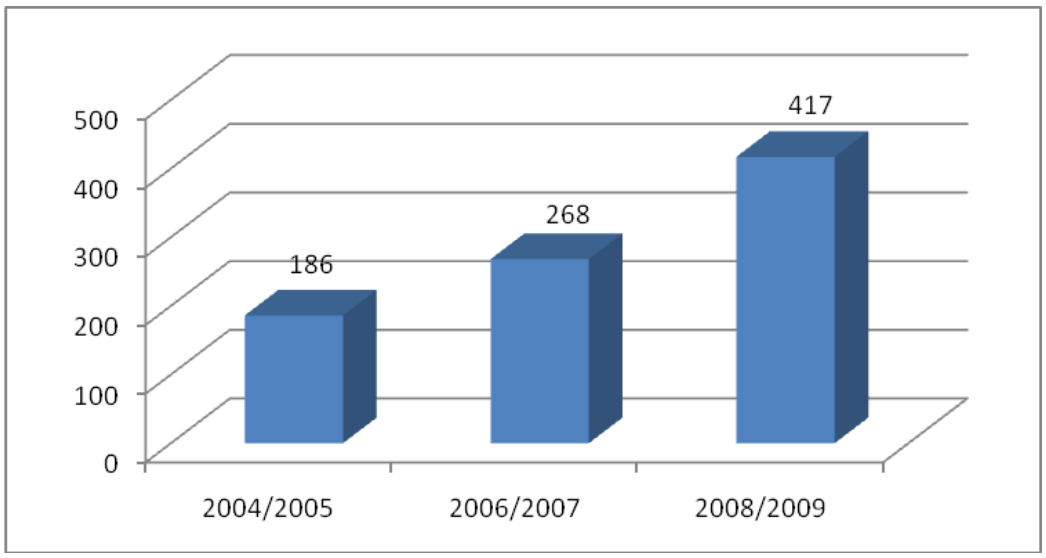

Chart 1

12 Leading Countries (2008/2009)

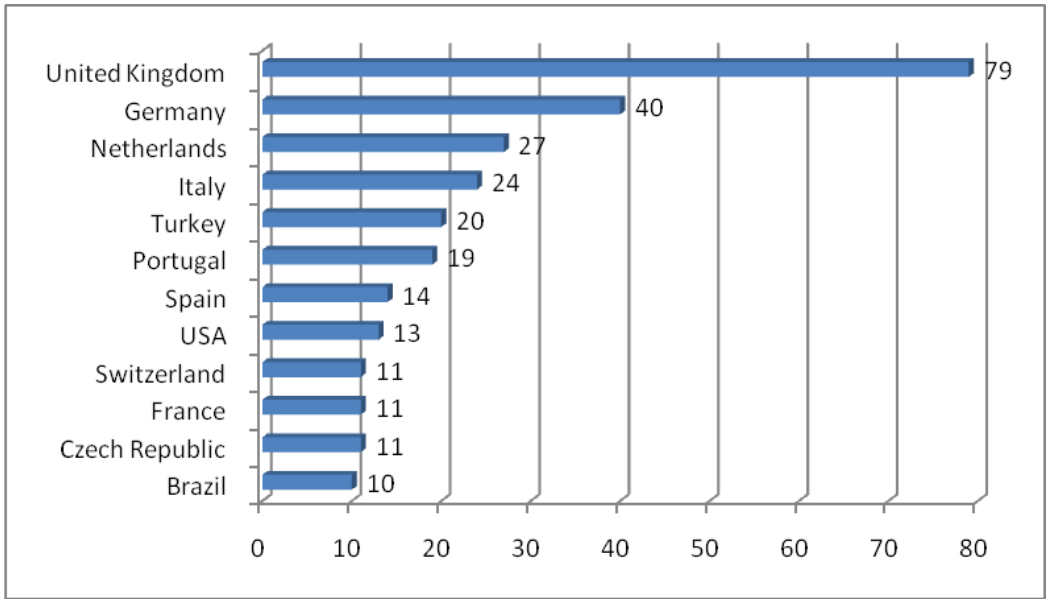

Chart 2

Bodo GRIMBACHER
Secretary

Treasurer's Report

Dear ESID members,

I hope you all spent a nice time during the recent Holiday Season!

I would like to provide you with few updates of our activities:

It is time to pay **your membership fee for 2010-2011**. The amount you have to pay is thesame as for 2008-2009. You can easily renew your membership on the ESID website - just login and follow the instructions! We accept only credit card payments, so please do not send cash or checks via mail. If you have any problems or questions regarding membership please contact Noa Sharon (esid@kenes.com) and she will be able to assist you promptly! We are implementing new membership benefits, so keep joining the community!

In line with one of the membership benefits, the second announcement of the next ESID biannual meeting in Istanbul is out! Please check the programme on the website www.esid2010.org and join us in that beautiful city! Remember that as an ESID member you are eligible for discounted congress fees!

With the valuable support of several sponsors I managed to help finance an ESID Junior Workshop at the Anna Meyer Children's Hospital in Florence on January 11 and 12, 2010. The organization of a workshop entirely dedicated to trainees will help to provide ESID Juniors a follow–up platform on learning processes, to stimulate discussions and interactions, and to reinforce the network. Furthermore, the financial support given for the workshop will help to establish a proper ESID Junior "budget" since any leftover funds from the meeting will be strictly restricted to other ESID Junior Educational Activities (travel grants, short-term fellowship etc.). You will find more details on the event in the ESID Junior corner.

Finally, as you might have learnt from the previous issue, from now on will be taking over the chief editorship of the ESID Newsletter from Esther de Vries. I am looking forward to this new challenge and with the support of you all I hope I can match all the great work, commitment and patience that Esther has shown over the past years.

All the best for 2010!

Eleonora GAMBINERI
ESID Treasurer

News & Views

ESID BIENNIAL MEETING - ISTANBUL, OCTOBER 6-9, 2010

Congress registration fees for ESID Members:

	Before 15 June, 2010	After 15 June, 2010	After 1 October, 2010
ESID MEMBERS	**EUR 350,-**	**EUR 450,-**	**EUR 500,-**
ESID MEMBERS withe less than 30 years old	**EUR 250,-**	**EUR 350,-**	**EUR 400,-**

News & Views — Continuing

PROGRAM IS NOW AVAILABLE ONLINE !

Visit the congress website at www.esid2010.org

and to get an overview of what this event has to offer you!

Final Report of Short-Term Fellowship

"Bone Marrow Transplant and Paediatric Immunology & Infectious Diseases"
at the Newcastle General Hospital

I am writing this essay, as the final report of my short-term fellowship in the "Bone Marrow Transplant and Pediatric Immunology & Infectious Diseases" units of the Newcastle General Hospital, which was kindly granted by the European Society for Immunodeficiencies (ESID) in August 2009.

Although I am still a junior member of the ESID, I have been working in the field of primary immunodeficiency diseases (PID) for more than ten years, since the time I was a medical student and research director of Students' Scientific Research Center in Tehran University of Medical Sciences. We organized a group of senior consultants and students to establish the Iranian Primary Immunodeficiency Registry. After graduation, I focused on this field at the Children's Medical Center, the main referral center for patients with PID in Iran, and Immunology, Asthma and Allergy Research Institute.

I have actively contributed in several PID projects, which lead to more than 150 published papers and presentations in international/national congresses. In addition to editing a number of books in the field of PID for patients and health case workers in the Farsi language, I am honored to be the editor of the text-book "Primary Immunodeficiency Diseases: Definition, Diagnosis and Management", which is the result of valuable contributions of more than 40 senior and junior scientists from more than 30 universities worldwide.

After completing the MSc-PhD programme at the University of Sheffield, UK, I applied for the short-term fellowship in "Bone Marrow Transplant and Pediatric Immunology & Infectious Diseases" at the Newcastle General Hospital, which was successfully awarded by the ESID.

I travelled to Newcastle upon Tyne at the end of August 2009, where I had the opportunity to see some attractions of the city, before attending the Newcastle General Hospital.

Newcastle upon Tyne is a lively and diverse city in the North East of England. Walking on both sides of the river Tyne and crossing the river through the bridges, especially the Millenium Bridge, was what I really enjoyed, as well as other interesting sites, including Greys Monument, Grainger Town, Opera House, Hadrian's Wall, Tynemouth Castle and Priory, Angel of the North, Cathedral Church of St Nicholas, Centre for Life, and the MetroCentre.
Newcastle General Hospital (NGH), Royal Victoria Infirmary (RVI), and Freeman Hospital are the three main hospitals of the city and I had the chance to visit the first two hospitals during my stay in Newcastle. Ward 23 of the NGH is the Children's Bone Marrow Transplant (BMT) unit, dedicated to Severe Combined Immunodeficiency (SCID) and related disorders. This is an active and well-developed unit for this group of sick children.

I attended the Immunology Clinic, Rheumatology Clinic, Infectious Diseases Clinic and Allergy Clinic for visiting out-patient cases with other consultants in Paediatric Immunology.

In the immunology clinic, a variety of patients with PID visited, including severe combined immunodeficiency (SCID), DiGeorge syndrome, IgA deficiency, chronic granulomatous disease (CGD) and MBL deficiency was very interesting, meanwhile discussions on approaches to the cases with possible diagnosis of PID and therapeutic options were very useful.

In the rheumatology clinic, I had the chance to visit some patients with rheumatologic disorders such as oligoarticular and polyarticular juvenile idiopathic arthritis (JIA), juvenile psoriatic arthritis, and osteogenesis imperfecta.

News & Views

Final Report of Short-Term Fellowship—Continuing

I also visited several patients with HIV infections in the infectious diseases clinic and a number of patients with allergic diseases (e.g., allergic rhinitis and food allergy) in the allergy clinic and discussions on the management of the patients was very useful.

Moreover, I participated in the BMT ward round and visited the hospitalized patients with other consultants in Paediatric Immunology. This multidisciplinary round with the BMT team was really an important part of my training. In addition to consultants of the ward, other specialists as well as nurses, virologist, microbiologist and others, if necessary, attend such rounds. Discussions with the BMT team on candidate patients for selecting best donors and deciding on appropriate chemotherapy conditioning regimens was one of my great interests, whilst managing the complications of patients after transplantation was a vital issue. Several patients with PID were treated or planned for the BMT during my visit from the NGH, such as different types of SCID, CGD, X-linked lymphoproliferative syndrome (XLP), Wiskott-Aldrich syndrome (WAS), hemophagocytic lymphohistiocytosis (HLH), Cartilage-hair hypoplasia (CHH), and immunedysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome.

Attending the paediatric research meeting was another activity, whereas several ongoing projects and future proposals were discussed.

I gained a valuable experience about the structure of a BMT unit and how excellent team work is needed for a successful BMT. Although it was a short period, I learned some primary knowledge and experience about pre-transplant conditions, selecting appropriate donors, admission strategies, selecting chemotherapy conditioning regimens, managing complications, discharge planning, and follow-up of the transplanted patients.

I would like to thank the ESID Educational Working Party, especially Professor Andrew Cant, for this award. I would like to add to this point that the short-term fellowship was an initiative of the ESID Juniors Working Party, which was not possible without the precious help from Dr Eleonora Gambineri (ESID Treasurer). Therefore I extend my special thanks to her and new chairperson of the ESID Juniors Working Party, Dr Crina Samarghitean.

I am also very thankful to Dr Andy Gennery, Dr Mario Abinun, Dr Julia Clark and Dr Mary Slatter for their valuable guidance during my stay there and to all the colleagues at the BMT unit and Pediatric Immunology & Infectious Diseases unit of the NGH.

Finally, I would like to encourage all ESID juniors to repeat this kind of activity, which are very useful for learning updates on diagnostic and therapeutic procedures in the field of PID.

Nima REZAEI, MD, PhD

nima_rezaei@farabi.tums.ac.ir

ESID Prague Spring Meeting, May 10 and 11, 2010

Institute of Immunology, 2nd Medical faculty and University Hospital Motol
Venue: Olympus headquaters, Prague – Czech Republic

I wish you all a great year 2010. On this occasion, I attach the draft programme for the 9th ESID Prague Spring Meeting, to be held May 10 and 11, 2010.

As always we try to attract our young colleagues to Prague, to learn and to share their knowledge. Registration for this year will open in January, 2010. You all are welcome! Please, let your young immunologists know about the event. This year we would also love to invite graduates from medical schools, who are willing to pursue their career in immunology and are looking for an immediate experience or possibly seeking PhD positions.

We believe that participation in the Prague event will be useful for everybody. A cultural programme is already planned, and we expect great science and a wonderful Prague experience. Topics will be amongst others: CVID, Th subsets, Th17, cases, junior presentations.

With regards and looking forward to seeing you in May,

Anna SEDIVA

News & Views—Continuing

The 34th J-Project Meeting was held in Tallinn, Estonia, 7-8 October 2009

The Meeting was organised by 3 Estonian societies: the Pediatric Society (K.Julge), the Society of Allergology and Immunology and the Society of Infectious Diseases. The main topic of the meeting was early detection, diagnostics, following and treatment of patients with primary immunodeficiencies (PID) in Estonia. All presentations were in Estonian; only the lectures of Prof. L. Marodi were in English.

Before the meeting on 7th October, there was a discussion about the diagnostics and treatment of PID in Estonia which where participated by Prof. L. Marodi and immunologists and pediatricians from Tallinn and Tartu.

The Meeting on 8th October started with the lecture by Prof. L. Marodi about aims and development of the J Project. Prof. L. Marodi gave an overview of the J Project achievements and also introduced molecular genetic testing available at the Debrecen Jeffrey Modell PID Reference Centre.

S. Velbri gave an overview about detection, diagnostics and treatment of PID in Estonia. The first patient with CVID was diagnosed in 1976 in Tallinn. In 30 years there have been over 200 patients diagnosed with PID, mainly antibody deficiencies. Estonia has participated in the ESID Registry since 1996. Estonian Patients Organisation for Primary Immunodeficiencies was organised in 1997. Estonia is a small country with a population of 1.3 million and therefore it is difficult to diagnose and treat rare forms of PID. It is necessary to have professional contacts in different countries.

A special part of the meeting was the analysis of different forms of PID. Prof. L. Marodi presented clinical characteristics and molecular genetic forms of hyper-IgE-syndrome.

Other presentations were about diagnostics, following and treatment of CVID in children (K.Ress, U.Putnik) and in adults (M.Varik). Cases of DiGeorge syndrome were analysed by R.Zordania. M.Vasar presented cases of hereditary angioedema. Interesting case reports were discussed: combination of XLA with Mohr-Traneberg syndrome in two brothers, Netherton syndrome in a girl, cases of chronic mucocutaneous candidiasis etc.

We hope that this meeting will promote early diagnosis and treatment of PID in Estonia.

Sirje VELBRI

The 36th J Project Meeting was held in Tehran, Iran, October 11-12, 2009

The 36th J Project meeting on primary immunodeficiency diseases (PID) was held on 11-12 October 2009 in Tehran, Iran. Head of the international pediatrics congress was Ali Rabbani, MD; organizers of the J Project Meeting were Asghar Aghamohammadi, MD, PhD and Nima Rezaei, MD, PhD.

Each year an International Congress on Pediatrics takes place in Tehran and several PID experts have attended these scientific congresses in Iran during the last decade. In 2005, the first International Congress on Immunodeficiency Disorders was organized in Tehran. A number of PID experts from different countries (USA, UK, Germany, France, Italy, Sweden, Spain, Japan, and Turkey) attended the congress to present an update in this field, whereas many scientists and researchers took part in this congress to increase their knowledge. This congress was a great event to further develop bilateral scientific exchange of Iranian scientists with other researchers of the world.

In October 2009, alongside the 21st Congress of Pediatrics, a joint meeting on Immunodeficiency Diseases was established. In order to have mutual scientific exchange with other researchers of the world, the scientific committee arranged a 2-day meeting, which was organized by the Department of Pediatrics, Children's Medical Center (Pediatrics Center of Excellence in Iran), Tehran University of Medical Sciences. The Jeffrey Modell Foundation (JMF) also supported the meeting.

The meeting focused on the linkages of fundamental sciences and patient-oriented research under the main theme of immunodeficiencies, whilst improving the awareness of physicians, pediatricians and other specialists on PID was the main objective of the meeting. More than 300 researchers and clinicians attended the meeting. The major part of the audience included general practitioners, pediatricians, and pediatric subspecialists; however, medical students, pediatric residents and fellows in the field of clinical immunology and infectious diseases also actively participated in the meeting.

News & Views—Continuing

The 36th J Project Meeting was held in Tehran, Iran, October 11-12, 2009 — Continuing

Some of the important topics that were presented during this meeting include:

- Novel monogenic disorders of the immune system - from genes to novel therapies
- Approach to children with recurrent infections
- Approach to children with chronic cough
- Approach to children with fever
- Approach to a patient with neutropenia
- Antibiotic therapy in respiratory and urinary infections
- Clinical manifestations and complications of primary immunodeficiencies
- Primary immunodeficiency diseases associated with neutropenia
- Immunological aspects of patients with disseminated BCG in North West Iran
- Odd presentations of chronic granulomatous disease

A poster session was also organized and presenters were asked to present their poster for 5 minutes.

Finally, we believe that the J Project is essential and useful and we would like to thank Prof. László Maródi for his initiative in this regard. We consider the event in Tehran as a successful J Project event, and we plan to repeat it in October 11-12, 2010 just after the ESID meeting in Istanbul. Therefore we invite all the ESID members to take part in our next J Meeting, as it would be easy to travel to Tehran from Istanbul and attendees hopefully will have a memorable time by travelling to both Turkey and Iran.

We are looking forward to continuing the successful cooperation and seeing you in Tehran.

Asghar AGHAMOHAMMADI

Nima REZAEI

Working Parties Reports

Report from the ESID Registries Working Party

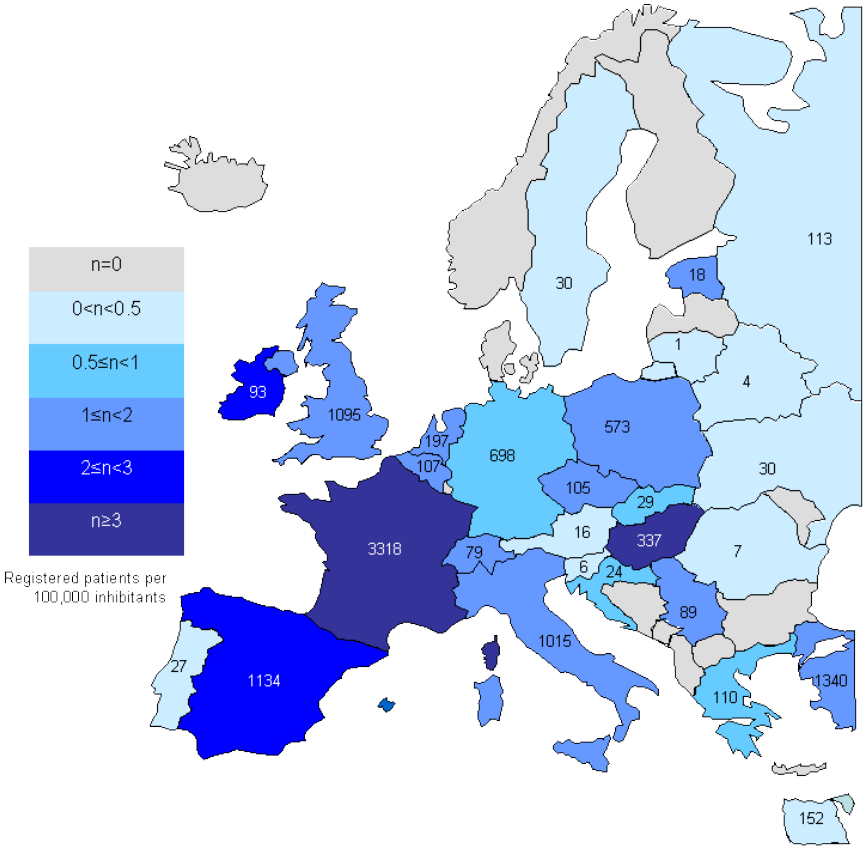

Fig.1: Registration progress by countries. The absolute number of patients is displayed in the map. The colours indicate the documentation rate in relation to the country population.

Working Parties Reports — Continuing

Report from the ESID Registries Working Party—Continuing

Current results and publications

As of December 21st, 2009, the ESID Database held data on 10,747 patients with a primary immunodeficiency disease. Of these, 9,702 were alive, while 824 were deceased. In the remaining 221 patients, the status was unknown. Of the 9,702 alive patients, the current treatment was documented in 8,548 patients (88%). Immunoglobulin replacement still represented by far the most frequent treatment in PID patients. It was applied in 3,587 (42%) of these patients.

While some basic statistics like these are updated regularly on the ESID website (www.esid.org/statistics.php), more detailed analyses have recently been published in Clinical and Experimental Immunology *Gathmann B et al.: The European internet-based patient and research database for primary immunodeficiencies: results 2006-08. Clin Exp Immunol. 2009 157 (Suppl 1):3-11* is an epidemiological overview of the data gathered in the ESID Database so far. *Ballow M et al: Immunodeficiencies. Clin Exp Immunol. 2009 Dec;158 Suppl 1:14-22.* focuses on the treatment of PID patients with immunoglobulin replacement and includes results in this field from the ESID Database.

Sabine El-Helou, German national data entry clerk within the PID-NET project

Publication awards

We again want to use this opportunity to encourage everyone working with the ESID Database to publish their results. With the support of PPTA, each year ESID awards the best publications using data from the ESID Database with prizes up to 5,000 €.

In 2010, the ESID Board will select a maximum of five publications to be awarded as follows:

- EUR 5,000 for the best publication
- EUR 4,000 for the second best
- EUR 3,000 for rank three
- EUR 2,000 go to rank four and
- EUR 1,000 are awarded to the fifth best publication

Applications for these awards can be submitted until February 28th, 2010. Publications must fulfil the following criteria:

(1) The date of publication must be in 2009.

(2) The publication must be based on data that has been collected at least in part in the ESID Online Database for Primary Immunodeficiencies

(3) The publication must mention the contribution of the ESID Database in its acknowledgements.

Applications shall be submitted to the ESID Board via Dr. Gerhard Kindle, Head of the ESID Registries Working Party, registry@esid.org

Documentation progress

The last months have seen a fast increase in patient numbers both in Hungary and The Netherlands. As we already mentioned in the last newsletter, The Netherlands are building up a national registry within the ESID Database since July 2009. The medical students who are registering the PID patients have by now documented almost 200 patients (see Fig. 1).

We hope to witness a similar progress in Germany where Sabine El-Helou has been employed as national data entry clerk within the PID-NET Project (see last newsletter) in November 2009. She is now starting to tour Germany in order to document PID patients in the ESID Database.

We are looking forward to 2010 and wish everyone a Happy New Year!

Gerhard KINDLE and Benjamin GATHMANN

Working Party Reports — Continuing

Report from the ESID juniors Working Party

ESID Summer School 2009

The seventh ESID Summer School in Primary Immunodeficiency Diseases took place in Bled, Slovenia, from 2 - 6th September 2009. The event has proved to be another astounding success.

The ESID Summer School was geared towards fellows in training, with a primary goal of education in the diagnosis, pathogenesis, and treatment of Primary Immunodeficiency diseases. The secondary goals of the Summer School were to attract and develop future scientists/clinicians in academic medicine and to increase the awareness of PIDs in clinical practice and in scientific discoveries. This year was the 10th year anniversary since this programme was successfully launched by doctors Helen Chapel and Anders Fasth.

Twenty six participants were selected from a diversity of countries: US, New Zealand, Canada, Brazil, Germany, Italy, UK, Portugal, Estonia, Netherlands, Spain, Czech Republic, Switzerland, Norway, Denmark, Turkey, Greece, and Slovenia. For the first time, every student had an assigned mentor, from which he got help and advice. The interactive mode allowed lively discussion and question sessions between the school faculty and students. This year the major topics of the Summer School were Hypogammaglobulinemia, T-cell Development, Thymus and Severe Combined Immunodeficiencies, and Innate Immunity.

A short survey handed to the participants after the meeting showed that the Summer School broadened their understanding and improved their ability to appreciate the scientific basis to the pathophysiology of Primary Immunodeficiencies. Their skills to develop a rational approach to patients with a possible Primary Immunodeficiency were improved significantly and also the skills to care for PID/PAD patients. The material presented in the Summer School were relevant to their research and/or clinical work and the topics presented in the school reinforced their interest in PID field. The lectures were good, comprehensive, well coordinated, incorporating recent developments in the field and shared freely. The faculty were prepared for the lectures, explained the material well and provided informative and representative examples. The discussions and questions session were important for the learning process and increased the understanding of the lectures. General organization and overall satisfaction was good. It was a good balance between the lectures and the cases included in the 'Discussion and Questions' session and the time was enough to interact and socialize.

We thank again our sponsors and mentors in making this event possible!

Working Party Reports — Continuing

Report from the ESID juniors Working Party—Continuing

ESID Junior Workshop

Another exciting workshop occurred in Florence on 11-12 January 2010! The event was hosted by Dr. Eleonora Gambineri (ESID Treasurer) and took place in the main lecture hall of Anna Meyer Children's Hospital.

Accomodation and meals were provided to successful applicants. Five different topics ranging from protocols in PIDs, T cell defects, stem cell transplantation, antibody defects and latest insights on PID were covered.

ESIDjuniors short term travel award

One scholarship of 1,000 Euros was awarded in 2009 to Dr. Nima Rezaei, from Iran. He successfully completed his short term visit in September in Newcastle General Hospital, UK. A full report is presented in this issue of the ESID newsletter. We hope other ESID juniors as well will be inspired by his success story and will follow his example.

We would like to thank again the ESID board, especially our Treasurer Eleonora Gambineri and Chair of the Educational Working Party, Andrew Cant and all the sponsors for their support in our activities.

We welcome your new suggestions, comments, ideas and activities for the ESID juniors working party.

Good luck in all your endeavours and look forward to meeting you ☺!

Wishing you a healthy, prosperous and wonderful 2010!

Crina SAMARGHITEAN

Report from the Clinical Working Party

Dear all, 2009 comes to an end. Old forms of primary immunodeficiencies have been given new names: Dock8, IL10receptor, Dectin1, CARD9 deficiency, just to mention some. The increasing number of primary immunodeficiency disorders (PIDD) makes it ever more challenging to diagnose PIDD. Therefore detailed experienced information on clinical and immunological phenotype of upcoming forms of immunodeficiency becomes essential. In February the website for immune phenotyping in immunodeficiency (www.IPIDnet.org) was launched. The purpose of IPID is to provide the current knowledge on the particular deregulation of the homeostasis of the immune system in specific PIDD. In addition IPID will develop standardized staining protocols and provide diagnostic guidelines for phenotyping the various PIDs. Recently the phenotyping of SCID and BAFF-R deficiency and a general protocol for T cell phenotyping as well as protocols for detection of γc and Stat5 phosphorylation in patients with T-B+NK- SCID (JAK3 and γc) were added. Protocols for CVID, DOCK8, ZAP70 deficiency, XLP, WAS, agammaglobulinemia and staining of B cell precursors in bone marrow samples are on their way. By summer 2010 I hope that we will have over 20 PID and all major protocols necessary for the flowcytometric evaluation of PIDD included in IPIDnet.

It will be very important to provide additional information on the clinical aspects especially of the new PIDD discovered every year. Therefore we will introduce a category on the website of the clinical WP of the ESID introducing clinical hallmarks of newly discovered PIDDs. I will therefore contact some of you who were involved in the discovery of these new entities to contribute short essays presenting the main manifestations of the respective PIDD. These essays can serve in the future as a basis for the definition of diagnostic criteria for these diseases.

Besides the strong interest in improving diagnosis of PIDD, the other project I had put forward when taking on the clinical WP was the challenge of the interface of immunodeficiency and autoimmunity. We have initiated this year a retrospective study on the use of immunosuppressive drugs in antibody deficiency disorders in adults. So far we have included three centres and collected data on nearly 80 patients. After a first evaluation of our questionnaire we are planning to open it up to other centres and hope that I can encourage some of you to participate.

Working Party Reports — Continuing

Report from the Clinical Working Party—Continuing

For this purpose, I plan to set up a platform on our website allowing all of you to announce clinical trials which you are currently running or planning. This initiative will hopefully increase the publicity of clinical trial activity within the ESID and foster the cooperation between many centres. I will prepare a form for entering the main information and make it available on the website as well as in another email I will send out in January 2010.

We will all benefit from increased cooperative activity like surveys and trials. Therefore, I ask you to get involved in the Clinical Working Party, develop project ideas and support the activities of others in order to improve patient care. Hope to see you all at the Clinical WP session in Istanbul. With the best wishes for 2010.

Klaus WARNATZ

Report from the ESID Education Working Party

The close of 2009 is a good time to reflect on a fulfilling and successful year for ESID education. In September the biennial summer school was held in Bled in Slovenia when 40 students and faculty met in very lovely surroundings for 4 days. Previous summer schools have been held in Spain and Portugal, so the move to Slovenia brought the summer school closer to the centre of Europe. Careful attention was given to feedback from previous summer schools and educational days with an emphasis on co-ordinating faculty members presentations and ensuring that there were plenty of opportunities for interaction, exchanging ideas, asking questions and learning from each other's experiences. Each student presented a primary immunodeficiency case, a great opportunity to learn how to succinctly present the key features of a case, formulating the key clinical questions and formulating a management plan. Each faculty member participated in every session as well as leading a session on their topic of special interest. Esther De Vries led the sessions on recognition and identification of PID, highlighting the highly acclaimed ESID diagnostic protocol. Jacques Van Dongen and Helen Chapel led a lively session of B cell disorders looking at both laboratory and clinical features. Georg Hollander brilliantly described T cell immunology and thymic physiology. Andrew Cant covered T cell disorders and haemopoetic stem cell transplantation and Eleonora gave an exciting talk on the new understandings of severe autoimmune disease such as IPEX. Steve Holland gave a highly original and captivating talk on innate immunity, with so much new information on topics such as NEMO and Hyopo IgV. Anders Fasth, who has contributed so much to summer schools over the years, told us about neutrophil disorders in his careful, clear and comprehensive manner. Crina Samarghitean also gave an interesting presentation on bioinformatics. The feedback was very encouraging with most aspects of the summer school being considered excellent!

The educational working party has also been very pleased to facilitate some awards to support younger doctors in research and training exchanges. Here is the list of our 2009 awardees:

Fabiola Caracseghi – *Travel Grant to the Prague Spring Meeting 2009*

Luis Ignacio Gonzales - *Travel Grant to the Prague Spring Meeting 2009*

Dr. Nima Rezaei – *ESID short- term fellowship*

As this newsletter goes to press, there has been a very successful ESID Junior Workshop in Florence organised and hosted by Eleonora Gambineri. This has been an exciting development which resulted in ESID Juniors asking for more educational opportunities. In combination with an event such as the Prague Spring School and the J project meeting we very much hope this will lead to still more Educational possibilities in the future.

Looking forward to ESID 2010 in Istanbul, there will be no less than 22 educational sessions throughout the congress, ranging from "Meet the Professor" breakfast sessions, to discussion workshops for discussing confusing or controversial topics, to larger lectures. Please remember to let us have your feedback as only in this way can we find out how educational activities can be improved and developed. Potential venues for the 2011 summer school are already being explored with some promising results. More about this later in the year!

Finally, as my term as chair of educational committee draws to a close, can I thank you all for your support, encouragement and interest, which has been so helpful. It has been a hugely enjoyable privilege to participate in the work of such a world leading, active and innovative society that brings the best of Europe into a cohesive and formidable force for the advancement, understanding and care of PIDs.

Andrew CANT

Working Party Reports — Continuing

Genetics Working Party

Dear All,

The next meeting of the working party will be in Vienna at EBMT on 20-22 March, 2010. We will be holding a working party session, business meeting and there will be an oral abstract session. At the business meeting we hope to finalise our revised conditioning guidelines which was discussed at the Cambridge meeting and which a number of us have been working on over the past few months and my thanks go to all of those who have contributed to this process. I hope we have a completed and approved document that we can make available on the website after the Vienna meeting.

I look forward to seeing many of you in Vienna.

Bobby GASPAR

PID care in development Working Party

J Project Meetings in 2010 (No. 39-45)

There will be another 7 J-Project meetings in 2010:

- Tirana (Albania), Georgina Kuli-Lito, April 8-9, gkuli_lito@hotmail.com;
- Porto Marina (Egypt), Aisha El-Marsafy, April 16-17, aisha_mars@hotmail.com;
- Kharkov (Ukraine), Liudmyla Chernyshova, May 19-20, chernyshova@ukr.net;
- Chelyabinsk (Russia), IrinaTuzankina, August 29-30, I.Tuzankina@iip.uran.ru;
- Tehran (Iran), Asghar Aghamohammadi, October 11-12, aghamohammadi@sina.tums.ac.ir;
- Podgorica (Montenegro), V. Miranović, November (TBA), vesmir@t-com.me;
- Debrecen (Hungary), László Maródi, December 3-4, lmarodi@dote.hu.

You are very welcome!

Laszlo MARODI

Interesting Papers

Update on primary immunodeficiencies (PIDs)

The updated classification of PIDs compiled by the International Union of Immunological Societies Expert Committee on Primary Immunodeficiencies after its biannual meeting in Dublin, Ireland, in June 2009, was recently published. Novel PIDs identified and reported in the last 2 years, have been added to the list. Careful analysis and prompt recognition of these disorders is essential for treatment and for survival and quality of life in patients affected with PIDs (Notarangelo, L. D et al, J Allergy Clin Immunol 2009, 124(6): 1161-78).

New syndrome

A novel syndrome with most probably autosomal recessive inheritance and unknown etiology was recently described. This new syndrome appeared in sisters born to consanguineous parents and presented with facial dysmorphism, developmental delay, cerebellar ataxia, optic atrophy and bone abnormalities. Both patients had repeated bacterial, viral and fungal infections consistent with combined immunodeficiency. Evaluation of the immune system showed depressed responses to mitogens or anti-CD3 antibody. Humoral immunity was also affected, both patients failed to mount an antibody response to vaccination (Roifman and Chitayat Clin Genet 2009:76: 449-457).

Hereditary folate malabsorption is a rare inborn error of metabolism due to mutations in the proton-coupled folate transporter (PCFT). Clinical presentation of PCFT deficiency may mimic severe combined immune deficiency (SCID). The authors report a 4-month-old female with failure to thrive, normocytic anemia, Pneumocystis jirovecii pneumonia and systemic

Interesting Papers — Continuing

cytomegalovirus infection. Immunological evaluation included hypogammaglobulinemia, absent antibody responses, and lack of mitogen-induced lymphocyte proliferative responses. PCFT mutations should be considered in infants with SCID-like phenotype, as the immunodeficiency is reversible with parenteral folinic acid repletion (Borzutzky, A et al, Clin Immunol 2009, 133(3): 287-94).

New gene

An autosomal recessive form of susceptibility to chronic mucocutaneous candidiasis associated with homozygous mutations in CARD9 was recently found. Chronic mucocutaneous candidiasis is characterized by persistent or recurrent infections of the mucosa or the skin with candida species. The phenotype of susceptibility to fungal infections in human CARD9 deficiency can be another example of a rare primary immunodeficiency that gives insight into the signaling pathway of immune regulation (Glocker, E. O et al, N Engl J Med 2009, 361(18): 1727-35).

Bioinformatics tools in PIDs

Many bioinformatics tools for PIDs are already freely available over the Internet. These bioinformatics tools help healthcare professionals in diagnosis, analysis and prediction. Currently, most of the resources are stand-alone and thus their integration will be a challenge for the future. Another challenge is to develop terminologies, ontologies and standards to achieve semantic interoperability (Samarghitean and Vihinen, Curr Opin Allergy Clin Immunol 2009, 9(6): 531-6).

The recently developed Resource of Asian Primary Immunodeficiencies (RAPID) helped in the development of an algorithm for prediction of candidate PID genes. Using a support vector machine learning approach, the authors predicted 1442 candidate PID genes using 69 binary features of 148 known PID genes and 3162 non-PID genes as a training data set. Six of the predicted genes have recently been experimentally confirmed to be PID genes. The remaining genes represent attractive PIDs candidates for testing in patients where the etiology is unknown (Keerthikumar, S. et al, DNA Res 2009, 16 (6): 345-51).

ESID registry database is a platform for epidemiological analyses and aims to develop new diagnostic and therapeutic strategies and also to identify novel disease-associated genes. The patient Internet-based database was developed in order to estimate the prevalence of PID in Europe as well as to establish and evaluate harmonized guidelines for the diagnosis and treatment of PID. Within 4 years, 7430 patients from 39 countries have been documented in the ESID database. The new results from ESID registry database have been recently published (Gathmann, B et al, Clin Exp Immunol 2009, 157 Suppl 1, 3-11).

An objective computational approach for phenotype analysis of common variable immunodeficiency (CVID) patients was recently published. Using six-color polychromatic flow cytometry, the authors analyzed B-cell phenotypes in a cohort of 48 CVID patients and 49 healthy donors. The Cut tree algorithm found 12 clusters. The new analytical approach enables a search in an objective computational environment for patient cohorts that are defined by similar B-cell profiles and thus contribute to the description of differences between CVID patient groups (Kalina, T, et al Cytometry A 2009, 75(11): 902-9).

A novel approach for nosology and systematic classification of PIDs based on parameters across several clinical, pathological, and physiological dimensions have been recently developed. This new approach combines existing clustering and network partition methods to classify PIDs. The new classification shares certain features with previous groupings, yet is different in a number of details (Samarghitean, Ortutay and Vihinen, J Immunol 2009, 183(11): 7569-75).

I hope you enjoyed the papers selected for this issue and we invite you to share other interesting articles you may have!

People interested to join the editorial board of ESID newsletter please send an email to Crina.Samarghitean@uta.fi.

Crina SAMARGHITEAN

Young Investigators Corner

Update on Th17 cells

The adaptive effector CD4+ T helper-mediated immune response is based on the development of distinct subsets that are characterized by different profiles of cytokine production. Classically naïve CD4+ T effector cells have been identified as two polarized main lineages, type 1 (Th1) or type 2 (Th2), in both mice and humans.

Th1 cells produce IFN-γ, they are mainly involved in protection against intracellular microbes and they are characterized by STAT4 activation and T-bet up-regulation. On the other side Th2 cells produce IL-4, IL-5, IL-9, and IL-13 and are involved in the protection against gastrointestinal nematodes. They express the transcriptional factors STAT6 and GATA3. In addition to their protective role against pathogens Th1 and Th2 are involved in the development of human disorders, such as autoimmune diseases and inflammatory chronic diseases in case of Th1 subpopulation and in the development of allergic diseases in case of Th2 cells.

A third type of Th cells named type 0 (Th0), that is able to produce both Th1 and Th2 cytokines, has also been detected.

More recently, IL-17-producing CD4+ T cells (Th17 cells) have been identified as a unique subset of Th cells that develops along a pathway that is distinct from the Th1, Th2 and Th0 cells differentiation pathways. The major breakthrough leading to discovery of Th17 lineage came from mouse models of autoimmunity such as the experimental autoimmune encephalomyelitis (EAE) and collagen-induced arthritis (CIA), two prototypical autoimmune mouse models that have historically been associated with Th1 responses.

Th17 cells seem to have a protective function against extracellular pathogens and fungi thanks to IL-17A production, that is able to induce recruitment, activation and migration of neutrophils granulocytes in the area of infection.

Human Th17 cells were found to be different from mouse Th17 cells both for some phenotypic and functional features and for the different mechanism of development. In mouse the concomitant activity of TGF-β and IL-6 appears to be necessary for initiation of Th17 differentiation from naïve CD4+ cells and their development is amplified by IL-21 and IL-23. In contrast, in human the combination of IL-1β and IL-6 seem to be involved in Th17 development, with the role of up-regulation mediated by IL-23. Th17 cells express the transcriptional factor ROR-γt (RORC in human) and they are also characterized by the expression of STAT3, CCR6, IL17A, IL-17F, IL-22, the chemokine CCL20 and IL23R.

Recently CD161, a new superficial marker of human Th17, has been described. CD161 is involved in trans-endothelial migration and its physiological ligand is the lectin-like transcript 1. Another member of the same family (C-type lectin domain family-2) has been found to be selectively expressed in the skin, where Th17 migrate during chronic inflammatory disorders. The hypothesis is that CD161 is important for the migration of effector Th17 cells to the tissues thanks to CCR6 recruitment to his ligand CCL20.

Cosmi et al. observed that in peripheral blood all Th17 cells were contained in to the CD161+ population and all CD161+CD4+ cell were CD45RA-CD45RO+ (memory) cells. Moreover CD161 expression was found in CD3+ cells identified in the skin of patients with psoriasis or in the gut mucosa of patients with chronic diseases. They also showed that some human Th17 cells also produce IFN-γ and express both ROR-γt and T-bet and they are able to shift toward Th1 phenotype in presence of IL-12 suggesting a flexibility of human Th17 cells and a possible developmental relationship betheen human Th1 and Th17 cells.

Different groups tried to induce the development of Th17 cells from naïve circulating CD4+ cells of adult subject without successfully results. Cosmi and al. demonstrated the ability of umbilical cord blood CD161+ cells to originate Th17 cell after polyclonal stimulation with anti CD3-CD28 mAb in presence of IL-1β and IL-23, supporting CD161 as a major surface marker of Th17 cells.

Sara CIULLINI MANNURITA

Annunziato F, Romagnani S. Do studies in human better despict Th17 cells? 2009, Blood, online.

Cosmi L, De Palma R, Santarlasci V, Maggi L, Capone M, Frosali F, Rodolico G, Querci V, Abbate G, Angeli R, Berrino L, Fambrini M, Caproni M, Tonelli F, Lazzeri E, Prronchi P, Liotta F, Maggi E, Romagnani S, Annunziato F. Human interleukin 17- producing cells originate from CD161+CD4+ T cell precursor, 2008, J Exp Med 205:1903-1916.

Romagnani S. Human Th17 cells, 2008, Arthritis Research & Therapy, 10:206

Take part in the Newsletter!

We are looking for volunteers to join the editorial board of ESID newsletter. People interested, please contact Editor in Chief, Esther de Vries, at esid@estherdevries.nl or Crina.Samarghitean@uta.fi.

Wish you good ideas and inspiration for many interesting and challenging papers! Do you have interesting articles you want to share with the whole ESID community?

Don't forget to send them to us.

STAY ON BOARD IN 2010 AND 2011!

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