INTERNATIONAL GENETIC EPIDEMIOLOGY SOCIETY

Newsletter – May 2014, Pre-Conference

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Letter from the President

Firstly, I would like to welcome Dr. France Gagnon as the incoming IGES President-Elect and Drs. Inke König and Jenny Barrett as new members on the IGES Board of Directors. I would also like to thank the outgoing Past-President, Dr. Suzanne Leal, and Board members Drs. Jenny Chang-Claude and Cornelia van Duijn, for the time and effort that they contributed to IGES during the past year. We should all remember that service to IGES is voluntary and that many of us are over-committed, but the time and effort of our past and current Officers and Board members is necessary for IGES to continue as a successful society, both academically and financially. I would also like to offer special thanks to Andreas Ziegler, as he moves from the position of President to Past-President, for his outstanding leadership during a year of fiscal austerity for IGES. I would also like to thank all the IGES members who made a tax-deductible contribution to IGES in 2013; your financial support is greatly appreciated. Finally, thanks to all those members who have joined the society this year. Remember that IGES membership dues are no longer included in the previous year's meeting registration fee and that meeting registration fees for non-members will be higher than those for members.

My goals for the coming year are to continue our efforts to ensure the long-term financial stability of IGES; to improve the institutional memory of IGES in terms of stated responsibilities and timelines for the Officers and members of the Board of Directors; to broaden the membership base; to strengthen the international reputation of the Society; and most importantly, to showcase the best that the field has to offer at our annual meeting to be held this year in Vienna, Austria from August 28 to 30, 2014. This year's meeting will be held in conjunction with both the International Society of Clinical Biostatisticians (ISCB) and Genetic Analysis Workshop 19 (GAW19). As always, we anticipate the comradery and intellectual focus and depth of a small, specialized academic society. Speaking for the Officers and the Board of Directors, I really look forward to to seeing you there.

Finally, IGES needs you! It is your Society. We particularly encourage the more junior members of IGES to volunteer. If you are interested in serving on a committee, please send an e-mail with a brief statement about on which committee(s) you might be interested in serving and a c.v. to afwilsonphd@gmail.com.

Alec Wilson

Treasurer's Corner

At the 2013 annual IGES meeting, it was decided to separate membership fees from the annual meeting registration, so if you haven't already signed up for 2014 IGES membership, be sure to visit our website and join our vibrant global community of scientists: http://www.geneticepi.org/. Membership will allow you to take advantage of reduced rates when attending the 2014 annual meeting in Vienna, which promises a very energetic program. Our meeting immediately follows the Genetic Analysis Workshop and the International Society for Clinical Biostatistics annual conference and we are pleased to offer a shared Mini-Symposium with ISCB during the first morning of our conference at no additional cost. Early bird registration rates are only valid until ***May 16, 2014***, so please register now to take advantage of this.

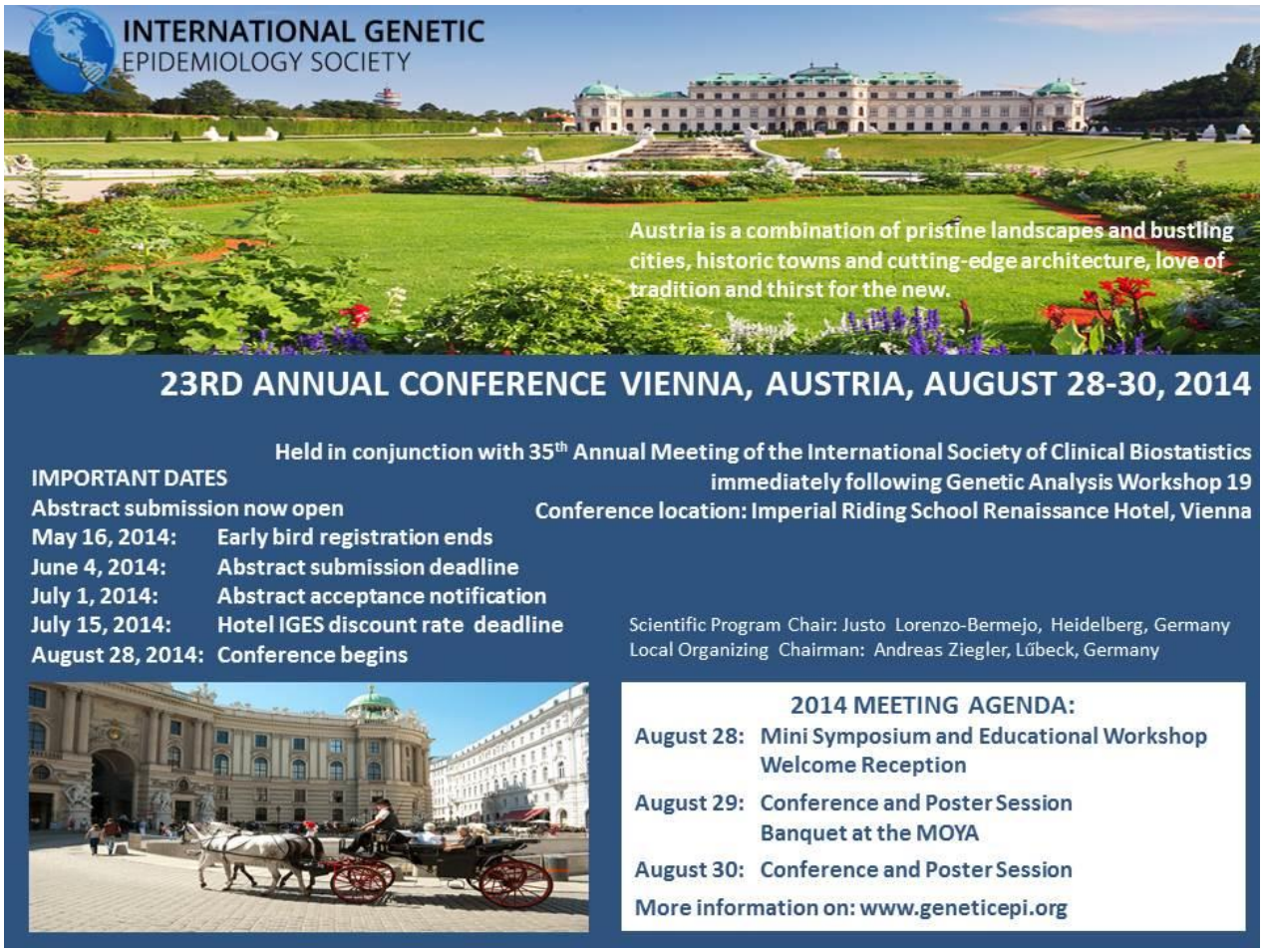
By now, you will have seen communication concerning the SEPA Transfer payment system being made available for our EU 25 Member State or EFTA Country members this year; we hope that this system will save on currency conversion fees. It has made the registration pages more cumbersome to work through, so we appreciate your patience and welcome your feedback on how the process worked for you to determine if we should continue this option. By using the SEPA funds deposited with UKSH, we anticipate savings in our vendor payments for European venues. Thanks go to Andreas Ziegler for arranging this opportunity and to Lynn Carrasco, DeLaine Anderson, and Gabriele Schatton for implementing the details.

The IGES Officers and Board Members have been actively pursuing ways to best use our resources in promoting our organization and its goals. Please join us at the annual meeting in Vienna to hear more on the progress we have made.

I look forward to seeing you all in Vienna!

Mariza de Andrade
IGES Treasurer

2014 Annual Conference in Vienna



Please visit http://www.geneticepi.org/iges-2014/ for registration, abstract submission, and current information on the Vienna Meeting.

CURRENT DATES:

May 16	***Early bird registration period ends***
June 4	***Abstract submission deadline***
July 1	***Abstract acceptance notification***
July 15	***Deadline for IGES discount rate in the conference hotel***

Program Committee

The Program Committee has set up an interesting program for the 2014 Annual Conference in Vienna, with first-class speakers:

Martin Posch
Vienna Medical University, Austria

Enrichment designs for the development of personalized medicine

If the response to treatment depends on genetic biomarkers, it is important to identify (sub-)populations where the treatment has a positive benefit risk balance. One approach to identify relevant subpopulations are subgroup analyses where the treatment effect is estimated in biomarker positive and biomarker negative groups. Subgroup analysis are challenging because different types of risks are associated with inference on subgroups: On the one hand, ignoring a relevant subpopulation one could miss a treatment option due to a dilution of the treatment effect in the full population. Even, if the diluted treatment effect can be demonstrated in an Overall population, it is not ethical to treat patients that do not benefit from the treatmemt, if they can be identified in advance. On the other hand selecting a spurious sub-population is not without risk either: it might increase the risk to approve an inefficient treatment (inflating the type 1 error rate), or may wrongly lead to restricting an efficient treatment to a too narrow fraction of a potential benefiting population. The latter can not only lead to reduced revenue from the drug, but is also unfavourable from a public health perspective. We investigate these risks for non-adaptive study designs that allow for inference on subgroups using multiple testing procedures as well as adaptive designs, where subgroups may be selected in an interim analysis. Quantifying the risks with utility functions the characteristics of such adaptive and non-adaptive designs are compared for a range of scenarios.

Christoph Bock
Research Center for Molecular Medicine of the Austrian Academy of Sciences, Austria

The relevance of epigenomics for personalized medicine

In my presentation, I will summarize the role of next generation sequencing for personalized medicine and highlight the relevance of bioinformatic and biostatistical methods for interpreting the vast amount of genome, epigenome and transcriptome data that are being generated at CeMM and at many genomics institutes world-wide. The talk will also discuss our ongoing work with the European BLUEPRINT project consortium (http://blueprint-epigenome.eu/) aimed at establishing comprehensive epigenome maps of hematopoietic cell types and various types of leukemia cells. I will conclude by outlining an integrated computational/experimental approach toward rational design of epigenetic combination therapies (Bock and Lengauer 2012 Nature Reviews Cancer), which we pursue in collaboration between the CeMM Research Center for Molecular Medicine and the Medical University of Vienna.

Krista Fischer
Tartu University, Estonia

Causal association structures in -omics data: how far can we get with statistical modeling?

This talk mainly concentrates on the setting where association of one genotype marker (typically SNP) with two correlated phenotypes is studied. In so-called "Mendelian Randomization" studies the main parameter of interest corresponds to a causal effect of one phenotypic trait on another trait, whereas a genetic marker is used as an instrument. Despite of the increasing number of publications using this methodological approach, the underlying assumptions are often overlooked. Therefore, many of the published effect estimates may actually be biased and misleading. One of the main untestable assumptions is the "no pleiotropy" assumption - the genotype has a direct causal effect on one phenotype only, whereas the effect on the second phenotype is fully mediated by the first one. When this is not fulfilled, the genotype is said to have a pleiotropic effect on both phenotypes, whereas another class of models is been designed to estimate such effects. However, we will show that mathematically one cannot distinguish between the two models: the model underlying the Mendelian Randomization scenario and the model for pleiotropic effect. We will discuss whether some sensitivity analysis methods may help to draw a correct conclusion here. In addition, we discuss another assumption underlying the Mendelian Randomization idea: the "no-treatment-effect heterogeneity" assumption. Here a parallel can be drawn with randomized clinical trials, where this assumption is crucial to allow for active treatment on the control arm. Using also simulation results, the effect of deviations from this assumption is studied.

Knut Rudi
Norwegian University for Life Sciences, Norway

Microbiome-genome interactions and human disease: an introduction and latest methodological developments

The interface hypothesis in explaining host-bacterial interactions in the human gut. Our gut microbiota is tremendously complex, outnumbering the host cells by a factor of ten and the number of genes by a factor of one hundred. The gut microbiota serves the main functions of extracting energy from the food, production of vitamins and other (essential) biomolecules, in addition to protection towards pathogens. However, despite major efforts we do still not know the basic mechanisms for host-bacterial interactions in the gut. We have therefore recently proposed the interface hypothesis, advocating the importance of positive host selection for mutualistic gut bacteria. I will present details about the hypothesis, and how it is supported from the current knowledge about the human gut microbiota.

Sebastian Zöllner, University of Michigan, USA

The benefit of coalescent theory in the framework of genetic association studies

Fine Mapping of Complex Trait Loci with coalescent methods in Large Case-Control Studies
Ziqian Geng, Paul Scheet and Sebastian Zöllner

Case-control studies are widely used to identify genomic regions containing disease variants. However, identifying the underlying risk variants for complex diseases is challenging due to the complicated genetic dependence structure caused by linkage disequilibrium (LD). By modeling the evolutionary process of a target region, coalescent-based approaches improve this identification by using all available haplotype information. Such methods estimate the genealogy at all sites in the region and thus model the probability of carrying risk variants at all loci jointly. From these probabilities we obtain Bayesian confidence intervals (CIs) where true risk variants are most likely to occur. Additionally, the genealogy at each position provides more information about the shared ancestry of neighboring sites. Indeed, such careful modeling of the shared ancestry of sequences is also beneficial in haplotyping and variant calling in regions of interests (ROI) where traditional hidden Markov approaches struggle. However, existing coalescent-based methods are computationally very challenging and can only be applied to samples below 200 individuals. Here, we propose a novel approach to overcome this difficulty, so that it can be applied to large-scale studies. First, we infer a set of clusters from the sampled haplotypes so that haplotypes within each cluster are inherited from a common ancestor. Then, we apply coalescent-based approaches to approximate the genealogy of ancient haplotypes at different positions across the ROI. Doing so, the dimension of external nodes in coalescent models is reduced from the total sample size to the number of clusters. Finally, we evaluate the position-specific cluster genealogy and their descendants' phenotype distribution, to integrate over all positions and establish CIs where risk variants are most likely to occur. In simulation studies, our method correctly localizes short segments around true risk positions for both rare (1%) and common (5%) risk variants in datasets with thousands of individuals. In summary, we have developed a novel approach to estimate the genealogy throughout sequenced regions. In fine mapping of complex trait loci, our method is applicable for large-scale case-control studies using sequencing data.

Invited talks will be financially supported by the ***International Biometric Society, German Region*** (IBS-DR), the ***German Society for Medical Informatics, Biometry and Epidemiology*** (GMDS) and the ***German Society for Epidemiology*** (DG-Epi).

In line with the talks by invited speakers, abstracts on **the following topics** are particularly welcome:

- Use of genetic data for clinical trial design (enrichment, adaptive and non-adaptive study designs…)
- Causal inference
- Mendelian randomisation
- Epigenetic data: applied and methodological research
- Microbiome data: applied and methodological research
- Population genetics and coalescent theory: applied and methodological research

Please submit your abstract by June 4, an extension of the abstract submission deadline will not be possible!

The 2014 Program Committee comprises:
Justo Lorenzo Bermejo (Chair), Celia Greenwood, Jeanine Houwing-Duistermaat, Andrew Paterson, André Scherag, Nathan Tintle, Alec Wilson (President) and France Gagnon (President-Elect).

Almost a year in advance, the Program Committee chooses topics of interest and speakers for the upcoming IGES meeting. Topic discussions are inspired by results of the participant survey at the preceding IGES conference. We would like to thank the 2013 IGES conference participants for their suggestions.

Justo Lorenzo Bermejo
Program Committee Chair

Education Committee

The IGES Education committee recommends activities concerned with information relevant to genetic epidemiology as it relates to the education of students in general, the training of professionals in genetic epidemiology, and to a lesser extent the awareness of genetic epidemiology by the general public. The committee is especially concerned with education at all levels relating to genetic epidemiology, particularly at the professional level, and aims to encourage liaison with the education committees of other groups. The committee also considers requests to communicate basic genetic epidemiology knowledge, its advances, and its applications to the public at large.

The IGES Education Committee works on a variety of educational and training initiatives each year. The primary focus of the group to date has been this year's education workshop, entitled **"Pharmacogenomics: When drug response gets personal"**, to be held in conjunction with the annual meeting August 28, 2014 from 2 to 5:30pm. This year, the Pharmacogenomics Research Network (PGRN) Statistical Analysis Resource (P-STAR) is sponsoring the education workshop.

Confirmed speakers include: Drs Chris Amos, Nancy Cox, Brooke Fridley and John Witte.
(See presentation titles and abstracts below)

Members on the IGES Education Committee are appointed for three-year terms. This year we welcome Ellen Goode, Heather Ochs-Balcom, Stephanie Santorico, and Silke Szymczak onto the Committee.

Elizabeth Gillanders
Education Committee Chair

Education Workshop

August 28, 2014 from 2 to 5:30pm
"Pharmacogenomics: When drug response gets personal"

Presentation titles:

- Brooke Fridley: ***"Pharmacogenomics: Past, Present and Future"***
- John Witte: ***"Assessing the genetic basis of drug response"***
- Nancy Cox: ***"Clinical Utility in Pharmacogenomics: Getting Beyond Individual Variants"***
- Chris Amos: ***"Smoking behavior and lung cancer risk related to nicotinic acetylcholine receptor variants and metabolic variants."***

Abstracts:

Brooke's Abstract: Pharmacogenetics is the study of the role of inheritance in individual genetic variation in response to drugs. In this post-genomic era, pharmacogenetics has evolved into pharmacogenomics, the study of the influence of genetic variation across the entire genome on drug response. Pharmacogenomics has been heralded as one of the first major clinical applications of the striking advances that have occurred and continue to occur in human genomic science. In this talk, I will provide an overview of pharmacogenomics and discuss the past, present, and future of pharmacogenomics in the 21st century.

John's Abstract: By definition, pharmacogenomic traits have an underlying genetic basis. Nevertheless, accurately estimating the heritability of drug response is important when designing studies and knowing how much genetic variation can—or has—been explained. Unlike most quantitative and qualitative traits, however, response to treatment has two unique, complicating factors: it is a gene-drug interaction and the outcome is often in terms of time-to-event. Here I will present and apply methods that address these two aspects when estimating the genetic basis (or heritabiiity) of pharmacogenomic traits.

Nancy's Abstract: Studies in pharmacogenomics have identified many individual variants with sufficiently large effect sizes to have clinical utility. Many of these are now the subject of implementation studies at a variety of levels. However, recent research on common diseases and complex traits has raised the possibility that mixed models allowing separately for the contribution of variants with larger effect sizes and a polygenic background may yield improved prediction. As medical centers move to having large-scale genome data routinely available on patients, as opposed to one-off genotyping for the prescription of specific drugs, the opportunity to build predictors of adverse events and efficacy using large scale genome data rather than individual (or small numbers of) variants becomes a real possibility. Using real examples from large-scale studies, we will contrast prediction based on individual or small numbers of variants with predictions based on large-scale information. We will also discuss efforts to implement these alternative approaches in EMR settings.

Chris's Abstract: In this presentation, I contrast the discovery of genetic variants that influence smoking behavior including initiation, daily consumption, and cessation. The most prominent associations are with the nicotinic acetylcholine receptor gene family on chromosome 15q25.1. These genes along with CYP2A6 strongly influence smoking behavior and also affect lung cancer risk. I will describe the striking impact that variation in these genes appears to have on the efficacy of pharmacological interventions to influence smoking cessation. Finally, I will describe studies of lung cancer risk and how these genes relate to it, along with a further discussion of the potential relevance of novel associations recently discovered for squamous lung cancer that may influence chemotherapeutic responses.

Publication Committee

The role of the IGES Publications Committee is to select the best paper from the previous year's volume of Genetic Epidemiology. The Committee is composed of nine senior IGES members with expertise covering the scope of the journal. This year, the Committee is reviewing 79 original research articles in Volume 37 of Genetic Epidemiology [2013]. The review process is underway, and the "Best Paper" will be announced in August during the Annual Meeting in beautiful Vienna!

France Gagnon
Publication Committee Chair

Young Investigators Committee

From the annual meeting:

- We had a great turnout at the 2013 IGES YI Mixer, which provided some 50 YI with an opportunity to share a meal and network with other YIs. This facilitated additional discussions with each other throughout the meeting.
- The 2013 IGES Lunch hosted a discussion of career advice between YIs and a handful of senior investigators. This was attended by around 50 YIs and we received requests for the advice slide show. We plan on hosting a similar lunch at the 2014 meeting, focusing on job search strategies.
- The IGES YI Facebook pages served as a location to search for potential roommates during the annual meeting. Let us know what sort of information you would like to see on the page, and we will add broader content.

Additional opportunities:

- The new IGES Facebook page (https://www.facebook.com/geneticepi?ref=hl) and Twitter account (https://twitter.com/Iges2013) provide a great opportunity to ask questions regarding the meeting and resources available.
- The 19th Genetic Analysis Workshop will be held August 24-27, 2014 in Vienna, Austria. This workshop offers a large genetic data set with real and simulated phenotype data for methods development and exploration. Researchers work on this data over the summer and present their findings at the Workshop. For more information, see www.gaworkshop.org.
- The American Society of Human Genetics annual meeting will be held October 18-22 in San Diego, California, USA. This large conference offers the opportunity to meet with thousands of your peers, as well as multiple workshops for various analytical tools, networking, career resources, and professional development. For more information, see www.ashg.org/2014meeting/.

Elizabeth Blue
Young Investigators Committee Chair

Genetic Epidemiology: Editor's Corner

Genetic Epidemiology needs good quality papers. We are running relatively low on papers submitted to the journal. I invite you to submit papers in all aspects of genetic epidemiology (applied and methodological) Examples include (but not limited to) gene-gene, gene-environment interactions, risk prediction models, methods to analyze DNA methylation, RNA seq data.

Genetic Epidemiology (impact factor 4.015) publishes a wide range of high quality manuscript in the fields of statistical genetics, epidemiology, and population genetics. I would like to emphasis that applied genetic epidemiology paper (particularly those coming from consortia) are of interest to the journal.

Please register on Wiley online library to receive email alerts for new content and saved searches. The website for registration is http://onlinelibrary.wiley.com/user-registration. Thanks and look forward to your active participation in the journal.

Sanjay Shete
Editor-in-Chief
sshete@mdanderson.org

Membership Committee

I would like to present you with the report for 2013 – 2014.

Members of the Membership Committee

Drs. Yan Sun (Chair, 2015), J**enny Chang-Claude** (2014)**, M. Daniele Fallin** (2014)**, David Fardo** (2015)**,** Ching-Ti Liu (2016), and Ronnie Sebro (2016). The year in the parenthesis indicates the end of the respective three-year term.

Activities 2013-2014

- Annual committee meeting at IGES 2013

  Members attending the 2013 Annual Meeting: Drs. Yan Sun (Chair), J**enny Chang-Claude, David Fardo and** Ronnie Sebro**; M. Daniele Fallin * (schedule conflict). Absentee:** Ching-Ti Liu

  We discussed the policy and terms of the membership committee. Each committee member will serve for a three-year term. We discussed strategies and new approaches to promoting IGES and the annual meeting with the IGES President.

- Promotion of IGES and annual meeting
  - List of meetings/conferences - promoting IGES and recruiting new members

    We compiled a list of relevant meetings/conferences at which we can advertise IGES. However, we will need a system to identify and track volunteers for these meetings.
  - IGES brochure / annual meeting poster

    We posted and distributed the poster/flyer of the IGES annual meeting at several meetings including the German Society of Epidemiology and ASHG annual meetings. We

also circulated these materials to investigators from China, where research in genetic epidemiology has been growing.

We worked with Dr. France Gagnon's group to design the IGES brochure and distributed it at the ASHG annual meeting.

- IGES ambassadors:
  We communicated with IGES ambassadors to advertise IGES and the annual meeting.

- Survey of 2013 IGES annual meetings
  We entered, combined, and summarized the data taken from a survey of 112 participants attending the 2013 annual meeting in Chicago. The presentation of the summary and our key observations was shared with the IGES leadership and will be shared briefly with all in Vienna.

Yan Sun
Membership Committee Chair

Communication Committee

The communication committee was founded in Chicago. Thus, this is the first report of this committee. The current members are Saoli Basu, Heike Bickeböller, Jessica Dennis, Claire Simpson, Kristel van Steen, and Jin Zhou.

Jessica Dennis is the IGES webmaster. Andrew Entwistle has agreed to stand in for Jessica during her maternity leave. Please note that each year we will request that a young scientist be the webmaster for one year. Please contact us if you are willing to volunteer. It is a great networking opportunity for you.

Jin Zhou has been taking care of Twitter and Facebook, which are new channels available to the society apart from their previous use by the young investigators committee.

The webpage has been subject to a number of changes, so we request that you visit regularly and take a look. The last change was a very recent update to the newest version of WordPress underlying our website. Please let us know if you encounter any problems.

The committee is working on a demand sheet for an internal website. As soon as the society is safely able to afford this, we would like to move in this direction. So please let us know your needs and concerns. The committee is also checking out possibilities for on-demand video conferencing for future meetings. However, we are not pursuing this for Vienna or Baltimore.

The committee also discusses potential content of this newsletter on a regular basis.

Heike Bickeböller
Communication Committee Chair

2014 IGES Officials

The names of all the IGES officials are available on our **website:**

http://www.geneticepi.org/organization/

The **officers are**: President: Alexander F. Wilson; Past President: Andreas Ziegler; President-Elect:France Gagnon; Treasurer: Mariza de Andrade; Secretary: Heike Bickeböller; Editor-in-Chief, Genetic Epidemiology: Sanjay Shete.

Board members are the officers and the following 6 people: Jenny Barrett, L. Adrienne Cupples, Josée Dupuis, Inke König, Andrew Morris, Kristel Van Steen

The **Education Committee** is led by Elzabeth Gillanders. The committee has 13 members. The newest members are Ellen Goode, Heather Ochs-Balcom, Stephanie Santorico and Silke Szymczak.

The **ELSI Committee** is chaired by Claire Simpson and has 14 members. Outgoing members are Alison Klein and Gail Jarvik.

The **Membership Committee** consists of Yan Sun (chair), Danny Fallin, Jenny Chang-Claude, David Fardo, the outgoing members Saurabh Ghosh, Hemant Tiwari and Dharambir Sanghera, and the incoming members Ching-Ti Liu, Anwar Santoso and Ronnie Sebro. There are many more active ambassadors to particular regions of the world.

The **Publication Committee** is chaired by France Gagnon. Standing member as editor of Genetic Epidemiology is Sanjay Shete. Further members are Alexander Wilson, Nancy Saccone, David Conti, Peter Kraft, Bertram Müller-Myhsok, Rasika Mathias and Shelley Bull.

The **Program Committee** included Justo Lorenzo Bermejo (Chair), Celia Greenwood, Jeanine Houwing-Duistermaat, Andrew Paterson, André Scherag, Nathan Tintle, Alec Wilson (President) and France Gagnon (President-Elect).

The **Young Investigators Committee** includes Elizabeth Blue (formerly Marchani) (chair), Katie O'Brian, Melanie Quintana, Lara Sucheston, Amy Spencer.

The **Communication Committee** is chaired by Heike Bickeböller (ex officio). Members are Saonli Basu, Jessica Dennis, Claire Simpson, Kristel van Steen, Jin Zhou.

The **IGES webmaster** is Jessica Dennis. Andrew Entwistle is standing in for Jessica during during her maternity leave. The **IGES Facebook and Twitter master** is Jin Zhou.

The **office** is organized by Delaine Anderson and Lynn Carrasco.

IGES Web Site: http://www.geneticepi.org/
IGES Facebook page: https://www.facebook.com/geneticepi?ref=hl
IGES Twitter page: https://twitter.com/Iges2013

Please note that the IGES Facebook and Twitter pages were only set up recently and are currently in a fledgling state.

IGES Facebook page exclusively for Young Investigators:
https://www.facebook.com/pages/International-Genetic-Epidemiology-Society-Iges-Next-Generation/174416209303988?ref=hl

This newsletter edition was proofread and formatted by Andrew Entwistle.