Scientific Report

European Science Foundation

European conference "Genomics of Complex Diseases: New Challenges" held in Granada, Spain on May 12-13, 2011

Organizer: Prof. Marta E. Alarcón-Riquelme

Organizing team: Dr. David López Herraez, Luisa Pinel and Alberto Ramírez Mena (informatician and presentation facilities)

Venue: Auditorium of the GENYO. Centro de Genómica e Investigaciónes Oncológicas Pfizer-Universidad de Granada-Junta de Andalucía, Granada, Spain.

Summary

When planning the conference, the main idea was to cover the genetics of lupus, in agreement with the BIOLUPUS objectives, but also to extend a bit more on the genomics of complex diseases. Systemic lupus erythematosus (SLE) is a complex disease, and the knowledge of genomics provides a deeper understanding of the possibilities of studying a disease as SLE.

When preparing the program, the plan was to initiate the talks with population genetics, providing as an example the studies performed in cardiovascular diseases (Prof. Ulf De Faire), but also include models of complex diseases. An important model in the study of complex diseases is the dog, a mammalian with great similitude to the human and sharing largely the environment of the human (Hannes Lohi). Then we were to continue with genetics of SLE (Tim Vyse) and diseases that share their genetic architecture with SLE, such as Systemic Sclerosis (Javier Martin) and Rheumatoid arthritis (Jane Worthington).

The second part of the program was aimed at having gene regulation, with two approaches (Esteban Ballestar and Amr Sawalha). Other types of genetic variation are also important, such as copy number variation (Alexandra Blakemore), and other types of potential regulatory mechanisms through retrotransposons (José Luis García Pérez).

A second step after identifying genes for complex diseases is also the understanding of how the polymorphisms or mutations lead to differences in gene expression and function (Sergey Kozyrev) and the combination of various types of variants and epigenetic phenomena is becoming of great interest (Paul Lizardi).

We should not forget that the clinical expression of complex diseases depends on the interaction between genes and environment, and potentially, important environmental factors such as infections should be considered. In fact, viral infections are thought to be important in the development of SLE (e.g. Epstein-Barr virus), however bacterial infections lie behind an important level of morbidity and mortality in SLE. Understanding how to study the presence of microbial infections in biological fluids using new types of methodology is of great importance (Alex Mira).

It is becoming clear that the genes identified to date do not explain the complete genetic contribution of genes to the development of SLE, and among the factors of major importance are rare mutations (Marta Alarcón-Riquelme). In addition, new and important technologies such as next generation sequencing will allow us to define the genetic architecture of complex diseases to a fine scale (Rasmus Nielsen and David Goldstein) but these also require very important computational efforts and a great deal of bioinformatics (Alberto Labarga), so we required the experience of researchers who are in the front line of next generation sequencing studies.

The major aim of the conference was to provide young scientists and students with a State-of-the-Art conference with many lessons for them to take home and new ideas to develop.

Description of the Scientific Content and Discussion at the Event

The Conference: May 12, 2011

The conference started at 9am by a welcome of Prof Alarcón-Riquelme, delineating the aims of BIOLUPUS and thanking the ESF for the funding for the organization of this conference for 5 minutes. Unfortunately Prof Ulf De Faire who was to give the first talk did not arrive (arrived the next day), and we started the session with Dr Hannes Lohi who provided an excellent presentation on dog genetics and the usefulness of this animal model in the genetics of complex diseases.

Dr Lohi was followed by Prof Tim Vyse, who is a Steering Board member of BIOLUPUS and who presented preliminary data on a genome-wide association scan for SLE that is being performed with over 4500 cases of SLE and over 9000 controls, the largest on this disease.

Dr Javier Martin talked about the genetics of Systemic Sclerosis (Scleroderma) and the genes that have been found that overlap with genes found in SLE.

Dr Jane Worthington gave an excellent talk, but in the bottom very similar to that of Dr Martin. Dr Worthington left the impression that most genes found in autoimmune diseases, with the exception of the HLA, are lupus genes. She also made emphasis on copy number variation and gene regulation. The session ended affirming that SLE is the prototype autoimmune disease.

The presentations of Dr Vyse, Dr Martin and Dr Worthington covered primarily the genetics of complex diseases regarding the study through genome-wide association scans.

Lunch was served as individual bags containing a sandwich while participants had time to look at the posters. We received a total of 33 abstracts. Of these 10 were selected as oral presentations and the rest were presented as posters.

After lunch, the first abstract session was given. It included the following presentations of 10 minutes each and 2 minutes of discussion:

1. Nadia Barrizzone: Rare variants in two functionally-related genes (TREX1 and PRF1) and susceptibility to autoimmune diseases.
2. Christian Enevold to present, but it was Dr Sören Jacobsen who presented: TLR7-rs3853839 polymorphism associated with systemic lupus erythematosus and nephritis in a Danish population.
3. Maria Fedetz. The autoimmune disease-associated KIF5A, CD226 and SH2B3 gene variants confer susceptibility for multiple sclerosis.

4. Sabrina Görgen. HLA-DRB1*04 is a novel fetal susceptibility allele in congenital heart block.
5. Elena Carnero Montoro. Functional relevance of a non-synonymous substitution in the CD5 gene (V471A) targeted for positive selection in East Asian populations.

Two excellent talks on epigenetics followed in the afternoon: Dr Esteban Ballestar provided a general overview on epigenetics and on the role of epigenetics and cancer while Dr Amr Sawalha gave a talk on epigenetics and SLE. Both talks were excellent.

The general participation was very good, there was ample discussion during the sessions and in fact enough time was given for discussions.

May 13th, 2011

The next morning was initiated with an excellent talk of Dr Alexandra Blakemore who gave a very good overview of copy number variation primarily on the topic of her research, obesity. In particular it was important to understand the methodologies involving recognition and genotyping of CNVs. Simple SNPs only tag simple CNVs, and validation of this type of variation and the functional consequences of their presence requires much more work than SNP genotyping.

Another type of regulation which may have unexplored functional implications are retrotransposons, and Dr García Pérez gave an excellent overview of what retrotransposons are and how they might be implicated in gene regulation.

Dr Sergey Kozyrev described several studies where the functional consequences of susceptibility variants are investigated in SLE. He described mainly variants in BANK1.

Finally, for the morning session Dr Paul Lizardi gave an excellent presentation on the investigation of the role of so called “junk” DNA, that is human sequences that are repeats, and their potential role in gene regulation and in particular in cancer. Many sequences such as LINE1 or other are repressed in somatic tissues because these lie within CpG islands and their activation may occur in cancer.

At the end of the morning, the second abstract session took place and the following abstracts were presented:
6. Lorenzo de la Rica. Dynamic Epigenomic profiling in autoimmune rheumatic disorders.
7. Eguzkine Ochoa. Identification of susceptibility genes to thrombosis in individuals with antiphospholipid antibodies.

8. Celine Berthier. Cross-species transcriptional network analysis defines shared inflammatory responses in murine and human lupus nephritis.
9. Klementy Shchtynsky. Epistatic relations between MAP2K4 and PTPN22 in development of rheumatoid arthritis.
10. José Ezequiel Martin. Identification of novel genetic markers associated with clinical phenotypes and auto-antibody subsets of systemic sclerosis through a genome-wide strategy.

Dr Ulf DeFaire arrived and was given time at the beginning of the afternoon session. He discussed the "disappointment" of the studies on the genetics of cardiovascular disease and how little clinical importance such studies have revealed of the genes identified. A presentation that gave much to think of.

Dr Carlsten Carlberg as rapporteur informed about the coming decisions on the topics for the European Union calls for FP8 and FP9. A very lively debate ensued on the role of research and the role of stakeholders in determining what researchers should do.

The presentation by Dr Alex Mira was excellent. An overview of the technological possibilities for the identification of bacteria in body fluids using pyrosequencing and next generation sequencing were provided. He gave various examples of studies ongoing.

Dr Alarcón-Riquelme presented a very succinct overview on rare mutations in SLE. Several have been identified and have been of importance in a disease like SLE: complement deficiencies, TREX1, SIAE, etc.

This presentation gave in a sense the introducing momentum for the next one. Unfortunately Dr Rasmus Nielsen could not come to the conference, but he sent a postdoc, Dr Anders Albrechtsen, who did a great job! His presentation went through various phases of the use of next generation sequencing and exome sequencing and bioinformatics in the identification of rare mutations and other types of mutations in complex diseases.

Also as a last minute cancellation, Dr David Goldstein did not arrive due to personal family issues. So the last speaker was Dr Alberto Labarga who gave an extensive talk on bioinformatics and several aspects of it.

The conference was ended with a short acknowledgement to the organizing team and all of the speakers by Dr Alarcón-Riquelme.

Also, Dr Alarcón-Riquelme was chairman for all the sessions.

Assessment of the Results and Impact on the Future Direction of the Field

Several participants came to us and expressed their utmost satisfaction with the conference, and particularly with the high academic level of the conference. I believe that 90% of the talks were academically excellent and the remaining of the talks were very good. I also believe students and even scientists involved learned definitely very much and that this type of conference, covering topics not just focused on a disease but on several topics that are important to learn to be able to study such disease is very important. In a way we organized the type of conference we would like to participate at. Even if it was unfortunate that we missed our Keynote speaker in the last minute, the conference was considered providing the latest on the field of genomics. I believe we could repeat this conference to give an update of the field and that this conference covered very advanced topics. It is very important to keep such a high academic level.

In general, the field of genomics, next generation sequencing and bioinformatics has recently started. While this conference was aiming at individuals not only interested in lupus but in all complex diseases, it was also aimed at providing those interested in lupus of the knowledge on genomics. Particular comments were given by clinical practitioners who were present (Dr Sören Jacobsen, Carlo Chizzolini) who expressed very deeply how this conference opened their eyes to what genomics really is and the level of science that is possible to achieve. This I believe is a very important discussion.

European Conference

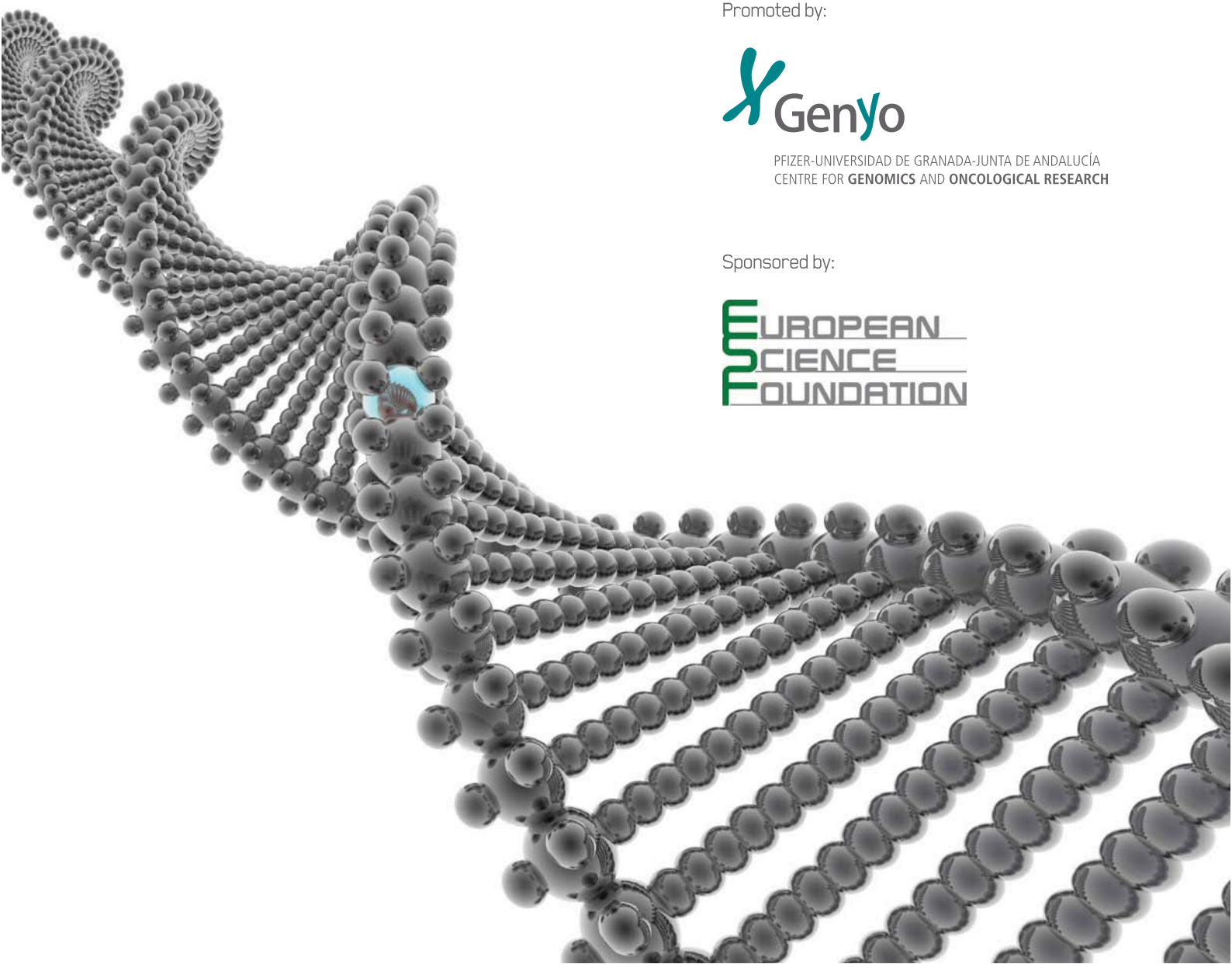
GENOMICS OF COMPLEX DISEASES: NEW CHALLENGES

Granada, Spain / May 12th and 13th, 2011

Conference Venue:
GENYO

Sponsored by:
European Science Foundation

Organized by:
BIOLUPUS Research Network



Promoted by:

Genyo

PFIZER-UNIVERSIDAD DE GRANADA-JUNTA DE ANDALUCÍA
CENTRE FOR **GENOMICS** AND **ONCOLOGICAL RESEARCH**

Sponsored by:

EUROPEAN SCIENCE FOUNDATION

European Conference

GENOMICS OF COMPLEX DISEASES: NEW CHALLENGES

Granada, Spain / May 12th and 13th, 2011

MEETING PROGRAM
THURSDAY MAY 12TH

08.30 Registration Conference

→ SESSION 1: GENETIC VARIATION AND DISEASE

09.00 Introduction and welcome to the meeting
Prof. Marta E. Alarcón-Riquelme GENYO and Centro Superior de Investigaciones Científicas (CSIC), Granada, Spain

09.05 Population genetics as a resource to identify disease susceptibility genes in cardiovascular disease
Prof. Ulf DeFaire Karolinska Institutet, Solna, Sweden

09.50 Dog Models for human complex diseases
Prof. Hannes Lohi University of Helsinki, Finland

10.35 Coffee Pause

11.00 State-of-the-Art in lupus genetic susceptibility: Lessons from a GWAS
Prof. Timothy Vyse King's College London, UK (11.00-11.45)

11.45 Shared genes in autoimmunity: Scleroderma and SLE
Prof. Javier Martin Centro Superior de Investigaciones Científicas (CSIC)

12.15 Shared genes in autoimmunity: Rheumatoid arthritis and SLE
Prof. Jane Worthington University of Manchester, UK

13.30 Lunch

14.45 Selected abstracts to be presented by students and postdocs

15.45 Coffee Pause

→ SESSION 2: THE GENOME IN DISEASE: GENE FUNCTION, REGULATION AND THERAPY - PART I

16.00 Epigenomics
Dr. Esteban Ballestar IDIBELL, Barcelona, Spain

16.40 Epigenetics of lupus
Dr. Amr Sawalha Oklahoma University, Oklahoma City, USA

17.45 Buses to Hotels

20:00 DINNER at Restaurante OLEUM

European Conference

GENOMICS OF COMPLEX DISEASES: NEW CHALLENGES

Granada, Spain / May 12th and 13th, 2011

MEETING PROGRAM
FRIDAY MAY 13TH

→ SESSION 2: THE GENOME IN DISEASE: GENE FUNCTION, REGULATION AND THERAPY - PART II

09.00 Copy number variation in complex diseases
Prof. Alexandra Blakemore Imperial College London, UK

09.40 Retrotransposons in the Human Genome: implications in disease
Dr. José Luis García Perez GENYO, Granada, Spain

10.20 Coffee Pause

10.40 Structure-function analysis of genetic variation in lupus
Dr. Sergey Kozyrev University of Uppsala, Sweden

11.20 Keynote Speaker: Epigenetic Instability Phenotypes in the Human Repeat Spectrum: From Genome-wide DNA Methylation Metrics to Real-time Imaging in Living Cells
Prof. Paul Lizardi University of Yale, New Haven, USA

12.00 Selected abstracts to be presented by students and postdocs

13.15 Lunch

→ SESSION 3: NEXT GENERATION SEQUENCING: POSSIBILITIES AND CHALLENGES IN THE STUDY OF COMPLEX DISEASES

14.30 Report on Conference on Personalized Medicine
Dr. Carlsten Carlberg Universty of Luxemburg and rapporteur of the BIOLUPUS Network for the European Science Foundation

14.50 Microbiomics and NGS
Dr. Alex Mira Centro Superior de Investigación en Salud Pública, Valencia, Spain

15.30 The role of rare genetic variants in lupus
Prof. Marta E. Alarcón-Riquelme GENYO and Centro Superior de Investigaciones Científicas (CSIC), Granada, Spain

16.10 Coffe Pause

16.30 The experience of exome sequencing
Prof. Rasmus Nielsen University of Copenhagen, Denmark

17.10 The bioinformatic challenge of Next Generation Sequencing
Dr. Alberto Labarga University of Granada, Spain

17.40 Keynote Speaker
Dr. David Goldstein Duke University, Durham, USA

18.25 End of the Meeting

European Conference

GENOMICS OF COMPLEX DISEASES: NEW CHALLENGES

Granada, Spain / May 12th and 13th, 2011

Conference Venue:
GENYO

Sponsored by:
European Science Foundation

Organized by:
BIOLUPUS Research Network

+INFO:
www.esf.org/activities/research-networking-programmes/medical-sciences-emrc/current-esf-research-networking-programmes/the-identification-of-novel-genes-and-biomarkers-for-systemic-lupus-erythematosus-biolupus/scientific-activities.html

Promoted by:

Genyo

PFIZER-UNIVERSIDAD DE GRANADA-JUNTA DE ANDALUCÍA
CENTRE FOR **GENOMICS** AND **ONCOLOGICAL RESEARCH**

Pfizer · Junta de Andalucía · Universidad de Granada

Sponsored by:

European Science Foundation

Parque Tecnológico de Ciencias de la Salud
Avenida de la Ilustración 114 | 18007 Granada | SPAIN
t +34 958 71 55 00 | **f** +34 958 63 70 71
www.genyo.es