



## EXTERNAL NEWSLETTER

ISSUE 6 - JUNE 2014

WWW.ABIRISK.EU

*Dear colleagues, dear friends and supporters of ABIRISK,*

*we are pleased to present you the sixth issue of the external newsletter of **Anti-Biopharmaceutical Immunization: prediction and analysis of clinical relevance to minimize the risk -ABIRISK- Project.***

*ABIRISK External Newsletter will be filled with interesting information mainly for all groups external to the ABIRISK consortium that may have an interest in our research and progress.*

*Please don't hesitate to forward this mail to anyone who could also be interested in reading it. If they want to receive their own newsletter in the future they can write at [newsletter@abirisk.eu](mailto:newsletter@abirisk.eu). If you're not interested in receiving our newsletter anymore, you can unsubscribe via mail.*

*In order to contribute to the contents of the newsletter, please send news, photos and other material related to ABIRISK areas of research at [newsletter@abirisk.eu](mailto:newsletter@abirisk.eu)*

*We hope you will enjoy reading our latest news.*

*Best regards,  
The ABIRISK management team*

## THE ABIRISK PROJECT

**ABIRISK** is an Innovative Medicine Initiative 3<sup>rd</sup> Call project on Anti-Biopharmaceutical Immunization. The project, which represents the first concerted effort to solve this problem, officially kicked off March 1<sup>st</sup>, 2012. ABIRISK project will aid in the creation of new, safer **biopharmaceuticals** and also generate tools to determine how individual patients are likely to respond to them both in clinical trials and after release to the market.

**ABIRISK Project** aims to provide an integrated approach to **anti-drug immunization**, bringing together, in an extensive and coordinated manner, a large network of clinicians from various specialties with broad experience in the care of patients treated with various type of **biopharmaceutical products** developing **anti-drug antibodies**, biologists familiar with the immune monitoring of patients, scientists specialized in the mechanisms of immunogenicity, methodologists and biostatisticians. In addition the collaboration with a large network of private pharmaceutical industries under the European Federation of Pharmaceutical Industries and Associations (EFPIA), will ensure direct transfer of the experimental findings into **biopharmaceutical product** development and patient management. Collectively, this group will critically evaluate the immunogenicity of existing **biopharmaceutical products** for **Hemophilia A, Multiple Sclerosis, and Inflammatory Diseases**. The **ABIRISK consortium**, constituting unique task forces for each of these complementary contributions, should improve our ability to predict immunogenicity and to minimize the risk of immunization against **biopharmaceutical products**.

The **ABIRISK project** consortium is presently made up of **thirty-eight partners, twenty-six** of which are **academic institutions, nine are EFPIA member companies** and **three** are small and medium enterprises (**SMEs**). Thirteen countries are represented: The United Kingdom, France, Italy, Germany, Switzerland, Denmark, Belgium, the Netherlands, Spain, Sweden, Austria, Israel and Czech Republic.

The consortium is co-ordinated by GlaxoSmithKline (Dr. Daniel Sikkema, Project coordinator) and Institut National de la Santé et de la Recherche Médicale (INSERM; Prof. Marc Pallardy, Managing entity), and will receive over €30 milion funding over 5 years from 1<sup>st</sup> March 2012.

**The list of ABIRISK partners and more information on the project can be found on the website ([www.abirisk.eu](http://www.abirisk.eu))**



The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° [115303], resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.  
[www.imi.europa.eu](http://www.imi.europa.eu)

### PROJECT NEWS

#### ABIRISK PRESENTED AT KEY IMMUNOGENICITY MEETINGS

At the **2014 AAPS National Biotechnology Conference - Advancing Health Through Innovations in Biotherapeutics** (San Diego, California, May 19-21 2014) **ABIRISK Project** was a **Hot Topic Session** on day 2 of the meeting.

The **Hot Topic Section** was chaired by **Bonita Rup** (ABIRISK Partner 29 Pfizer) and presentations were focused on **ABIRISK Work Package 3 (WP3)** activities. **WP3** of the ABIRISK project is entirely dedicated to technologies of immunogenicity prediction. The main objectives of WP3 are to evaluate the relevance of existing approaches, to develop new predictive assays and to address the specific effects of aggregates on immunogenicity. After a brief overview of IMI and ABIRISK in general and the goals of WP3, **Sebastian Spindeldreher** (ABIRISK Partners 30 Novartis Pharma) and **Bernard Maillère** (ABIRISK Partner 5 Commissariat à L'Energie Atomique et aux Energies Alternatives - CEA), **WP3 co-leaders**, presented details of their WP's recent progress.

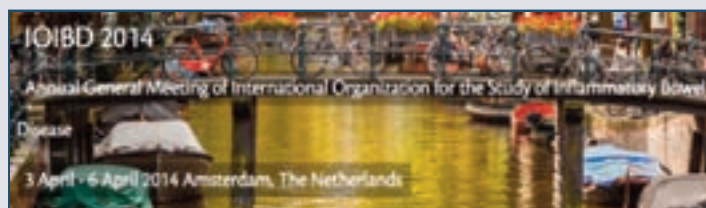


#### CORAL GABLES SYMPOSIUM 2014

At the **2014 Coral Gables Symposium** (Miami, Florida, April 7-8 2014) a **whole Session** was dedicated to **ABIRISK Project**. The **Session** was chaired by **Sebastian Spindeldreher** (ABIRISK Partners 30 Novartis Pharma) and opened by **Florian Deisenhammer** (ABIRISK Partner 18

University of Innsbruck – IMU; ABIRISK Work Package 1 co-leader) presentation focused on **ABIRISK Work Package 1** activities and entitled **“WP1 – Non-drug related immunogenicity factors in biopharmaceutical therapies”**. Florian's talk was followed by **Claudia Mauri** (ABIRISK Partner 8 University College London – UCL; ABIRISK Work Package 2 co-leader) **“WP2 – Are regulatory B cells affected in patients having adverse reactions to biological drugs?”** and **Bernard Maillère** (ABIRISK Partner 5 Commissariat à L'Energie Atomique et aux Energies Alternatives – CEA; ABIRISK Work Package 3 co-leader) **“WP3 – Evaluation and development of technologies for predicting immunogenicity”** presentations.

**Yehuda Chowers** (ABIRISK Partner 13 Rambam Medical Center) was invited to discuss the management of clinical worsening of patients on anti-TNFs treatment to the **2014 Annual General Meeting of International Organization for the Study of Inflammatory Bowel Disease** (Amsterdam, The Netherlands, April 3-6 2014).



The **International Organization for the Study of Inflammatory Bowel Diseases (IOIBD)** is the only international worldwide organization devoted to these chronic and sometimes disabling diseases involving different parts of the gastrointestinal tract. The mission of the IOIBD is to promote the health of people with IBD worldwide by setting the direction for patient care, education and research.

**Sylvia Julien** (ABIRISK Partner 37 IPSEN Innovation) has been invited to present **ABIRISK Project** at the **Exploratory Clinical Development World Europe Meeting** (London, UK, June 3-5 2014) in the context of immunogenicity risk mitigation. The **Exploratory Clinical Development World Europe Meeting** is considered the largest and most influential European event for top pharma & biotech representatives working within exploratory development & early phase clinical trials.

## UPCOMING EVENTS

### SEPTEMBER

#### EUROTOX 2014

The **50<sup>th</sup> Congress of the European Societies of Toxicology** will be held at the **Edinburgh International Conference Centre, Edinburgh** from the **7<sup>th</sup> to the 10<sup>th</sup> September 2014**.

The Conference aim is to "Advance Science for Human and Environmental Health" and there is an exciting programme highlighting new and innovative science and current regulatory topics. There will be a mix of plenary and keynote lectures, symposia, workshops and a full continuing education programme. In addition, there will be interactive poster sessions and a dynamic trade exhibition. EUROTOX 2014 will be the meeting place for toxicologists from around the world to come together to meet and discuss the key issues facing the discipline today.

There will be an attractive social programme, including traditional music and a ceilidh. Edinburgh is an ideal base to explore the impressive beauty of the rest of Scotland.

### NEW PUBLICATIONS PRODUCED BY ABIRISK PROJECT

#### **A novel tree-based procedure for deciphering the genomic spectrum of clinical disease entities**

Mbogning C, Perdry H, Toussile W, Bröet P

*J Clin Bioinforma.* 2014 Apr 16;4(1):6.

Dissecting the genomic spectrum of clinical disease entities is a challenging task. Recursive partitioning (or classification trees) methods provide powerful tools for exploring complex interplay among genomic factors, with respect to a main factor, that can reveal hidden genomic patterns. To take confounding variables into account, the partially linear tree-based regression (PLTR) model has been recently published. It combines regression models and tree-based methodology. It is however computationally burdensome and not well suited for situations for which a large number of exploratory variables is expected.

In the present study **ABIRISK Philippe Bröet's team from Partner 2 Institut National de la Santé et de la Recherche Médicale (INSERM)** developed a novel procedure that represents an alternative to the original PLTR procedure, and considered different selection criteria. A simulation study with different scenarios has been performed to compare the performances of the proposed procedure to the original PLTR strategy.

Results reported in this study indicated that the proposed procedure with a Bayesian Information Criterion (BIC) achieved good performances to detect the hidden structure as compared to the original procedure. The novel procedure was used for analyzing patterns of copy-number alterations in lung adenocarcinomas, with respect to Kirsten Rat Sarcoma Viral Oncogene Homolog gene (KRAS) mutation status, while controlling for a cohort effect. Results highlight two subgroups of pure or nearly pure wild-type KRAS tumors with particular copy-number alteration patterns.

In conclusion, this study reported that the proposed procedure with a BIC criterion represents a powerful and practical alternative to the original procedure. Proposed procedure performs well in a general framework and is simple to implement.



### **The case for measuring anti-drug antibodies in people with multiple sclerosis**

Lundkvist Ryner M, Farrell RA, Fogdell-Hahn A

*Expert Rev Clin Immunol. 2014 Apr 30. [Epub ahead of print]*

The advent of biopharmaceuticals (BPs) has led to significant improvements in the treatment of many chronic inflammatory diseases, and the number of BPs on the market and of diseases treated reflects their success. However, repetitive parenteral administration and intrinsic immunogenic properties of the drug can elicit an immune response, leading to production of anti-drug antibodies (ADA).

This is a major limitation of the use of BPs and has to be taken into consideration in clinical practice and during drug development.

In this editorial **ABIRISK Partners Karolinska Institutet and University College London** describe, due to the increased knowledge about the immunogenicity of BPs and regular ADA testing in patients, an optimized long-term treatment for the individual and thus optimal use of health care resources.

The authors conclude that, although this field has already been extensively investigated in the treatment of multiple sclerosis with IFN- $\beta$ , there is a clear need for consensus from academia, health care providers and the BP industry in managing ADA across all BPs and diseases.



## RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

### **Interleukin-10 produced by B cells is crucial for the suppression of Th17/Th1 responses, induction of T regulatory type 1 cells and reduction of collagen-induced arthritis.**

Carter NA, Rosser EC, Mauri C.

*Arthritis Res Ther. 2012 Feb 8;14(1):R32*

### **Expression of IL-2, IL-17 and TNF-alpha in patients with Crohn's disease treated with anti-TNF antibodies.**

Katz LH, Kopylov U, Fudim E, Yavzori M, Picard O, Ungar B, Eliakim R, Ben-Horin S, Chowers Y.

*Clin Res Hepatol Gastroenterol. 2014 Mar 5. pii: S2210-7401(14)00018-7.*

**Interferon beta treatment of multiple sclerosis increases serum interleukin-7.**

Lundström W, Hermanrud C, Sjöstrand M, Brauner S, Wahren-Herlenius M, Olsson T, Karrenbauer V, Hillert J, Fogdell-Hahn A.

*Mult Scler.* 2014 May 12.

**Therapeutic drug monitoring in inflammatory bowel disease: current state and future perspectives.**

Vande Casteele N, Feagan BG, Gils A, Vermeire S, Khanna R, Sandborn WJ, Levesque BG.

*Curr Gastroenterol Rep.* 2014 Apr;16(4):378.

**MiR-126: a novel route for natalizumab action?**

Meira M, Sievers C, Hoffmann F, Derfuss T, Kuhle J, Kappos L, Lindberg RL.

*Mult Scler.* 2014 Mar 5.

**MS disease activity in RESTORE: A randomized 24-week natalizumab treatment interruption study.**

Fox RJ, Campbell Cree BA, De Sèze J, Gold R, Hartung HP, Jeffery D, Kappos L, Kaufman M, Montalbán X, Weinstock-Guttman B, Anderson B, Natarajan A, Ticho B, Duda P.

*Neurology.* 2014 Mar 28.

**Novel monoclonal antibodies for therapy of multiple sclerosis.**

Knier B, Hemmer B, Korn T.

*Expert Opin Biol Ther.* 2014 Apr;14(4):503-13. 7676.

**FoxA1 directs the lineage and immunosuppressive properties of a novel regulatory T cell population in EAE and MS.**

Liu Y, Carlsson R, Comabella M, Wang J, Kosicki M, Carrion B, Hasan M, Wu X, Montalban X, Dziegiel MH, Sellebjerg F, Sørensen PS, Helin K, Issazadeh-Navikas S.

*Nat Med.* 2014 Mar;20(3):272-82.

**Daclizumab high-yield process in relapsing-remitting multiple sclerosis (SELECTION): a multicentre, randomised, double-blind extension trial.**

Giovannoni G, Gold R, Selmaj K, Havrdova E, Montalban X, Radue EW, Stefoski D, McNeill M, Amaravadi L, Sweetser M, Elkins J, O'Neill G; for the SELECTION Study Investigators.

*Lancet Neurol.* 2014 Mar 18. pii: S14744422(14)70039-0.

**HLA alleles as biomarkers of high-titre neutralising antibodies to interferon- $\beta$  therapy in multiple sclerosis.**

Núñez C, Cénit MC, Alvarez-Lafuente R, Río J, Fernández-Arquero M, Arroyo R, Montalbán X, Fernández O, Oliver-Martos B, Leyva L, Comabella M, Urcelay E.

*J Med Genet.* 2014 Apr 19.

### ABIRISK COMMUNICATION TOOLS

#### PRESS RELEASE

Updating the original version generated by IMI Communication Office, **ABIRISK kick-off meeting fact sheet** has been created to promote ABIRISK project to broad audience mainly through institutional websites of ABIRISK partners, highlighting that the project has been started.

#### PROJECT BROCHURE

Official **ABIRISK Brochure** has been created and distributed to ABIRISK partners to disseminate information about the project in any suitable occasion (meetings, congresses, workshops, exhibition, shows or open forum, etc.) to broad audiences.

#### SCIENTIFIC NEWSLETTER

The **ABIRISK Scientific Newsletter**, an update on ABIRISK topics-related literature and international regulation, is sent to all consortium members and key opinion leaders in the different ABIRISK fields each month, posted on ABIRISK website and advertised on LinkedIn in several Immunogenicity-focused groups.



#### PROJECT WEBSITE

The main source for information on the project is ABIRISK website ([www.abirisk.eu](http://www.abirisk.eu)) where you will find the list of ABIRISK partners and their contact, more detailed information on the project, recent news on the project, all ABIRISK publications and press release, and the ABIRISK Scientific Newsletter.

**ABIRISK WEBSITE has been visited by a monthly average of over 900 people worldwide in the first 6 months of 2014!**