ABIRISK

EXTERNAL NEWSLETTER

ISSUE 12 - DECEMBER 2015

WWW.ABIRISK.EU

Dear colleagues, dear friends and supporters of ABIRISK,

we are pleased to present you the twelfth 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. 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

We hope you will enjoy reading our latest news.

Best regards,
The ABIRISK management team

THE ABIRISK PROJECT

ABIRISK is an Innovative Medicine Initiative 3rd Call project on Anti-Biopharmaceutical Immunization. The project, which represents the first concerted effort to solve this problem, officially kicked off March 1st, 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 1st March 2012.

The list of ABIRISK partners and more information on the project can be found on the website (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.'

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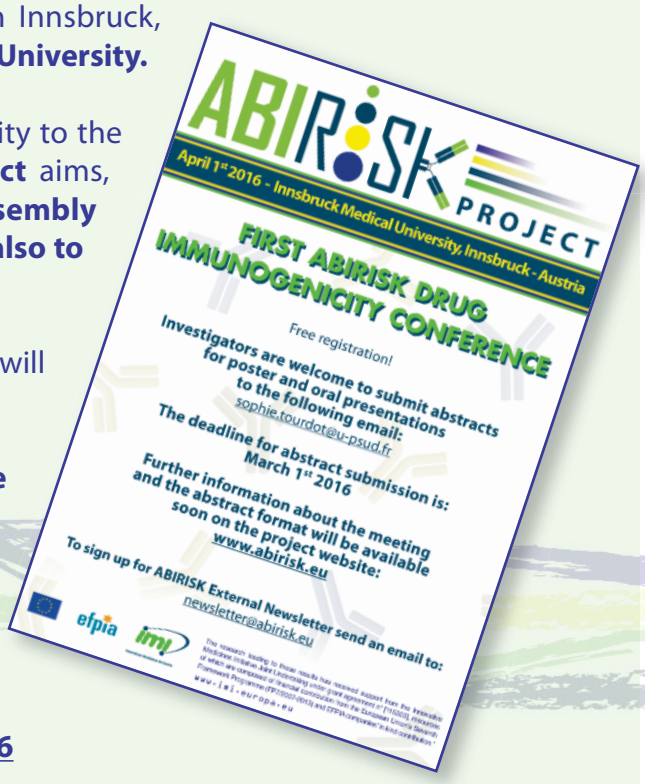
PROJECT NEWS

ABIRISK 2016 GENERAL ASSEMBLY AND DRUG IMMUNOGENICITY CONFERENCE

The 2016 **ABRISK General Assembly** will be held in Innsbruck, Austria, on 29-30 March 2016, at the **Innsbruck Medical University.**



In order to increase awareness and improve the visibility to the international scientific community on **ABIRISK project** aims, objectives and expectations, this year the **General Assembly scientific day** will consist of a scientific meeting **open also to non-ABIRISK members:**

The First ABIRISK Drug Immunogenicity Conference will take place on **1 April 2016** all day.

The registration to the Drug Immunogenicity Conference is free of charge!!!

Investigators are welcome to submit abstracts for poster and oral presentations to the following email: sophie.tourdot@u-psud.fr

The deadline for abstract submission is: 1 March 2016

Abstracts must be written in English. Maximum 2,500 characters (approximately 340 words), including spaces but excluding title and contact information of the authors.

PLEASE NOTIFY IF YOUR ABSTRACT IS SUBMITTED FOR EITHER ORAL OR POSTER PRESENTATION OR ONLY FOR POSTER PRESENTATION

Oral presentations duration is 10 minutes plus questions.

Notifications of acceptance of the abstracts and selection as oral presentation or poster will be sent to the corresponding author of the abstract by **15 March 2016 at the latest.**

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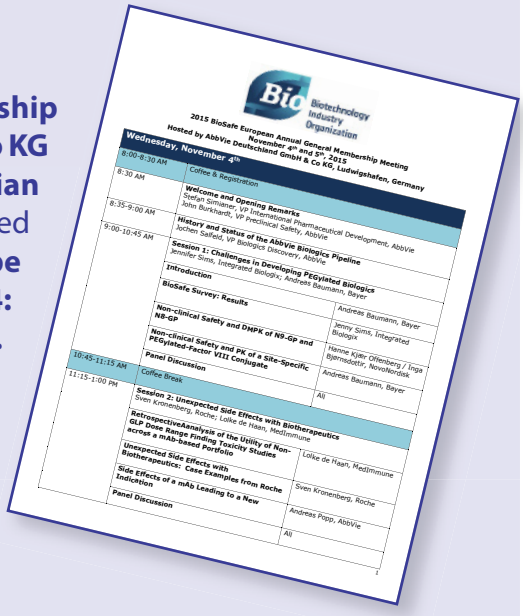
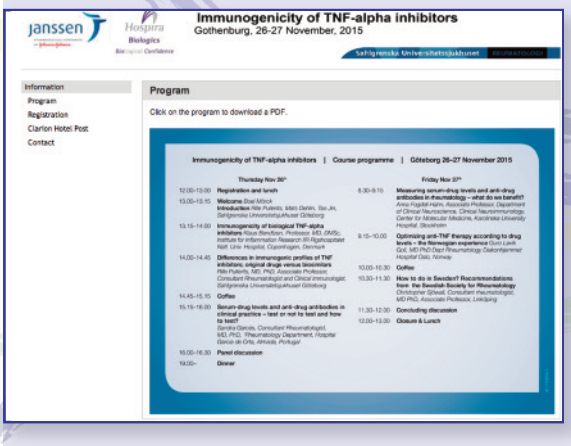
ABIRISK presented at key immunogenicity meetings

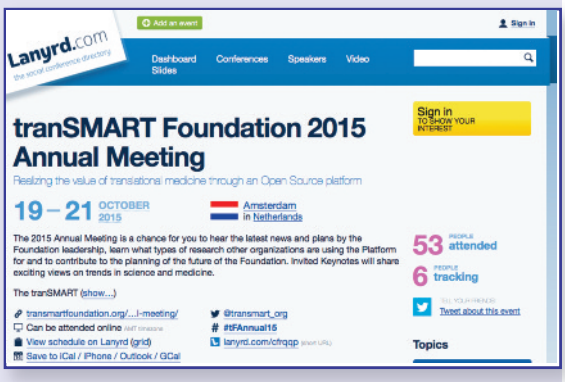
At the **2015 BioSafe European Annual General Membership Meeting**, taking place at the **AbbVie Deutschland GmbH & Co KG in Ludwigshafen, Germany**, on 4-5 November 2015, **Sebastian Spindeldreher** (ABIRISK Partner 30 Novartis Pharma AG) was invited to give a talk entitled **"Immunogenicity Prediction-Can it be Done?"**. Sebastian's presentation was included in the **Session 4: Immunogenicity and PKPD - from Prediction to Interpretation.** The meeting's goal was to provide industry experience and perspectives gained to help ensure common understanding and continued application of scientific principles with respect to key issues in preclinical safety evaluation of biopharmaceuticals.





Anna Fogdell-Hahn (ABIRISK Partner 17 Karolinska Institutet) has been invited to give a talk at the course **"Immunogenicity of TNF-alpha inhibitors"** in Goteborg, Sweden, on 26-27 November 2015. Anna's lecture was entitled **"Measuring serum-drug levels and anti-drug antibodies in rheumatology - what do we benefit?"** and it was focused on most important items related to the immunogenicity of biopharmaceuticals currently utilized in the treatment of some rheumatic autoimmune diseases as well as on how the ABIRISK Project is contributing in improving the knowledge in the field.

Pierre Doennes (ABIRISK Partner 39 SciCross AB) presented the **ABIRISK database and eTRIKS collaboration** at the **tranSMART Foundation 2015 Annual Meeting** in Amsterdam, Netherland, on 19-21 October 2015.
The meeting was a chance for the attenders to hear the latest news and plans by the Foundation leadership, learn what types of research other organizations are using the platform for and to contribute to the planning of the future of the Foundation. Pierre' presentation was entitled "The ABIRISK tranSMART platform" and focused on the ongoing collaboration with eTRIKS and described ABIRISK approach to integrate data.



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UPCOMING EVENTS

12th ANNUAL PEGS BOSTON

Boston, USA, 25-29, April 2016

CHI's flagship biologics event will return to Boston's trendy **Seaport District April 25-29, 2016.**

With record-breaking attendance in 2015, **PEGS Boston** attracts an international delegation of nearly 2,000 participants including conference delegates, speakers, exhibitors, sponsors and guests representing over 30 countries.

Participants value the in-depth short courses, access to 22 conferences, and wide-ranging presentations delivering new unpublished data, case studies, innovation and insight.

The vast exhibit hall will be packed with 125 exhibiting companies and more than 200 research posters on display providing valuable viewing of innovative new technologies, as well as abundant networking with biopharma researchers and industry representatives.

68th AAN ANNUAL MEETING

Boston, USA, 25-29, April 2016

The **68th AAN Annual Meeting** will take place in **Vancouver, BC, Canada from April 15 to April 21, 2016.**

The **AAN Annual Meeting** is the world's largest gathering of neurologists, bringing together more than 10,000 neurology professionals across the globe to network, discuss cutting-edge research, and take part in top-rated education programing across a wide variety of topics.

As part of its new format, the **2016 AAN Annual Meeting** will feature **Experiential Learning Areas** positioned throughout the convention center from Friday through Thursday. These areas offer dynamic and interactive learning opportunities designed to promote learning outside of a traditional classroom.

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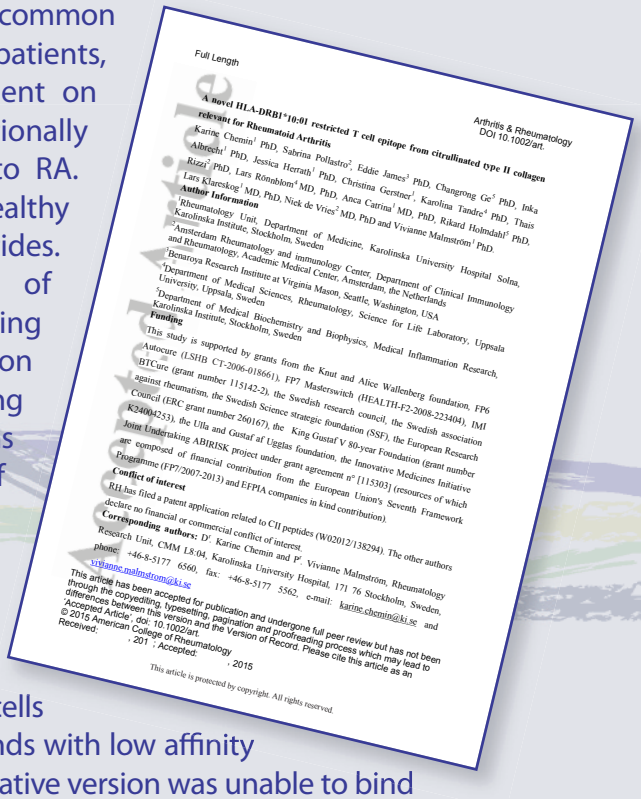
NEW PUBLICATIONS PRODUCED BY ABIRISK PROJECT

A novel HLA-DRB1*10:01 restricted T cell epitope from citrullinated type II collagen relevant for Rheumatoid Arthritis

Karine Chemin, Sabrina Pollastro, Eddie James, Changrong Ge, Inka Albrecht, Jessica Herrath, Christina Gerstner, Karolina Tandre, T.S. Rizzi, Lars Rönnblom, Anca Catrina, Rikard Holmdahl, Lars Klareskog, Niek de Vries, Vivianne Malmström.

Arthritis Rheumatol. 2015 Dec 29. [Epub ahead of print]


Full Length

A novel HLA-DRB1*10:01 restricted T cell epitope from citrullinated type II collagen relevant for Rheumatoid Arthritis

Arthritis & Rheumatology
DOI 10.1002/art.

Karine Chemin[1] PhD, Sabrina Pollastro[2], Eddie James[3] PhD, Changrong Ge[3] PhD, Inka Albrecht[1] PhD, Jessica Herrath[1] PhD, Christina Gerstner[1], Karolina Tandre[4] PhD, Thais Rizzi[2] PhD, Lars Rönnblom[4] MD, PhD, Anca Catrina[1] MD, PhD, Rikard Holmdahl[2] PhD, Lars Klareskog[1] MD, PhD, Niek de Vries[5] MD, PhD and Vivianne Malmström[1] PhD.

Author Information

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[4]Department of Medical Sciences, Rheumatology, Science for Life Laboratory, Uppsala University, Uppsala, Sweden
[5]Department of Medical Biochemistry and Biophysics, Medical Inflammation Research, Karolinska Institute, Stockholm, Sweden

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Conflict of interest

RH has filed a patent application related to CII peptides (W02012/138294). The other authors declare no financial or commercial conflict of interest.

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Antibodies against citrullinated collagen type II (Cit-CII) are common in sera and synovial fluids of Rheumatoid Arthritis (RA) patients, whereas the known CII T cell epitope is not dependent on citrullination. The study aimed to identify and functionally characterize Cit-CII restricted T cell epitopes relevant to RA. PBMCs from HLA-DRB1*10:01 positive RA patients and healthy donors were *in vitro* stimulated with candidate CII peptides. CD154 up-regulation was measured as a marker of antigen-specific activation and anti-HLA-DR blocking experiments confirmed HLA restriction. Cytokine production was measured by Luminex technology. Direct peptide binding assays using HLA-DRB1*10:01 and *04:01 monomeric proteins were performed. The T cell receptor (TCR) β chain of CD154-enriched antigen-specific T cells was sequenced with high-throughput sequencing.

A novel citrullinated CII peptide was identified based on its ability to activate CD4+ T cells from HLA-DRB1*10:01 individuals. When stimulated *in vitro*, Cit-CII autoreactive T cells produced pro-inflammatory cytokines. Cit-CII(311-325) binds with low affinity to HLA-DRB1*10:01 but not to HLA-DRB1*04:01 while the native version was unable to bind either protein. Finally, Highly Expanded Clones (HECs) were identified in the TCRβ repertoire of Cit-CII(311-325) stimulated PBMCs.

Results reported in this study illustrate the ability of the citrullination process to create T cell epitopes from CII, a cartilage-restricted protein relevant to RA pathogenesis. The exclusive binding of Cit-CII(311-325) to HLA-DRB1*10:01 suggests that recognition of citrullinated epitopes might vary between individuals carrying different RA-associated HLA-DR molecules.

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NEW PUBLICATIONS PRODUCED BY ABIRISK PROJECT

Immunogenicity of long-lasting recombinant factor VIII products.
Ing M, Gupta N, Teyssandier M, Maillère B, Pallardy M, Delignat S, Lacroix-Desmazes S; ABIRISK consortium
Cell Immunol. 2015 Dec 19. [Epub ahead of print]

Replacement therapy for patients with hemophilia A using plasma-derived or recombinant factor VIII (FVIII) is complicated by the short half-life of the FVIII products and by the occurrence of neutralizing antibodies in a substantial number of patients.


ARTICLE IN PRESS

Contents lists available at ScienceDirect

Cellular Immunology

journal homepage: www.elsevier.com/locate/ycimm

Review article

Immunogenicity of long-lasting recombinant factor VIII products

Mathieu Ing, Nimesh Gupta, Maud Teyssandier, Bernard Maillère, Marc Pallardy, Sandrine Delignat, Sébastien Lacroix-Desmazes, on behalf of the ABIRISK consortium

ARTICLE INFO

ABSTRACT

1. Introduction

In the recent years, enormous efforts have been invested to develop new generations of coagulation factors with extended half-lives. Presumably, the use of long-lasting FVIII products should reduce the frequency of administration to the patients and drastically improve their quality of life. The question of their immunogenicity remains however unanswered as yet.

The authors of this review propose a summary of the different strategies developed to enhance the half-life of FVIII, including fusion of FVIII to the Fc fragment of the human IgG1 or to human serum albumin, or attachment of polyethylene glycol. Based on the available literature, the authors hypothesize on the potential benefits or risks associated with each of the latter strategies in terms of immunogenicity of the newly derived hemostatic drugs.

RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

Contribution of enhanced engagement of antigen presentation machinery to the clinical immunogenicity of a human IL21 receptor-blocking therapeutic antibody.
Xue L, Hickling T, Song R, Nowak J, Rup B
Clin Exp Immunol. 2015 Sep 24.

The immunogenicity of biosimilar infliximab: can we extrapolate the data across indications?
Ben-Horin S, Heap GA, Ahmad T, Kim H, Kwon T, Chowers Y.
Expert Rev Gastroenterol Hepatol. 2015 Sep;9 Suppl 1:27-34.

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RECENT PUBLICATIONS GENERATED BY ABIRISK PARTICIPANTS OUTSIDE THE PROJECT

Pharmacokinetic considerations in the treatment of multiple sclerosis with interferon-β.
Hegen H, Auer M, Deisenhammer F.
Expert Opin Drug Metab Toxicol. 2015 Sep 30:1-17.

Late-onset neutropenia after treatment with rituximab for rheumatoid arthritis and other autoimmune diseases: data from the AutoImmunity and Rituximab registry.
Salmon JH, Cacoub P, Combe B, Sibilia J, Pallot-Prades B, Fain O, Cantagrel A, Dougados M, Andres E, Meyer O, Carli P, Pertuiset E, Pane I, Maurier F, Ravaud P, Mariette X, Gottenberg JE.
RMD Open. 2015 Jun 30;1(1):e000034.

Subcutaneous Ustekinumab Provides Clinical Benefit for Two-Thirds of Patients With Crohn's Disease Refractory to Anti-Tumor Necrosis Factor Agents.
Wils P, Bouhnik Y, Michetti P, Flourie B, Brixi H, Bourrier A, Allez M, Duclos B, Grimaud JC, Buisson A, Amiot A, Fumery M, Roblin X, Peyrin-Biroulet L, Filippi J, Bouguen G, Abitbol V, Coffin B, Simon M, Laharie D, Pariente B; Groupe d'Etude Thérapeutique des Affections Inflammatoires du Tube Digestif (GETAID).
Clin Gastroenterol Hepatol. 2015 Sep 29.

Daclizumab HYP versus Interferon Beta-1a in Relapsing Multiple Sclerosis.
Kappos L, Wiendl H, Selmaj K, Arnold DL, Havrdova E, Boyko A, Kaufman M, Rose J, Greenberg S, Sweetser M, Riester K, O'Neill G, Elkins J.
N Engl J Med. 2015 Oct 8;373(15):1418-28.

Twenty-eight-week results from the REALISTIC phase IIIb randomized trial: efficacy, safety and predictability of response to certolizumab pegol in a diverse rheumatoid arthritis population.
Weinblatt ME, Fleischmann R, van Vollenhoven RF, Emery P, Huizinga TW, Cutolo M, van der Heijde D, Duncan B, Davies O, Luijtens K, Dougados M.
Arthritis Res Ther. 2015 Nov 15;17(1):325.

Efficacy and safety of tabalumab, an anti-BAFF monoclonal antibody, in patients with moderate-to-severe rheumatoid arthritis and inadequate response to TNF inhibitors: results of a randomised, double-blind, placebo-controlled, phase 3 study.
Schiff M, Combe B, Dörner T, Kremer JM, Huizinga TW, Veenhuizen M, Gill A, Komocsar W, Berclaz PY, Ortmann R, Lee C.
RMD Open. 2015 Aug 12;1(1):e000037.

Optimizing anti-TNFα therapy: Serum Levels of Infliximab and Adalimumab Associate With Mucosal Healing in Patients with Inflammatory Bowel Diseases.
Ungar B, Levy I, Yavne Y, Yavzori M, Picard O, Fudim E, Loebstein R, Chowers Y, Eliakim R, Kopylov U, Ben-Horin S.
Clin Gastroenterol Hepatol. 2015 Oct 29

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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**) 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 1300 people worldwide during 2015!

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