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INTRODUCTION

A growing number of medicines are based on biological molecules such as proteins and monoclonal antibodies. These novel drugs have resulted in new, more effective treatments for a number of serious conditions. Yet sometimes these medicines trigger a response from the patient's immune system, which can decrease the effectiveness of the drug or cause severe side effects.

The aim of the IMI-founded ABIRISK project **"Anti-Biopharmaceutical Immunization: Prediction and Analysis of Clinical Relevance to Minimize the Risk",** is to shed new light on the factors behind this immune response. 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 (BPs)** 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.

The ABIRISK consortium (presently made up of thirty-five partners, twenty-four of which are academic institutions, nine are EFPIA member companies and two are small and medium enterprises, with thirteen countries represented), has been designed to meet all of these requirements in order to target three types of disorders: **Hemophilia A, Multiple sclerosis and Inflammatory diseases: inflammatory rheumatisms (including rheumatoid arthritis) and inflammatory bowel diseases.**

ABIRISK Project will collect data both retrospectively from patients suffering from various types of diseases and treated with various BPs at European centers with a high level of experience in clinical research and will prospectively recruit additional patients in dedicated studies during the 5 years of this program. Guidelines and Standard Operating Protocols for the study of anti-drug immunization will be established and used to standardize the collection of prospective data from these patients.

ABIRISK Project thus represents a unique opportunity to create an interdisciplinary task force of clinical centers especially designed to study immune responses against biopharmaceuticals.

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WELCOME

Dear Reader,

We would like to welcome you to the August 2014 issue of the **ABIRISK Scientific Newsletter**. The Scientific Newsletter gives you a monthly update on the most relevant literature related to ABIRISK topics published around the globe, both inside and outside ABIRISK consortium.

This month, we chose to highlight the work by Hedl and colleagues who elegantly evidenced a loss-of-function for the rs7282490 risk allele in the ICOSLG 734 Immunity region associated with Inflammatory Bowel Disease.

In addition, you will find in this issue some regulatory news on biopharmaceuticals from the European Medicines Agency

We look forward to your visit on **ABIRISK** website for more information and updates on the program.

Enjoy reading !

Best wishes

The ABIRISK management team

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LITERATURE

This month's selected article

Inflammatory bowel disease (IBD) is characterized by dysregulated intestinal immune homeostasis and involves a multifaceted interplay of host genetics and environmental influences. This complex interaction between host genetics and environmental influences have started to unravel through recent advances in the field, which include data generated from genome-wide association studies (GWAS). Multiple loci are associated with IBD, but as of today a functional explanation is missing for most of them. In this paper, Hedl and colleagues elegantly evidenced a loss-of-function for the rs7282490 risk allele in the ICOSLG 734 Immunity region associated with IBD.

Firstly, the authors showed expression of ICOS on monocyte-derived dendritic cells (MDDCs) and more importantly, on intestinal myeloid-derived cells known to mediate early microbial recognition in the intestine. Then, they could demonstrate that ICOS:ICOSL interactions on these cells amplify pattern-recognition receptor (PRR)-induced signaling and cytokine secretion, through amplification of NOD2-initiated signaling. Indeed, ICOSL was required for optimal cytokine secretion upon TLR2, TLR3, TLR4, TLR5 and TLR9 stimulation on MDDCs.

As conserved arginines in the ICOSL in the proximal cytoplasmic tail recruit a PKC-RACK1-JNK signaling complex, the authors went on to compare the PPR-induced cytokine secretion profile of rs7282490 ICOSLG *GG* and *AA* carriers. They found that for GG carriers cytokine secretion was diminished. Further, the authors demonstrated that the rs7282490 risk allele G in the ICOLSG region was associated with increased likelihood of Ileal Crown disease phenotype.

Pattern Recognition Receptor Signaling in Human Dendritic Cells is Enhanced by ICOS Ligand and Modulated by the Crohn's Disease ICOSLG Risk Allele.
Hedl M, Lahiri A, Ning K, Cho JH, Abraham C.
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Immunogenicity

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Arthritis Rheumatol. 2014 Jul 30.

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Is there still a role for abatacept in the treatment of lupus?
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Basic immunology

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BMC Med Genomics. 2014 May 8;7(Suppl 1):S8.

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REGULATION

EMA

Human medicines European public assessment report (EPAR): Plegridy,peginterferon beta-1a
Authorized
July 2014

Opinion/decision on a Paediatric Investigation Plan (PIP): daclizumab
Therapeutic area: Neurology (updated)
July 2014

Human medicines European public assessment report (EPAR): Cimzia, certolizumab pegol
Revision: 11, Authorised
July 2014

Human medicines European public assessment report (EPAR): Avonex, interferon beta-1a
Revision: 20, Authorised
July 2014

Human medicines European public assessment report (EPAR): Rebif, interferon beta-1a
Revision: 28, Authorised
July 2014

Pending EC decision: RoActemra, tocilizumab
Opinion date: 24-Jul-2014

Pending EC decision: Humira, adalimumab
Opinion date: 24-Jul-2014

Human medicines European public assessment report (EPAR): Remicade, infliximab
Revision: 41, Authorised
July 2014

Human medicines European public assessment report (EPAR): Simponi, golimumab
Revision: 17, Authorised
July 2014

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Withdrawn application: Simponi, golimumab
Post-authorisation
July 2014

Opinion/decision on a Paediatric Investigation Plan (PIP): Humira, adalimumab, Therapeutic area: Immunology-Rheumatology-Transplantation/Gastroentology-Hepatology
Updated
July 2014

Opinion/decision on a Paediatric Investigation Plan (PIP): ocrelizumab, Therapeutic area: Neurology
Updated
July 2014

Human medicines European public assessment report (EPAR): MabThera, rituximab
Revision: 33, Authorised
July 2014

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