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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 Re 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 rheumatism (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.

## WELCOME

Dear Reader,

We would like to welcome you to the June 2015 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.

From now on, we will draw your attention to a selection of articles each month that we think make a difference in their respective fields.

In addition, you will find in this issue some regulatory news on biopharmaceuticals

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*

## LITERATURE

### This month's selected articles

1. This study was conducted in the largest cohort to date of patients with borderline inhibitor tests and/or positive personal history of inhibitors, followed up in a routine clinical practice setting:

[Evaluation of safety and effectiveness of factor VIII treatment in haemophilia A patients with low titre inhibitors or a personal history of inhibitor. Patient Data Meta-analysis of rAFH-PFM Post-Authorization Safety Studies.](#)

Romanov V, Marcucci M, Cheng J, Thabane L, Iorio A.  
Thromb Haemost. 2015 May 28;114(1).

2. This review of epigenetic factors that may contribute to autoimmune disease highlights a number of genes that are subject to epigenetic regulation that we are interested in for immunogenicity. Some of these genes or gene products we measure in predictive assays or have already been shown to have genetic relatedness to immunogenicity, such as HLA-DR, IL10 and FOXP3. The review includes methylation, histone acetylation and variance in non-coding RNAs (including miRNA) as well as prospects for epigenetic therapy :

[Epigenetics in autoimmune diseases: pathogenesis and prospects for therapy.](#)

Zhang Z, Zhang R.  
Autoimmun Rev. 2015 May 27.

3. An interesting work on affinity/avidity in a well-defined prospective study population using an attractive method :

[Antibody dissociation rates are predictive of neutralizing antibody \(NAb\) course: a comparison of interferon beta-1b-treated Multiple Sclerosis \(MS\) patients with transient versus sustained NABs.](#)

Gibbs E, Karim ME, Oger J; Steering Committee of the BENEFIT study.  
Clin Immunol. 2015 Mar;157(1):91-101.

## Immunogenicity

### [Cross-reactive and pre-existing antibodies to therapeutic antibodies - effects on treatment and immunogenicity.](#)

Van Schie KA, Wolbink GJ, Rispens T.  
MAbs. 2015 May 11:0.

### [Anti-adalimumab antibodies in juvenile idiopathic arthritis: frequent association with loss of response.](#)

Skrabl-Baumgartner A, Erwa W, Muntean W, Jahnle J.  
Scand J Rheumatol. 2015 May 14:1-4

### [Antibody dissociation rates are predictive of neutralizing antibody \(NAb\) course: a comparison of interferon beta-1b-treated Multiple Sclerosis \(MS\) patients with transient versus sustained NAb.](#)

Gibbs E, Karim ME, Oger J; Steering Committee of the BENEFIT study.  
Clin Immunol. 2015 Mar;157(1):91-101.

### [Monoclonal antibodies in excess: A simple way to avoid immunogenicity in patients?](#)

Chaigne B, Watier H.  
J Allergy Clin Immunol. 2015 Apr 27.

## Methods

### [Biomimetic biosensor to distinguish between inhibitory and non-inhibitory factor VIII antibodies.](#)

Kocot C, Schindler AR, Le Blanc A, Schmalenberg M, Miesbach W, Spannagl M, Luppia PB.  
Anal Bioanal Chem. 2015 May 10.

### [Comparison study of two commercially available methods for the determination of golimumab and anti-golimumab antibody levels in patients with rheumatic diseases.](#)

Martín S, Del Agua AR, Torres N, Pascual-Salcedo D, Plasencia C, Ruiz-Argüello B, Martínez A, Navarro R, Nagore D.  
Clin Chem Lab Med. 2015 May 6.

### [Analytical and clinical evaluation of a new immunoassay for therapeutic drug monitoring of etanercept.](#)

Llinares-Tello F, de Salazar JR, Senabre-Gallego JM, Santos-Soler G, Santos-Ramírez C, Salas-Heredia E, Molina-García J; AIRE-MB Group<sup>a</sup>.  
Clin Chem Lab Med. 2015 Feb 7.

## Animal models

### [Cross-Species Scaling of Monoclonal Antibody Pharmacokinetics Using a Minimal PBPK Model.](#)

Zhao J, Cao Y, Jusko WJ.  
Pharm Res. 2015 May 5.

## Biomarkers

### [Prediction of treatment response to adalimumab: a double-blind placebo-controlled study of circulating microRNA in patients with early rheumatoid arthritis.](#)

Krintel SB, Dehlendorff C, Hetland ML, Hørslev-Petersen K, Andersen KK, Junker P, Pødenphant J, Ellingsen T, Ahlquist P, Lindegaard HM, Linauskas A, Schlemmer A, Dam MY, Hansen I, Horn HC, Jørgensen A, Raun J, Ammitzbøll CG, Østergaard M, Stengaard-Pedersen K, Johansen JS.  
Pharmacogenomics J. 2015 May 5.

### [Biomarkers as potential treatment targets in inflammatory bowel disease: A systematic review.](#)

Murdoch T, O'Donnell S, Silverberg MS, Panaccione R.  
Can J Gastroenterol Hepatol. 2015 May;29(4):203-8.

## Systemic Lupus Erythematosus

### [Targeting interferons in systemic lupus erythematosus: current and future prospects.](#)

Mathian A, Hie M, Cohen-Aubart F, Amoura Z.  
Drugs. 2015 May;75(8):835-46.

## Rheumatoid Arthritis

### [Interpreting the multi-biomarker disease activity score in the context of tocilizumab treatment for patients with rheumatoid arthritis.](#)

Reiss WG, Devenport JN, Low JM, Wu G, Sasso EH.  
Rheumatol Int. 2015 May 31.

[Comparative Effectiveness of Tocilizumab and TNF Inhibitors in Rheumatoid Arthritis Patients: Data from the Rheumatic Diseases Portuguese Register, Reuma.pt.](#)

C Romão V, Santos MJ, Polido-Pereira J, Duarte C, Nero P, Miguel C, Costa JA, Bernardes M, Pimentel-Santos FM, Barcelos F, Costa L, Melo Gomes JA, Pereira da Silva JA, Branco JC, Canas da Silva J, Pereira da Silva JA, Fonseca JE, Canhão H.

Biomed Res Int. 2015;2015:279890.

[Cost-effectiveness of abatacept, rituximab, and TNFi treatment after previous failure with TNFi treatment in rheumatoid arthritis: a pragmatic multi-centre randomised trial.](#)

Manders SH, Kievit W, Adang E, Brus HL, Moens HJ, Hartkamp A, Hendriks L, Brouwer E, Visser H, Vonkeman HE, Hendriks J, Jansen TL, Westhovens R, van de Laar MA, van Riel PL.

Arthritis Res Ther. 2015 May 22;17:134.

[Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force.](#)

Smolen JS, Breedveld FC, Burmester GR, Bykerk V, Dougados M, Emery P, Kvien TK, Navarro-Compán MV, Oliver S, Schoels M, Scholte-Voshaar M, Stamm T, Stoffer M, Takeuchi T, Aletaha D, Andreu JL, Aringer M, Bergman M, Betteridge N, Bijlsma H, Burkhardt H, Cardiel M, Combe B, Durez P, Fonseca JE, Gibofsky A, Gomez-Reino JJ, Graninger W, Hannonen P, Haraoui B, Kouloumas M, Landewe R, Martin-Mola E, Nash P, Ostergaard M, Östör A, Richards P, Sokka-Isler T, Thorne C, Tzioufas AG, van Vollenhoven R, de Wit M, van der Heijde D.

Ann Rheum Dis. 2015 May 12. pii: annrheumdis-2015-207524.

[Effectiveness of Rituximab for the Treatment of Rheumatoid Arthritis in Patients with Prior Exposure to Anti-TNF: Results from the CORRONA Registry.](#)

Harrold LR, Reed GW, Shewade A, Magner R, Saunders KC, John A, Kremer JM, Greenberg JD.

J Rheumatol. 2015 May 1.

[Rheumatoid Arthritis - Anti-TNF.](#)

Chaabo K, Kirkham B.

Int Immunopharmacol. 2015 May 8.

[CD8+T cell profiles in patients with rheumatoid arthritis: The effect of anti-TNF therapy on CD45RA/CCR7 subsets.](#)

Souto-Carneiro MM, Lorenz HM.

Arthritis Rheumatol. 2015 May 4

## Inflammatory Bowel Diseases

[Review article: The pharmacokinetics and pharmacodynamics of drugs used in inflammatory bowel disease treatment.](#)

Quetglas EG, Armuzzi A, Wigge S, Fiorino G, Barnscheid L, Froelich M, Danese S.  
Eur J Clin Pharmacol. 2015 May 27.

[Infliximab is superior to other biological agents for treatment of active ulcerative colitis: A meta-analysis.](#)

Mei WQ, Hu HZ, Liu Y, Li ZC, Wang WG.  
World J Gastroenterol. 2015 May 21;21(19):6044-51.

[Vedolizumab: A New Opponent in the Battle Against Crohn's Disease and Ulcerative Colitis.](#)

Poulakos M, Machin JD, Pauly J, Grace Y.  
J Pharm Pract. 2015 May 6

[Withdrawal of anti-tumour necrosis factor  \$\alpha\$  therapy in inflammatory bowel disease.](#)

Papamichael K, Vermeire S.  
World J Gastroenterol. 2015 Apr 28;21(16):4773-8.

[Use of Intravenous Immunoglobulin for Patients with Inflammatory Bowel Disease with Contraindications or Who Are Unresponsive to Conventional Treatments.](#)

Merkley SA, Beaulieu DB, Horst S, Duley C, Annis K, Nohl A, Schwartz DA.  
Inflamm Bowel Dis. 2015 May 19.

[Briakinumab for treatment of Crohn's disease: results of a randomized trial.](#)

Panaccione R, Sandborn WJ, Gordon GL, Lee SD, Safdi A, Sedghi S, Feagan BG, Hanauer S, Reinisch W, Valentine JF, Huang B, Carcereri R.  
Inflamm Bowel Dis. 2015 Jun;21(6):1329-40.

[Biomarkers of Inflammatory Bowel Disease: From Classical Laboratory Tools to Personalized Medicine.](#)

Viennois E, Zhao Y, Merlin D.  
Inflamm Bowel Dis. 2015 May 15.

[Characterizing unmet medical need and the potential role of new biologic treatment options in patients with ulcerative colitis and Crohn's disease: a systematic review and clinician surveys.](#)

Gordon JP, McEwan PC, Maguire A, Sugrue DM, Puelles J.  
Eur J Gastroenterol Hepatol. 2015 May 7.



## Multiple Sclerosis

[A systematic review of drugs in late-stage development for the treatment of multiple sclerosis: a focus on oral synthetic drugs.](#)

Safavi M, Nikfar S, Abdollahi M.

Inflamm Allergy Drug Targets. 2015 May 28.

[CD4 cell response to interval therapy with natalizumab.](#)

Berkovich R, Togasaki DM, Cen SY, Steinman L.

Ann Clin Transl Neurol. 2015 May;2(5):570-4.

[Daclizumab reverses intrathecal immune cell abnormalities in multiple sclerosis.](#)

Lin YC, Winokur P, Blake A, Wu T, Romm E, Bielekova B.

Ann Clin Transl Neurol. 2015 May;2(5):445-55.

[The Effect of Vitamin A Supplementation on FoxP3 and TGF- \$\beta\$  Gene Expression in Avonex-Treated Multiple Sclerosis Patients.](#)

Saboor-Yaraghi AA, Harirchian MH, Mohammadzadeh Honarvar N, Bitarafan S, Abdolahi M, Siassi F, Salehi E, Sahraian MA, Eshraghian MR, Roostaei T, Koohdani F.

J Mol Neurosci. 2015 May 19.

[Vitamin d in multiple sclerosis and central nervous system demyelinating disease-a review.](#)

Burton JM, Costello FE.

J Neuroophthalmol. 2015 Jun;35(2):194-200.

[Vitamin D3 administration to MS patients leads to increased serum levels of latency activated peptide \(LAP\) of TGF-beta.](#)

Åivo J, Hänninen A, Ilonen J, Soilu-Hänninen M.

J Neuroimmunol. 2015 Mar 15;280:12-5.

## Hemophilia

[Danger signal-dependent activation of human dendritic cells by plasma-derived factor VIII products.](#)

Miller L, Weissmüller S, Ringler E, Crauwels P, van Zandbergen G, Seitz R, Waibler Z; **ABIRISK consortium.**

Thromb Haemost. 2015 May 7;114(2).

[Pharmacokinetic properties of BAY 81-8973, a full-length recombinant factor VIII.](#)

Shah A, Delesen H, Garger S, Lalezari S.  
Haemophilia. 2015 May 8.

**Basic immunology**

[Regulation of tumour necrosis factor signalling: live or let die.](#)

Brenner D, Blaser H, Mak TW.  
Nat Rev Immunol. 2015 May 26;15(6):362-74.

**Opinions/Commentaries/Across diseases reviews**

[Recommendations on the use of biosimilars by the Brazilian Society of Rheumatology, Brazilian Society of Dermatology, Brazilian Federation of Gastroenterology and Brazilian Study Group on Inflammatory Bowel Disease-Focus on clinical evaluation of monoclonal antibodies and fusion proteins used in the treatment of autoimmune diseases.](#)

Azevedo VF, de Souza Meirelles E, Kochen JA, Medeiros AC, Miszputen SJ, Teixeira FV, Damião AO, Kotze PG, Romiti R, Arnone M, Ferreira Magalhães R, Maia CP, de Carvalho AV.  
Autoimmun Rev. 2015 May 1

## REGULATION

### EMA

[Human medicines European public assessment report \(EPAR\): Enbrel, etanercept](#)

Revision: 44, Authorised  
May 2015

[Human medicines European public assessment report \(EPAR\): Humira, adalimumab](#)

Revision: 38, Authorised  
May 2015

[Referral: Article 20 procedures, Tysabri, natalizumab](#)

May 2015

[Opinion/decision on a Paediatric Investigation Plan \(PIP\): Benlysta, Belimumab](#)

Therapeutic area: Immunology-Rheumatology-Transplantation

Updated  
May 2015