

2011, N°2

October 2011

Message from the coordinator



How tightly or loosely should a network be coordinated in order to optimize its outputs? Many times I have contemplated on the above, wondering whether my next mass email would bring the partners closer, or it will just add to the increasing entropy of spam. Well, I think that a network is like a river. In the long term, it is the flowing water

– it's energy, it's force – that will define its limits, much more than the banks. PreDicta is overflowing with energy, with all the groups being dynamically productive in their respective fields, streams of energy steadily joining to produce synergies, the body of the major river.

With just a few weeks to our first birthday, we can of course be happy for starting sharply and setting up robust structures for the project to develop on solid grounds. Two major cohorts have been set-up: the pediatric preschool-to-school has already started to recruit in its five centres, while the adult rhinitis/polyps protocol was re-

ceived with much enthusiasm by the partners, several of which offered to participate voluntarily, in addition to the ones originally planned! The various experimental models, including mice, epithelial cells, lipid mediators, virus chips, DNAzymes have advanced significantly and are ready to either receive samples or proceed to their next phase.

Mobility has been excellent (or excessive in my case...), with several junior scientists moving among centres for training in new techniques and transferring technology. In addition, our networking continues expanding: for example, WP1 has initiated a collaboration

with the Ohio State University College to use transcriptomics on the cohort's samples, while several 'spin-off' projects are being generated between the partners.

Of course, we're still in the beginning. We still have ahead of us the conquest of a deeper understanding of the mechanisms that make asthma persist, including lots of publications, hot debates and translational outputs that will make the world a better place. I can see these coming, which makes me continuously enthusiastic about this great group and project!

See you all in Athens!

Nikos Papadopoulos
National and Kapodistrian
University of Athens

What's new in PreDicta's Work packages?

*Progress made in
PreDicta work
packages from
month 7 to 12
(April 2011 to
September 2011)*



First PreDicta kids recruited for WP1 cohort!



**Predicta WP1 Team
at the Medical Uni-
versity of Lodz**

*Dorota Zarominska ,
Nurse , Anna So-
banska M.D. , Pe-
diatrician
Marek L. Kowals-
ki M.D. , Center
Leader with Hubert ,
one of the first re-
cruited children*

In WP1: Longitudinal cohort

The Pediatric cohort set up has been completed and all centres have received permission to start from their Ethics Committees. Although according to the original planning an electronic diary system should have been ready, this has been delayed due to procedural reasons (what some may, not completely unjustified, call bureaucracy...). Therefore we decided to start using paper diaries and regular PEF meters and to employ the electronic system as soon as it is ready. All centres have or are about to recruit their first patients; in fact the first PreDicta kid was recruited in Lodz on the 19th of August (congratulations to the Polish team!).

The laboratory part has also been optimized and is ready to go. In fact, after the suggestion of Tuomas Jartti, a collaboration with Octavio Ramilo and Asun Mejias from the Ohio State University College to use transcriptomics on the cohort's samples has been set up. Thank you Tuomas for the suggestion and welcome to Octavio and Asun in the PreDicta family!

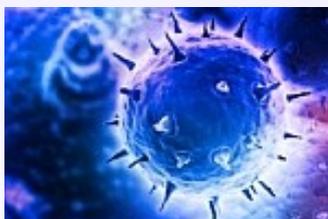
In WP2: Mouse models

The team at BRFAA Athens lead by Vangelis Andreakos reported in EMBO Mol Med a novel role for an anti-viral type III IFN IL-28A (also known as IFN-I2) in modulating CD4⁺ T cell responses in a mouse asthma model. This study was performed as part of Task 2.3 which aims to investigate the importance of innate immune responses to rhinovirus infections in asthma. For Task 2.1 (repeated rhinovirus infections) a manuscript from the Johnston Lab (IC London) entitled *The generation of antibody responses to human rhinovirus in a mouse model of infection* has been prepared for submission to Mucosal Immunology. Collaboration between BRFAA Athens and IC London led to the award of an

EACI short term fellowship. This enabled a member of the BRFAA team (Aikaterini Chairakaki) to join IC for 3 months during which the first studies to investigate dendritic cell responses to rhinovirus infection *in vivo* were performed (Task 2.5).

In WP3: Epithelial models

Recruitment of allergic-asthma, allergic non-asthmatic, non-allergic asthmatic and control individuals continues. Growth of lower airway (bronchial) and upper airway (nasal) epithelial cells is now well established within the labs of the Predicta collaborators. Through the efforts of Dimitri Thanos's team (BRFAA), we are currently optimising assays that will be highly useful in determining why some of these individuals have impaired innate immunity to rhinovirus infection. These include assays that will assess the ability of single cells to produce IFN- β or not, and whether or not IFN- β is being driven from one allele or two. This will be the first time these assays have been used in primary cell types. Preliminary data is currently being generated for the other objectives in this WP, including the investigation of epithelial cells to produce pro-Th2 molecules.



WP4: Virus-Bacteria interactions

In the past months the protocol for WP4 (Virus-Bacteria interactions: Evaluation of the effect of viral infections and bacterial colonization in adults with allergic rhinitis and nasal polyps) has been finalized by input of the different cooperating centers.

We are now with more participants in the study: the project will be running in Ghent (Belgium), Lodz (Poland), Turku (Finland) and Athens (Greece). We are very happy with the interest to cooperation of the different centers, this will certainly add to the value of the study.

After this phase, we can start the application to the ethical committees. If this runs as smooth as we hope, we can start recruitment of patients before the end of 2011.

In WP5: Immune regulation

During the last months, we investigated the influence of viral infections on allergen-specific T regulatory cells in healthy and allergic immune response. We will analyze surface molecules related to T cell activation and tolerance in the presence and absence of RV-infected epithelial culture supernatants. After characterizing their cytokine profile, blocking mAbs and siRNA against major cytokines will be used. The hypothesis is that there can be an influence on ongoing memory Treg cell response as well as an indirect effect via dendritic cell subsets.

In WP6: Resolution of inflammation

Method development for the assessment of lipid mediators in culture supernatants of human bronchial epithelial cells and mouse lung tissue has progressed. Katerina Chairakaki from BRFAA got trained on rhinoviral infection models at Sebastian Johnston's lab in London

In WP7: Diagnostics

Several RV sequences have been aligned and areas of interest identified, expressed and purified. The WP progresses according to PreDicta work plan.

In WP8: Interventions

To develop and characterize DNAzymes according to their cleaving ability of rhinovirus RNA, we focus on the human rhinovirus internal cis-acting regulatory element (CRE) as

well as sequences from the 5'UTR containing the 5' cloverleaf structure. Corresponding sequences from three viral strains (HRV 1b, HRV 16, HRV 29) were cloned into a target vector and reverse transcribed back into tRNA.

Following, we have so far analysed 45 DNAzymes complementary within a 1000bp target region close to the CRE-element, and new ones for both the 5' UTR region and the CRE element are in preparation. No active DNAzymes could be found yet. In parallel, positive controls using active DNAzymes from T-Bet and GATA-3 were established in collaboration with TransMit Marburg.



PreDicta Skin Prick Test protocol (WP1)

ALLERGOPHARMA (<http://www.allergopharma.de>) agreed to provide skin prick test solutions free of charge to support PreDicta Workpackage 1. The skin prick solutions will be shipped to the participating centers in Athens, Ghent, Lodz and Erlangen. The agreement was negotiated by Vicky Xepapadaki and Nikos Papadopoulos from NKUA.

Klosterfrau Award 2012 for Research of Airway Diseases in Childhood

The Klosterfrau Award for Research of Airway Diseases in Childhood is being granted to outstanding researchers and research groups in the field of childhood airway diseases.

The "Klosterfrau Research-Award for Airway Diseases in Childhood" will be awarded to researchers in basic science, pneumology and pediatrics whose work is orientated to a better understanding of airway diseases in children, especially those suffering from bronchial asthma, congenital disorders of the airway tract as well as primary diseases of the lung parenchyma.

The prize is endowed with 30.000 € and will be given to one person or team, of which 10.000€ will remain at the individual disposal of the awardee, whereas 20.000€ will have to be invested into further research of the winner or his team.

Guidelines for Applicants

- Applicants should not be older than 40 years (this limit will not be handled too strictly by the scientific committee)
- Applications must be submitted by an individual applicant
- **There is no special application form required**
- The work may not be older than 2 years (publication after September 2009 or accepted for publication)
- The work should be clinical or basic research in airway diseases, by a researcher whose major clinical training and work has been in pediatrics
- The majority of the research work should have been performed by the applicant
- Applications should contain a short statement of the head of the research group who confirms his/her support of the application
- A short curriculum vitae and a publication list are obligatory
- A summary of the work must be attached which outlines the clinical relevance to airway diseases in childhood and identifies questions arising from the work which need to be answered in the future

Applications shall be sent **by email only** to Prof. Dr. Dr. h. c. D. Reinhardt, Chairman of the International Scientific Board:

dietrich.reinhardt@med.uni-muenchen.de; info@prof-reinhardt.de

Deadline: December 16th, 2011

Next events



PreDicta 2nd consortium meeting

PreDicta will hold its second consortium meeting in Athens, Greece, on 17-18 October 2011. Workpackages leaders will present the work performed during the 1st year of the project. About 30 participants are expected.

Pediatric Allergy and Asthma Meeting – PAAM 2011 –

The EAACI Pediatric Allergy and Asthma Meeting – PAAM 2011 – will be held in Barcelona, Spain, on 13 – 15 October 2011. This Meeting will be attended by internationally renowned speakers from Europe and around the world, and the scientific programme addresses not only specialists in Pediatric Allergology, but also general pediatricians, specialists in Pediatric Pulmonology and Gastroenterology, general practitioners and researchers dealing with children with allergic diseases.



PreDicta members participating: Nikos Papadopoulos (NKUA), Vicky Xepapadaki (NKUA), Patrick Holt (member of the Scientific Advisory Board)