ERS SHORT-TERM RESEARCH TRAINING FELLOWSHIP

ZVORISTEANU Anca Valeria

Fellowship Number STRTF 46-2010
ERS Short-Term Research Training Fellowships Application

No. STRTF 46-2010 - Dr. ANCA VALERIA ZVORISTEANU

Section 1 - Fellowship Sought

Fellowship number: STRTF 46-2010
Title of proposed project: IL-10 produced by macrophages suppresses antiviral innate IFNs in rhinovirus-infected macrophages and epithelial cells
ERS Fellowship programme: STRTF
Keywords: IL-10, macrophages, rhinoviruses, asthma
Expected starting date: 01.01.2011
Expected finishing date: 31.03.2011
Do you intend to return home after the Fellowship? Yes

What are you plans after the Fellowship? Clinical Hospital Oradea have got moden laboratory appliance, the main issue remaining is the lack of experience of the medical staff in experimental work. Receiving the ERS STRF fellowship will allow me to learn techniques such cell/virus titration, ELISA, RT-PCR and perform the study. Obtaining the Fellowship will put me in an excellent position to initiate further studies in asthma field, together with Prof Nanulescu and his group, when I return back to Romania after the completion of this project.

Section 2 - Applicant personal details

Title: Dr.
Last name: ZVORISTEANU
First names: ANCA VALERIA
Gender: Female
Date of birth: 01.09.1970
Nationality: ROMANIA
Present position: MD Specialist in Allergy and Clinical Immunology
Since when: 2002
Name and address of the home institution: Clinical Hospital Oradea, Allergy and Immunology Department, Republicii Street Nr 37, Oradea, Bihor, Romania
Country: ROMANIA
Telephone: 0040 744 580301
E-mail: ancazvori@yahoo.com
ERS membership number: 133374
Are you now based in your Home country?: Yes
Are you now based in your Host country?: No - ROMANIA
Home/Host address: Dacia Street, nr 37, BL AN 54, ap 16, Oradea, Bihor, Romania

Section 3 - Home supervisor

Title: Prof.
Last name: NANULESCU
First names: MIRCEA VICTOR
Present position: Consultant Professor of Pediatrics and Pediatric Respiratory Medicine
Since when: 1993
Name and address of the home institution: Clinical Hospital Oradea, Allergy and Immunology Department, Republicii Street, nr 37, Oradea, Bihor, Romania
Country: ROMANIA
Telephone: 0040 744 510287
Fax:
E-mail: nvmircea@cluj.astral.ro
ERS member?: Yes
ERS membership number: 80933

Section 4 - Host supervisor

Title: Prof.
Last name: JOHNSTON
First names: SEBASTIAN L.
Present position: Professor of Respiratory Medicine
Since when: 2000
Name and address of the home institution: Department of Respiratory Medicine, National Heart and Lung Institute, MRC & Asthma UK Centre in Allergic Mechanism of Asthma, Centre of Respiratory Infection, Imperial College London, Norfolk Place, London, W2 1PG, United Kingdom
Country: UNITED KINGDOM
Telephone: 44 (0) 2075943764
Fax: 44 (0) 2072628913
E-mail: s.johnston@imperial.ac.uk
ERS member? Yes
ERS membership number: 113528

Section 5 - Professional qualifications and experience of the applicant

Postdoctoral researcher since: --
PhD holder since: --
MSc holder since --
MD holder since 1996

Other: MD Specialist in Allergology and Clinical Immunology 2002
Senior Specialist in Allergy and Clinical Immunology 2008

List degrees/diplomas/field of study/ years in which obtained and name of institutes):
- MD Licence Degree, 1996, University of Medicine and Pharmacy 'V. Papilian', Sibiu, Romania
- MD Specialist in Allergology and Clinical Immunology Degree 2002, 'N. Malaxa', Institute of Allergology and Clinical Immunology, Bucharest
- Senior Specialist in Allergy and Clinical Immunology, 2008

Number of years fulltime research experience 0

Please provide other information on your research experience (part time, full time, while working, while studying, etc.)
part time research experience

Number of years professional experience (list: years, position, name of employer) 9 years professional experience as a clinician

Last two positions:
Position 1
Name of employer Clinical Hospital Oradea, Allergy and Immunology Department
From-To: 2002

Do you have 1 first author publication: No

Main publication as a co-author:
-P. Chereches, A. Zvoristeianu, M. Nanulescu, Growth Velocity at Children with Asthma Treated with Inhaled Corticosteroids, Allergy-Journal of EAACI, no 57, pag 194, July 2002, vol 57, ISSUE s73
-D. Dumitrascu, A. Zvoristeianu, The Prevalence of Allergic Diseases in
Section 6 - ERS Fellowship application details

Number of publications in international peer-reviewed periodicals as per date of this application

In English: 1
In other language: 3

Professional societies or associations of which you are a member:
ERS-European Respiratory Society
EAACI-European Academy of Allergology and Clinical Immunology
UCB-Institute of Allergy
WAO -Romanian Society of Allergology and Clinical Immunology

6.1 For International Fellowship applications:

Explain why the objectives of the research project are not attainable in Europe

Are the facilities and skills not available in a European Host unit?

Why is going abroad essential?

6.2 Type of the previous ERS Fellowship for which you are asking for a continuation:

Title of the previous ERS Fellowship for which you are asking for a continuation:

Type of award:

Fellowship number:

Year of award:

Start date:

End date:

Home Supervisor name and unit address:

Host Supervisor name and unit address:

Briefly inform us about the success of the earlier Fellowship. Which skills or objectives did you attain until this point?

Why is an extension essential? What are the new techniques or results to be acquired, and what will be the expected added value it would bring?
6.3 ERS Fellowship application for extension of previous support from other sources

Title of the previous Fellowship or Research project for which you are asking for an extension with ERS support:

Year of award:
Start date:
End date:
Type of the previous Fellowship/Project which you would like to extend with ERS funds:
Home Supervisor name and unit address:
Host Supervisor name and unit address:
Candidate status:
Candidate funded by:
Project’s facilities, resources, materials, operational funds initiated and supported by:

Briefly inform us about the success of the earlier Fellowship/Project. Which skills or objectives did you attain so far?

Why is an extension essential?

6.4 Previous ERS Fellowship recipient applying for a NEW ERS Fellowship

Title of the previous ERS Fellowship:
Year of award:
Type of award:
Fellowship number:
Start date:
End date:
Home Supervisor name and unit address:
Host Supervisor name and unit address:

Briefly inform us about the success of the earlier ERS Fellowship:

What was the impact on your career, on patient care
in your Home unit, etc?

Why are you re-applying for an ERS Fellowship?

What are the new techniques or results to be acquired and what will be the expected added it would bring?

Why is an extension essential? Why do you think you should be reconsidered/refunded?

6.5 ERS Fellowship re-application after a previously rejected project

Re-application with exactly the same title, research project, duration, Host/Home units and application files:

Re-application with the same project and general content but with improved application files, project description, etc.:

What are the minor amendments in this re-application? (methodology, objectives, timelines, etc.):

Re-application with similar project but with major amendments (other title, other duration, other Host unit, etc.):

Yes:

Title of the previously rejected ERS Fellowship application:

Type of the previously rejected ERS Fellowship:

Fellowship number of the previously rejected ERS Fellowship:

Date of negative notification:

Exact duration requested
previously:
Home Supervisor name and unit address:
Host Supervisor name and unit address:
What are the major amendments in this re-application?
CURRICULUM VITAE

PERSONAL DETAILS
Name: Anca Valeria ZVORISTEANU          DOB: 1th September 1970
Address: 16, Hegel Street, Sibiu, Romania
Phone No: +40 744 580301;  E-mail: ancazvori@yahoo.com

EDUCATION
-1990-1996: Faculty of General Medicine, University of Medicine and Pharmacy “Victor Papilian ” Sibiu, Romania
-1996 - 2002 Residency in Allergy and Clinical Immunology
-2002 - present: Specialist in Allergy and Clinical Immunology

FOREIGN LANGUAGES
English: written/spoken

WORK EXPERIENCE
-2002 - present -Specialist in Allergy and Clinical Immunology at the Clinical Hospital Oradea –Ambulatory -Department of Allergy and Immunology, Republicii Street, no 37, Oradea, Bihor, Romania

COURSES/CONTINIOUS MEDICAL EDUCATION/GRANTS
-EAACI Summer Course”Environment, Sports and Allergy”, Rome 14-16 September 2000-Vilasimius 16-20 September 2000
-EAACI Summer Course” Modern Trends in Allergy and Clinical Immunology” Kiev, Ukraine 30 august-4 September 2001
-EAACI Summer School” Highlights on Allergic Rhinitis and Its Impact of Asthma-ARIA”21-25 August, 2002, Sofia, Bulgaria
-EAACI Summer Course “Flowcitometry and Allergy”， Bilbao,7-11 September 2002
-Course “Asthma at children”, Cluj, 10-12 April, 2003
-“Flowcytometry Techniques” Course-Cantacuzino Institute, Bucharest, 15-31 March 2004
- GA2LEN/EAACI Summer School “Dubrovnik, Croatia, 26-30 September, 2004
- CMR Course “The Treatment of Allergic Diseases”, Oradea, 15 December 2004 (lector)
- Medical Management Training, Oradea, 28 January-01 February 2005
- GA2LEN/EAACI Summer Course “Asthma and Allergy- Bringing the Gap between Basic and Clinical Science”, Rotterdam, The Netherlands, 27-31 Aug 2005
- ERS/ATS Joint School Course on “Basics in Asthma”, Oslo, Norway, June 8-10, 2005
- ERS School Course on “Medical Aerosols” Budapest, Hungary, 25-26 November 2005
- Course “Allergy, Congestion and Inflammation”, Oradea, 01. January-30. December 2006
- EAACI Course “Food Allergy Training”, Hindsgavl Castle, April 8-11, 2006
- The Annual Conference of the Romanian Society of Allergology and Clinical Immunology, Cluj-Napoca, Romania, 24-26 March 2006
- The Congress of Romanian Society of Allergology and Clinical Immunology, Targu-Mures, Romania, 26-28 April 2007
- Specific Immunotherapy Training, Bucharest, 11 April 2007
- The Congress of EAACI, Goteborg, Sweden, 9-13 June 2007
- ERS Annual Congress, Stockholm, Sweden, 15-19 September 2007
- Summit Evolving Paradigms in the Treatment of Histamine –Mediated Allergic Disease, Athens, Greece, 26-28 February 2009
- AAAAI Annual Meeting –Washington, DC, March 13-17, 2009
- CMR Course the Respiratory Pathology, From the Etiology to the Treatment, Oradea, 23 March, 2009
- CMR Course The Role of the Nasal Corticosteroids in the Treatment of Inflammatory Nasal Obstruction, Oradea, 25 November, 2009 (lector)
- Specific Immunotherapy Training, Brasov, Romania, 19-20 March, 2010
- ATS International Conference, New Orleans, Louisiana, May 14-19, 2010
- UCB Allergy School “For a Global Management of Respiratory Allergy”, Belgium, 28-29 May, 2010
- Art Forum 2010 Advances in Respiratory Therapeutics Forum, Rome, 12 June, 2010
- CMR Course The Modern Management of Allergic Rhinitis, Oradea, 15 June, 2010 (lector)
- EAACI/GA2LEN Allergy School, Lifestyle Intervention in Allergy and Asthma, Sardinia, Italy, September 9-12, 2010
1. Diana Dumitrascu, Anca Zvoristeau, Dana Ranta: The Influence of the Environmental Factors, the Increased Prevalence of Allergic Diseases in Children Age 10-13 Years old in Cluj County - presentation at National Conference of the Allergy and Clinical Immunology Society 1998, UMF Medicine Journal Cluj University, 1998


8. P. Chereches, M. Farcau, A. Zvoristeau: Risk Factors for Skin Hypersensitivity in Children With Asthma, poster presentation at national Conference of the Romanian Allergy and Clinical Immunology Society, Cluj-Napoca 2003, pag 115
9. A. Zvoristeanu: **Ambrosia Allergy**-local project research, 2005-2008 Allergy and Allergenic Plants, [www.aspbihor.ro](http://www.aspbihor.ro)

10. Clinical Study, A **Randomised Double-Blind Placebo-Controlled study To Assess The Safety of Oral Microincapsulated Ragweed Pollen Extract Administered For One Year**, 2007, Principal Investigator,

11. A **Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy, Safety and Tolerability of Two Doses of ACT-128800, an Oral SIP1 Receptor Agonist, administered Up To Twenty-Eight Weeks in Patient With Moderate to Severe Chronic Plaque Psoriasis**, 2010, Pulmonary Function Tests, Co-investigator
PROJECT: IL-10 produced by macrophages suppresses antiviral innate IFNs in rhinovirus-infected macrophages and epithelial cells

Summary
One current view on allergic asthma pathogenesis is that IL-10 treatment may prove to be a successful therapeutic strategy. However, in relation to virus-induced asthma, there are data that IL-10 downregulates mediators associated with Th1 responses and antiviral activity. The aim of this study is to determine if one cause of the deficient IFN production in asthmatic airway cells could be increased production of the suppressor cytokine IL-10 by alternatively activated macrophages.

Work plan
To study in vitro if:
1. Upon rhinovirus infection alternatively activated macrophages produce less antiviral IFN-α/β/λ and more suppressor cytokine IL-10, type 2 chemokines, and fibrotic factors (arginase 1, FIZZ1) and harbor more virus as compared to normal subjects.
2. IL-10 treatment of RV-infected epithelial cells and macrophages decreases IFNs and increases virus load.

Reasons for selecting the Host
Prof Johnston’s group has a long interest in studying the role of monocytes/macrophages in virus-induced asthma exacerbations, previously demonstrating the increase of IL-10 production by in vitro RV infection in peripheral blood mononuclear cells from asthmatics. He has recently reported that macrophages sustain limited rhinovirus replication and that macrophages from asthmatic produce less IFN-α/β/λ as compared to normal subjects ex vivo upon rhinovirus infection. All methods to be employed are available and daily used in Prof Johnston’s laboratory.

The value of the project for my career
My main interest is Allergology and Immunology and I treat many patients with asthma, children and adults. In the last 5 years, in this part of country we have been confronted with an increase of incidence of ragweed allergic diseases. I have been involved in a project initiated by the Local administration and Health authorities which aim is to prevent, detect, treat and monitor this disease. I was actively involved in research activities in asthma field in Romania, at the level available here and I am interested in studying the laboratory immunology technique (in the asthma field, in particular). In the last years, in Romania, there is a constant progress in asthma therapy, therefore the Clinical Hospital Oradea have got modern laboratory appliances, the main issue remaining is the lack of experience of the medical staff in the experimental research. Receiving the ERS STRF fellowship will allow me to learn techniques such cell/virus culture, virus titration, ELISA, RT-PCR and perform the study. I hope that by working hard I will generate interesting data which will be published. Obtaining the Fellowship will put me in an excellent position to initiate further studies in this field, together with Prof Nanulescu and his group, in order to personalized treatments at the state of the art, when I return back to Romania after the completion of this project.
Background of the project Activation via different signaling pathways results in MØ with different phenotype and functions: classically activated MØ (caMØ), type II activated MØ (MØ-II), and alternatively activated MØ (aaMØ). aaMØ are induced by IL-4, IL-13, TGF-β and ingestion of apoptotic material. aaMØ have increased anti-inflammatory, phagocytic and profibrotic functions. aaMØ produce also high levels of IL-10, that via autocrine activity mediated through binding to IL-10 heterotetramer receptor (IL-10R, composed of two of each of the receptor chains IL-10Rα and IL-10Rβ), inhibits antigen-presenting function, type I IFN, IL-12 production and microbicidal activity of macrophages. Also, by acting on T cells IL-10 induces regulatory T cells thereby creating an immunosuppressive environment. It was reported that TARC/CCL17 and IL-10 inhibit caMØ generation from resident MØ. It was recently suggested that IL-10 and regulatory T cells could be of therapeutic benefit in the treatment of allergic diseases. There are however data suggesting that IL-10 activities could be detrimental in virus-induced asthma.

Importance of the topic and the reason for pursuing the research now Respiratory viral infections are the major cause of asthma exacerbations in adults and children. Alveolar MØ play a key role in the responses to virus infection and alternative activation of MØ by excess IL-4 may diminish antiviral responses. In RSV-infected children, IL-10-production by peripheral blood mononuclear cells (PBMC) correlated with recurrent wheezing on follow-up and RSV bronchiolitis. Rhinovirus uptake by MØ has been demonstrated and Prof Johnston’s group has previously investigated the potential interactions between rhinoviruses and monocytes in terms of intracellular replication, surface costimulatory molecule expression and cytokine production and reported limited rhinovirus replication in monocyte-derived macrophages (MDM). He also reported that in vitro rhinovirus infection of PBMC induces a shift towards the type-2 phenotype (increased IL-10 and decreased IFN-γ and IL-12) in atopic asthmatic compared to normal volunteers; RV inactivation decreased levels of IL-10, suggesting that RV-replication in monocytes induced the major part of IL-10 production. IL-10 is involved in dowregulation of mediators associated with Th1 responses and antiviral activity. Type-III IFN (interferon lambda 1/2/3 also referred to as IL-29/IL-28A/IL-28B) are related to both type-I interferons and IL-10, have antiviral activity and signal through a heterodimeric receptor composed of CRF2-12 (IFN-λ-R1/IL-28Rα) and CRF2-4 (IL-10-R-β/IL-10-R2) chains. In one study of human monocytes IL-10 acted as an antagonist to IFN-λ1 functions, suggesting a feedback mechanism which regulates the function of IFN-λ.

There are data suggesting that the dominant macrophage phenotype in atopic asthmatic subjects is alternatively activated characterized by increased production of IL-10. It was previous shown that IL-10 decreases mediators with antiviral activity implying that IL-10 effects might be unfavorable in virus-induced asthma. Johnston et al reported deficient induction of innate IFN-α/β/λ by RV16 in bronchoalveolar cells, which was correlated with severity of RV16-induced asthma.
exacerbation and virus load in experimentally infected asthmatic volunteers\textsuperscript{26} (Laza-Stanca et al submitted). We think IL-10 might play a role in decreased IFN-α/β/λ and increased viral susceptibility in asthmatics. To support our hypothesis, we investigated whether RV increases MØ IL-10 (Fig. 1 and Fig. 2) and type 2 chemokine MDC (data not shown) production in MDM and whether this is further increased by IL-4-treatment. RV16 induced IL-10 production in a dose dependent manner; inoculum from which virus had been filtered\textsuperscript{27} and soluble-ICAM-1 coated or UV-inactivated RV16 did not induce IL-10, confirming that RV16 replication induces IL-10 production, and not virus receptor binding, phagocytosis of the virus or soluble factors in the virus inoculum (Fig. 1 & 2).

Furthermore, RV16-induction of IL-10 was significantly amplified in IL-4-pretreated MDM (data not shown). Our preliminary data confirm that macrophage RV16 infection induces IL-10 production, which is further increased by IL-4-pretreatment of macrophages. These data support our hypothesis that macrophages in asthmatic subjects produce more suppressor IL-10 and less antiviral IFN-α/β/λ and that IL-10 may play a role in the impaired antiviral immune responses in asthmatic subjects.

Material and methods Due to the large number of macrophages necessary for the \textit{in vitro} studies we will use blood monocyte-derived macrophages (MDM). Monocytes will be prepared from PBMC by positive sorting using anti-CD14-conjugated magnetic beads and differentiated to macrophages by culturing with GM-CSF\textsuperscript{17}. Stock solutions of RV16, a major group and RV1b, a minor group, are available and are kept at –70°C.

1. Do upon RV infection aaMØ produce less IFN-α/β/λ and more IL-10, type 2 chemokines and fibrotic factors and harbor more virus as compared to caMØ? MDM pretreated with IL-4 (aaMØ) or IFN-γ (caMØ) will be exposed to RV16 at MOI from 0.1 to 10 RV16/cell for 1 h, washed with PBS and cultured in RPMI 1640 supplemented with 2% FCS for 72 h. Cell lysates and supernatants will be collected at various time points after the infection (6h/12h/24h/48h/72h). Supernatants will be used to titrate RV16 release and to measured cytokine/chemokine production (IL-10, IFN-α/β/λ, PARC, TARC, MDC) and arginase-1 by ELISA.
RNA will be extracted from cells and used to assess viral RNA and IL-10, IFN-α/β/λ, IFNL-R1 and IL10-R2, PARC, TARC, MDC, arginase-1 and FIZZ1 mRNA expression by qPCR Taqman. In order to assess whether the observed changes are specifically due to RV-replication, purified as well as UV-inactivated RV preparations will be also used. Virus persistence and replication at macrophage level and differences between susceptibility to virus infection between caMØ and aaMØ will be assessed by measuring virus titre in culture supernatants and cell mRNA levels by RT-PCR. Soluble factors levels will be correlated with the level of virus replication and persistence. RV serotype specificity and responses to RSV and influenza will be investigated to determine the generalisabilty of the findings to other virus types.

2. Does IL-10 decreases IFN-α/β/λ and increases virus load in epithelial cells and macrophages?

In order to examine if IL-10 negatively modulates IFN-α/β/λ, RV-infected epithelial cells or MDM will be treated with IL-10 up to 72h and innate IFN levels and virus titre measured in supernatants. We will also use blocking anti-IL-10 Ab (neutralizing anti-IL-10, BD) and measure IFN-α/β/λ and virus levels in MDM infected with RV16.

**Statistical analysis** Testing for statistical significance in the time-course and dose-response studies will be undertaken by analysis of variance (ANOVA). Correlations between production of cytokine mRNA/protein and virus titre will be investigated by Spearman’s rank correlations.

**Conclusion** Other scientists are investigating whether treatments that raise the level of IL-10 could be used to treat asthma, as IL-10 seems to help some people with severe asthma who experience ongoing symptoms. It is therefore incredibly important to know how such treatments might affect people in other situations, such as those with milder asthma who know that colds make their symptoms worse. This research should provide important information as to whether people whose asthma is made worse by virus infections should avoid any treatment likely to increase the level of IL-10.

References to recent publications in the project field from the host and others
3. Gary-Gouy H et al. Type I interferon production by plasmacytoid dendritic cells and monocytes is triggered by viruses, but the level of production is controlled by distinct cytokines. *J Interferon Cytokine Res* 22, 653-659 (2002).
CURRICULUM VITAE

Name
Mircea V. Nanulescu

Date of birth
14th August 1940

Address
3 rd Paediatric Clinic
University of Medicine and Pharmacy – Cluj
Campeni Street, no 2-4, 3400, Cluj-Napoca
Tel/Fax 0040 64 432018  Tel 0040 74
Email nvmircea@cluj.astral.ro

Qualifications
1965 MD- University of Medicine and Pharmacy Bucharest
1972 Paediatric Degree, University of Medicine and Pharmacy Cluj
1974 Ph.D Degree, University of Medicine and Pharmacy Cluj
1979 Consultant in Paediatrics, University of Medicine and Pharmacy,
    Bucharest, Romania
1994 Consultant in Nephrology, Board of Health Romania
1999 Paediatric Respiratory Medicine Degree
2000 Consultant in Paediatric Respiratory Medicine, Health Ministry

Present post
Consultant Professor
2003- The President of the Romanian Society of Paediatric Respiratory
Medicine

Previous Appointments
1980-1990 Lecturer in Paediatrics, University of Medicine and Pharmacy Cluj
1990-1993 Associate Professor University of Medicine and Pharmacy, Cluj
1991-2005 Director of 3rd Pediatric Clinic, Cluj, Romania
1993-2005 Professor of Paediatrics University of Medicine and Pharmacy Cluj
1997-2002 Professor of Paediatrics- University “Vasile Goldis”, Arad
1998-1999 Professor in Public Health University “ Babes-Bolyai”, Cluj

Other Position Held
1985-1989 Secretary of the Paediatrics Department within the Union of Medical
Scientific Association - Cluj branch
1996-2004 Member of the Faculty Board
University of Medicine and Pharmacy Cluj
1998-2005 Director of the Nursing College
University of Medicine and Pharmacy Cluj
2000-2004 Vice-President of the Paediatric Nephrology Association Romania
2000-2004 Member in the Paediatric Board of the Health Ministry Romania

Achievements
1987-1988 Foundation of Medical Centres and Editor of National Guidelines
“National Guide for Management of Acute Respiratory Infection in
Children”
1992 AIDS Centre for Medical Assistance and Screening for the New-born”
    Cluj
1998 Coordinator of the Paediatric Expert Group for the Implementation in
    Romania of  GINA Guideline Establishment of Foundations and
    Associations
1997 Establisher and President of the Foundation and Association “The
    protection of Asthmatic Children”, Cluj-Napoca
1998 Establisher and Vice-President of Paediatric Nephrology Association
Romania

1999 Coordinator of the Regional Centre for derulation the program “The prophylaxis of Asthma in Children”
2003 Establisher and President of the Romanian Society of Paediatric Respiratory Medicine
2008 Coordinator of the Medical Practical Guide “Allergic Rhinitis in Children”

Collaboration Programmes with Centres Abroad
1992 Cooperation Program with Healthcare Leadership Council-USA(Humana Inc Louisville and Baylor University, Dallas). This assistance program offered for 3rd Paediatric Clinic: medical equipment (value $50,000), medical literature (25 monographies, 10 subscriptions to paediatric journals1996, 1997, 1998, 1999) grants for training in Louisville and Dallas USA (11 physicians, 6 nurses, 3 psychologists).
1996-1997 Cooperation Program with “Amsterdam Medical Centre”. This program offered 7 grants for training and congress participation

First Implementation in Paediatrics Practice in Romania
- prolonged artificial ventilation in infants
- prolonged laryngeal intubation for management of obstructive laryngitis
- aerosol therapy by intermittent positive pressure
- peritoneal dialysis in children

Creation and Assessment of Medical Technologies
- transcutaneous oxymeter
- monitor for respiratory control
- device for oxygen humidification

Organization of National and International Conferences
2000 Lectures in collaboration with University Louisville, Kentucky, USA
2001 Workshop “The Asthma Therapy in Children”, Cluj
2002 Workshop “The Chronic Nasal Obstruction” Cluj
2003 The first National Conference of the Romanian Society of Paediatric Respiratory Medicine, “Asthma in Children”, Cluj-Napoca
2005 Workshop on Paediatrics in collaboration with University Louisville(Kentucky, USA), Cluj
2005 The second National Conference of the Romanian Society of Paediatric Respiratory Medicine “Asthma in Children. Viral Acute Respiratory Infections”
2010 National Conference with International Participations of the Romanian Society of Paediatric Respiratory Medicine

Invited Lecturer
- International 2
- National 68

Honours and Awards
Title Associate Distinguished Professor 1992, 1989
Diploma: 75 Years of Romanian-Pharmaceutical Education in Transilvania 1994
Excellency Diploma given by the Romanian Society of Respiratory Medicine 2010
Mircea Nanulescu

Publications List


CURRICULUM VITAE

Name  Sebastian L Johnston  Date of birth  30th March 1959

Address  Department of Respiratory Medicine  
   National Heart and Lung Institute and  
   Wright Fleming Institute of Infection & Immunity  
   Imperial College of Science, Technology & Medicine  
   Norfolk Place, London W2 1PG  
   Tel 020 7594 3764  Fax 020 7262 8913  
   Email s.johnston@ic.ac.uk

Qualifications  
   1982  MB BS (Guys Hospital, London UK)  
   1993  PhD (University of Southampton UK)  
   2000  FRCP (London UK)

GMC registration number  2620176

Present Post  
   Sept 1999 -  Professor of Respiratory Medicine  
   National Heart and Lung Institute  
   Imperial College London

Previous Appointments  
   July 1996 – Aug 1999  Senior Lecturer in Medicine, Respiratory Medicine &  
   Respiratory Infection, University of Southampton

   Jun 1992 - Jul 1996  Lecturer in Medicine and Respiratory Medicine  
   University of Southampton

   Jan 1994 - Jan 1995  MRC Travelling Research Fellow  
   University of Iowa, Iowa, USA.

Research Grants  

<table>
<thead>
<tr>
<th>Date</th>
<th>Awarding Body</th>
<th>Purpose of Award</th>
<th>Duration</th>
<th>Amount</th>
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<tr>
<td>2005</td>
<td>Asthma UK Grant number 05/067</td>
<td>Role of macrophage-type 1 interferon production in rhinovirus induced asthma exacerbation.</td>
<td>3 yr</td>
<td>£168,992</td>
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<td>2006</td>
<td>Firestone Institute for Respiratory Health</td>
<td>The Diary of Asthma and Viral Infections Study</td>
<td>1 yr</td>
<td>£66,150</td>
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<td>2006</td>
<td>Asthma UK Grant number 06/050</td>
<td>Regulation of MUC5B expression by respiratory virus infection: role in the pathogenesis of asthma</td>
<td>3 yr</td>
<td>£196,153</td>
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<td>2006</td>
<td>British Lung Foundation Grant number PO6/13</td>
<td>Regulation of rhinovirus induced INF-β and pro-inflammatory cytokine production in bronchial epithelial cells from asthmatic and normal individuals</td>
<td>3 yr</td>
<td>£119,979</td>
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<td>Year</td>
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<tr>
<td>2006</td>
<td>Medical Research Council</td>
<td>Role of oxidative and nitrative stress and histone de-acetylation in rhinovirus induced acute exacerbations of COPD</td>
<td>4 yr</td>
<td>£991,076</td>
</tr>
<tr>
<td>2007</td>
<td>Medical Research Council</td>
<td>Mechanisms of deficient innate immune responses in asthma</td>
<td>3 yr</td>
<td>£1,219,732</td>
</tr>
<tr>
<td>2007</td>
<td>Medical Research Council</td>
<td>Biomarkers to target antibiotic and steroid therapy in COPD exacerbations</td>
<td>3 yr</td>
<td>£1,063,284</td>
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<td>2007</td>
<td>Wellcome Trust</td>
<td>Centre for Respiratory Infection</td>
<td>3 yr</td>
<td>£3,400,000</td>
</tr>
<tr>
<td>2008</td>
<td>Asthma UK</td>
<td>Alveolar macrophage IL-10/IFN-λ production in rhinovirus induced asthma exacerbations</td>
<td>3 yr</td>
<td>£156,085</td>
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<td>2008</td>
<td>European Research Council</td>
<td>Human and mouse models of rhinovirus induced acute asthma exacerbations</td>
<td>5 yr</td>
<td>€2,497,762</td>
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<td>2008</td>
<td>Biomedical Research Centre</td>
<td>Respiratory Theme Award</td>
<td>1 yr</td>
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<td>2009</td>
<td>NIHR</td>
<td>Senior Investigator Award</td>
<td>5 yr</td>
<td>£60,000</td>
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<td>2009</td>
<td>Biomedical Research Centre Project Grant P26095</td>
<td>Translational studies in a human model of rhinovirus induced acute exacerbations of asthma</td>
<td>2 yr</td>
<td>£143,418</td>
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<td>2009</td>
<td>Wellcome Trust</td>
<td>Immune Regulation of Viral Lung Disease</td>
<td>5 yr</td>
<td>£1,500,000</td>
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<td>2010</td>
<td>NH-MRC grant 631075</td>
<td>The role of microRNAs in antiviral and inflammatory responses during experimental rhinovirus infection</td>
<td>3 yr</td>
<td>A$583,500</td>
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</table>
Major Publications

1. Papadopoulos NG, Stanciu LA, Papi A, Holgate ST and Johnston SL. A defective type 1 response to rhinovirus in atopic asthma. Thorax 2002;57:328-32


