CONTACT

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PERSONAL DATA

Born:21 December 1975, Athens, Greece. Citizenship: Hellenic (Greek). Marital Status: Married, two children. Languages: Greek, English, French.

TITLES

Medical Doctorate (MD): University of Crete, Greece, 2000.

Doctorate (PhD): University of Crete, Greece, 2004.

Pulmonary Specialist Title: Hellenic Ministry of Health, Athens, Greece, 2007.

ORGANIZATIONS

Hellenic Medical Association: member

Hellenic Thoracic Society: member,

European Respiratory Society: member.

EDUCATION

MD: 09/1994-07/2000, School of Medicine, University of Crete, grade 82.6%, top 5th percentile.

PhD: 02/2001-02/2004, “"Comparison of airway inflammation between severe persistent asthma and COPD”; School of Medicine, University of Crete, grade: excellent.

Postdoctoral fellowships

01/2005-04/2006, Lung Pathology Unit, National Heart and Lung Institute, Imperial College, London, UK.

08/2007-06/2008, Dept of Thoracic Medicine, School of Medicine, University of Crete, Greece.

Medical specialty training

04/2002-01/2005 Respiratory Medicine, Venizelion Hospital, Crete, Greece;

04/2006-08/2007 Respiratory Medicine, University Hospital of Heraklion, Crete, Greece; board certification by the Hellenic Ministry of Health (Prefecture of Crete).

POSITIONS

06/2014-present: Senior researcher (Group Leader, Respiratory Immunity and Immunoregulation Team), Applied Biomedical Research and Training Laboratory "Marianthi Simou", National and Kapodistrian University of Athens.

09/2010-present: Director, Respiratory Function Laboratory, Hygeia Hospital, Athens, Greece.

09/2010-06/2014: Research Fellow, Applied Biomedical Research and Training Laboratory "Marianthi Simou", National and Kapodistrian University of Athens, Greece.

09/2008-09/2010: Pulmonary Consultant, Hellenic National Health System, Department of Critical Care and Pulmonary Services, General Hospital Evangelismos, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

06/2008-09/2008: Lecturer of Pneumology (non-tenure-track), Department of Critical Care and Pulmonary Services, General Hospital Evangelismos, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece.

04/2006-09/2007: Pulmonary Fellow, University Hospital of Heraklion, Crete, Greece.

04/2002-01/2005 Pulmonary Fellow, Venizelion Hospital, Crete, Greece.

10/2000-12/2001: Primary Healthcare Practitioner, Hellenic National Health System, Arcalochori District Medical Center, Crete, Greece.

SCIENTIFIC OUTPUT

Teaching activities: 2011: Post-graduate course in COPD, University of Athens; 2008-2010: Undergraduate teaching of Respiratory Medicine, Evaggelismos Hospital; 2007: Postgraduate Seminar in Respiratory Medicine, University of Ioannina; 2006: Immunology and Cellular Biology of the Lungs Seminar, European Respiratory Society and Hellenic Thoracic Society; 2006: Seminar of Continuous Medical Education in COPD, Hellenic Thoracic Society; 2004: Clinical workshop on COPD, Nikea General Hospital, Athens.

Abstract presentations: Several abstracts presented at National and International scientific meetings, including the American Thoracic Society and European Respiratory Society International meetings.

Invited lectures: 2011: Genes and Asthma, Hellenic Thoracic Society (HTS); 2011: The role of dendritic cells in COPD, University of Athens; 2008: Recent advances in COPD research, HTS; 2008: The role of flow cytometry in BAL and sputum samples in the diagnosis and research of pulmonary disorders, Hellenic Flow Cytometry Society; 2007: Experimental research in COPD. University of Ioannina; 2006: Dendritic cells in pulmonary host defence and disease, HTS; 2006: Is COPD an autoimmune disorder? HTS.

Peer-reviewed publications: 32 papers, as per list below.

Book Chapters: N.M. Siafakas, E. Tzortzaki and M. Tsoumakidou. Antibiotics in COPD in ‘’Long – term intervention in COPD’’, eds: R. Powels, D. P. Postma, S. Weiss, Marcel – Dekker, inc publication, 2004.

Commissions of trust: (2004-Today) Reviewer, articles submitted to Thorax, European Respiratory Journal, Respiratory Research, Respiration, Respiratory Medicine, BMC Pulmonary Medicine, Cytokine, Recent Patents On Inflammation & Allergy Drug Discovery, Current Drug Targets, Current Medicinal Chemistry, Journal of Medicine and Medical Sciences. (2008)

Reviewer, applications submitted for research fellowships, European Respiratory Society. (2008)
Reviewer, abstracts submitted at the European Respiratory Society congress.

Bibliometric indices

Papers (PubMed). Total: 32; years:14; papers/year: 2.29.

Document type. Articles: 24, reviews: 5, letters: 3.

Author. First: 22; last:1.

Citations (Scopus). Total: 661; citations/year: 47; uncited papers:1 ; uncited papers/year:0.07.

h-index:14.

Impact Factor (ISI): Cumulative impact factor: 173.468; mean impact factor: 5.421.

PROFILE

I currently serve as a Senior Researcher and Group Leader of the Respiratory Immunity and Immunoregulation Team at the Applied Biomedical Research and Training Laboratory "Marianthi Simou" of the National and Kapodistrian University of Athens, Greece. My research activities focus on elucidating the mechanisms of immune tolerance in groups of cigarette smoke-exposed subjects, ranging from healthy smokers, to Chronic Obstructive Pulmonary Disease (COPD) and lung cancer patients.

My past research focused on understanding the function of cellular and molecular components of the respiratory immune system in the context of COPD and their clinical implication. With co-workers we elucidated a critical mechanism of ectopic lymphoid follicle formation in the lungs of patients with COPD: chronic inflammation activates lung B cells to express lymphotoxin, in turn up-regulating CXCL13, which creates a positive feedback loop and promotes B cell migration. In parallel studies, we yielded critical insights into the molecular and cellular links between persistent/recurrent respiratory tract infections, such as occurs in patients with COPD, and inflammation-induced immunosuppression. In specific, we identified for the first time the existence of an immunosuppressive cell network encompassing regulatory lung CD1c-expressing conventional dendritic cells and IL-10-secreting T regulatory cells in COPD and dictated the increased levels of neutrophil elastase and of the pro-inflammatory cytokines IFNγ and TNFα, as a possible cause.

My current research activities focus on understanding the nature of the link between COPD and lung cancer and on elucidating the mechanisms of lung cancer immune evasion. Building on our earlier work that points to a major role of pulmonary dendritic cells in suppressing immunity under inflammatory conditions, we are testing the hypothesis that chronic inflammation promotes lung cancer immune evasion by suppressing dendritic cells and is further working to identify novel molecular and cellular pathways exploited by lung cancer cells to suppress dendritic cells. Our specific questions are: 1. Which is the role of dendritic cells in lung cancer immune escape and progression? 2. How local stimuli modify dendritic cells in favour of tumor tolerance? 3. How dendritic cells elaborate pulmonary stimuli to suppress cancer immunity? With my current work I aims to construct a conceptual framework of the link between dendritic cells and lung cancer and hope to identify therapeutic targets that can switch from tumor tolerance to anti-tumor immunity.

MAJOR ACHIEVEMENTS

My early research concentrated on characterizing airway inflammation in obstructive airway disorders. During initial studies, my team and I found that severe persistent asthma and COPD, both associated with non-reversible airflow limitation, can be distinguished on the basis of sputum inflammatory patterns, i.e. sputum eosinophilia and higher ratio of T helper versus T cytotoxic cells found in asthma (Clin Exp Allergy 2004;34:234-40). These findings were completed by those of others, collectively establishing sputum analysis for the assessment of patients with asthma and COPD. In subsequent work, we examined the involvement of airway inflammation and oxidative stress in severe acute exacerbations of COPD. We found that nitrosative stress increase along with levels of pro-inflammatory mediators at the onset of COPD exacerbations (Chest 2005;127:1911-8). This work was expanded by studies designed to pharmacologically target inflammatory and oxidative pathways, so as to prevent or treat disease exacerbations. In parallel studies, I sought to better understand phenotypes of obstructive airway disorders. We analysed the inflammatory profile of a subgroup of patients with asthma, termed noneosinophilic asthmatics and showed that they share several cellular and molecular indices with eosinophilic asthmatics, both of which can be distinguished from COPD patients (Chest 2006;129:1194-202). Over all these early publications translated to numerous citations from studies published in major respiratory journals and references in chapter of books focusing on obstructive airway diseases.

At that early time when I was investigating the cellular and molecular mechanisms of obstructive airway disorders, a relatively newly discovered cell type was beginning to attract the attention of scientists with interest on respiratory immunology. i.e. the dendritic cell. Considering that T cell responses were prominent on both asthma and COPD and that dendritic cells emerged as major orchestrators of such responses, I decided to focus on the role of pulmonary dendritic cells in obstructive arway diseases. However, early studies on human lung dendritic cells were hampered by their scarcity and the lack of dendritic cell-specific markers. So, we developed a novel approach for the functional analysis of human dendritic cells, based on their immunomagnetic separation from bronchoalveolar lavage fluid cells (Immunol Cell Biol 2006;84:267-73) and validaded markers that could be used for the immunohistochemical detection of dendritic cells in human lung tissue explants (Histopathology 2007;51:565-8). Analysis of dendritic cells in the bronchial mucosa of asthmatics showed that smoking significantly decreased numbers of mature dendritic cells and cells expressing the effector cytokine IFNγ (Am J Respir Crit Care Med 2007;175:919-25). These novel findings prompted us construct the hypothesis that patients with smoke-related disorders have low pulmonary defense against respiratory pathogens due to impaired dendritic cell maturation (Am J Respir Crit Care Med 2007;176:833, Am J Respir Crit Care Med 2008;177:1180-6). In our follow-up study, we discovered that the lungs of patients with COPD are also lacking mature dendritic cells (Chest 2009;136:726-33). To establish a pathogenetic link between COPD, lung dendritic cells and immune suppression, we purified dendritic cells from the lungs of patients with COPD and developed novel ex vivo models of T cell responses with primary lng dendritic cells. Our recently published work identifies a novel tolerogenic circuit encompassing suppressive lung dendritic cells and regulatory T cells in patients with COPD and further highlights IL-10 and IL-27 as potent therapeutic targets that could block development of this circuit (J Allergy and Clin Immunol 2014;134:944-54). In parallel recent studies I investigated the mechanisms of lymphoid follicle formation in the setting of COPD. That work showed that lymphoid follicles may be induced by lung B cells via a CXCL-13 dependent mechanism and implicated toll-like receptor and lymphotoxin receptor signalling in the above mechanism (Am J Respir crit Care Med 2013;131:187:1192-202).

To summarize, my contributions to the field of airway diseases were translated to achievement of scientific autonomy and establishment of an independent research team in less than 10 years.

Important milestones in this effort were publications in esteemed respiratory and immunology journals, the establishment of novel experimental models and major Research Grants awarded from the Hellenic Thoracic Society.

COLLABORATIONS

Dr. Vassilis Soumelis (2013-present), Integrative Biology of Human Dendritic cells and T cells, Marie Curie Institute, Paris, France. High throuput gene expression analysis of intratumoral dendritic cell subsets in patients with lung cancer.

Prof. Sebastian Johnston (2012-2013), Respiratory Medicine and Allergy, National Heart and Lung Institute, Imperial College, London, UK. Characterization of the COPD lung microenvironment during experimental rhinovirus infection.

Dr. Paschalis Sideras (2012-2013), Immunobiology, Biomedical Research Foundation of the Academy of Athens, Greece. Identification of lung B cell-derived CXCL13 and its association with lymphoid follicle formation in COPD.

Dr. Georgina Xanthou (2010-2013), Cell Biology, Biomedical Research Foundation of the Academy of Athens, Greece. Functional analysis of lung dendritic cell-induced T cell responses in patients with COPD.

Prof. Peter Jeffery (2005-2008), Lung Pathology, National Heart and Lung Institute, Imperial College, London, UK. Investigation of lung dendritic cell phenotypes in the bronchial mucosa of patients with COPD.

Prof. Teresa Tetley (2005-2006), Lung Cell Biology, National Heart and Lung Institute, Imperial College, London, UK. Phenotypic characterization of lung dendritic cells in surgical resection specimens from patients with COPD.

REPRESENTATIVE PUBLICATIONS

Tolerogenic signaling by pulmonary CD1c+ dendritic cells induces regulatory T cells in patients with chronic obstructive pulmonary disease by IL-27/IL-10/inducible costimulator ligand. Tsoumakidou M, Tousa S, Semitekolou M, Panagiotou P, Panagiotou A, Morianos I, Litsiou E, Trochoutsou AI, Konstantinou M, Potaris K, Footitt J, Mallia P, Zakynthinos S, Johnston SL, Xanthou G. *J Allergy Clin Immunol.* 2014 Oct;134(4):944-954.

CXCL13 production in B cells via Toll-like receptor/lymphotoxin receptor signaling is involved in lymphoid neogenesis in chronic obstructive pulmonary disease. Litsiou E, Semitekolou M, Galani IE, Morianos I, Tsoutsa A, Kara P, Rontogianni D, Bellenis I, Konstantinou M, Potaris K, Andreakos E, Sideras P, Zakynthinos S, Tsoumakidou M. *Am J Respir Crit Care Med.* 2013 Jun 1;187(11):1194-202.

Dendritic cells in chronic obstructive pulmonary disease: new players in an old game. Tsoumakidou M, Demedts IK, Brusselle GG, Jeffery PK. *Am J Respir Crit Care Med.* 2008 Jun 1;177(11):1180-6.

Cigarette smoking alters bronchial mucosal immunity in asthma. Tsoumakidou M, Elston W, Zhu J, Wang Z, Gamble E, Siafakas NM, Barnes NC, Jeffery PK. *Am J Respir Crit Care Med.* 2007 May 1;175(9):919-25.