

DR GEORGHIOS SANTIS

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Department of Respiratory Medicine & Allergy*5th Floor Thomas Guy House*Guy's

PERSONAL INFORMATION

Nationality: British
Date of birth : 2nd December 1958

QUALIFICATIONS

MB ChB 1985
MRCP 1986
MD 1992
FRCP 1998

UNDERGRADUATE EDUCATION

1978 - 1983
University of Leicester
Distinctions in Medicine and Paediatrics

CURRENT POST

1995 - present
Reader in Respiratory Medicine GKT School of Medicine
Consultant Physician to Guy's & St Thomas' NHS Trust

PREVIOUS POSTS

House Physician and Surgeon - Leicester Royal Infirmary 1983-84

molecular and biological factors that influence outcome in treated and control patients is under development. This work is being carried out in collaboration with Antigenics, an USA based company.

Ph D STUDENTS

Since my appointment, I have been responsible for the supervision of 3 PhD students. Ms E Davison has been awarded her PhD this year. Dr J Whitehouse, who registered for her PhD as a part-time student in December 1997, and Mr I Kirby, who registered in October 1998, will be completing their experimental work by April 2001 and would be submitting their thesis in the same year.

GRANTS

Cystic Fibrosis Trust

Genetic - Phenotype studies in adults with cystic fibrosis

1.9.1989 - 31.8.1991 (£33,000) (with Prof ME Hodson)

Wellcome Trust

Gene Therapy for cystic fibrosis (Advanced Clinical Training Fellowship)

1.6.1993 - 31.7.1994 (£72,750)

Wellcome Trust

Structure-Function Studies of Adenovirus Type 5 Fiber Protein

1.11.1995 - 31.3.1997 (£55,250)

Special Trustees for St Thomas' Hospital:

Recombinant Adenovirus Vectors for Targeted Gene delivery

As Firm Head, I am actively involved in the teaching of cardiac, respiratory and ENT medicine for Year 3 undergraduate medical students. In addition, I am responsible for the Lung Oncology Special Study Module (2 students/rotation) and the Symposium on Lung Cancer, both in Year 3. I lecture on Virus Vectors for the B.Sc. course in Molecular Medicine (Gene Therapy module). I also participate regularly in the teaching of specialist registrars in Respiratory Medicine.

RESEARCH ACTIVITIES

My current research interests are in developing molecular therapies for respiratory diseases, in particular carcinoma of the lung. Specific areas of research include:

The molecular basis of adenovirus-host cell interactions.

We have been investigating the molecular and structural determinants of adenovirus attachment. Our main achievement was the identification of contact residues and the definition of the receptor-binding site of adenovirus type 5 fibre protein. We have also contributed in the characterisation of the receptors involved in virus cell attachment and internalisation. We are actively investigating immunogenic epitopes in two viral capsid proteins in order to understand the determinants of virus immunogenicity. Finally we have constructed adenovirus vectors with novel receptor targeting specificity and we have studied their biophysical properties in detail. We are currently probing adenovirus-cell interactions using FRET microscopy and time-resolved anisotropy.

The characterisation of high order transcriptional regulatory elements in the developing and mature lung.

We are concentrating on the transcriptional regulation of TTF-1, a transcription factor that is critical in the developing and mature lung. This work, which relies heavily on transgenic mouse analysis, indicates that high order regulatory elements for TTF-1 are located at least 45Kb upstream of the TTF-1 gene. Future work in this field will involve detail dissection of these regulatory elements in order to incorporate these into an appropriate expression vector for stable physiological gene expression in the lung.

Development of biological therapies for lung cancer.

We are the first group to begin an investigation into the role of Oncophage, a patient specific tumour vaccine, as adjuvant therapy in resectable non-small cell lung carcinoma. Work on the

SHO in Medicine - Leicester Royal Infirmary 1984-85
SHO in Nephrology - Middlesex Hospital 1985
SHO in Cardiology - National Heart Hospital 1985
SHO in Respiratory Medicine - Brompton Hospital 1986
Registrar in Medicine - Middlesex Hospital 1986 - 1988
Research Fellow - National Heart & Lung Institute 1988 - 1990
Senior Registrar - Brompton Hospital 1990 -1994
Wellcome Trust Advanced Training Fellow - Institute of
Molecular & Cell Biology and Transgene, Strasbourg, France-
1992-1994

CLINICAL ACTIVITIES

Since my appointment I have established a multidisciplinary service for patients with lung cancer and a service for the rapid assessment of patients with suspected lung malignancy. The service now meets all national and international standards of treatment and includes a weekly multidisciplinary meeting followed by a parallel clinic. As Lead Clinician for Lung Cancer at GKT Cancer Centre, I was responsible for submitting the Trust application for funds for Lung Cancer from the Department of Health. As a consequence of our successful application, additional posts have been funded (specialist nurse, data co-ordinator and consultant sessions in pathology, radiology and palliative care). I have established a network of interested clinicians in Southeast Thames area to facilitate clinical research in lung cancer, aiming to improve our low level of participation in national and international clinical trials in this area. Finally, I am involved in forming a TeleMedicine link between cancer units and the GKT Cancer Centre

TEACHING ACTIVITIES

Burd DAR, Santis G, Millward TM.

Severe extravasation injury: An avoidable iatrogenic disaster?

British Medical Journal. 1985; 290:1579-80

BOOK CHAPTERS

Santis G Molecular genetics of cystic fibrosis and Marfan's syndrome.

In Annual of Cardiac Surgery. Editors Yacoub MY and Pepper J:
April 1992

Santis G Molecular genetics of cystic fibrosis. (1st edition)

In Textbook of Cystic Fibrosis. Editors Geddes DM and Hodson
ME: July 1994

Santis G. Molecular genetics of cystic fibrosis. (2nd edition)

In Textbook of Cystic Fibrosis. Editors Geddes DM and Hodson
ME: January 2000

Worldwide survey of the $\Delta F508$ mutation.

American Journal of Human Genetics 1990; 47: 354 - 59

European Working Group on CF genetics

Santis G, Osborne L, Knight RA co-authors.

Gradient of distribution in Europe of the major CF mutation and of its associated haplotype.

Human Genetics 1990; 85: 436 - 447

Santis G, Osborne L, Knight RA, Hodson ME, Ramsay M.

Genetic influences on pulmonary severity in cystic fibrosis.

Lancet 1990; 335: 294-295

Santis G, Osborne L, Knight RA, Ramsay M, Williamson R, Hodson ME.

Cystic fibrosis haplotype association and the $\Delta F508$ mutation in adult British CF patients.

Human Genetics 1990; 85: 424 - 6

Santis G, Osborne L, Knight RA, Hodson ME.

Linked marker haplotypes and the $\Delta F508$ mutation in adults with mild pulmonary disease and cystic fibrosis.

Lancet 1990; 335: 1426-29

Friedland J, Santis G, Smith M.

Infectious mononucleosis as a cause of bilateral hilar lymphadenopathy.

Postgraduate Medical Journal 1988; 64: 799-800

Burd DAR, Santis G.

Iso-osmolar contrast media

British Medical Journal 1984; 289: 836

Theodorou N, Westaby D.

Pleural effusions associated with pancreaticopleural fistula.

Thorax 1993; 48: 867-868

Udwadia Z, Santis G, Stevens M, Simonds A.

The use of nasal ventilation to facilitate weaning in patients with chronic respiratory insufficiency: clinical and economic outcome.

Thorax 1992; 47: 715-718

Osborne L, Santis G, Schwarz M, Klinger K, Hodson ME, Knight RA.

Incidence and expression of the N1303K mutation of the cystic fibrosis (CFTR) gene.

Human Genetics 1992; 89: 653-658

Santis G, Hodson ME, Strickland B.

High resolution computed tomography in adult cystic fibrosis patients with mild lung disease.

Clinical Radiology 1991; 44: 20-22

Osborne L, Santis G, Knight RA, Hodson ME.

A mutation in the second nucleotide binding fold of the cystic fibrosis transmembrane conductance regulator.

American Journal of Human Genetics 1991; 48: 608-612

Santis G, Osborne L, Knight R.A., Hodson M.E.

Independent genetic determinants of pancreatic and pulmonary status in cystic fibrosis.

Lancet 1990; 336: 1081-84

Cystic fibrosis Genetic Analysis Consortium

Santis G., Osborne L., Knight R.A.: co-authors

its high affinity receptor CAR

Journal of General Virology 1999 80 (6): 1519-1527

Davison E, Kirby I, Elliott T, Santis G:

*The human HLA-A*0201 allele, expressed in hamster cells, is not a high-affinity receptor for adenovirus type 5 fiber.*

Journal of Virology 1999 73(5): 4513-4517

Davison E, Diaz R-M, Hart I, Santis G, Marshall J.

Integrin alpha5beta1-mediated adenoviral infection is enhanced by the integrin-activating antibody TS2/16:

Journal of Virology 1997 71: 6204-6207

Dean M, Santis G.

Phenotypic diversity and tissue expression of CFTR gene.

Human Genetics 1994; 93(4): 364-68

Cystic Fibrosis Genotype/Phenotype Consortium (Santis G: co-author)

Correlation between genotype and phenotype in cystic fibrosis

New England Journal of Medicine 1993; 329: 1308 - 1313

Osborne L, Lynch M, Middleton P, Alton E, Geddes D, Hodson ME, Pryor JM, Santis G.

Nasal epithelial ion transport and genetic analysis of infertile men with congenital bilateral absence of the vas deferens

Human Molecular Genetics 1993; 2: 1605-1609

Santis G.

Pulmonary severity and genotype

Pediatric Pulmonology 1992; 8: 140-141

Williams SG, Bphupalan A, Zureikat N, Thuluvath PJ, Santis G,

and can be modulated by changes in beta1 integrin function

Journal of Gene Medicine 2001;3: 550-559

Kirby I, Davison E, Beavil AJ, Wickham TJ, Roelvink PW, Kovesdi I, Sutton BJ, Santis G:

Adenovirus type 9 fiber knob binds to CAR with reduced affinity compared to the fiber knobs of other CAR-binding adenovirus serotypes

Journal of Virology 2001 75(15):7210-4.

Kirby I, Davison E, Beavil AJ, Soh CP, Wickham TJ, Roelvink PW, Kovesdi I, Sutton BJ, Santis G:

Identification of contact residues and definition of the CAR binding site of Adenovirus type 5 fiber

Journal of Virology 2000; 74(6): 2804-13.

Kirby I, Davison E, Beavil AJ, Soh CP, Wickham TJ, Roelvink PW, Kovesdi I, Sutton BJ, Santis G:

Mutations in the DG loop of adenovirus type 5 fiber knob protein abolish high-affinity binding to its cellular receptor CAR.

Journal of Virology 1999; 73 (11): 9508-14

Santis G, Evan TWE.

Molecular Biology Molecular Biology for the Critical Care Physician (Part I)

Critical Care Medicine 1999; 27 (4): 825-831

Santis G, Evan TWE.

Molecular Biology Molecular Biology for the Critical Care Physician (Part II).

Critical Care Medicine 1999; 27 (5) 997-1003

Santis G, Le-Grand V, Hong S-S, Kirby I, Davison EA, Pavirani A, Imler J-L, Bergelson J, Mehtali M, Boulanger P.

Molecular determinants and serotype specificity of Ad5 fiber binding to

Previous:

Member AFLM (France) Committee of Experts

Auditor, MB Ph.D. program at UMDS

MAJOR INVITED LECTURES

American Cystic Fibrosis Congress - Washington, USA; October 1992

Genotype-Phenotype relationship in cystic fibrosis

European Congress on Human Genetics - Hamburg, Germany; July 1993

The genetic basis of CBAVG

British Thoracic Society - London; December 1998

Gene Therapy for Lung Cancer

National Institutes of Health - Bethesda, USA; October 1999

Characterisation of the CAR binding site of adenovirus 5 fiber protein

PUBLICATIONS

Kirby I, Lord R, Sutton BJ, Santis G:

Biophysical properties of recombinant adenovirus type 5 fibre knob-RGD fusion properties

Journal of Virology In press 2003

Whitehouse J, Lee YC, Antoniou M, Santis:

Analysis of the transcriptional regulation of Thyroid Transcription factor 1 (TTF1) gene in transgenic mice suggests the presence of an LCR like element upstream of the TTF1 promoter.

Gene in press 2003

Davison E, Kirby I, Whitehouse J, Hart IR, Marshall JF, Santis G.

Adenovirus type 5 uptake by lung adenocarcinoma cells in culture correlates with expression of CAR, is mediated by alpha5beta1 integrin

Improving outcomes in lung cancer

1.4.1999 - 31.3.2002 (£180,000)

Special Trustees for Guy's & St Thomas' Hospital

Biomolecular Interactions between Adenovirus type 5 fiber protein and its cellular receptors

1.1.01 - 31.12.2003 (£167,420)

BBSRC

Biophysical analysis of the molecular interactions that determine cell entry and trafficking by human adenoviruses

1.6.2001 - 31.5.2004 (£182,060 plus the cost of synchrotron radiation.)

MRC-Ph.D. studentship (with Prof. J Ward)

Molecular characterisation of Tryp-1 channels in human airway smooth muscle

1.10.2001-30.9.2004

COMMITTEE MEMBERSHIP

Current:

Lead Clinician-Lung Tumour Group GKT Cancer Centre

Member-Steering Committee GKT Cancer Centre

Chairman-Southeast Lung Cancer Research Network

Chairman-Southeast Lung Cancer Tumour Working Group

Member-Southeast London Cancer Network Policy Group

Member of the Academic Board, KCL

1.10.95-31.9.96 (£57,875)

Special Trustees for Guy's Hospital: Targeting of recombinant adenovirus vectors by modification of the penton base protein

1.10.96-31.9.97 (£33,600)

Wellcome Trust

Structure-Function Studies of Adenovirus Type 5 Fiber Protein

1.4.1997 - 30.6.2000 (£139,750)

Special Trustees for Guy's & St Thomas' Hospital

Biomolecular Interactions between Adenovirus type 5 fiber protein and its cellular receptors

1.6.1998 - 31.5.1999 (£34,420)

Wellcome Trust

Transcriptional regulation of thyroid transcription factor 1 (TTF-1)

1.11.1997 - 31.7.2001 (£192,658)

Wellcome Trust

Identification of molecular targets of thyroid transcription factor 1 (TTF-1)

1.7.98 - 31.6.2000 (£88,976) (with Dr CD Bingle)

Department of Health