



# REPORT: UNIVERSITY OF CAPE TOWN LUNG INSTITUTE: 2000-2010





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2000-2010

## INTRODUCTION

This report presents a summary of the activities and achievements of the Lung Institute for the years 2000 to 2010, its first 11 years. The Institute was constituted in 1998 and the custom-built clinical research centre building commissioned in April 2000. The founding mission of the Institute is **to serve as a centre of excellence for the study and application of knowledge and health in diseases of the lungs and respiratory tract relevant to the needs of Southern Africa**. While this mission has remained central to its activities, its sphere of involvement has broadened in recognition of the relatedness of all health needs and the importance of addressing these in a co-ordinated and comprehensive manner. An assessment of whether the Institute has fulfilled its mission and become a centre of excellence both in research and in the application of knowledge, can be viewed from various perspectives. For UCT, the Institute represented an experiment; the potential of a research facility, structured as a company, to provide value both to the university, and to society. Could its unique structure and positioning enable it to perform functions and provide opportunities that supplemented those offered by the university? It was to serve as part of an extended platform for teaching and research, providing facilities and equipment for clinical services that might not be available elsewhere. In addition it was positioned to provide outreach services to the wider community, not constrained by a primary focus upon registered students. But was it a viable business proposition, relying chiefly on income generated from research? From the perspective of the scientific community, would its research be of a standard that would gain international recognition and even become a thought leader? Finally, what contribution would it make to health services and the community?

The operations of the Institute are organized in clinical research units (CRUs) each with a different focus. Over the 11 years there have been changes; new CRUs have formed, and others closed, reflecting the Institute's response to emerging health needs and strategic opportunities such as the outbreak of multi-drug tuberculosis (the formation of a Center for TB Research Innovation and the Lung Infection and Immunity Unit), and a call to assist in the strengthening of primary care services (the Knowledge Translation Unit). Units that have moved from the Institute are the Infectious Diseases Unit – to the UCT Institute for Infectious Diseases and Molecular Medicine and the Occupational Health Unit and Asbestos Trust, to larger premises. A shortage of space within the building has become a limiting factor, the staff complement on the Institute's payroll having increased to more than 70. The Institute's annual budget is almost R40 million, but its researchers also contribute to successful grant applications for projects based at UCT and other universities. Scientific publications to which its staff have contributed number more than 380, and the Institute has mentored and provided support for several PhD and Masters degree students. Financial and facility management has been of a high standard under the competent supervision of the manager, administration staff and the Finance Committee, with the Institute Board providing guidance and support.

The Institute acknowledges with gratitude fruitful collaborations with National, Provincial and local authority departments of health, several universities in South Africa and abroad, with the South African Medical Research Council and with many other organizations and research groups. Funding through grants and contracts has also been received from a large number of sources which have contributed to the success of the Institute. These are listed in the CRU reports that follow and are acknowledged with gratitude.

Attempting to summarize the work of many researchers over more than a decade is not an easy task. This report cannot do justice to the quality of their work, nor describe its value and significance. Many projects have been omitted, and some staff and collaborators may have been overlooked. However, the publications list that follows is a complete record of the publication outputs of the Institute and is perhaps the best measure of productivity.

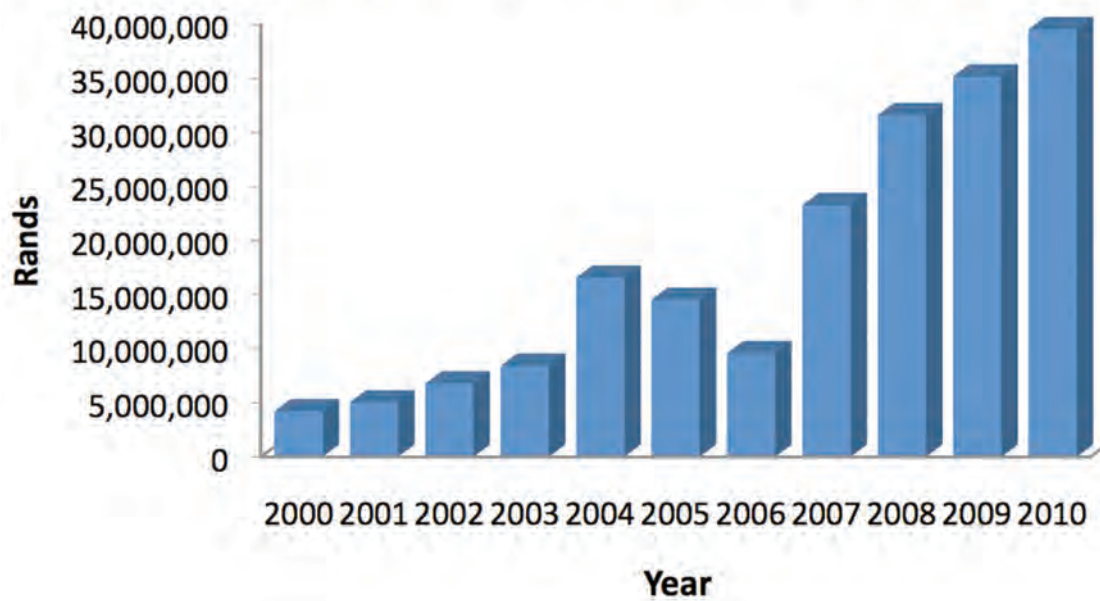
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**Occupational Medicine Clinical Research Unit (OMCRU)** Special mention must be made of a colleague whose death in 2004 cut short a very productive career. Professor Neil White was an enthusiastic participant in the formation of the Institute and founded the Occupational Medicine Clinical Research Unit (OMCRU). A champion for the rights and health of workers, he followed the path of using science to promote change. His work in the Institute included the development of an online teaching programme for occupational health practitioners (Radiological Occupational Lung Disease Surveillance programme), studies of retired mine-workers, a community survey of health problems relating to the petrol refinery in Cape Town, a study of a community exposed to sulphur fumes from a fire at an explosives factory, and surveillance of workers exposed to asbestos. He mentored students in Occupational Medicine and several other disciplines, assisting them with their projects. OMCRU provided offices for the Provincial Medical Advisory Panel established in terms of the Compensation of Occupational Injuries and Diseases Act, of which he was the chair. After Neil's death, Dr Greg Kew became head of the Unit, assisted by Professors Rodney Ehrlich and Mohamed Jeehbay and Dr Jim te Water Naude, until it disbanded in 2008.

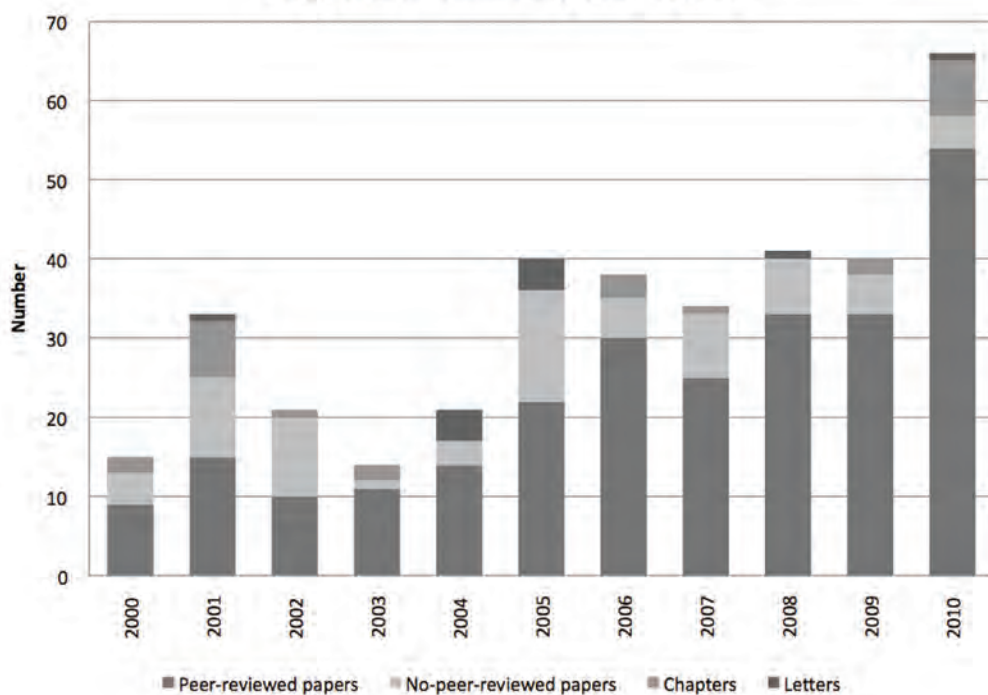
Besides the CRUs listed below, the Institute has provided accommodation and infrastructural support to several **independent researchers and projects:**

1. Dr Douglas Wilson (in association with Professor Gary Maartens (Department of Pharmacology, UCT)) in research on diagnostic algorithms for the diagnosis of TB in patients with HIV/AIDS.
2. Dr Jean Nachege and Professor Gary Maartens in association with Dr R Chaisson of the Johns Hopkins University, Baltimore, in an NIH-funded project on supervised therapy for patients with HIV/AIDS receiving ART, and related topics.
3. The Asbestos Trust (Dr Jim te Water Naude) responsible for the evaluation and compensation of workers affected by occupational exposures to asbestos in South Africa.
4. Several students on Discovery and Fogarty fellowships in the Faculty of Health Sciences have been provided mentorship, and assistance with the management of their project and finances.

## Lung Institute - Annual Turnover



## Lung Institute: Publications 2000 to 2010



## HIGHLIGHTS FROM THE CLINICAL RESEARCH UNITS:

### Lung Clinical Research Unit

**Head: Professor Eric Bateman**

The Lung Clinical Research Unit has served as the core research unit of the Institute since it was founded in 2000. Its broad objective is to perform research and provide highly specialized services in the field of pulmonology. Its activities have spanned epidemiology, clinical evaluation of new drugs and treatment approaches for airways diseases, rhinitis, pneumonia and diffuse parenchymal lung diseases and other diseases, the testing of tuberculosis vaccines, research in lung physiology, quantitative imaging and other methods of evaluating the lungs, and health systems interventions. Work begun in the unit gave rise to the Knowledge Translation Unit, and the Centre for TB Research Innovation.

#### Facilities and Activities

LCRU operates in a custom-build clinical trials facility that conforms to rigorous requirements demanded by local and international regulatory bodies

- Equipped for clinical and physiological studies
  - o Full complement of lung function and exercise testing apparatus
  - o Chest radiology
  - o Sleep study laboratory
  - o Laboratory for processing of biological specimens
  - o Pharmokinetics laboratory
  - o Pharmacy
  - o Archiving and records

A specialized pulmonology service is offered to researchers from other units, institutions and referring physicians. These include:

- o Clinical assessments
- o Dynamic lung volumes (flow volume loops, PEF, home monitoring etc.)
- o Static lung volumes (body plethysmograph)
- o Impedance pletysmography (IOS)
- o Cardiopulmonary exercise testing (cycle and treadmill, 6 minute walk etc.)
- o Metronome-paced dynamic hyperinflation testing
- o Oximetry
- o Bronchial challenge tests with allergens and methacholine
- o MIPS and MEPS
- o Diffusing capacity
- o Induced sputum to assess bronchial inflammation: cytology, microbiology, proteomics, metabolomics, etc.
- o Skin prick testing
- o Nasal antigen challenge testing
- o Exhaled nitric oxide testing

## Research

- Epidemiology – researching the causes and burden of common respiratory diseases in Southern Africa and in particular of asthma, allergic diseases and chronic obstructive pulmonary disease (COPD). We have conducted several community-based studies involving questionnaires, skin testing, chest radiography and lung function testing. We were the first centre in Africa and the fourth globally to utilize the internationally accepted BOLD methodology for studying the prevalence of COPD in the community. Our research has highlighted the multifactorial origins of COPD in South Africa and the special impact of previous pulmonary tuberculosis, domestic and environmental pollution, substance abuse as well as high levels of tobacco smoking.
- Studies of risk factors and mechanisms of disease in COPD associated with HIV and TB infections.
- Tuberculosis research – assessment of the clinical safety of a new vaccine being developed for tuberculosis.
- Lung physiology – evaluation of new methods of assessing lung function, including metronome-paced assessment of dynamic hyperinflation, and tests of airway hyper-responsiveness and exercise tolerance.
- Digital radiology – in collaboration with the CTBRI, the development of automated reading of digital chest radiology and quantitative assessment of high resolution computerized tomography images.
- Occupational and environmental lung disease – field studies in risk industries and detailed assessments of patients with occupational lung diseases, in collaboration with the Occupational Diseases CRU and Department of Public Health.
- Clinical evaluation of new drugs and treatment approaches in asthma, COPD, allergic rhinitis, pneumonia and other diseases. The research team has gained an international reputation as a centre for drug evaluation. More than 120 phase II, III and IV clinical studies have been performed to date, ranging from single-centre investigator-initiated projects to multicenter international trials.
  - Classes of drugs evaluated include short, long and ultra-long acting beta2-agonists, short, long and ultra-long acting anticholinergics, inhaled corticosteroids, dual pharmacophores, several varieties of antibiotic, selective phosphodiesterase-4 inhibitors, a topical phospholipase A inhibitor, anti-IgE antibodies, anti-IL5 monoclonal antibodies, anti-IL 13 monoclonal antibodies, inhaled and injected recombinant gamma-interferon, CRTH2 inhibitors, anti-histamines, leukotriene receptor antagonists, combinations of long-acting beta2-agonists and inhaled corticosteroids, of long-acting beta2-agonists and anti-cholinergics, theophyllines, and several biological and novel agents for the treatment of airways diseases.
  - Contracting companies: Actelion, ALK-Abello, Almirall, Altana, Amgen, AstraZeneca, Aventis, Byk Madaus, Boehringer Ingelheim, Bristol Myers Squibb, Chiesi, Criterium, Eli Lilly, Forest, GlaxoSmith Kline, Hoffman la Roche, Intermune, Janssen Pharm, Kyowo Hakko, MDS Pharma, MSD, Morria Biopharmaceuticals, Morton, Nycomed, Novartis, Pfizer, Replidyne, Sanofi Aventis, Schering Plough, Sky Pharma.
- Evaluation of non-pharmacological methods for treating asthma including rehabilitation programmes, lung volume reduction surgery (as part of the Canadian MRC Trial) and the Fenzian device (Eumedics).
- Evaluation of allergic diseases in patients with HIV on ART.

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## Teaching and Training

- A Tuberculosis for Clinicians course is offered annually for pulmonologists and physicians from the Netherlands and has been opened to local physicians
- Chest Radiography Reporting and Recording (CRRS) courses once or twice yearly
- Courses on Lung Physiology and Exercise Testing were held in 2008 and 2009 with the assistance of UCT visiting professor Christopher Cooper from the David Geffen School of Medicine, UCLA, USA.
- Occasional lectures to groups of visiting physicians and/or pulmonologists from Greece, China, and various countries in Africa and the Middle East.
- Supervision of projects for B Technology degrees (4)
- PhD degrees (4)
- Masters degrees: MPH (3), MTech (2), MPhil, MMed (6)
- Research experience for undergraduate students from UCT and UWC (Physiotherapy, biokinetics, and MBChB)
- In-service training for registrars in pulmonology (Certificate in Pulmonology), Medicine, Occupational Medicine, and Occupational Health
- In-service training and career advancement for staff, especially those from historically disadvantaged backgrounds.

## Service and Outreach

- Funding of self-initiated research on health issues for which external funding is not available forms an important part of the Institute's commitment to serve. Examples of projects are pilot studies and early work on PALSAs (2001 & 2002) and PALSAs PLUS (2003), the Lung Health 2002 study, the BOLD study (2004), the Tuberculosis in Obstructive Lung Disease (TOPD) project (2009 & 2010), the HIV-related obstructive lung disease (HALO) study (2009 & 2010) and several smaller studies. These have created opportunities for post-graduate students and provided valuable information on topics relevant to the wider community and health services.
- Participation in public health awareness activities; World Asthma Day, World TB Day, World COPD Day, the Year of the Lung 2010, the UCT Wellness Week (annual), and in organizing and staffing Information and Lung Testing stalls in public places from time to time.
- Training physicians, occupational nurses and other categories of staff in lung function testing: On-site training has been provided by LCRU staff in several places in South and sub-Saharan Africa.
- Professor Bateman has lectured, conducted seminars and workshops in numerous countries, including developing countries and has played a major role through GINA and as a representative of the American Thoracic Society in improving the care of patients with asthma and COPD.

## Current Staff

- Physicians 7 (full-time 1), 5 clinical technologists, 2 laboratory technologists, 2 pharmacists (part-time), 3 nurses, one clinical trial assistant (part-time), and 3 administrators.
- Visiting Professors:
  - o Professor Christopher Cooper, Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine, UCLA, USA (5 months in 2008)
  - o Professor Luis Taborda Barata, Department of Medical Sciences, Faculty of Health Sciences, University of Beira Interior, Covilhã, Portugal (6 months in 2010)

## Honours and Special Achievements

- Dr A Jithoo (2001 to 2005) received the Glaxosmithkline Pulmonology Research Fellowship for 2004/2005, the Best Junior Investigator Award at the 2003 South African Thoracic Society Congress, Department of Medicine Prize for the best Clinical Research Presentation at the 30th Annual Research Day 2003 and a prize for the best young clinical investigator in the Master of Medicine (UCT) course in 2003.
- The Gaining Optimal Asthma Control Study (lead author Professor Bateman) published in the leading respiratory journal, the American Journal of Respiratory and Critical Care Medicine in 2004, was the most cited paper in the journal for 3 successive years (a record for the journal), and the findings reported formed the basis for a major revision in the goals of asthma treatment and the way in which asthma is managed.
- A paper entitled Identifying “Well-controlled” and Not Well-controlled” asthma using the Asthma Control Questionnaire (senior author E.D. Bateman) published in 2006 was one of the top 10 most cited papers in the international journal, Respiratory Medicine, for 3 years.
- Professor E D Bateman is currently the Chair of the Global Alliance for Asthma and an Executive member of the Global Alliance Against Chronic Respiratory Diseases. He serves on the editorial boards of 7 international medical journals and is an invited lecturer at numerous international meetings each year. He has an A-rating from the National Research Foundation.

## Funding

- SA Medical Research Council
- World Health Organisation (Stop TB Programme)
- Research for International Tobacco Control (Canada)
- South African Thoracic Society
- Discovery Foundation
- NIH (USA)
- Allergy Society of South Africa
- National Research Foundation
- Fogarty Research Fellowship
- CDIA (Canada)
- Aeras
- American Thoracic Society
- Pharmaceutical companies listed above.

## Collaborations

- Departments of Public Health and Paediatrics, and the Divisions of Infectious Diseases in the Health Sciences Faculty, UCT
- Chronic Diseases in Africa (CDIA) initiative (UCT)
- Royal Brompton Hospital, London
- David Geffen School of Medicine, University of California Los Angeles (UCLA)
- New York University School of Medicine and Bellevue Hospital
- Stellenbosch University (Desmond Tutu Tuberculosis Research Unit)
- South African Medical Research Council
- Institute of Infectious Diseases and Molecular Medicine (UCT)
- Faculty of Health Sciences, University of Beira Interior, Portugal
- Extensive collaborations in different projects with researchers abroad.
- Pharma companies listed above.

## **Allergy and Diagnostics Clinical Research Unit**

### **Head: Professor Paul Potter**

ADCRU focuses on the diagnosis and management of allergic diseases in Southern Africa. It is a highly specialized clinical component of the Allergology Unit in the Department of Medicine at UCT and provides a nationally unique diagnostic service for practitioners and major hospitals.

Its activities include a diagnostic and research allergology laboratory service, a clinical trial research unit, a specialised allergology consultation service, training for undergraduates, fellows and postgraduate students in the field of allergology, nurse education in allergy (in association with the The National Asthma Education Programme) and a pollen monitoring service in the Western Cape.

Additional special facilities and services include aerobiology pollen monitoring, allergen skin prick testing, double-blind placebo controlled and open food challenge testing, drug allergy titrated skin testing, volumetric air sampling and services for patients with complement immunodeficiency.

### **Research activities:**

#### **Clinical Trials:**

- Clinical trials (40) for pharmaceutical companies in the fields of seasonal and perennial allergic rhinitis, allergic conjunctivitis, asthma (adult and paediatric), atopic dermatitis, urticaria, angioedema and hereditary angioedema.
- Classes of agents studied include anti-histamines, bronchodilators, inhaled corticosteroids, biological standardization of allergens and sublingual immunotherapy.
- Contracting companies: ALK-Abello, Altana Madaus, AstraZeneca, Aventis, Boehringer Ingelheim, Clindev, Criterium, Hoechst Marion Roussel, Leti, MDS Pharma, Merrel Dow, MSD, Morria, Novartis, Nuvisan CDS, Rhone Poulenc Rorer, Schering Plough, Shire, Stallergenes, UCB, 3M.

#### **Basic Research:**

- Diagnosis and follow up of latex allergy in Western Cape hospitals (ongoing studies using micro array and a 10 year follow up questionnaire)
- Heterogeneity of cytokine immunological responses to sublingual allergen immunotherapy
- Characterization of the allergens in Mopane worm allergy
- Utility of the sulphido leukotriene release test (CAST) in patients on grass immunotherapy (SLIT) and in patients with angioedema
- Collaborative research with the University of Cardiff in the area of complement C6 deficiency

#### **Applied Research:**

- Pharmacokinetic studies of novel antihistamines in young children.
- Efficacy of a bradykinin receptor antagonist in acute episodes in patients with hereditary angioedema.
- Long term efficacy and safety of a non-steroidal anti-inflammatory topical treatment for children with atopic eczema.
- Clinical trials on new inhaled steroids and combination inhaled therapy for children with asthma.
- The prevention of recurrent wheezing using a leukotriene receptor antagonist.
- The efficacy and safety and effect on quality of life of novel antihistamines

### **Teaching and training:**

- Projects for medical students' Special Modules (e.g. angioedema, bee venom, asthma)
- Projects for MSc Students (e.g. dietetic food allergy, complement C6 deficiency, food allergy in eczema)(2 students)
- Supervision or co-supervision of 3 PhD students.
- Allergology Diploma students (4 students)

### **Service and outreach**

- General allergy consultation service for private patients and patients from the tertiary hospitals requiring specialised procedures or investigations.
- An immunotherapy clinic for initiation and follow up of sublingual immunotherapy and administration of venom immunotherapy.
- A comprehensive allergy diagnosis laboratory service for the Lung Institute, the NHLS, and private laboratories.
- A telephonic advisory service for doctors throughout South Africa requiring advice for managing patients with allergies.
- An immunodeficiency register linked to the SA National Immunodeficiency Register (on line).
- Provision of pollen counts using the Burkard spore trap to researchers for planning clinical trials in patients with seasonal allergies and for guiding immunotherapy and seasonal pharmacotherapy.
- The training of doctors for the Diploma in Allergy and in the near future for sub-specialization in Allergology.
- Training of nurses for the National Asthma Education Programme Education Diploma in asthma care.
- Information for patients and doctors (allergy education brochures, protocols for desensitization and treatment algorithms).

### **Current staff:**

Professor (1, fulltime), Emeritus professor (part-time), paediatrician (1), medical officers (4), collaborating research clinicians (2), nurse (1), clinical trial co-ordinators (2), scientist (PhD) (1), technologist (1), technician (1), aerobiologist (part-time – 1), executive secretary (1), receptionist (1).

### **Honours and special achievements:**

Professor Paul Potter serves on the Board of Directors of the World Allergy Organization (WAO) (representing Africa) and as Chair of the WAO Speciality and Training Council. He has a NRF B rating, is an Honorary Member of the Georgian Allergy Society, and a Fellow of the Malaysian Society for Allergy and Immunology, the American College of Allergy and the American Academy of Allergy and Clinical Immunology. He has successfully motivated for recognition by the HPCSA of Allergology as a sub-speciality.

### **Funding:**

South African Medical Research Council, the Allergy Society of South Africa, pharmaceutical companies for clinical trials, and income from provision of laboratory and clinical services.

## Knowledge Translation Unit

### Heads: Dr Beverly Draper and Dr Lara Fairall (Research)

The Knowledge Translation Unit (KTU) develops and provides training in the use of clinical guidelines. Guidelines are easy-to-follow algorithmic documents for daily use by primary care practitioners (usually nurses), for the diagnosis and management of priority diseases. Guidelines are customized to local needs, integrate management across diseases and are in line with and responsive to current evidence and national policies. Educational outreach to ensure knowledge translation into practice is performed in accordance with current principles of adult education and in line with current national training policies. The unit focuses on health systems research to evaluate the effectiveness of this approach and promotes the uptake of research findings in clinical practice, both locally and internationally.

### Projects:

- **PALSA PLUS** (Practical Approach to Lung Health and HIV/AIDS in South Africa), is an evidence-based primary health care guideline accompanied by a groundbreaking on-site training programme that equips nurses to diagnose and manage respiratory diseases including TB, HIV/AIDS and STIs in primary care settings.
- **STRETCH** (Streamlining Tasks and Roles to Expand Treatment and Care for HIV) was developed to support the integration and decentralisation of HIV services, including re-prescription and antiretroviral treatment initiation in selected adults by nurses. Based on PALSA PLUS, it was implemented in selected primary care facilities in the Free State province.
- **PALM PLUS** (Practical Approach to Lung health plus HIV/AIDS in Malawi), is an adaptation of PALSA PLUS operational in the Zomba district of Malawi.
- **Primary Care 101** is an expansion of the PALSA PLUS guideline to address 40 common presenting symptoms and 17 chronic conditions in adults.
- **Free State Monitoring and Evaluation Programme** The unit has supported the monitoring and evaluation of the Free State's antiretroviral treatment programme.

### Research Activities:

Major research projects include the following:

- A pragmatic randomised controlled trial to assess the effects of educational outreach to nurses on tuberculosis case detection and primary care of respiratory illness in Free State primary clinics (instruction in the use of the Practical Approach to Lung Health in South Africa (PALSA) guidelines), 2003
- A pragmatic randomised controlled trial to assess the effects of educational outreach to nurses on the primary care of tuberculosis and HIV/AIDS in Free State primary clinics (instruction in the use of PALSA Plus guidelines (incorporating management of patients with HIV/AIDS)), 2004/5

- A pragmatic randomised controlled trial to assess the effects of educational outreach to nurses on the care of patients with tuberculosis and HIV/AIDS in primary care clinics in the Western Cape (using PALSAPlus), 2006/7
- Streamlining Tasks and Roles to Expand Treatment and Care for HIV in primary care clinics in the Free State. 2008/10
- Strengthening human resources and improving clinical outcomes through an integrated guideline and educational outreach in a resource-poor setting, the Zomba district of Malawi. 2009/10
- Effectiveness of an integrated care guideline training programme on the processes and outcomes of non-communicable chronic diseases in primary care clinics in South Africa. Western Cape primary clinics, 2011.
- Data from the Free State Anti-Retroviral Treatment programme is being used in research projects coordinated by leDEA (International Epidemiologic Databases to Evaluate AIDS).

#### **Teaching and Training:**

- Each project has provided opportunities for post-graduate students (PhD projects (6)) at UCT and collaborating universities and given rise to several publications.
- Training is an integral part of KTU activities, and although directed principally at primary care nurses, involves all categories of clinic staff. In addition, where adopted as policy, PALSAPlus is being included in curricula of nursing colleges and in universities for the training of nurses.
- Progress is being made in including the PALSAPLUS approach in the curriculum for medical students.
- In the accelerated roll-out phase of PALSAPLUS commissioned by the Minister of Health, Dr Aaron Motaalehi in 2009, to expand access to ART, the KTU training team has overseen the training of more than 800 trainers and more than 12 000 primary care nurses have received instruction using the KTU training methods.

#### **Service and Outreach**

- PALSAPLUS is currently being used in all 9 provinces of South Africa and is being rolled out in partnership with the provincial training centres. The KTU supervises training in each province, training outreach trainers who in turn deliver training on site at primary health care facilities.
- The STRETCH programme has provided valuable insights on the delivery of care to patients with HIV receiving ART that will be applied in the programme to expand access to ART in primary care facilities in South Africa.
- Primary Care 101 programme is being developed and tested in the Western Cape as a potential way of extending the benefits of the PALSAPLUS approach to patients with other chronic diseases.
- The original and later versions of the guidelines were funded by the Institute at risk until funding partners were found.
- At the request of the WHO (PALSAP Programme), KTU staff have lectured and facilitated at WHO PAL workshops in several developing countries.
- A co-operative agreement has been reached with Dignitas International, a medical humanitarian organization based in Toronto, which works with communities to increase access to life-saving HIV/AIDS-related treatment and care, to expand the PALSAPLUS approach to other countries in Africa.

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## **Current staff**

Current staff comprises 4 physicians (two in research and one in guideline development and one in project management), educationalists (3), scientists (2), information technologist (1) and project managers and administrators (3).

Collaborating scientists: Professors Eric Bateman, Max Bachmann (East Anglia), Merrick Zwarenstein (Toronto), Dingie van Rensburg (Free State) and Simon Lewin (London School of Tropical Medicine and Hygiene, UK) and Drs Pat Mayers (Nursing, UCT), Chris Seebregts and Carl Lombard (SA MRC), Dr Angeni Beeckie.

## **Special Achievements**

Adoption of PALSA PLUS for roll-out in provinces in South Africa.

## **Funding**

- International Development Research Centre (Canada)
- Belgium Technical Co-operation
- South African National Department of Health
- Western Cape Department of Health
- Free State Department of Health
- UK Medical Research Council
- Discovery Foundation
- Irish Aid
- CIDA (Canada)
- National Institutes of Health (USA).

## **Collaborations**

- Chronic Diseases in Africa initiative (UCT)
- UCT Health Sciences Faculty Departments of Medicine, Public Health, Family Medicine, Psychiatry and Nursing
- South African Medical Research Council
- Free State and Stellenbosch Universities
- Norwich Medical School, University of East Anglia, UK
- Norwegian Knowledge Centre for the Health Services, Oslo, Norway
- Sunnybrook Research Institute, Department of Health Policy, Measurement and Evaluation, University of Toronto
- Mediciens Sans Frontiers
- Dignitas International (Canada)
- London School of Tropical Medicine and Hygiene, UK.

## Center for TB Research Innovation

### Head: Dr Rodney Dawson

The primary objective of the CTBRI, which was established in 2006, is to assist in the search for new drugs and treatments for tuberculosis. Projects include methods of assessing the extent of disease and the impact of HIV infection on lung health. This has involved the development of methods for the quantitative assessment of chest radiographs (both manually and semi-automated) and of CT scans of the chest.

### Facilities and Activities

- Early Bactericidal Activity (EBA) study facility for up to 10 patients, with regulation quality infection control measures, supporting laboratory and other services.
- A Phase III TB Study network including an outpatient facility at the Institute and satellite facilities at the Chapel Street Clinic in Woodstock (renovated with Institute funds) and the Langa Community Health Centre, where a four-roomed facility was constructed in 2007.
- A digital chest radiology unit.

### Research Activities

- EBA studies. Five studies involving new drug entities and more than 100 patients with active pulmonary tuberculosis have been completed to date.
- The centre has enrolled more than 250 patients with tuberculosis into 2 multicenter international Phase III studies of novel TB drug regimens.
- The development of a Computer-Assisted Diagnostic system for the diagnosis of tuberculosis from digital chest radiographs (in collaboration). The unit has collected a large cohort of patients and analysis has begun.
- An NIH-funded study of recombinant interferon-gamma immunotherapy in the treatment of pulmonary tuberculosis.
- An NIH-funded 5-year longitudinal study of 220 HIV-infected adults on ART to investigate episodes of lung infection (aetiology and immunology) and the development of chronic lung disease.
- Projects in MDR and XDR tuberculosis.
- Development of a modified Chest Radiology Review System (CRRS) for reading digital chest radiographs.

### Teaching and Training

- An annual or twice-yearly training course for researchers in the use of the Chest Radiology Review System (CRRS) developed by the Institute. More than 75 readers have been trained and certified.
- Provision of a project for one PhD student.

### Service and Outreach

- Two pulmonologists assist with clinics and registrar training in the Respiratory Clinics and Respiratory ICUs at Groote Schuur Hospital.
- Monthly outreach clinics are held at Brewelskloof Hospital in Worcester.
- In 2009, funds raised from courses were used to assist two physicians from Brewelskloof hospital to attend an international TB congress (IUATLD Congress).
- The Unit funded the renovation of the Chapel Street Employees Wellness Clinic responsible for caring for employees of the City of Cape Town.

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## **Current Staff**

- The staff complement includes two pulmonologists (full-time), 3 medical officers, 3 registered nurses, 7 enrolled nurses and nursing assistants, 2 laboratory technicians, 1 pharmacist, 2 drivers, 2 technical support staff and 2 administrators.

## **Funding**

- Research grants from the NIH (USA), EDCTP (EU), FDA and Dutch Innovation.
- Contract research including from the Global Alliance for TB Drug Development and several pharmaceutical companies.
- Radiology projects have been funded by the EDCTP, Rogan Delft (Ltd) and Dutch Innovation.

## **Collaborations**

- Institute for Infectious Diseases and Molecular Medicine (UCT)
- Tiervlei Trials Centre (EBA studies)
- Brewelskloof Hospital
- City of Cape Town (use of clinic facilities)
- Bellevue Hospital and New York University School of Medicine, New York (Professor William Rom)
- University of Nijmegen Medical Centre, Netherlands

## Lung Infection and Immunity Unit

### Head: Professor Keertan Dheda

The LIU seeks to improve the survival and health people with lung infections associated with poverty e.g. tuberculosis (TB), HIV, and pneumonia, through prevention, diagnosis and management, and to increase understanding of protective immunity against these diseases.

The major areas of interest are drug-resistant TB, diagnosis of pulmonary infections including TB, immunopathogenesis of TB, and interventions to improve outcomes in patients with pulmonary infections.

### Facilities and Activities

- The major facilities of the LIU are located the Department of Medicine (offices and well-equipped laboratories), but the Institute provides a base for its many field and outreach activities.
- The UCT laboratories cover approximately 500 square metres and include a category 3 laboratory (BSL3), an advanced molecular biological platform, and two flow cytometers including a multi-colour LSR2 instrument.
- Recruitment and clinical profiling of patients for studies is performed in clinics and hospitals.
- The unit has developed the infrastructure for the developing and validating of new TB diagnostic technologies including LAMP, Gene Xpert and the HAIN MDR plus and SL assays.
- Aptamer and proteomics technology is being explored to identify new diagnostic targets.
- Molecular epidemiological and drug susceptibility testing for XDR TB are undertaken by staff based and co-supervised at the University of Stellenbosch.

### Research activities

Examples of recent research outputs include the following;

- Early treatment outcomes and HIV status of patients with extensively drug-resistant tuberculosis in South Africa: a retrospective cohort study. *Lancet*, 2010. This is the largest cohort of XDR-TB patients (more than 200) in which treatment outcomes have been examined. It provided several policy recommendations, including the value of moxifloxacin and HAART to improve outcomes.
- High Incidence of Hospital Admissions with Multidrug Resistant and Extensively Drug Resistant Tuberculosis among South African Health Care Workers. *Ann Internals Med*. 2010. This study revealed that the incidence of active MDR or XDR-TB was ~ 6-fold higher in healthcare workers in South Africa than in controls, and point to the need for intensified HCW screening, infection control programs, and use of newer rapid diagnostic tools in symptomatic HCWs.
- Cerebrospinal T Cell Responses Aid the Diagnosis of Tuberculous Meningitis in a HIV and TB Endemic Population. *Am J Respir Crit Care Med*. 2010. This is the first large study demonstrating that TB meningitis can be rapidly diagnosed in a high burden setting.
- Within-subject variability and boosting of T-cell interferon-gamma responses after tuberculin skin testing. *Am J Respir Crit Care Med*, 2009. This paper defines the reproducibility of the assay and informs on interpretation of results around the cut point. This impacts on the way these tests are used globally and will have implications for national guidelines in several countries.

# REPORT:

## UNIVERSITY OF CAPE TOWN LUNG INSTITUTE: 2000-2010

### Teaching and training

- The Unit currently has 13 registered post-graduate students, 8 PhD or MD students, and 5 Masters students. Two PhD and 2 Masters students have graduated.
- Courses co-organised by the Unit include a Scientific Writing Course and an XDR/MDR Tuberculosis Course.

### Service and Outreach

- Clinical outreach activities by researchers are provided at four primary care clinics in Cape Town, the Brooklyn Chest Hospital (weekly clinics for MDR and XDR TB patients), and Gordonia Hospital in Upington in the Northern Cape (two-monthly).
- Professor Dheda serves on the MDR National TB Advisory Committee, and also on the UK Drug Resistant TB Advisory Network.

### Current staff

- Staff include 13 post-graduate students, 3 laboratory technicians, 3 medical scientists, 6 research nurses, 3 research assistants, 2 data managers, and 2 administrators.

### Honours and Special Achievements

- Professor Dheda was awarded a South African National Research Foundation Chair and MRC Career Development Award in 2008, a UCT Fellows Young Researcher Award from UCT in 2009 and the 2010 International Union against Tuberculosis and Lung Disease Scientific prize. He serves on the editorial boards of Plos One and International Journal of Tuberculosis and Lung Disease.
- The Unit was awarded a European Developing Country Trial Partnership award valued at \$4.1million for the development and validation of new diagnostic technologies for TB.

### Funding

- SA Medical Research Council
- National Research Foundation
- European Union FP7
- EDCTP
- NIH (USA)
- Fogerty
- Discovery Foundation
- Polio Research Foundation
- SA Thoracic Society

## Collaborations

- National Health Laboratory Service
- Institute for Infectious Diseases and Molecular Medicine (UCT)
- University of Zimbabwe College of Health Sciences
- SA Medical Research Council – Unit for Clinical and Biomedical Research
- University Teaching Hospital, Zambia
- University of Nijmegen Medical Centre, Netherlands
- University College, London
- Klinikum Universitat Munchen – Department of Infectious Diseases and Tropical Medicine
- Karolinska Institutet, Sweden
- Foundation for Innovative Diagnostics (FIND), Germany
- Liverpool School of Tropical Medicine
- London School of Tropical Health and Hygiene
- University of Florida
- CSIR
- Botswana Harvard Aids Institute; Partnership for HIV Research and Education
- Stellenbosch University
- Biomedical Research and Training Institute, Zimbabwe
- College of Medicine, University of Malawi
- University of Medicine and Dentistry of New Jersey
- Leiden University Medical Centre
- New York University School of Medicine and Bellevue Hospital
- Dipartimento di Scienze Biomediche, Italy
- University of Western Australia

## The Skin and Hair Centre

### Head: Professor Gail Todd

The Skin and Hair Centre has focused on clinical trials on new dermatologicals and has provided a variety of services for patients with disorders of skin and hair. These include consultations, a day care centre, patient counselling, a problem cases clinic for dermatologists and an oral diseases clinic (Professor Josh Hiller). Consultant dermatologists include Emeritus Professor Norma Saxe, and Drs M Penny, S Pather and N Khumalo. A social worker specialising in the psycho-social aspects of skin diseases has provided counseling and assistance with patients' maintenance plans. Outreach functions included liaison with schools and the workplace in order to facilitate understanding and acceptance of skin diseases and their management in the community. The Day Care Centre has provided highly skilled phototherapy from dermatology trained staff, and personalised care to patients suffering from chronic skin diseases such as eczema, psoriasis and vitiligo. It is the first dermatology centre of its kind in South Africa.

### PUBLICATIONS

(since 2000, all Units combined)

Success in research involves collaboration and teamwork. The publications listed have involved researchers at the Lung Institute to varying degrees; some as lead contributors and others as one of many collaborators. As the Institute forms part of the research platform of the Division of Pulmonology in the Department of Medicine, the publications are regarded as outputs from both the Institute and University, and especially publications on projects with a major laboratory component. Authors and co-authors associated with the Institute are presented in **bold** type.

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## Contact Details

UCT Lung Institute  
George Street  
Observatory  
7925  
Tel: +27 21 406 6850  
<http://www.lunginstitute.co.za>

Managing Director: Professor Eric Bateman  
Email: [eric.bateman@uct.ac.za](mailto:eric.bateman@uct.ac.za)  
Tel: +27 21 406 6901

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