ANALYSIS

UCT's contribution to medical genetics in Africa - from the past into the future

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The Division of Human Genetics (DHG), Faculty of Health Sciences, University of Cape Town (UCT) – established in 1972 – recently celebrated its 40th anniversary. We review its history, current status and future objectives.

Dr Stuart Saunders, former Professor of Medicine and Vice-Chancellor of UCT, played a pivotal role in initiating the DHG. Dr Peter Beighton served as Professor of Human Genetics from 1972 to 1999. In this period, the initial focus was on medical genetics and the development of cytogenetic, biochemical and molecular laboratories, with the help of Prof Jacquie Greenberg. Fourteen clinical and scientific DHG members obtained doctorates; of these, 8 achieved full professorial status.

Current Head of the Department, Prof Raj Ramesar, succeeded to the Chair in 1999. Expansion of the molecular laboratories followed. The DHG now has comprehensive programmes for postgraduate scientific training, research and service.

Publications during the lifetime of the DHG include more than 540 articles in peer-reviewed medical, genetic and scientific journals, 20 books and contributions to over 40 chapters/editorials in scientific and medical genetic books.

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From the past

Medical genetics emerged from the broader fields of anthropology and population genetics in the 1960s, when, following advances in cytogenetics and biochemistry, it became evident that new concepts and knowledge in the field had clinical applications. Academic and clinical genetic facilities began to be established in major centres, predominantly in Europe and the USA.

In South Africa (SA) precursors of this process included the anthropological contributions of Prof Phillip Tobias at the University of the Witwatersrand. Similarly, Prof M C Botha of the University of Cape Town (UCT) was active in the laboratory aspects of population genetics. Another notable contributor was Dr Geoffrey Dean, a physician in Port Elizabeth, who documented the familial nature of a form of porphyria which affected several thousand descendents of a single Dutch progenitor. By the late 1960s, UCT had a well-established unit in the Department of Medicine dedicated to the study and management of porphyria, under Prof Lennox Eales.

At the start of the 1970s, Prof Stuart Saunders, as Chair of Medicine, mandated a Senior Lecturer to become involved in the clinical aspects of genetic disorders. Concurrently, cytogenetic facilities were established within the Department of Physiology. The post of full Professor of Human Genetics was established within the Department of Medicine, and on 1 April 1972 (regarded by many as an appropriate date) Prof Peter Beighton was formally appointed to this Chair. The cytogenetics unit was transferred from Physiology to Human Genetics.

A programme of lectures in medical genetics was introduced in the undergraduate curriculum. Routine genetic clinics were established at Groote Schuur Hospital (GSH) for diagnosis, prognostication and genetic counselling, and a partnership with the genetic clinic at Red Cross War Memorial Children's Hospital (RCWMCH) was initiated. It soon became necessary to provide biochemical laboratory facilities.

At this early stage, the main research thrust was the assessment of the presence and frequency of genetic disorders in the various populations of SA.[1] This service-orientated translational research provided a basis for the development of clinical and laboratory facilities appropriate to local circumstances. A weekly genetic clinic at the Princess Alice Orthopaedic Hospital was in line with the Head of Department's special interest in genetic skeletal disorders; the study of several hundred affected persons laid the foundations for local research in this field.[2] Genetic disorders were causative in a significant portion of individuals with physical handicaps, intellectual dysfunction, visual disturbance and profound childhood deafness.[3] Numerous institutions in the Cape provided care and education for these persons, for whom diagnostic screening was initiated. In time, additional technical, nursing and medical posts were established, permitting institutional screening in other regions of SA. Regular outreach genetic clinics were held in peripheral centres.[4] Large-scale epidemiological investigations were undertaken in a rural Xhosa community and among the San population of the western Kalahari. In the 1980s, advances in technology facilitated the establishment of a pregnancy counselling clinic at GSH with antenatal diagnostic services.[5]

The political situation in SA impeded international interaction, particularly with Africa (the only other medical genetics unit on the continent being in Cairo). In different circumstances, links with overseas universities could have been highly productive. Despite the adverse socio-political situation, a highlight was the role played by the Department of Human Genetics, in conjunction with Prof J P van Niekerk (Dean) and Dr Ernette du Toit, in the revocation of the Mixed Marriages Act in 1985.

Molecular biology began to impact medical genetics; in the early 1980s the biochemistry laboratory in the Department of Human

Emeritus Prof Peter Beighton was the first Head of the Division of Human Genetics (1972 - 1999); from 1983 to 1998 he was Director of the UCT/MRC Unit for Medical Genetics. Dr Karen Fieggen is a senior specialist and Head of Clinical Genetic Services. Dr Ambroise Wonkam is a clinical specialist and oversees the undergraduate and postgraduate teaching of clinical genetics. Prof Raj Ramesar has been the Head of Department since 2000. He is a registered genetic counsellor and Director of the MRC Genetics Research Unit at UCT. Prof Jacquie Greenberg is a medical scientist and genetic counsellor, and heads up the molecular genetics diagnostic laboratory.

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Genetics was expanded, with subsequent developmental research and medical genetic applications.[6] Clinical and laboratory staff were encouraged to undertake research and the establishment of a Medical Research Council (MRC) unit in the department provided impetus. Clinicians who trained in the department had Fellowship qualifications in Medicine or Paediatrics and several successfully completed doctoral research projects. Scientific staff were equally active; 14 had obtained doctorates by 1999, 8 of whom subsequently achieved full professorial status in SA or overseas. Longstanding professional collaborations and friendships with past doctoral graduates have continued. Ongoing clinical and molecular genetic studies have resulted in interdisciplinary, national and international research projects which have made major contributions: http://web.uct.ac.za/depts/genetics/neuro and http://web.uct.ac.za/depts/genetics/retina.

In the 1990s the scope of medical genetics continued to widen, the staff establishment of the Division of Human Genetics (DHG) increased and local, peripheral and outreach clinics flourished with the support of the cytogenetics and molecular laboratories. Medically orientated genetic research was supplemented by laboratory studies and new directions followed.[7-9] At the end of 1999 PB was succeeded by Prof Raj Ramesar.

From 2000 to the present

Despite national and provincial crises in filling vacant posts and/or creating new ones, great efforts have been made to maintain the excellence of clinical teaching and training in the medical genetics subspecialty. Recognition, on the part of other disciplines, of the value of genetics in understanding the basis of disease and in guiding management has been of particular assistance, with many senior clinicians undertaking higher degrees within the field. The training of registrars in medical genetics has commenced. The trend of a growing genetic footprint in each health sciences discipline may turn out to be the ultimate success story of our Faculty. Research momentum has been strengthened with the establishment of a National Colorectal Cancer Research Consortium,[10] and a MRC Human Genetics Research Unit (http://www.mrc.ac.za/mrcnews/july2005/colon.htm).

With a focus on genetic developments in Africa, the advent of the African Society of Human Genetics (AfSHG; http://www.afshg.org) led to commitment to establish a continental genomics research network. Pressure from the AfSHG resulted in relocation of its headquarters from the National Institutes of Health (NIH) in the USA (where its President, Prof Charles Rotimi, is based) to the DHG within the Department of Clinical Laboratory Sciences. Collaboration of the AfSHG with the NIH (USA) and the Wellcome Trust (UK) led to the establishment of the Human Heredity and Health: Africa programme (H3Africa; http://www.h3africa.org) for funding large-scale genomic research networks on the African continent. The DHG, with its commitment to promote genetics within as many disciplines as possible, within UCT and elsewhere, is viewed as a key role player in the work of the AfSHG and H3Africa.

In March 2010 the Division hosted an International Joint Conference of the African and Southern African Societies of Human Genetics, which attracted a stellar list of researchers in the field. The meeting's purpose was to define research priorities and develop study designs required to improve health in African populations. Since the H3Africa meeting, both the Wellcome Trust and the NIH have launched competitive doctoral and post-doctoral fellowship grant opportunities for young African scientists, and have established local reference centres. The Southern African Human Genome Programme, launched in January 2011, will further extend these initiatives.[11] With international support and interest in ensuring the interconnectivity and applicability of genetics and genomics in the health of our continent, UCT has a notable role to play in integrating genomics research and translation with other medical disciplines.

Current genetic services in SA

The objective of a good genetic service is 'to help people with a genetic disadvantage to live and reproduce as normally and responsibly as possible'.[12] Ideally, the service should include diagnosis, counselling and comprehensive care for those individuals whose lives could be affected by a genetic condition. This is as necessary in an emerging economy such as SA, where limited resources adversely affect the adequacy of facilities for the disabled, as in the developed world.

Currently, comprehensive genetic services are available in the 3 main urban centres of SA and offer fully integrated clinical, counselling and laboratory facilities, as well as specialist academic training. They provide outreach clinics within their provinces and others. Notably, in 2011 there were only 17 medical geneticists, of whom 9 were in full-time practice, and 26 genetic counsellors – as listed on the GC-SA email list of the Southern Africa Society of Human Genetics (http://www.sashg.org).

The shortage of trained genetic professionals leaves much of the population without access to appropriate services, despite recognition of the role of genetics in monogenic disorders and common mutltifactorial diseases such as cancer, diabetes and heart disease. Formerly, trained nurses were key providers of genetic services but competing needs, made worse by the HIV epidemic, have resulted in attrition of posts for both nurse counsellors and medical geneticists. Moreover, there is no provision for the emerging profession of genetic counselling which, in the multilingual and multicultural society of SA, demands indigenous language speakers to convey complex genetic concepts.

UCT – 1 of only 4 training centres for specialist medical geneticists and offering 1 of only masters degrees in genetic counselling in the country – has a clear responsibility for training genetic healthcare professionals for South Africa and, arguably, for the rest of Africa.

Outreach programmes and prenatal, paediatric and adult clinical services have been provided to over 40 000 patients over the last 2 decades, through GSH and RCWMCH. Diagnostic laboratory services and a thriving translational research environment have ensured that UCT is at the forefront of medical genetics in SA and the rest of Africa. Its future central role is to contribute to genetic healthcare while training genetic specialists and contributing to the teaching of undergraduate students.

Medical genetics in sub-Saharan Africa

According to the World Health Organization, 7.6 million children are born annually with severe genetic conditions or malformations that are predominantly genetic in origin; 90% are born in low- or middle-income countries.[13] However, genetic conditions receive little attention outside the industrialised world, with the main focus being on communicable diseases such as HIV and malaria. Yet, haemoglobinopathies alone represent a health burden equivalent to that of communicable and other major diseases.[14]

Most sub-Saharan African countries lack clinical and diagnostic facilities for genetic medicine and have no capacity for research.[15] Furthermore, human genetics research in sub-Saharan countries has often failed to address the ethical obligation to build capacity in those countries exploited for such research. For example, among 50 studies published since 1989 in which Cameroonian DNA samples were used, less than 20% included a Cameroonian collaborative centre.[16] The concern is that, despite the potential of genetic knowledge to improve

health and to promote equity, commercial development of genomics will widen the gap between the developed and developing world.[17]

This prompted inauguration of the AfSHG, which provides a forum for scientists to meet, network and collaborate.[18] A highlight of the 2007 AfSHG meeting in Cairo was the launch of the African Genome Project.[19] Discussions between African and international scientists and funding agencies led to the Wellcome Trust Frontiers Meeting ('Genetic diversity in health and disease in African populations') in Cameroon (13 - 15 March 2009). As a result, the H3Africa initiative was launched with the goal of developing a large-scale genomics research programme in Africa to study genetic diversity in health and disease in African populations.[20] Researchers from African and non-African countries are currently involved in researching aspects of the human genome in relation to human origins, diversity and disease susceptibility.[21]

There is also need to improve genetic literacy in sub-Saharan Africa.[22] Collaboration between international and African universities will assist with the development of new curricula for medical undergraduates, and the establishment of registrar/resident training programmes. Internship training for medical scientists and genetic counsellors, together with BSc programmes, could be developed.

In conclusion, governments and international health agencies should recognise the importance of medical genetics to the global community; yet, they tend to neglect the field when global health issues are discussed. UCT's Afropolitan policy could facilitate initiatives deserving of advocacy and encouragement from the international community, on the part of African geneticists.

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