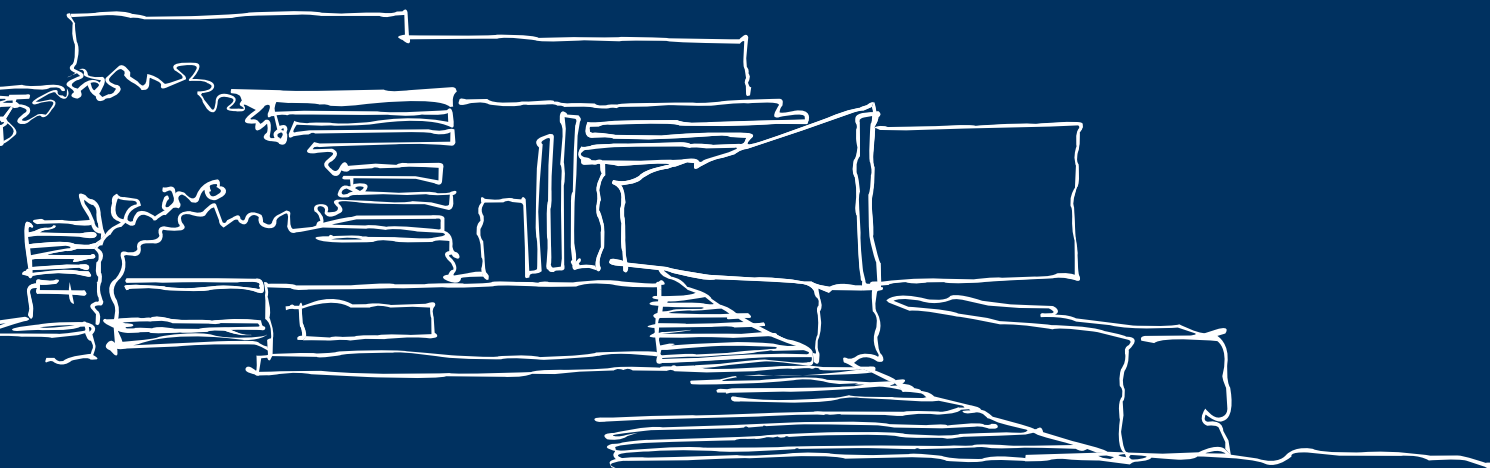


AAS-STIAS  
WORKSHOP REPORT  
**STEM CELL SCIENCE AND APPLICATIONS**  
27 JUNE TO 1 JULY 2016

A CREATIVE SPACE FOR THE MIND



# ABOUT AAS AND ABOUT STIAS

## STIAS

The Stellenbosch Institute for Advanced Study is a high-level research institute dedicated to innovative thinking, the production of new knowledge and the nurturing of emerging leaders. It was established in 1999 as an independent Public Benefit Organisation with its own Board of Directors. Over the past sixteen years STIAS has become established as a prime research destination on the continent of Africa.

Its aim is to provide a creative space for the mind where leaders in their respective disciplines can devote their undivided attention to innovative projects of their own choosing, free from the distractions of lecturing and administrative responsibilities.

While it belongs to the family of institutes for advanced study like Princeton, Berlin, Uppsala, Stanford, Harvard, and others, STIAS is distinguished by three aspects: It serves all disciplines, not only the natural sciences, social sciences or the humanities; it concentrates on interdisciplinary discourse and projects; and it has a special focus on Africa.

## AFRICAN ACADEMY OF SCIENCE

The African Academy of Sciences (AAS) is a pan-African organisation headquartered in Nairobi, Kenya, which aims to drive sustainable development in Africa through science technology and innovation. The AAS utilises its membership pool which consists of a community of excellent scientists to engage with governments and policy makers on the continent. The membership comprises individuals who have reached the highest level of excellence in their field of expertise and have made contributions to the advancement of the field on the continent.

To date AAS has recognised 330 AAS Fellows and Associate and Honorary Fellows who are proven science, technology and innovation leaders, policy advisors and thinkers most of whom live and work throughout the continent.

The activities of the AAS are broadly categorised into Recognising Excellence through the election of scientists into AAS Membership as Fellows/Associate Fellows and Affiliates (a programme to mentor young professionals into world class research leaders), and Awarding Prizes; Providing think tank services for shaping the continent's strategies and policies and Programmatic activities.

The AAS is the only continental academy in Africa enjoying the support and recognition of NEPAD and the African Union as well as several governments and major international partners. These bodies also recognise the think-tank functions of the Academy and its increasing role in setting the research agenda for the future development of the continent.

Up to twenty research fellows are hosted at the STIAS Wallenberg Research Centre at any one time. The Institute strives to provide an interface between the global research community and Africa in Africa. It serves as a meeting point not only between North and South, but also between East and West by including projects and fellows from Latin America, Asia and Oceania.

STIAS fellows are expected to be resident at STIAS for the duration of a fellowship, with no academic obligations other than pursuing the proposed research project. The only other duties are to share in the discussion over lunch which is served daily, and to participate in the Thursday STIAS fellows' seminar where fellows in turn present their work to other fellows and invited academics from the local community.

More information about applying for the regular fellows programme at STIAS is available at

**[www.stias.ac.za/application-to-the-stias-programme](http://www.stias.ac.za/application-to-the-stias-programme)**

The AAS is implementing programmes in partnership with pan African and international organisations. In 2015, the AAS launched the Alliance for Accelerating Excellence in Science in Africa, a platform created in collaboration with the New Partnership for Africa's (NEPAD) Agency. AESA is an agenda setting and funding platform to support the development of Africa's research leadership and promote scientific excellence and innovation to overcome some of Africa's developmental challenges.

The AAS is governed by:

- A General Assembly, that consists of AAS Fellows and meets regularly to hear from the Governing Council receive financial and activity reports and to approve the Academy's programmes;
- A Governing Council that consists of 14 officers elected by the General Assembly and meets twice a year to create and review the Academy's programmes, approve audited accounts and appoint members of the Management Committee;
- A Management Committee that consists of the President, the Secretary General, the Treasurer and the Executive Director;
- The Secretariat based in Nairobi, headed by an Executive Director.

More information is available at: **<http://aasciences.ac.ke>**

## ACKNOWLEDGEMENT

We appreciate the foresight of Prof. Dorairajan Balasubramanian of L. V. Prasad Eye Institute (LVPEI) in India and Prof. Abdallah Daar of the University of Toronto in Canada, who conceptualised building the capacity of young African scholars in stem cell science as well as Prof. Vivaldo Moura-Neto, Instituto Estadual do Cerebro Paulo Niemeyer in Brazil a supporter and long-term mentor in this initiative. Sincere gratitude goes to Dr Christoff Pauw, Programme Manager, STIAS; Ms Nel-Mari Loock, Programme Administrator and all STIAS staff for hosting the workshop as well as Swedish Riksbankens Jubileumsfond who together with STIAS, co-funded the workshop.

Special thanks go to the resource persons, including those who availed their laboratories for the practical session, who shared their knowledge and their vision for building capacity of African scientists in stem cell science as well as the opportunity they provided for mutual co-operation.

Our gratitude is extended to Prof. Jacque Greenberg, University of Cape Town, for her valuable session on the importance of ethical

consideration in this emerging field of science as well as to other experts who gave insights into the work that they are undertaking in this field.

The workshop would not have been so successful without the young professionals – potential mentees. We thank them for sharing excerpts of the interesting scientific work they are each undertaking, their stimulating and constructive discussions, their willingness to expand the pool of mentees in stem cell science and promote this field in Africa

We also thank Ms Olivia Osula, African Academy of Sciences, who worked with STIAS to deliver a successful workshop as well as her colleagues, Ms Janet Kariuki and Deborah-Fay Ndhlovu.



**Prof. Berhanu Abegaz**  
Executive Director, AAS



**Prof. Hendrik Geyer**  
Director, STIAS



*From left to right: Prof. Abdallah Daar, Prof. Hendrik Geyer, Prof. Berhanu Abegaz and Prof. Dorairajan Balasubramanian*

# EXECUTIVE SUMMARY

New and emerging knowledge in frontier medicine provides an opportunity to develop alternative therapies for prevention, diagnosis and treatment for diseases that plague the continent including the rising cases of Non Communicable diseases. Stem cell science has great potential to provide much needed solutions to reduce Africa's disease burden. It is however, still an emerging field. Much research still needs to be done to fully understand the potential of stem cells and regenerative medicine in treatment.

For Africa there are the additional challenges of shortage of expertise as well as inadequate infrastructure for research in this field. It is therefore important to promote this field as a career option and build the capacity of both established and young scientists, collaborate and share knowledge, expertise and facilities within the continent and globally so as to establish this field of frontier medicine in Africa.

The African Academy of Sciences and the Stellenbosch Institute for Advanced Study joined forces to hold the workshop on *Stem Cell Science and Applications* in South Africa from 27 June to 1 July 2016. This was the third workshop on stem cell science and regenerative medicine organised by AAS and partners.

By bringing together over 30 participants from Africa, Brazil and India, the two organisations are continuing an ongoing *Capacity Building in Cell Biology and Regenerative Medicine* programme started by the AAS and partners in 2012. The goal of this programme is to build capacity and mentor future generations of young African scientists in the areas of stem cell science through training provided by various resource persons in this field.

A workshop was organised in 2013 with support from the World Academy of Sciences (TWAS) and the National Commission for Science Technology (NACOSTI) in Kenya. In 2014, AAS submitted a proposal to the InterAcademy Panel (IAP) to fund the next phase of the programme comprising a second workshop and a mentor-mentee component.

The workshops provide a forum for young scientists to interact with these resource persons and are an opportunity to identify young professionals who could be mentored in the mentor-mentee component of the programme. The latter is accomplished through short-term research visits undertaken by the young professionals at the laboratories of the resource persons.

The presentations and feedback allowed scientists to share ideas to help advance their respective research areas. The practical sessions during the laboratory visits also allowed participants to acquire knowledge about various types of equipment and techniques used in stem cell research from institutions in South Africa. It was eye opening and inspiring for participants who wish to advance their careers in stem cell science.

For STIAS and the AAS the success also comes with the lessons shared of how to overcome the challenges that scientists face in stem cell research. The recommendations provided by participants not only show the commitment to growing this field of research despite the challenges but also how such a forum provides networking opportunities for scientists to share facilities and knowledge. The participants mapped a way forward that includes recommendations to:

- Continue to raise the profile of the field so that more young people are aware of the career opportunities it offers and its impact in combatting diseases.
- Improve collaboration between stem cell researchers and clinicians. Researchers should educate clinicians on cell biology as they are the bridge between the public and scientists.
- Allow scientists to share facilities and expertise to enable peers to access resources to conduct research in stem cell sciences.
- Mentor young scientists in grant writing and create a database to avail funding schemes for the field. This would enable the young scientists to apply and access funding to continue their stem cell research.
- Organise a fourth workshop to expand the pool of mentees and mentors as well as stem cell knowledge
- A group on Stem Cell Research for Africa comprising the young scientists present was established to begin addressing African Capabilities in orienting Stem Cell and Regenerative research so as to combat African Health Issues. The group has a Chairperson with regional Co-ordinators from Central, Eastern, Northern, Southern and Western Africa

AAS, STIAS and partners should now use the recommendations to shape the future of the stem cell science programme in Africa.

## BACKGROUND

New and emerging knowledge in frontier medicine provides an opportunity to develop alternative therapies for prevention, diagnosis and treatment for diseases that plague the continent including the rising cases of non-communicable diseases (NCDs). Building Capacity of African Scientists in Cell Biology and Regenerative Medicine (CBRM) through mentoring by experts from scientifically advanced countries of the South will enable Africa to cope with these health challenges.

The workshop provided a forum for young African Scientists to interact with frontier experts in CBRM from India, Brazil and China. Information was shared on the potential of cell therapy/regenerative medicine to address global health concerns in general and those that are specifically relevant to Africa as well as the status of cell therapy/regenerative medicine in Africa.

STIAS and AAS share common goals which have been evident from the onset of the relationship. Both organisations aim to support science at the highest level; both have a specific emphasis on Africa and its emerging place in global scholarship and both share a vision for young researchers and the future of science on the continent. The workshop on *Stem Cell Science and Applications* is the first concretisation of these shared goals. The workshop forms part of the STIAS long-term theme

*“Health in Transition”* and is the first in a series of planned joint AAS-STIAS events.

AAS organised a *sensitization* workshop on *Capacity Building in Cell Biology and Regenerative Medicine* in November 2013 in Nairobi, Kenya and a second workshop in August 2014 on *Training and Mentoring African Scientists in Stem Cell and Regenerative Medicine Research*. Early career scholars were identified to take part in the mentorship component of the project whereby young professionals would travel to laboratories of the experts for short-term research visits.

In 2015, seven mentees underwent training at various institutions—the National Centre for Cell Sciences (NCCS), Pune, India; the LV Prasad Eye Institute in Hyderabad, India; the Institute of Biomedical Sciences of the Universidade Federal do Rio de Janeiro (UFRJ), Brazil; the Institute for Cellular and Molecular Medicine at the University of Pretoria, South Africa and the Islet Research Laboratory, Anatomy and Histology at Stellenbosch University, South Africa. Two of the mentees who undertook their research visits at the Universidade Federal do Rio de Janeiro (UFRJ) obtained scholarships to undertake PhD courses in Brazil under the overall mentorship of Prof. Vivaldo Moura-Neto, one of the lead resource persons collaborating on the CBRM project.

## OBJECTIVES

The AAS-STIAS workshop assessed the progress of collaborations established so far from on-going CBRM activities, highlighted new training and research opportunities and presented the participants with a platform to plan or launch their careers in stem cell science. The workshop also provided opportunities for networking among a multidisciplinary team of experts in the field.

Additional early career scientists would be identified to be designated as mentees and undertake research visits at laboratories in India, Brazil and South Africa as well as identify additional experts to provide the training. The workshop was to be “the launching pad for active stem cell practice in Africa.”<sup>1</sup>

## FORMAT

The third workshop combined a series of lectures and demonstrations of hands on techniques at the Islet Research Laboratory of Stellenbosch University, the *International Centre for Genetic Engineering and Biotechnology* (ICGEB) and the *Division of Cell Biology* at the University of Cape Town. It also consisted of dedicated networking sessions where young professionals had discussions with the experts to identify individual areas of research interest in which the former could be trained. It also provided

opportunities for networking between laboratories in Africa and identifying the current work being undertaken as well as potential areas of synergy nationally, regionally and across the continent.

A multidisciplinary team of experts in the of cell biology from Brazil, Canada, India, Kenya, Nigeria, South Africa and Sudan were invited as speakers.

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<sup>1</sup> Prof. Dorairajan Balasubramanian, Director of Research at L. V. Prasad Eye Institute in India



## RESOURCE PERSONS

The key resource persons who contributed to the workshop were:

- Prof. Abdallah Daar, University of Toronto, Canada
- Prof. Dorairajan Balasubramanian, L. V. Prasad Eye Institute (LVPEI), Hyderabad, India
- Prof. Susan Kidson, University of Cape Town, South Africa
- Dr Venant Tchokonte-Nana, Stellenbosch University, Cape Town, South Africa
- Prof. Iqbal Parker, International Centre for Genetic Engineering and Biotechnology (ICGEB), Cape Town, South Africa
- Prof. Jose Garcia Abreu, Universidade Federal do Rio de Janeiro (UFRJ), Brazil
- Prof. Fabio Almeida Mendes Universidade Federal do Rio de Janeiro (UFRJ), Brazil

- Dr Anjali Shiras National Centre for Cell Sciences (NCC), Pune, India
- Prof. Keolebogile Shirley Motaung, Tshwane University of Technology, South Africa
- Dr Bade Ogundipe, University of Ibadan, Nigeria

Other experts included Dr Marianne Mureithi, KAVI-Institute of Clinical Research, University of Nairobi (KAVI-ICR), Kenya; Prof. Jacquie Greenberg, University of Cape Town, South Africa; Prof. Kathy Myburgh, Stellenbosch University, South Africa; Dr Hiba BadrEldin Khalil Ahmed, Al Neelain University, Sudan; Dr Atunga Nyachio, Institute of Primate Research, Kenya; Dr Kevin Dzobo, International Centre for Genetic Engineering and Biotechnology (ICGEB), South Africa; Dr Mari Van de Vyver, Stellenbosch University South Africa and Prof. James O. Olopade, University of Ibadan, Nigeria.

## WHY STEM CELL SCIENCE IN AFRICA?

Stem cell science is a growing field across the globe. Since their discovery in 1963 by Canadian scientists, Ernest McCulloch and James Till, there have been various developments in the field starting with the cloning of Dolly the sheep in 1996 and the method of inducing pluripotency in normal cells in 2007. In Africa the field is still fledgling but workshop participants recognised and

emphasised its importance given the regenerative abilities of stem cells that offer a potential for treating various diseases.

Stem cell science can provide solutions to the rising burden of non-communicable diseases (NCDs) in Africa, which the World Health Organization is predicting to overtake communicable, maternal and perinatal diseases as the leading cause of death by 2030 (WHO Global Status Report on Non-communicable Diseases 2010). There certainly is a case for focusing on them.

At the moment NCDs account for 23 percent of the disease burden on the continent, contributing to a rise in medical costs and the impact on human development. Diabetes for example can compromise foetal development. Half of the people who die from NCDs are people in their productive years which is a loss for African society and industries. As such, investing time and money on stem cell research to address diseases which will have a huge economic burden on Africa is essential to ensure that the continent continues on the path of growth and improves the lives of its people.

The field still has a lot of potential for growth according to Prof. Abdallah Daar from Canada's University of Toronto. Scientists do not know enough and the field is still equally new on the continent. Mechanisms for scaling up organ development, for example, are still to be studied. For Africa, this means unexplored career options and research fields for both established and young scientists.



Left: Dr Farisai Chidwondo

# DEFINING STEM CELLS

Stem cells show a lot of promise in the field of regenerative medicine but what exactly are they?

Stem cells have been classified broadly into three categories<sup>2</sup>:

- Adult stem cells,
- Multipotent mesenchymal stem cells
- Pluripotent stem cells which include embryonic stem (ES) cells and induced pluripotent stem cells (iPSCs).

Adult stem cells are found throughout the body in both children and adults and divide and reproduce infinitely, often to repair dying cells and regenerate damaged tissues. They are also called somatic cells and are isolated from a tissue such as fat cells and the umbilical cord. Adult stem cells have been successfully used to treat leukaemia. They are however, difficult to multiply into large numbers. They are rare and comprise 0.1 percent of cells in many of the organs in the body.

A typical example of adult stem cells are skin epidermal cells (keratinocytes). These can be harvested from donor skin samples, cultured *in vitro* and used for research or for treatment (i.e. for burns). They are regarded as uni potent adult cells and can only be grown into skin cells.

Mesenchymal stem cells on the other hand can be obtained from a variety of tissues, including bone marrow, umbilical cord, foetal and adipose (fat) tissues. Bone marrow cells have been used for treating haematological conditions for over 70 years and typically, these transplanted cells home into and populate the recipient's bone marrow and when the transplant is successful, they differentiate into all the blood cell types. In culture, many studies have shown these cells to differentiate into several different cells types including adipocytes, chondrocytes and osteoblasts.

Pluripotent stem cells are capable, at least *in vitro*, of differentiating into all the types of cells in the body. Although the ability of pluripotent cells to become a part of a fully functional normal tissue remains to be proven, many animal studies and some human studies provide exciting prospects.

Human embryonic stem (hES) cells are derived from the inner cell mass of the early developing embryo and can be considered as the 'gold standard' of pluripotency. They can differentiate or develop into various types of cells in the body making them pluripotent. However, they require that embryos be destroyed to obtain these cells, which according to Prof. Jacque Greenberg from the University of Cape Town, has meant that the "harvesting and use of hES cells is limited by their availability and regulated by complex ethical and moral issues."



Prof. Susan Kidson

Adult cells can be reprogrammed into embryonic stem cells by introducing genes from an embryo to become induced pluripotent cells (iPSCs). Induction of human pluripotent stem cells is achieved by cellular reprogramming of somatic cells mediated by transcription factors. Cellular reprogramming is the reversion of differentiated cells to an undifferentiated state of pluripotency. Stem cells have the unique ability to either self-renew or get committed to become differentiated [cells of different lineages]. Stem cells can be differentiated into the middle (mesoderm), internal (endoderm) and external (ectoderm) germ layers. Cells of the middle layers are cardiac, skeletal muscle, kidney and gut. The skin and neural cells are the external layer cells while the stomach, colon, liver, pancreas, urinary bladder, trachea, lungs, pharynx, thyroid, parathyroid, intestines and gallbladder cells are examples of the internal layer cells.

Induced pluripotent stem cells (iPSCs) are currently used as cellular or biological models of certain diseases. They could potentially be used to treat some of the diseased or damaged tissue of the individual from whom they have been created, in the future. They are more commonly used as they are not regulated by ethical issues.

<sup>2</sup> This section on the definition of stem cells has been taken from part of Prof. Jacque Greenberg's presentation at the workshop on "stem cells kept simple" and Dr Anjali Shiras' presentation on 'cell based therapies with iPS Cells'.

# WORKSHOP INTRODUCTORY REMARKS

The facilitator Dr Christoff Pauw, Programme Manager at STIAS, welcomed all participants from different parts of the continent to the Stellenbosch Institute of Advanced Study (STIAS). He traced the beginning of the AAS-STIAS collaboration to a meeting and discussions he had with the AAS Executive Director a few years earlier. The workshop on *Stem Cell Science and Applications* is an example of the shared ideas and the beginning of greater collaboration between STIAS and AAS.

The Director of STIAS, Prof. Hendrik Geyer, informed participants that the AAS-STIAS collaboration was further strengthened following discussions held with Prof. Abegaz when he undertook his fellowship at STIAS in 2014. AAS and STIAS prioritize building capacity of young scientists by providing direct support to the young research community in Africa.

Prof. Geyer also mentioned the presence of Prof. Abdallah Daar who is actively involved in the STIAS long-term research project *Health in Transition* and who has been involved also in previous CBRM workshops. He underscored the importance of inter-disciplinary collaboration in science and particularly the novel area of Stem Cell and Regenerative Medicine.

He referred to the AAS 10th General Assembly that had taken place the week prior to the workshop which provided an opportunity to celebrate excellence and discuss the future of science in Africa. There was concern of globalization as a form of neo-colonization but Africa should ensure that science on the continent develops on its own terms with the continent's needs in mind.

He also talked of the STIAS *Iso Lomso programme* where young researchers apply for STIAS fellowship and the institute facilitates their stay at various institutes of advanced studies and also provides support at their home institutions. STIAS identifies this as a very important direction to help with some of the barriers young researchers come across in Africa.

The Executive Director of the African Academy of Sciences, Prof. Berhanu Abegaz said that the association with STIAS has been very rewarding and acknowledged Dr Pauw's significant role towards the success of the AAS-STIAS collaboration. He gave a presentation on the status of the Academy and emphasized on its three mandates: Recognizing excellence, Think Tank function and STI Programmes.

Prof. Abegaz gave a background of the AAS fellowship and expounded on the need for greater gender, discipline and country balance to address underrepresentation. South Africa for example is leading in S&T on the continent but its membership numbers are not indicative of this. He also talked of the AAS Affiliates Programme whose aim is to create an enabling environment for young researchers in the continent.

An overview of the programmatic arm of AAS, the Alliance for Accelerating Excellence in Science in Africa (AESA) was given, AESA is an agenda setting and funding platform established by AAS together with the New Partnership for Africa's Development Agency (NEPAD) and funded by Wellcome Trust (WT), Bill and Melinda Gates Foundation (BMGF) and the UK Department for International Development (DFID). Several programmes - Climate Impact Research Capacity and Leadership Enhancement (CIRCLE), Grand Challenges Africa (GCA), Developing Excellence in Leadership, Training and Science (DELTAS) Africa Initiative and Good Financial Grant Practice Programme (GFGP) - currently fall under AESA.

Prof. Abegaz told the participants that CBRM is one of the AAS programmatic activities under the broad strategic objective of "Health and Wellbeing". The conceptual developers of the programme Prof. Dorairajan Balasubramanian, L. V. Prasad Eye Institute in India and Prof. Abdallah Daar, University of Toronto in Canada first shared their idea of initiating capacity building in the field of cell biology and regenerative medicine at the TWAS General Meeting in China in September 2012. The meeting in China was also attended by Prof. Vivaldo Moura-Neto, Instituto Estadual do Cérebro Paulo Niemeyer, who has since been one of the lead resource persons collaborating in the CBRM programme.

The proposal of the meeting in China was to initiate capacity building in the field by (a) having experts go to a specific centre in Africa and hold a hands-on workshop; (b) host colleagues from Africa for short periods of time in the laboratories of resource persons in India, China and Brazil, and (c) explore any other possibilities. The parties at the meeting requested AAS to take leadership in organising CBRM activities.

Two workshops have been organised which subsequently resulted in successful mentor-mentee relationships that saw seven young scientists make short term research visits to their respective mentors' laboratories in India, Brazil and South Africa. He appreciated all those who made the programme a success.

He advised those attending the workshop for the first time to critically evaluate what was right for them in mapping out their futures in the area of stem cell science. He informed them that there would be opportunities for them to meet one on one with mentors at the workshop to help them make these decisions.

Dr Pauw acknowledged support from Nel-Mari (STIAS), Olivia, Deborah and Janet (AAS) He encouraged the participants to speak to the various resource persons and engage with each other.



# POTENTIAL FOR APPLICATION OF STEM CELL SCIENCE IN AFRICA

In addition to offering an effective strategy for fighting non communicable diseases, stem cells can provide alternative organs. It was mentioned that many patients especially in Africa die while on waiting lists for organ transplants hence organ bio-engineering is necessary and inevitable. Essentially, stem cells would offer an alternative supply of organs as they can be grown in the laboratory.

Recent breakthroughs in the area, according to Prof. Daar from the University of Toronto, Canada, include a human heart regenerated from stem cells by researchers from the Massachusetts General Hospital and Harvard Medical School in the United States. Other organs that have been grown in the lab using stem cells by international scientists include human muscles and kidneys. Prof. Iqbal Parker from the International Centre for Genetic Engineering and Biotechnology (ICGEB) also gave an example of scientists at the University College London who can weave threads made of stem cells into almost any form, leading to artificial transplants whose resulting synthetic tissue can be adapted to many different purposes. These are areas that African scientists can potentially use to model their stem cell research.

Adult stem cells can be used as an alternative to animal models. Animals models can be costly to keep and sometimes produce erroneous results because animal responses to human diseases and drugs can be different. There is a description on subsequent pages of this report on how a team led by Prof. Susan Kidson from the University of Cape Town developed a disease model of Spinocerebellar ataxia type (SCA7) using skin cells.

Drugs are not equally effective in all tissues of the body. Differentiated stem cells can be used to assess how drugs work in different tissues and why they target specific tissues. This would be essential for African scientists involved in drug development.

Prof. Daar in his presentation *Can Regenerative Medicine Make a Difference to the Management of Organ Failure in Africa*, noted that globally, organ transplant was still far from being fully developed but strides were being made. One of the challenges of organ transplant is the severe immunosuppression when preparing the patients' immunity against allogeneic rejection. It was noted that microbes are becoming resistant to antibiotic treatments which is likely to plunge the world to the pre-antibiotic/penicillin era.

About 30% of the global population is overweight. Obesity and malnourishment are both strong risk factors for diabetes type II and its complications, Prof. Daar stated. The value of regenerative medicine in many diseases including Arthritis, Burns, Dementia and Spinal cord injuries was stressed. Participants were urged to scale up research and clinical therapies in order to benefit the patients in need.

## Stem Cells to regenerate the damaged outer surface of the human cornea

Stem cells are also being used to repair damaged corneas in India; this was pointed out by Prof. Dorairajan Balasubramanian of the L. V. Prasad Eye Institute in India. He talked about *Stem Cell Biology and its Specific Applications in Two Areas of Eye Care – the Cornea and the Retina*. He showcased the natural mechanism of *corneal abrasion* and gave a video demonstration of current technology in corneal transplant in humans. The limbus of the eye is area rich in stem cells with the potential to regenerate almost all of the conjunctival layer and especially the corneal layers.

Clinicians in India have so far performed 1,500 operations since 2004. The method involves cultivating limbal stem cells on human amniotic membrane and applying it on the patient's eye. This procedure is called Cultivated Limbal Epithelial Transplantation or CLET. More recently, such cultivation can be done on the patient's own eye (rather than in a culture laboratory, so that the need for a stem cell culture lab can be avoided); this simpler method is referred to as Simple Limbal Epithelial Transplantation or SLET.

While this procedure works for the damaged cornea, thanks to the presence of stem cells in the limbus surrounding the cornea, there are no known stem cells in the retina and therefore the use of iPS cell is inevitable for any use of regenerative therapies of the retina of the eye.

## How does the ectoderm decide between neural or epidermis? May the Wnt pathway solve the question?

At the Universidade Federal do Rio de Janeiro (UFRJ), Prof. Jose Garcia Abreu is looking into the possibility of Wnt pathway as the answer to the question on how the ectoderm decides between neural and epidermis cells. The concept of neural induction has been postulated years ago based on experiments done in frog and avian embryos. The commitment of the ectoderm cells to a more specialized fate is first observed by the acquisition of the expression of cytokeratin which a differentiation marker for epidermis formation while sox2 is an early marker for neural tube formation.

In the neural default model, neural induction is the first step towards the formation of the neural plate. In amphibians during neural induction, every cell at the animal pole will become destined to go into the formation of the neural tube. The presence of BMP in intact growing cells has been noted to program cells to give rise to the epidermis. However, when these cells become dissociated they differentiate into multipotent neural cells. It has been demonstrated that BMP inhibition is not sufficient for neural induction in other models. The key players for neural induction differ across species (for example, BMP, FGF and WNT). It is most likely that at least a minimum two factors will be needed in deciding the fate of the ectoderm towards the formation of the neural tube.

Wnt proteins require a lipid modification for receptor binding and activity. Zhang et al report that Notum, a secreted Wnt antagonist, is a Wnt deacylase that inactivates Wnt proteins and is required for vertebrate neural induction and head development. Deacylated Wnt forms oxidized-oligomers, suggesting that acylation is essential for Wnt structure.<sup>3</sup>

Notum is found in the presumptive early ectoderm as well as the primitive streak and Henson's node OF CHICK EMBRYO. Notum silencing induces epidermal formation in frogs. These evidences in different embryo models put Wnt as key signaling pathway implicated in neural induction.

## Lessons from the embryo to cell and regenerative biology

Prof. Fabio de Almeida Mendes, from UFRJ explained that the understanding of regenerative biology is partly dependent on a clear comprehension of all the details processes and factors that guide embryogenesis and embryology. The frog *Xenopus laevis* lays many eggs and the development of their fertilized eggs into tadpole can be monitored by visual observation with the naked eye. The organisers of gastrulation instruct the migrating cells to form different layers. These organisers also induce axis formation leading to the two axis, dorsal-ventral and anterior-posterior.

Different proteins have cysteine-rich (CR) domains e.g. tolloid related metalloproteinase. Fifty-six (56) different proteins have CUB-domains containing proteins 1 (CDCP 1), for example, cubulin has 27 CUB domains. CDCP 1 is a transmembrane protein and is important for tumour survival, migration by activating Src kinase and PKC. CUB domain of CDCP 1 binds to TGF- $\beta$ 1 and TGF- $\beta$ 2. CDCP 1 increases TGF- $\beta$ 1 signaling pathway in luciferase reporter assay. It also increases the number of p-smad2 positive cells and as well increases smad-2 phosphorylation.

## Induction of human pluripotent stem cells and there *in vitro* differentiation: Looking forward to regenerative medicine

Dr Anjali Shiras of the National Centre for Cell Science (NCC), in India spoke on cell based therapies with iPS Cells. She highlighted the induction of human pluripotent stem cells and their *in vitro* differentiation as a way forward in regenerative medicine.

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<sup>3</sup> Notum is required for neural and head induction via Wnt deacylation, oxidation and inactivation, Xinjun Zhang et al, Dev Cell. 2015 Mar 23; 32(6): 719–730

Somatic cells reprogramming gives rise to induced pluripotent stem cells (iPSCs); upon differentiation of iPSCs, cells of different lineages may be obtained. *In vitro* differentiation of Pluripotent Stem Cells can be initiated under the regulation of Leukaemia Inhibitory Factor (LIF), growth factor, genetic manipulation and small molecules to yield cells. Cells may be differentiated as embryonic bodies, on stromal cells or on extracellular matrix. Germ layer differentiation of iPSCs can be achieved by using cytokine/growth factor and inhibitor supplementations. The differentiation induction of iPS cells into neural cells, cardiac cells, pancreatic beta cells and hepatocytes holds promise for its use in regenerative medicine.

Apart from the differentiation of iPSCs, there are direct-lineage reprogramming strategies for obtaining cells of different lineages from somatic cells. The process is fast and direct with no risk of teratoma formation. A recent study in 2015 has documented on a small-molecule-driven direct reprogramming of mouse fibroblasts into functional neurons without genetic manipulation.

The technology of Induced Pluripotent Stem Cells can be applied in regenerative medicine, disease modelling, gene corrections and therapy, drug screening, personalized medicine, among others. Several recent studies have shown the derivation of iPSCs from patients with Alzheimer's disease (AD), Parkinson's disease, ALS and spinal muscular atrophy.

Advantages of disease-specific iPS cells include: recapitulation of *in vivo* phenotype in a dish which would allow future use in drug screening; circumvention of cross species differences and ethical constraints; potential for cell-based therapies; responsive candidate drugs; possibility of many compounds to be tested simultaneously; and also the opportunity to improve preclinical predictions by allowing therapeutic testing of multiple cell lines. However, generation of clinical grade iPSC for every patient is time-wise and economically impossible. Presently iPSC technologies require 3 months for generation of cells, while safety and quality control takes 6 months. It is very expensive to derive a single iPS line. Allogenic banking from homologous HLA donors in Japan has stock of 75 iPS cell-lines and in the United Kingdom, a pool of 150 cell-lines. The stocks are enough to cater to 80% of Japan and 93% of UK populations respectively.

## CAVEAT IN USING STEM CELLS

As there is still a lot of research to be done in the field of stem cell biology, workshop participants emphasised that scientists still need to be conservative on what stem cells can do.

# ONGOING STEM CELL RESEARCH IN AFRICA

As stem cells are already showing a potential in treating various diseases, workshop participants outlined how they are using them in their research.

## Recent Advances in Stem Cell Therapy

Prof. Iqbal Parker, International Centre for Genetic Engineering and Biotechnology (ICGEB) in South Africa, informed participants that ICGEB is a centre of excellence for both research and training in the fields of genetic engineering and biotechnology, addressing the needs of developing countries and economies in transition.

He gave some facts about disease prevalence and burden in the Sub Saharan Africa [HIV/AIDS, malaria, & TB – 25%; neglected infectious diseases – 27%; and non-communicable diseases – 23%]. According to WHO non-communicable diseases are likely to surpass infectious diseases as the leading cause of mortality in Africa. Cardiovascular disease alone is the largest/leading contributor to the disease burden, and by projection, would dominate mortality trends in future. Consequently Prof. Parker explained that there is a need to rethink strategies about fighting diseases in Africa and how stem cell therapy can be implemented.

Culturing of pluripotent stem cells may be employed for drug development toxicity tests, experiments to study development and gene control, and generation of tissue/cells for therapy. Stem cells have crucial properties of self-renewal and pluripotency. The unique nature of the different types of Stem cells [embryonic, adult and induced pluripotent stem cells] and the potential uses/applications of stem cells in the treatment of various disorders and diseases were highlighted.

Prof. Parker outlined the procedure used for the production of the first synthetic trachea, based on biological 3D printing, which was developed at University College London and seeded with stem cells for implantation into a male patient. This invention has greatly improved the chances for creation of artificial tissues and thus could lead to artificial transplants. He concluded by describing the process for the production of cell-derived extracellular matrix [ECM] and highlighted some related research articles he co-authored recently.

## Islet cells recovery in STZ-diabetes model: Beta cell regeneration or islet reorganisation?

Some of the challenges associated with diabetes mellitus research are limitation in islet regeneration of the adult pancreas, little or no access to donor pancreas for whole pancreas transplantation and the problem of immunosuppression. Thus it appears that Islet beta-cell transplantation remains the ultimate hope as a therapeutic option for Type 1 diabetes. The field of stem cell biology and regenerative medicine have promoted renewed interest in islet regeneration as a source of new islets. However, the first major step towards this is to develop an experimental model of type 1 diabetes mellitus.

At Stellenbosch University, Dr Venant Tchokonte-Nana is researching on treating diabetes with regenerated insulin cells from adult pancreas. He is regenerating Islet beta cells (those that produce insulin) and administering them to rats injected with Streptozotocin (STZ), a naturally occurring chemical that damages the DNA of  $\beta$  cells of the pancreas and mimics type 1 diabetes.

Dr Tchokonte-Nana and his team have shown that the use of STZ to mimic type 1 diabetes in the laboratory does not model the pathophysiology of Type 1 diabetes but rather allows to study of complications of hyperglycaemia. With the regenerated Islets, the rats were clear of diabetes however hyperglycaemia occurred 120 days after nephrectomy. Histology revealed the beta cell destruction and the injected islets were thought to have been probably reorganised. Islet cell organization is crucial for the maintenance of islet functions. The team is researching to understand what happens to the cells 120 days post nephrectomy that causes the disease to return.

In response to a question on the differences between naturally occurring diabetes mellitus and experimentally induced chemical diabetes mellitus, Dr Tchokonte-Nana explained that the former is caused by the autoimmune destruction of beta cells of the islets of the pancreas while the experimentally induced by chemicals is as a result of direct destruction of the beta cells of islet of pancreas. He was also asked for how long can the rat remain normoglycaemic before nephrectomy and he said that this had not been determined but there is a long term clinical success in humans as long as the immune system is suppressed.



*Prof. Iqbal Parker and Prof. Susan Kidson*

## Modelling neural degeneration in Spinocerebellar ataxia type 7 using iPS Cells

In her presentation, Prof. Susan Kidson from the University of Cape Town in South Africa, noted that the goal of stem cell research is to translate results gotten from the laboratory to the clinic and the discovery of induced pluripotent stem cells (iPS) has led to the transformation of the understanding of biological research. It has opened up the world of stem cell biology more than proffering solutions.

Genes do not die and they do not get deleted but can be switched on or off. Whenever a cell differentiates from an embryonic stem cell to an adult stem cell, the differentiated cell follows a process of changes in gene activity. This involves the inactivation/switching off of embryonic-specific genes and a concurrent activation/switching on of differentiation-specific genes. The end result of this differentiation 'programme' is a specialized cell.

This makes genetic cell reprogramming of a differentiated adult stem cell into an induced pluripotent stem cell an interesting reality – by deactivation/switching off of differentiation-specific genes and a reactivation/switching on the embryonic-specific genes.

At Prof. Kidson's laboratory, they are using induced pluripotent stem cells to understand changes in gene expression of ataxin and tubulin proteins during differentiation. SCA7 is a late-onset neurodegenerative disease caused by an abnormal stretch of the glutamine amino acids in the sequence of the ataxin protein leading to gait ataxia, macular atrophy of the eye and blindness.

Prof. Kidson's team has successfully reprogrammed cells of SCA7 patients and control fibroblasts into iPSCs. Differentiated neural and photoreceptor cells exhibit appropriate morphology and expression of cell type-specific genes and proteins.

Numerous dysregulated transcripts were identified in SCA7 patient-derived neural and retinal cells, which may be explored in future studies to give further insight into pathogenic mechanisms. It was noted that SCA7 NPCs appear particularly susceptible to proteasomal stress.

## Dreams for the Future of Tissue Engineering and Regenerative Medicine on African Continent Based on Medicinal Plants

Prof. Keolebogile Shirley Motaung at the Tshwane University of Technology in South Africa is exploring the use of medicinal plants in tissue engineering of articular cartilage. She explained that the three key ingredients of tissue engineering are morphogenetic signals which is plant based morphogenetic factors, responding stem cells, and extracellular matrix scaffolding. She further explained that tissue morphogenesis is initiated and governed by inductive signals (morphogens) based on dynamic and reciprocal tissue interactions. According to Prof. Motaung, medicinal plants have been an integral part of the African culture but their role in tissue engineering constructs remain unexplored.

She is screening medicinal plants to identify compounds that can effectively be used in tissue engineering of articular cartilage particularly for treating joint defects. Prof. Motaung is using *Pterocarpus angolensis* (also known as the African nutmeg and traditionally used for treating malaria, gonorrhoea, wounds and inflammation) in her study. The effects of *P. angolensis*, was explored in *in vitro* assays and on the expression of collagen type II from the superficial and middle zone chondrocytes of bovine articular cartilage.

She found that the bark and root extracts of the plant were not toxic to the superficial and middle zone chondrocytes but *induced the proliferation of chondrocytes*. She stated that the findings of the



Prof. Susan Kidson



Prof. Shirley Motaung



research highlight the key role which *P. angolensis* extracts can play the most important role in cartilage regeneration. Her team is yet to identify the active compounds in the plant that regenerate cartilage and also bone.

### Adult progenitor cells: *in vitro* and *in vivo*

In giving an overview of cell differentiation in Muscle Injuries, Prof Kathy Myburgh of Stellenbosch University explained that adult progenitor cells are undifferentiated cells found throughout the body, and have the ability to divide to replenish dying/dead cells and regenerate damaged tissues. While embryonal stem cells are involved in development of an embryo/foetus, adult progenitor cells are involved in cell repair/regeneration. Muscle cells are multinucleated post-mitotic cells that do not divide. However satellite stem cells are found at the periphery lying underneath skeletal muscle basement membrane. These stem cells are normally in a quiescent state but when activated they undergo cell

Muscle injuries are caused by trauma, loading or pathological disease and human daily rigorous/adventurous activities (exercise-induced muscle damage). These injuries lead to the activation of muscle stem cells as a result of cytokines oversecretion. When muscle stem cells become activated, they proliferate, differentiate, migrate and eventually fuse with the overlying muscle cell.

MyoD and myogenin are responsible for muscle stem cell proliferation and differentiation respectively while TGF- $\beta$  inhibits muscle cell proliferation and differentiation. Elevated level of TGF- $\beta$  leads to transdifferentiation.

### Prospects of Ocular Stem Cell Science in Nigeria

In Nigeria, Dr Ayobade Ogundipe from the University of Ibadan is looking at Stem cell treatment in Ocular Surface diseases, especially after damage to the limbus and the consequent corneal epithelial limbal stem cell deficiency. According to Dr Ogundipe, the eye offers a unique opportunity in science and its clinical application of using stem cells. The ocular surface stem cells are harvested with minimal invasion and they can be used in treating diseases and even prevent complications like the cornea opacity.

Cornea epithelium is constant lost and replaced in all individuals. The ability to renew the epithelial cells is through a healthy limbal stem cells. Damage to the limbal stem cells may arise from congenital conditions or from acquired conditions like chronic inflammation, trauma, especially chemical injury, neoplasia, surgery and other causes. Extensive damage at the limbus may lead to partial or total limbal stem cells deficiency. This manifests as persistent epithelial defect, conjunctivalization of cornea, vascularization or fibrovascularization. Replacing epithelial cells in the case of damage does not offer the solution but limbal stem cells offer hope. Limbal stem cells are the precursors of the corneal epithelial cells. Thus, he has started practising both CLET, and more recently SLET in Nigeria, after attending a short workshop on these, held at the LV Prasad Eye Institute at Hyderabad, India.



Prof. Kathy Myburgh

His research is on the use of autologous stem cells from the healthy eye to be transplanted directly to the damaged eye after removing the fibrovascular growth on the cornea by a procedure referred to as Simple Limbal Epithelial Transplant (SLET) or using the limbal stem cells harvested from live relation or from cadaver in a procedure referred to as aSLET. This procedure, however, carries a higher risk of graft rejection.

SLET has been shown to be a successful procedure. Studies have shown a 71.9 percent success rate with the results being even better for children for at 80 percent. He, however, said the procedure faces challenges of lack of donor stem cells, rejection of tissue allograft and that extraocular sources of stem cells not being as good as limbal stem cells.

Future research is into using iPSCs and MSCs derived from the bone marrow of the patient to treat corneal limbal stem cell deficiency especially where it is difficult or impossible to get tissue from the patient being treated and living relations are not available or willing to donate limbal tissue. This would be by cultivating the limbal stem cells from the patient's iPSCs and MSCs in the laboratory and transplanting them to the diseased eye.

# ASPIRATIONS TO BUILD COMPETENCY IN STEM CELL SCIENCE IN AFRICA

Some young experts are currently undertaking research work at established stem cell laboratories in Africa. They too shared the scope of their work as described below.

## Establishment of Assays and Systems for Culture and Manipulation of Haematopoietic Stems Cells and Mesenchymal Stem Cells

Researchers at the Kenya AIDS Vaccine Initiative Institute of Clinical Research, University of Nairobi are establishing a cord blood bank. They have been isolating mesenchymal stem cell (MSCs) and haematopoietic stem cell from cord blood. A sample of blood is taken from a new-born baby's umbilical cord and adipose tissues. This is cultured and maintained for use as disease model.

The team, led by Dr Marianne Mureithi, obtained cord blood from 34 pregnant women and isolated CD34, which they cultured for two weeks and characterised to have haematopoietic cells. The team plans to conduct long term cultures whose results they hope to use to lobby the public to establish a cord blood bank if successful.

The team also obtained adipose tissues from surgeons at the university hospital which they broke down using collagenase and centrifugal force to extract and isolate cells. The surgeons have been using adipose tissues to treat wounds but without a proper analysis to see if they really contained stem cells. Dr Mureithi's study shows the extracted cells from the adipose tissue contain 54 percent of mesenchymal stem cells confirming their existence for surgeons who are using them to treat wounds.

## Stem Cells Treating Myocardial Infarction; an experimental study

Dr Hiba BadrEldin Khalil Ahmed, Al Neelain University in Sudan is concentrating her stem cell research on the bone marrow. Myocardial Infarction (MI) also known as a heart attack is one of the leading causes of death worldwide. Stem cells offer hope in treating MI and it has shown positive outcome in mice models. Wister albino Rats are easy models to use in studying MI and low cost too.

Homing is the phenomenon whereby cells migrate to the organ of their origin. By homing, transplanted mesenchymal stem cells are able to travel to and engraft or establish residence in the bone marrow. Various chemokines and receptors are involved in the homing of MSCs. Stem cells also home to other organs (especially in response to stress signals). This technology has been used to deliver stem cells in treatment of MI and has offered hope, especially use of autologous BM cells- the major source of stem cells.

The study is assessing the clinical outcome of using the above mentioned technique in MI rats, the homing efficacy and compare

the outcome of using intracoronary and intravenous injection. The markers of interest are Troponin 1, SDF-1, MCP-3, GRO-1 and VEGF.

Dr Ahmed assured participants that the human bone marrow donors are volunteers and follow proper consent protocol. The procedure is not invasive and only takes a very small amount from healthy donors. So far there have been no rejection cases.

## Stem Cells in Regenerative Medicine and Cancer

Dr Kevin Dzobo, from ICGEB Cape Town / University of Cape Town, informed participants that much research has been done in the field of stem cells to find solutions to the problem of organ shortage. Regenerative Medicine and Tissue Engineering are fields of research that have existed for over 60 years. However, challenges such as (a) the inability to expand cells *in vitro*; (b) inadequate biomaterials and (c) inadequate vascularity has resulted in few clinical advances.

For regenerative medicine to be successful, solutions can be found by studying the biology of the growth factors, cell differentiation, molecular mechanisms and cell-matrix interactions. Importantly, scaffolds or biomimetic ECMs should replicate the biochemical and structural properties of the tissue being replaced or repaired.

In two of their studies published in *Stem Cell Review and Reports* and *International Journal of Molecular Sciences*, Dr Dzobo and colleagues illustrates the importance of the cellular microenvironment in directing both embryonic and adipose-derived stem cell fate and that the nature and composition of the extracellular matrix is a crucial determining factor. With cartilage defects being one of the main problems experienced by many people, chondrogenically differentiated adipose-derived mesenchymal stem cells represent a viable therapeutic option for the treatment of such defects.

In addition to trying to expand both embryonic and mesenchymal stem cells on 3D polymeric scaffolds, Dr Dzobo and colleagues are also studying mesenchymal stem cells role in both esophageal and breast cancer cell growth. Mesenchymal stromal/stem cells (MSCs) especially represent an area being intensively researched for tissue engineering and regenerative medicine applications. MSCs may provide the opportunity to treat diseases and injuries that currently have limited therapeutic options, as well as enhance present strategies for tissue repair.

Their results published in *Stem Cells International* shows the influence of tumour microenvironment on cancer cell behavior and provides alternative therapeutic targets for potential regulation of tumour cells. These MSCs from WJ offer only short term effects on cancer cells and further studies are needed before WJ-derived MSCs can be used as a therapeutic option for several cancers. In

another review article, published in *Omics Journal of Integrative Biology* (in press) the team also discuss the role of cancer stem cells in cancer initiation, progression and metastasis.

### Stem Cell Impairment in Chronic Inflammatory Conditions and its Implications for Autologous Cell Therapy

At Stellenbosch University in South Africa, Dr Mari van de Vyver is carrying out studies to (a) better our understanding of why stem cells become impaired in diabetes and (b) how this impairment can be corrected so that these stem cells can be used for the treatment of non-healing wounds. Non-healing wounds is a major complication of Type 2 diabetes mellitus. The impaired wound healing results due to abnormal keratinocyte/fibroblast migration, impaired proliferation, cellular apoptosis, M1 macrophage polarization, endothelial dysfunction and nerve damage. Dr. van de Vyver predicted that in the next 15 years, Africa might have 14 million people with wounds that are slow to heal as the number of diabetes patients rises.

She is exploring the use of alternative therapies for treating non healing wounds. Her team has so far isolated mesenchymal stem cells (MSCs) from the bone marrow of obese pre-diabetic and healthy mice. The study indicated that bone marrow stem cells from the healthy mice had a faster population doubling time (7 days) than the cells from pre-diabetic mice (18 days). The study also showed that stem cells from pre-diabetic mice have an altered gene expression profile and are unable to migrate. The work led to the team concluding that there needs to be an understanding of the cellular changes that affect the multi-functional properties of MSCs to provide an effective regenerative strategy.

### Therapeutic Efficacy and Safety of Oogonial Stem Cells (OSCs) Injection into Baboon Ovary

Infertility is a big concern for affected families according to Dr. Atunga Nyachieo from the Institute of Primate Research in Kenya. For both men and women experiencing infertility, most treatment options rely on the premise that both partners produce functional gametes. For those couples where one or both partners are unable to produce functional gametes, no treatment options are currently available other than the use of donor gametes. Donation of gametes coincides with the loss of a genetic link with the child, which many couples do not accept.

An alternative to produce functional gametes is to use germline progenitors which are present in the gonads, the ovarian stem cells in the females. It has been demonstrated that oogonial stem cells (OSCs) are able to develop into oocyte *in vitro* and *in vivo in mice* leading to offsprings but successful validated procedures for *in vitro* and *in vivo* OSC cultures leading pregnancy has not been demonstrated in humans and other primates. Dr Nyachieo seeks to determine a model for stem cells derived fertility treatment. He is carrying out experimental studies on baboons with infertility by injecting them with Oogonial Stem Cells (OSC).

OSC are undifferentiated cells that have the capacity to develop as germ cells. Dr Nyachieo and his team are looking at creating stem cell derived gametes. Their study aims to isolate OSCs from baboon ovary, culture them in the laboratory and inject them in the ovary. Successful injection of OSC leading to production of viable oocytes that can be fertilized and lead to pregnancy will be a proof of concept for OSC and will pave way for application to human. This will contribute to addressing infertility especially in cases of loss of functional gametes.

### Current Research Work: Developing and Maintaining Neural Stem Cells in Nigeria

Prof. James Olopade from the University of Ibadan, Nigeria proposes to use unique African rodents such as the African giant rat and the greater cane rat to study neural stem cells using comparative cryostructural and comparative genomics studies. These unique rodents have been shown to have unique neurobehavioral patterns differing from the normal Balb/C mice.

His aim is the development, maintenance and characterization of neural stem cells from unique African rodents starting with the African Giant Rat and the Greater Cane Rat. This will enable him to contribute to drug testing of neurotherapeutic agents using indigenous sources, and also through characterization define the presence of any unique genomic sequence in the neurocellular populations. He was advised to consider also the naked mole rat in his research.

Poor power infrastructure and lack of gene sequencing facilities are a few of the constraints. Prof. Olopade and his team are looking at novel ways to overcome the challenge of unstable power supply in Nigeria so that they can set up a centre of Excellence in Africa for neural stem cells research. He sought to establish collaborations with physicians in Nigeria and Centres of Excellence for Neural Stem Cell research overseas.



# BUILDING CAPACITY FOR STEM CELL SCIENCE IN YOUNG AFRICAN RESEARCHERS

## Skills learned from CBRM research visits and previous workshops

As part of the efforts to build stem cell sciences in Africa, the AAS and partners provided an opportunity for young African scientists to be mentored by experts in the field in 2015. The AAS organised short-term research visits under the CBRM programme for seven early career African scholars/mentees to receive training in laboratories of experts in India, Brazil and South Africa. Six of these mentees as well as some of the young scientists from previous CBRM workshops shared their experiences.

## Use of Skin Stem Cells in the Treatment of Wounds

Dr Farisai Chidzondo from the University of Zimbabwe outlined the achievements of her project as an AAS mentee in the CBRM programme. She highlighted the challenges encountered by people in Zimbabwe such as lack of adequate power supply which leads to the use of open fires, often resulting in burns and chronic wounds. This has prompted the need for wound healing regimens such as skin stem cells.

Culturing of these cells can aid in understanding the process of how wounds heal by observing how cells migrate. She proposes to use lectins which have been shown to have the ability of binding to sugar moieties on cells and stopping inflammation.

She also highlighted the various laboratory techniques she acquired during her research visit in Pune, India, such as handling cell culture, viability testing of cells, extraction of total RNA, synthesis of cDNA, protein transfer and western blotting. She was also invited by Prof. Kidson to the University of Cape Town where she learnt culturing of human adult skin keratinocytes and mouse embryonic fibroblasts and effects of different concentrations of serum on the growth of cells. Armed with these skills, she managed to get a grant of US\$4 000 from her home institution, the University of Zimbabwe, to support her cell culture work on keratinocytes.

## My Journey as a “Mentee in Cell Biology and Regenerative Medicine” under The African Academy of Sciences Mentorship Program

Ms Dorcas Wachira from the Kenya Medical Research Institute (KEMRI) shared her mentorship journey, which started in November 2013 during the first CBRM workshop. The second workshop on Training and Mentorship in Stem Cell Research and Regenerative Medicine was held in Aug 2014 with hands on practical session at KAVI-ICR. She went for a research visit at the Institute for Cellular and Molecular Medicine at the University of Pretoria, South Africa, 18th May to 12th June 2015, hosted by the Institute's Director, Professor Michael Pepper.

During the visit she learnt the following techniques; isolation of adult stem cells from adipose tissue, phenotypic characterization of mesenchymal stem cells, stem cell culture and passaging of cells, freeze/thawing of stem cells and viability testing, Isolation of RNA from stem cells, assessment of RNA integrity and quality, cDNA synthesis and qPCR.

Her current research activities include Functional Consequences of Singular and Concurrent Application of IL-21 and Rapamycin on Tumor Antigen Specific T Cells *in vitro* in Adoptive T cell Therapy. So far, she has managed to acquire cell lines (T2 cell lines) from ATCC and have successfully carried out cell culture. The adoptive T cell therapy will be done in-vitro and in-vivo in NOD-SCID mice. The aim is to determine the impact of singular and concurrent application of Rapamycin and IL-21 on tumor AFP and differential analysis of transcriptomes during singular and concurrent application of IL-21 and rapamycin.

In addition, Ms Wachira is mentoring other scientists including one of the participants at this workshop and two MSc students. Her goals are to establish a stem cell research unit; capacity building and to form collaborations.

## Study of Tumor Stem-Like Cells from Glioblastoma and Medulloblastoma: Contributions to Diagnostic and Therapy

Lucy Macharia from the Universidade Federal do Rio de Janeiro is working on the *Study of Tumor Stem-like cells from Glioblastoma and Medulloblastoma* as contributions to diagnostics and therapy.

Glioblastoma is one of the most aggressive human primary brain tumors with an average survival of about fifteen months while medulloblastoma is the common primary brain tumor in children. Despite recent advances in cancer biology, the current diagnostic tools are highly invasive treatment outcomes have not changed significantly over the past decade (Siebzehnruhl et al. 2011). Necrosis and microvascular hyperplasia are hallmarks of GBM reflective of a hypoxia situation. HIF-1 is regulated by the cancer microenvironment which in turn contributes to deregulation of a group of MicroRNAs that regulate genes associated with drug resistance, stemness state, angiogenesis and invasion. Stem-like cells have been shown to contain self-renew properties and are highly proliferative and represent a minor population in the tumor mass.

This study therefore aims to find microRNA biomarkers that can complement diagnosis and prognosis in glioblastoma and medulloblastoma and to investigate the role played by hypoxia and their stem-like cells. microRNA are stable and can be used to reverse the cancer stem cell like properties through up-regulation and down-regulation of genes (modulation). Glioblastoma cell



lines GBM 02, GBM03, GBM11, GBM95, U87 and T98G and Medulloblastoma cell lines D425, D283, D458 and DAOY will be used in this study. Primary culture and culture of the cell lines will be performed. Stem cell characterization will be done using oncosphere culture and clonogenicity assays while western blotting and immunocytochemistry will be performed to determine the expression levels of target proteins and markers. RT-qPCR will be used to evaluate the expression of MicroRNAs in GBM and MB and a comparison will be made between hypoxia and normoxia and between normal cell lines and their respective stem-like cells. *In vivo* experiments will be performed in mice.

## Stem Cell Technology: Current Status and Future Trends in Tanzania

Dr Dennis Russa from the Muhimbili University of Health and Allied Sciences in Tanzania shared the current status and future trends of stem cell techniques in Tanzania. He has carried out various cell manipulation techniques such as cell culture, antibody and fluorophore staining, immunocytochemistry and fluorescent imaging.

From studies he has conducted, some of the novel findings included the inhibition of  $\text{Ca}^{2+}$  metabolism during mitosis,  $\text{Ca}^{2+}$  mediated anti-cancer mechanism and the elucidation of  $\text{Ca}^{2+}$  spark/burp signals in different cells whose significance is yet to be established. Dr Russa is currently sensitizing and raising the awareness of therapeutic potential of stem cells, liaising with the Tanzania commission for Science and Technology (COSTECH) to take up the leadership role in stem cells work in the country, advocating the stem cell concept through publications and recruiting young scientists to pursue a career in stem cells research and therapy. Challenges being faced are many but the lack of tissue culture facilities, inadequate expertise (technicians and post-docs) and lack funding and the major setbacks

## Multi-Drug Resistance in Glioblastoma: The involvement of ABC Transporters in Glioblastoma Stem-like Cells

Ms Caroline Muriithi from the Universidade Federal do Rio de Janeiro, Brazil, presented the work she will do as part of her PhD study which focuses on multi-drug resistance in glioblastoma. Glioblastoma stem-like cells are able to initiate tumours in individuals and they are resistant to conventional cancer therapies. These GSCs have a characteristic phenotype such as capacity to resist oxidative stress, elevated capacity for DNA damage repair, quiescence and high expression of drug efflux channels that make them resistant to treatment.

Her work will concentrate on the drug efflux channels from the ABC transporter family due to the conflicting studies on the role of these proteins in Glioblastoma. The ABC membrane transporters are efflux channels used to block drug induced cell cytotoxicity. These ATP-dependent transporters are highly expressed in GSCs. Their action ensures that drug levels in the GSCs remains at sub-

optimal levels, thereby rendering these drugs impotent.

The main ABC membrane transporters involved in multi-drug resistance in Glioblastoma are P-glycoprotein, MRPs, BCR-P. There is need to study the expression of these transporters on different GMB cells lines. The implications of inhibiting these transporters on chemo resistance to tumor drugs like Doxorubicin, Temozolomide and the signalling pathways involved in increased expression of ABC proteins in GSCs need to be investigated. She was advised to consider using primary cell lines from a Glioblastoma tumors.

## Current Work and Future Plans Relating to Stem Cells and Regenerative Medicine

Ms Clare N. Kimani from the Institute of Primate Research in Kenya examined the effects of neuroinflammation on neurogenesis and olfaction. Neurogenesis is regulated by a very complex microenvironment comprising the vascular network, different growth and neurotropic factors, changes in the electrical and chemical environment and support by glial cells.

The role of neuroinflammation in regulating neurogenesis and neuroprotection is not clear. However, some of the mediators of the inflammatory response have been shown to have a role in the regulation of neurogenesis and neuroprotection. Studies need to be conducted to increase the potential therapeutic value of regulating neuroinflammation in cellular regeneration in the diseased brain.

Consequently, understanding the mechanisms underlying the effect of neuroinflammation in proliferation, fate determination, migration and differentiation of neural stem cells will be useful in developing specific approaches to target the damaging effect of inflammation in neurogenesis. The study will investigate the effects on molecular promoters of neurogenesis, VEGF and BDNF in a mouse model of neuroinflammation.

## Comparative Analysis of Wound Healing and Regenerative Ability in Different Mammals

Dr John Muturi Kimani from the University of Nairobi presented a comparative analysis of wound healing and regenerative ability in different mammals. According to Dr Muturi some of the model organisms for regeneration include arthropods (insects, crustaceans and arachnids) and echinoderms.

There is generally poor regenerative ability in mammals, examples of regeneration in mammals include; epithelial renewal e.g skin and intestine, red blood cell replacement, deer antler regeneration in deers, hair cycling (external ears closure of rabbits and spiny mouse). Additionally, the mammalian foetal skin regenerates perfectly though repair of skin wounds in adults occurs by fibrosis resulting in a scar.

There are interspecific differences that exist in the content and organisation of the skin and similarly between species which affects the way skin wounds heal. The naked mole rat (*Heterocephalus glaber*) with scarce hair on its skin (almost hairless) has a long lifespan compared to other mammals.



Mr Oluwaseun Ahmed Mustapha

The naked mole rat provides an opportunity to examine how skin structure, immunity and lifespan affects healing. Despite lacking adnexa that interrupts dermal replacement in other rodents the naked mole rat takes longer to heal.

### The stem cell potential of the adult hippocampus

Mr Mosab A Mohammed from the Al Neelain University in Sudan explains that Neurogenesis in the brain of adult mammals occurs throughout life, and has been clearly demonstrated at two locations under normal conditions: the subventricular zone (SVZ) of the lateral ventricles and the subgranular zone (SGZ) of the dentate gyrus in the hippocampus. In the adult brain, the hippocampus is a crucial structure for the formation of certain types of memory, such as episodic memory and spatial memory.

In this project, Mr Mosab and his team are investigating the stem cell potential of the adult Hippocampus by identifying the role of adult-born neurons, behavioral test to evaluate memory function and loss in hippocampus. The team used the cyclin D2 Knockout (cD2KO) model to check the relevance of newborn neurons to hippocampus-dependent memory processes. Using the Morris water maze paradigm they showed that the lack of adult neurogenesis strongly impairs spatial learning and memory.

They also analyzed the expression of cyclin D2 and cyclin D1 in the different subsets of SGZ progenitors and found that the cD2 population is highly proliferative and the cD1 population is mostly quiescent; Furthermore cD2 exclusively expressed in neural stem cells (type 1; NSC) and, together with cD1, also in the subsequent intermediate progenitor stages, this means that cD2 is indispensable for the division of NSCs.



Ms Lucy Macharia

### Investigating the role of a FAM111B mutation in hereditary fibrosing poikiloderma using induced pluripotent stem (ips) cell models

Ms Dimakatso Gumedde from the University of Cape Town, South Africa, presented her project based on finding out how FAM111B mutation causes Poikilodermas which is affecting a South African family. This is a disease where sufferers don't have sweat glands and their Achilles tendon hardens causing them to walk on toes.

Her study is assessing how the FAM111B functions using stem cell disease models. The function of FAM111B is unknown. The team also sought to determine the expression of FAM111B as well as markers that are activated and up-regulated during fibrogenesis. All of the iPSC clones expressed pluripotency markers (i.e. OCT4, TRA-1-60 & NANOG) and germline (endoderm, mesoderm & ectoderm) markers following *in vitro* differentiation indicating their ESC-like phenotype. Gene expression of fibrosis markers (transforming growth factor-  $\beta$ 1,  $\alpha$ -SMA, COL1A1, COL3A1, TGF- $\beta$ R1, type 1 collagen and tissue inhibitors of metalloproteinases), which are upregulated during fibrogenesis, no chromosomal abnormalities were detected in any of the clones. Preliminary qRT-PCR findings showed a difference in FAM111B expression between patient and control dermal fibroblasts.

## OTHER SCIENTIFIC RESEARCH IN AFRICA

Much fascinating scientific work was presented by other young scientists, including AAS Affiliates, who are involved in different areas of research in Africa. The next phase of CBRM will continue to offer mentorship opportunities. It is expected that these young professionals will join the growing pool of mentees in the CBRM programme.

### Origins and reservoirs of zoonotic viruses: coronaviruses as a paradigm for the transmission interface between wildlife, livestock and humans

Dr Augustina Angelina Sylverken from the Kumasi Centre for Collaborative Research in Tropical Medicine in Ghana shared her study on origins and reservoirs of zoonotic viruses. Her theme, 'One health concept', works through integrative effort of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals and the environment.

The study showed bats are the major source and host of coronaviruses (CoV), such as Severe Acute Respiratory Syndrome (SARS)-CoV and the Middle East Respiratory Syndrome (MERS) CoV. They have found some signs of these viruses as well as related ones in bats confirming this theory and are now raising awareness among communities in Ghana about how animal and health interactions can promote the transmission of these viruses.

The team carries out sensitization in local communities and collaborates with them to obtain samples for study. The challenges that Dr Sylverken and her team face include insecurity of farmers, language barriers and unwillingness of farmers to disclose their livestock size.

She highlighted some of the benefits of the work as One health concept' enabling them to explore transmission interfaces; the research is interdisciplinary as it includes Ecology, Microbiology, Veterinary, Social Sciences; technology transfer as serological and molecular-based assays are applicable in human and veterinary diagnosis and there is capacity building as the team is composed of Post Docs, PhDs, MScs and interns among others.

### Exploring the African pharmacopoeia as source of new therapies: screening efforts at the Biotechnology Unit, University of Buea (Cameroon)

This study explores new therapies for handling Malaria. Dr Denis Zofou from the University of Buea in Cameroon gave an overview of natural products as a source for malaria treatment. An estimated 80% of populations in Africa, Asia and Latin America relies on Traditional Medicine. 61% of the 877 small molecules introduced to the drug market worldwide during 1981-2002 was inspired by natural products (NP: 6%, NP derivatives: 32% and NP mimics: 23%). Quinine and Artemisinin are typical examples.

In Cameroon, herbal medicine plays a major role in daily health care including malaria treatment and prevention. There are 500

medicinal plant species used by traditional medicine practitioners and regulated by the Office of Traditional Medicine (Public Health Ministry) and local administrative authorities.

Dr Zofou is involved in a project to create a register of traditional medicine that will be partly used for treating malaria, to prepare medical plant data for the different types of malaria by developing their pharmacopoeia in Cameroon. His group has screened over 200 plant species and have isolated about 70 components from four plant species (including edible plants) and tested, 15 with promising activity ( $IC_{50} < 5\mu\text{g/mL}$ , less or no toxicity on mammalian cell-lines), especially from edible plants. Many of the claims of traditional medicine practitioners can be verified by using simple bio-assays, and the success rate is by far higher than if random systematic screening of plants is carried out.

Dr Zofou had been inspired by the presentations by resource persons at the workshop particularly that of Dr Tchokonte-Nana on stem-cell and regenerative medicine to design animal model for diabetes and Prof. Motaung on using medicinal plants to stimulate cell regeneration.

### Population genetics and immunology of *Plasmodium falciparum* in natural populations of Southwestern Cameroon

In spite of the successful implementation of improved and sustained nationwide malaria control strategies, the disease still remains a significant problem in Cameroon. Dr Tobias Obejumo Apinjoh from the University of Buea, is studying the parasite diversity and polymorphisms that result to drug resistance in *Plasmodium falciparum*, the parasite that carries malaria.

Dr Apinjoh's study is being carried out in Southwestern Cameroon where the disease still remains prevalent attributing to 44 percent of hospitalisations and 18 percent of deaths despite the successful implementation of improved and sustained nationwide malaria control strategies.

His study has focused on five species of malaria transmitting mosquitoes and understanding how parasite diversity contributes to the failure of anti-malaria parasite control measures. They are also assessing how parasites evade natural immune responses which may jeopardize the effectiveness of vaccines. Part of their work includes policy advocacy to ensure that policymakers are aware of growing antimalarial drug resistance and to join in efforts to combat it.

Malaria still remains a significant problem in southwestern Cameroon with up to 20% asymptomatic *P. falciparum* infections. *MSP1/2* and *GLURP* *P. falciparum* genetic diversity is high, reflecting high transmission intensity in the area. There are high mutation rates in *pfdfhr* and *pfdfhs* mutations indicative of accumulating resistance to SP in the area. More SNP data, increased sample size and continuous monitoring will provide definitive picture

## The development, production and characterization of adult neural stem cells from the greater Cane Rat

Mr Mustapha Oluwaseun Ahmed from the Nigeria's Federal University of Agriculture presented his study on the development, production and characterisation of Adult Neural Stem Cells from the greater Cane Rat (*Thryonomys swinderianus Temmick*). This study was conducted on the background of increasing neurological disorders in Nigeria due to industrialisation and unregulated population growth.

Reports have shown that Nigeria has the 2nd gas flares in the world. Gas flaring has been associated with myelination defects and demyelination. Neuro-degenerative and demyelination can be remedied by use of adult neural stem cells. Nigeria has a rich plant biodiversity which could be used for herbal treatment. However, Nigeria generally is limited in cell-culture system facilities that can be used in drug testing to establish efficacy of a given compound.

To overcome the limitation of cell culture, animal models are used in drug testing. The indigenous greater cane rat and African Giant rat have been shown to have a well developed sense of smell and have been used in sniffing compounds without showing any sign of neural disorders. This study was designed to establish whether the two rats have a neural stem cells niches that alleviates neural disease.

## Pharmacological study of a pro-angiogenic snake venom protein

Dr Zohra Aloui from Institut Pasteur de Tunis focused on the pharmacological study of a pro-angiogenic snake venom protein. She discovered a protein that can stimulate angiogenesis and restore cardiac function but needs to be protected in drug delivery because it is not stable in human serum.

*Macrovipera lebetina transmediterranea* also known as the blunt nose or leperine viper is a venomous viper subspecies endemic to North Africa. This snake is known to produce a venom with ability to enhance capillary permeability. Aloui has been able to purify the protein responsible of this activity (ICPP), establish its primary sequence, classified and show that it has 52% identity to human Vascular Endothelial Growth Factor "VEGF". The protein (ICPP) is also shown to stimulate differentiation of embryonic stem cells into a vascular network and improve respiratory function in heart after acute ischemia/reperfusion. For this reason, the protein (ICPP) has been proposed to be used to develop remedies.

Her current objective is to establish the bioactivity of the nano-sized carrier-conjugated protein (ICPP) in mice and cell culture. Her work involves use of the following methods; endothelial cell proliferation, wound healing assay and matrigel assay. Investigating novel molecules that modulate vessel growth is essential to the development of new drugs in angiogenesis as well as on regenerated damaged tissue.

## Inflammatory markers as emerging risk factors of cardiovascular diseases in HIV

Bernadette Jani from the University of Zimbabwe studies inflammatory markers as emerging risk factors of cardiovascular diseases in HIV, which found that interrupting antiretroviral therapy can lead to higher mortality and cardiovascular diseases events. Cardiovascular diseases is an inflammatory process that take decades to develop. In HIV-seronegative persons, high-sensitivity C-reactive protein is a biologic marker of CHD risk.

HIV infection induces chronic inflammation, despite adequate suppression of HIV replication with antiretroviral therapy, resulting in elevations of several biological markers associated with cardiovascular diseases risk in HIV-seronegative persons. Jani measured CD4, platelets activation and biomarkers of inflammation IL-6 and IL-4 in HIV-uninfected persons, HIV-infected and not taking antiretroviral drugs, and HIV-infected under antiretroviral therapy. Her study demonstrated that interruption in antiretroviral therapy is associated with higher mortality and cardiovascular diseases events postulated to be related to inflammatory mediators such as interleukin-6.

Her work also demonstrated high platelet activation and induced lipid abnormality in person under antiretroviral therapy despite its involvement in increasing life expectancy. Specific antiretroviral agents have been associated with higher rates of myocardial infarctions and elevations in markers of inflammation such as interleukin-6 in persons with cardiovascular diseases events. Her work helps the understanding of biomarkers of inflammation associated with the development of cardiovascular diseases in the setting of HIV infection and the use of antiretroviral therapy.

Despite the fact that HAART increases longevity, and reduces the number of AIDS related deaths, there is a considerable increase in the number of non AIDS related deaths, due to CVDs. This may be attributed to the persistent inflammation caused by HIV itself, traditional risk factors or may be exacerbated by the therapy itself. Thus the best way to move forward maybe checking the levels of biomarkers of inflammation then administer HAART in combination with anti inflammatory drugs such as statins ,to better management of the diseases. HAART reduces viral load and boosts CD4 count , but inflammation remains persistent as evidenced by the surrogate biomarkers of inflammation.

## Applications of induced pluripotent stem cells: A statement of professional development in stem cell science

Dr Nkiruka Azubike from the University of Nigeria's presentation was on applications of induced pluripotent stem cells: a statement of professional development in stem cell science noted how stem cells have revolutionised practice of medicine. However, the field of stem cells and regenerative medicine in general was deficient or completely non-existent in Nigeria due to lack of funding and skilled personnel. Azubike's current research is on use of medicinal to remedy cardiotoxicity in albino rats.



The study involves screening plants that have therapeutic effect against myocardial infarction, the death of heart muscle secondary to prolonged lack of oxygen supply. Due to the limitation occasioned by use of animal models in establishing the mechanical of action of plants extracts, Azubike would like to explore the traditional remedies using invitro Somatic and stem cells cultures.

### Stem cell research: Pathway to sickle cell therapy?

Dr Idowu Aimola from Nigeria's Ahmadu Bello University presented on the pathway to sickle cell therapy where he explained how adult hemopoietic progenitor stem cells can be used as experimental models for the screening of potential foetal hemoglobin inducers as an alternative treatment to sickle cell anaemia, which has been traditionally treated with Hydroxyurea, which causes side effects and doesn't work in 50% of people. There is increased prevalence of sickle cell anemia in developing countries with much burden being seen in Sub-Saharan Africa.

Adult haemapotetic stem cells can be isolated from peripheral blood using glycerol density gradient. There is also a possibility of getting haemapotetic stem cells in extramedullary organs like spleen.

### Regenerative medicine and severe acute malnutrition

Ms Christine Ichugu from Kenya Medical Research Institute (KEMRI) is carrying out research on the impact of inflammation on mesenchymal stem cells and T memory stem cells in severe acute malnutrition. Severe acute malnutrition is of major public health concern particularly because of its association with infections. It is among the most prevalent causes of immunodeficiency affecting as much as half of the population in disadvantaged communities.

Severely malnourished children experience higher mortality risk due to infections, therefore, early immune reconstitution to prevent infections and re-infections could decrease mortality in these children. The study further adopts T cell memory stem cells in correcting T cell immunodeficiency which is observed in protein energy malnutrition. Cell-based therapies are being adopted in treating inflammatory diseases because they are multifocal, have an ability to reduce inflammation and stimulate repair.

## HANDS-ON SESSIONS AT LABORATORIES

Participants visited the laboratories of some of the resource persons in Cape Town to see and learn practically some of the techniques applied in stem cell research. These were the laboratories of Prof. Susan Kidson at the University of Cape Town Division of Cell Biology, Prof. Iqbal Parker at the International Centre for Genetic Engineering and Biotechnology (ICGEB) and Dr Venant Tcholonte-Nana at the Stellenbosch University ISLET Research Laboratory.

At the University of Cape Town, the mentees learnt cell counting where cultured cells were counted manually using a hemocytometer. The lab uses trypsinized cells diluted in normal media. They also learned how to test cells for contamination by mycoplasma which can be missed by microscopy. The importance of aseptic techniques was emphasized. The test for mycoplasma contamination uses hook stain, an immunofluorescent stain that is cheaper than DAPI stain, then imaged on a confocal microscope. The mentees also attended a seminar on "Remodelling or repurposing of drugs already in use for cancer" conducted by two PhD students at the lab.

The mentees who visited ICGEB were received by Dr Ariella Rowe who oriented them to the four laboratories at the centre. Lab 1 is the bench work lab. Lab 2 is for infectious agents and immunology. The equipment included biohazard level 2, DNA extraction equipment and Gel documentation system. Lab 3 is for flow cytometry, where flow cytometry techniques were demonstrated including cell sorting and retrieval. Lab 4 is for cell and tissue culture where the procedures learnt included media preparation, general procedures for cell culture, co-culturing of two cell lines, cell counting using an automated counter and viability testing.

The Head of Division of Anatomy and Histology, Prof. Benedict Page and the Dean of Research, Dr Van Pittus welcomed the mentees at the Islet Research Laboratory, Department of Biomedical Sciences, Stellenbosch University. They were given a tour of the facilities including the departmental museum, theatres, animal facility and laboratories. Mentees were shown how islet cells were harvested from the pancreas of a rat and preparation of a primary culture was demonstrated. They were also taken through protocols for immunocytochemistry identifying pancreatic islet stem cells. The Islet research group focuses on Islet cells with the aim of finding a new source of donor islet cells for islet replacement therapy.



# ETHICAL CONSIDERATIONS FOR USING STEM CELLS IN AFRICA

Prof. Jacquie Greenberg educated participants on ethical issues in stem cell research. Regenerative medicine involves the use of stem cells and DNA, and by extension a human being. Dr Greenberg emphasised that it is because of this that researchers have a huge responsibility towards ethical considerations. The need to respect patients as sources of information for research was highlighted.

With each new technology come new challenges. Stem cell science is advancing at an unprecedented rate with thousands of research papers being published every year and many clinical trials for a wide range of conditions underway as registered in ClinicalTrials.gov. The field has brought with it more complex and multifaceted ethical issues and there is need to change legislation to match this growth with considerations on how to get permission from individuals who donate their biological material for both scientific inquiry and essentially for their potential therapeutic ability, i.e., consent protocols.

Issues to be addressed when compiling informed consent forms for stem cell related research were presented including what the patient would need to know. At the Department of Genetics, University of Cape Town, genetic counsellors are trained who act as the interface between the patient and the clinician and the laboratory. The specialist areas include inherited neurodegenerative and retinal degenerative diseases, induced pluripotent stem cells as a “disease in a dish” model, gene silencing and gene-based therapies, translational genetics and genetic counselling.

Guidelines for informed consent for prospective studies on stem cells should take a tiered approach to consent that allows participants to tailor their consent. Participants could opt to have their cells used in research for their genetic conditions only and not for future research (opt-out). This would require additional oversight and monitoring to make sure that the use of cell lines

is adhered to. However, there could also be the option for there-consenting of patients, if their cells are used for another purpose (opt-in).

There is a need to be explicit when conveying information to participants especially regarding the controversial issues of the study e.g. that the germ line derivatives and reproductive applications will not be attempted or developed, or reproductive cloning of humans. They should also be aware that the cells are immortalised so they are going to be used for a long time and if the patient feels like they want to withdraw, they may but without any effect on their disease management There is need to explain to the patient what you are going to do in a language that is comprehensible. Patient confidentiality must be guaranteed.

The guidelines on Ethics in Health Research from the Ministry of Health in South Africa recognize five key ingredients; Patient autonomy, Respect for basic rights, Confidentiality, Researcher accountability and Researcher balance. In addition, the *South African Oversight Committee* requires that researchers give reports on what they are working on, what they have published and discoveries made. Researchers also have to apply for permits to import or export DNA.

Stem cell science has real prospects for treatment and the ultimate goal is to develop the research results into therapy. However, it is imperative that false promises are not generated from the information that is passed to the public i.e., there is a need to balance hype and hope. In instances where scientists work with journalists or reporters, the scientists must insist that they will not engage with a journalist or reporter unless the scientist is allowed to review the article before it is published. Ethical issues must be taken seriously by scientists, medical practitioners, legislators, journalists and lay people.

QUESTIONS		ANSWERS
1.	Since the area of stem cell research is relatively new particularly to Africa, do review teams understand stem cell research?	The obligation is on the researcher to educate the ethics team. The team should be diverse but still have experts on the subject. There is need to build capacity.
2.	What would it cost to generate IPCs?	For 1 year for one student to generate stem cells would cost about 100,000 Rand. Collegiality is important. Keep eyes open for funding opportunities.
3.	The area of stem cell research is neglected with respect to funding opportunities, what can be done?	You need to start with what you have and make the most of it. Patient support groups are known to fund certain research areas. An example is the group ‘Genetic Alliance’.
4.	Why is there a lot of ethical misconduct with stem cell research in some parts of the world?	There is a need to address these issues as they come up and re-evaluate ourselves at the individual level.
5.	Is there a legal framework for regulation of stem cell research in South Africa?	There is a Tissue Act, in Chapter Eight of the Health Act. There process of developing legislation is ongoing.
6.	What advice can be given regarding ethical committees and their contribution as most current committees comprise mostly clinicians who might not have the same goals as researchers?	Ethical committees should comprise medical, scientific, laymen and cultural representatives. They should have at least 3 experts i.e. a clinician, scientist/researcher and an ethics person.



*Prof. James Olopade and Dr Oluwaseun Mustapha*



## FUTURE OF THE CELL BIOLOGY AND REGENERATIVE MEDICINE PROGRAMME

Participants noted that some of the challenges limiting African scientists from effectively pursuing stem cell research include lack of tissue culture and gene sequencing facilities, lack of expertise (technicians and post-docs), unreliable power supply and inadequate funding. In addition, the field is new globally and there are not many mentors for young people wishing to pursue a career in the field, especially in Africa. They commended initiatives such as the Stem Cell Science and Applications workshop organised by the AAS and STIAS as useful since they provide a network to share expertise and infrastructure.

Participants gave their views on the Cell Biology and Regenerative Medicine programme and proposed the next steps in terms of structures and mentor-mentee aspects of the programme. Suggestions included: mentoring young scientists in grant writing; establish a joint communication forum to share issues and solutions related to stem cells and regenerative medicine; developing an African database and showcase to stakeholders and the general public what the current group in the CBRM programme is doing - this would be a source of awareness and information and have a database also where available funding schemes can be accessed and need capacity building in science communication to reach the public and policy makers.

### Creating awareness about stem cell science and its applications

Participants recognised that there needs to be concerted efforts to raise the profile of the field so that more young people are aware of the career opportunities it offers and that Africa as a whole come to know of the impact it can have on science. Participants should

showcase their work to stakeholders including policy makers and the general public to raise awareness of the impact of stem cell sciences. Ensuring that policymakers are aware of its impact would enable the scientists to lobby for resources.

#### Proposals included:

- to set up a platform that will raise awareness about the importance of cell biology in Africa
- to share funding and research opportunities as well as new publications in the field
- to increase collaboration among stem cell scientists in Africa
- to identify individual specializations so as not to duplicate effort but gain the most from the different capacities nationally and regionally
- to make use of facilities in the region and initiate exchange visits to various cell biology facilities
- to compare and enhance university syllabi on cell biology in Africa
- to stimulate further mentorship with experienced scholars world wide
- establish a joint communication forum to share information related to stem cells and regenerative medicine
- Dr Tchokonte-Nana is willing to provide support for the next stem cell workshop and AAS may contact him in this regard



## Expanding stem cell science into translational research

Scientists should not restrict themselves to stem cell and regenerative medicine. They should think of cell biology in general and then break it down into various compartments for study. They could take advantage of their diverse research backgrounds. The aim is to think of other applications of cell biology towards providing tangible solutions i.e. translational research. It was suggested that the theme for the next workshop be expanded based on this.

In addition, there should be collaboration between stem cell researchers and clinicians. The latter are the bridge between the public and scientists. Researchers should educate clinicians on what they are doing in the laboratory.

It was suggested that CBRM workshops be organised in various regions of the continent as a way to promote the programme as well as attract awareness, bring in more mentees, mentors as well as public support.

## Building capacity – Infrastructure

The young scientists together with the experts and resources persons are advised to aim at building capacity and sharing facilities and expertise. They may explore ways to encourage networking between national organisations and regional organisations and find commonalities which will work together. This would strengthen regional centres and ensure that they worked together instead of competing.

Laboratories may be synergized to work together to push the Stem Cell agenda and research forward. It is just as important to identify individual specializations among the laboratories nationally and regionally so as not to duplicate efforts but to complement on-going research work on stem cells. Facilities may be shared at national

and regional level and laboratories may provide access to scientists from other countries. This would also enable them gain from each other's different areas of expertise

It would help to have a critical mass of people involved in each region. This sharing of resources would strengthen inter Africa collaboration. The scientists may look towards gaining expertise within the continent utilizing the available facilities in different countries particularly for basic techniques. They would then go out of the continent to gain expertise and use facilities that cannot be found within Africa. This would also lead to more productive collaboration.

Participants were urged to make use of the capacity available in South Africa. Some stop gap measures could be used – scientist working, for example, in laboratories that had frequent power failure could spend some time in a country that did not suffer the problem like South Africa and carry out their work there. This is something that happens in practice and some students can even be sent abroad to do some of the work.

Long-term solutions such as obtaining support to generate power at the local level, using alternative sources of generating power cost effectively and including experts in other fields to help find solutions. Engineers could be approached and apprised on the importance of cell biology research and requested to come up with appropriate solutions.

## Building capacity – Training opportunities

Participants were informed about a PhD programme in Brazil that could take in students from Africa. It is specific to developing the relationship between Brazil and Africa and would be important for those at the workshop. One of the experts, Prof. Jose Garcia Abreu from the Federal University of Rio de Janeiro, had in June 2016 become coordinator of the graduate programme in Morphological Sciences.





The programme is autonomous and is not subject to the university rules. It is hosted in the university but grants go directly from the ministry of higher education to the programme – to Prof. Abreu directly.

It is the highest PhD programme in morphological sciences in Brazil. There are over 400 graduate students; more than 110 in PhD and Masters, 40 postdocs, 40 technicians and.; 6 technology facilities More information is available at [www.pcm.icb.ufrj.br](http://www.pcm.icb.ufrj.br). The website is currently in Portuguese but will be translated into English.

There is also TWAS Fellowship available specifically to Africa and Brazil. For this fellowship, potential students are required to find a supervisor and apply for the programme. Two CBRM mentees, Lucy Macharia and Caroline Muriithi, were awarded fellowships through it. There is also Doctorate Sandwich Programme whereby individuals could undertake PhD studies in their own countries and spend a year in Brazil or undertake their PhD study in Brazil and spend one year in their country.

Prof. Abreu invited all to join the graduate programme, emphasizing that they were 'looking for brains not for Brazilians' i.e. looking for people who want to make a difference through science. He offered to assist those who were interested in applying. It was agreed that this would be an excellent opportunity for the young professionals.

Mosab Ali Awad Mohammed invited participants to apply for a Scientific Writing Workshop that would be held at Al-Neelain University in collaboration with IBRO, in Khartoum, Sudan January 14-19, 2017. The workshop's objective is to help young African investigators acquire skills and develop strategic means to communicate with the broad neuroscience community and, in particular, to publish scientific articles in peer-reviewed journals. A call would be sent out to all participants.

## Building capacity – Personal motivation

Participants were encouraged that their enthusiasm for cell biology would enable them to achieve desired results in their research work. It was up to the scientists to make their voices heard back in their countries for example take it upon oneself to convince someone to buy a generator, and not wait on someone else. They may also involve the ministers, local administrators and vice chancellors, by approaching them and letting them know that their nationals have been trained in stem cells and applications and ask them to ensure that there are running facilities back home to work from. It was suggested that these officials also be invited to cell biology workshops.

It was also advised that participants take a step by step approach. Beginning the process was crucial. Establishing a stem cell laboratory is challenging. However, it is not impossible and the scientists could begin by introducing a stem cell laboratory in their institutions establishing own protocols in a special part of the laboratory. They may not have sophisticated instruments but this should not discourage them. They could also collaborate with private laboratories. The next step would be to make experimental researches. This will give them confidence to establish stem cell work in their countries. With this set up they could then seek more funding to enable them push the agenda forward. This approach and determination has enabled Dr Hiba BadrEldin Khalil Ahmed to carry out work on stem cells at Al Neelain University in Sudan.

Another example was given of Brazil which established laboratories from humble beginnings. Initially they built 20 to 30 laboratories out of ship containers with air conditioning and storage. It was meant to be temporary but has now become a huge facility and accommodates 20 professors. It is a shared laboratory. The young scientists were encouraged to start small like this. Facilities and equipment last long and are an investment.



## Role of AAS and STIAS

There was also a discussion on the role and goals of the Mentor-Mentee relationship. There is a need to increase capacity in terms of training. The mentorship should now be expanded to include a new pool of Mentors to enhance the quality of research and innovation that will be initiated by the young mentees. Another workshop should be organised to select another cohort of mentees and to bring in more mentors from other countries.

It is hoped that after five years there will be a pool of young people established in the field and some mentees will become mentors in their own right and mentors could become collaborators. This is the ultimate goal of this programme.

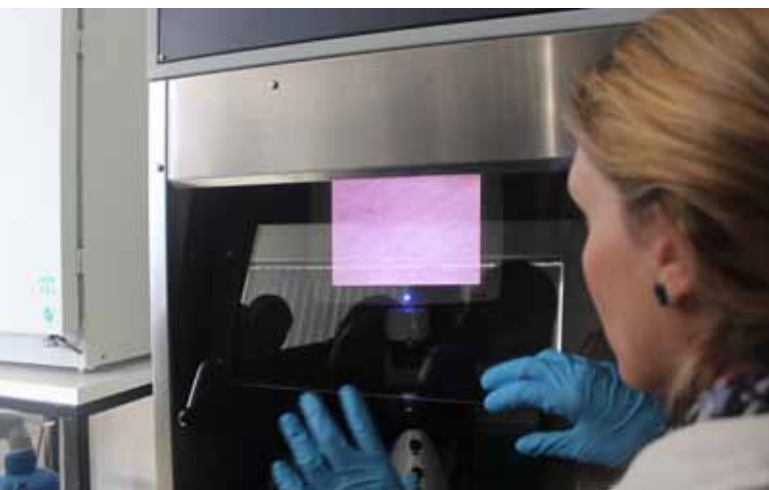
Participants learned that AAS and STIAS are not cell biology research institutions but are both interested in developing science. Both institutions realise that cell biology has great potential. Young scientists should realise that there is a window of opportunity- AAS STIAS, resource persons – who are prepared to respond to their needs and expectations. The ownership of that process however should pass to the young scientists. One way is to appoint a number of coordinators representing the five regions of the continent.

AAS, STIAS and the resource persons would not wait another year to organise an activity for them but have the young scientists propose what they wanted to undertake. They could for example take advantage of their robust communication channel and come up with a joint proposal for activities that they consider should be funded with a budget which AAS can present to a funder.

Participants were encouraged to build capacity both through the CBRM programme and other AAS programmes as one programme cannot provide all they needed.

## Establishing a Stem Cell Group

The young scientists, following the advice of the mentors, established a group on Stem Cell Research for Africa that will begin addressing African Capabilities in orienting Stem Cell and Regenerative research so as to combat African Health Issues.



The Chairperson of the group is Dr Marianne Mureithi from the KAVI-Institute of Clinical Research, University of Nairobi working with regional Coordinators: Dr Zohra Aliou from the Institut Pasteur de Tunis (Northern Africa); Mr Mosab Ali Awad Mohammed from Al Neelain University in Sudan (Eastern Africa); Dr Denis Zofou from the University of Buea in Cameroon (Central Africa); Dr. Nkiruka Azubike from the University of Nigeria (Western Africa) and Dr Farisai Chidzwondo from the University of Zimbabwe (Southern Africa,) All the young scientists in the group were encouraged to be active members.

It was agreed that the group should:

- Prepare a publication and proposal to request AAS and other funders to undertake the proposed research activities of the group
- Undertake joint research projects
- Consider joining a professional society - this will help in bringing people in the same field together.
- Work towards the application of their research in stem cells and not just basic science
- Identify and focus on Africa specific problems
- Part of the group to consider spending time at STIAS to work on the proposal away from their usual work.
- The group would work with AAS, STIAS and the resource persons towards having more mentees trained, producing more publications on stem cell science and working on joint projects
- Keep communicating as networking is very important for working together

The resource persons all indicated their support for the CBRM programme. The group was advised to make use of the contacts that they had made with resource persons at the workshop to expand their knowledge. They further asked the scientists to contact them whenever they required information or advice.

Prof. Balasubramanian said that it is important to note that the CBRM programme was initiated by academies –Indian National Science Academy (INSA), The World Academy of Sciences (TWAS), Brazilian Academy of Sciences (BAS) and African Academy of Sciences (AAS). AAS will continue to support the programme. AAS is now in a better position as it can attract interest and funds from various partners such as the Grand Challenges Africa (GCA), Wellcome Trust (WT), Bill and Melinda Gates Foundation (BMGF), etc.

Collaboration is faster through academies. He informed participants that he would explore the possibility of hosting clinicians from Africa to spend some time in India at institutes working on stem cells.

It was agreed that the CBRM programme had been a success and STIAS and AAS were appreciated for organising this third workshop. The young scientists must transfer the knowledge they have acquired at this workshop back to their institutions.

# ANNEXES

## ANNEX 1: INTERVIEWS WITH THE AAS COMMUNICATIONS MANAGER

Some scientists were requested to give first-hand accounts of how the Cell Biology and Regenerative Medicine Programme had benefitted their scientific career. Their stories showcase the success of the programme. The impact could be useful when engaging funders and policy makers to show the importance of this field of research in Africa. The stories end with the views of Prof. Balasubramanian, one of the key scientists who envisioned this programme.

### Studying burn wounds in Zimbabwe

**Participating in an African Academy of Sciences stem cell sciences workshop has helped a Zimbabwean biochemist to learn tissue culture, train others and access a grant to research the treatment of burn wounds using stem cells.**

When Farisai Chidzwondo, a biochemist from the University of Zimbabwe, almost lost a sister to burn wounds at the age of eight she vowed she would help patients in the same condition.

The opportunity came with the African Academy of Sciences' Cell Biology and Regenerative Medicine programme, an initiative to mentor early career scientists in cell biology. She attended the workshop on *Training and Mentoring African Scientists in Stem Cell and Regenerative Medicine Research* that the AAS organised in 2014 where she learnt about how stem cells can be used in treating various diseases including burn wounds.

The programme also matched Chidzwondo with Dr Anjali Shiras, an established researcher at India's National Centre for Cell Sciences, Pune. This enabled her to travel to the Asian country in January 2015 to learn laboratory techniques to culture, multiply and use stem cells. It also resulted in an invitation to spend time with Prof. Susan Kidson at the University of Cape Town in South Africa where she learnt to culture keratinocytes.

Stem cells are classified into adult stem cells, which are found throughout the body and reproduce infinitely, often to repair dying cells and regenerate damaged tissues; mesenchymal stem cells which can be obtained from a variety of tissues, including bone marrow, umbilical cord, foetal and adipose or fat tissues; and pluripotent stem cells that are capable of differentiating into all the types of cells in the body.

This knowledge helped her to successfully apply for a \$4 000 grant from the University of Zimbabwe to enable her to start a project to grow skin cells and to teach tissue culture to her honours students. When she was accepted in the workshop Chidzwondo had no knowledge on tissue culture.

"But now we know how to grow cells and test lectins, which are carbohydrate binding proteins. We have also tested components that people use to speed up the healing of wounds from burns and assess their effect. With this knowledge we can advise people

on what to use and not to use to heal burn wounds," she said.

Chidzwondo presented her work to senior researchers and other early career researchers at the workshop on *Stem Cell Science and Applications* organised by the AAS and the Stellenbosch Institute of Advanced Studies in June this year.

She is not stopping here though. She plans to scale up her project to encompass grafting skin cells.

"My progress so far would have not been possible without the support of the AAS and my mentors," she said.

### How an AAS initiative has helped grow an early career researcher's career

**An African Academy of Sciences stem cell programme has helped Caroline Muriithi from Kenya's Institute of Primate Research to find a PhD scholarship.**

Attending the first workshop on stem cell sciences helped me to decide to pursue a career in stem cell sciences.

For a time, I wasn't sure what career path to follow until the workshop on Capacity Building in Cell Biology and Regenerative Medicine organised by the African Academy of Sciences in Nairobi, Kenya, in 2013. I have a background in infectious diseases but wanted to change to cancer research. I wasn't sure what areas in cancer research to focus on until my meeting with Prof. Vivaldo Moura-Neto from the University of Rio de Janeiro in Brazil and his team. Prof. Moura-Neto and his team shared their work on cancer stem cell research, which sparked my interest into the subject.

The AAS also organised my visit to Prof. Moura-Neto's laboratory at the University of Rio de Janeiro's Institute of Biomedical Sciences. He helped me to develop a PhD project and successfully apply for a scholarship at the Brazilian university where I have been pursuing my doctoral studies since June this year. My project studies the causes of multi-drug resistance in glioblastoma, a common and aggressive brain tumour. I am studying how glioblastoma cells remove drugs from the system making them ineffective in cancer treatment. In addition, little is known about cancer cells particularly the cell of origin.

I am hoping to contribute knowledge to the subject that will be crucial for finding cancer therapies.

I would like to see more young people pursue the field of stem cell science because of the opportunities it offers to grow their careers and find solutions to address health challenges in Africa. It is good to see organisations, such as the AAS and senior researchers offer such opportunities for young people.

Early-career researcher's project seeks to find how mutations in a gene is causing a rare condition in a South Africa family.

Meet Dimakatso Gumede, a PhD student from South Africa's University of Cape Town (UCT), who is studying how FAM111B, a gene that is causing a rare condition in a South African family functions using stem cell disease models.

In 2005, a 26-year South African woman with a multiple condition including skin lesions, sclerosis, no hair and arm and hardened Achilles tendon causing her to walk on toes walked into the Groote Schuur Hospital. She had a high intolerance of heat that necessitated her to sit in a fridge to cool down. Her condition intrigued researchers led by Dr Nonhlanhla Khumalo, a dermatologist at UCT, who were keen to find out her family history.

Her brother and father who had died at 30 and 56, respectively, had similar symptoms. Another 31-year-old brother and half-sister suffered from the same condition, which Dr Khumalo subsequently termed Hereditary sclerosing poikiloderma and published a paper describing the family and disease. The family are the only known sufferers in South Africa. Ten years later Gumede chose the family as the subject of her PhD study.

"The function of the FAM111B gene, which causes the disease is still unknown. I am assessing how it functions using stem cell disease models," she said.

She presented the work to her peers and senior researchers at the *Stem Cell Science and Applications* workshop organised by the African Academy of Sciences and the Stellenbosch Institute of Advanced Studies in South Africa in June this year.

Gumede has taken part in other stem cell sciences workshops organised by the African Academy of Sciences.

"My project is uncharted territory. It has been good to know from the workshops that there are experts who can assist by giving feedback or availing their laboratories where needed," Gumede said. "The first workshop in 2013 was important for most of us early career researchers who took part especially when noting the progress that has been made since then. Many have taken to stem cell science research and are conducting projects in the area, which wasn't the case when we began."

Prof. Balu speaks on the progress of the stem cell sciences programme

In 2012 Prof. Dorairajan Balasubramanian, the Director of Research at the L. V. Prasad Eye Institute in India was part of the team that conceived the programme for training young researchers in stem cell sciences. The Cell Biology and Regenerative Medicine Programme has to date held three workshops and funded seven young researchers to visit laboratories of their mentors in Brazil, India and South Africa. Prof. Balasubramanian, popularly known as Prof. Balu, is happy with how the programme has progressed so far. He spoke to the AAS about how it began and its benefits.

### **What inspired the programme?**

The promise that stem cell science has in medicine, for example, is enormous. I remember speaking about my project at the meeting and it generating excitement. Our project repairs damaged corneas using stem cells. Such treatments for patients with eye conditions are not common in Africa. We discussed how Africa and India share similar problems and saw opportunities for collaboration and especially for training young scientists in the field.

### **Has the programme progressed to your expectations? What have been its benefits?**

Science is about bringing people together and indeed to be a scientist is to be a citizen of the world. This is what the workshop has done and it has been a pleasure to meet people from different continents including some young ambitious scientists who have sought solutions to problems and worked together for a common goal.

We have all found the space to get feedback on our work. Young scientists have also had the opportunities to visit established researchers in their labs to see how they work, learn various new techniques, the equipment that can be used and opportunities in stem cell sciences.

### **Why is stem cell science important?**

Stem cells are like embryos out of which a whole life is formed. We can make a tissue or organ using stem cells or correct a defect. This is the promise that stem cell technology offers.

### **What should be the future of the programme?**

From the three workshops we have held so far we have seen a lot of interest from various parts of Africa. There are opportunities for growth and to train more young scientists from other parts of the continent.



## ANNEX 2: LIST OF WORKSHOP PARTICIPANTS

	NAME	COUNTRY	INSTITUTION	EMAIL
<b>Resource Persons</b>				
1	Jose Garcia ABREU	Brazil	Universidade Federal do Rio de Janeiro, Brazil	garciajr@icb.ufrj.br
2	Abdallah DAAR	Canada	University of Toronto, Canada	a.daar@utoronto.ca
3	Dorairajan BALASUBRAMANIAN	India	L. V. Prasad Eye Institute, India	dbala@lvpei.org
4	Susan KIDSON	South Africa	University of Cape Town, South Africa	susan.kidson@uct.ac.za
5	Fabio Almeida MENDES	Brazil	Universidade Federal do Rio de Janeiro, Brazil	mendes@icb.ufrj.br
6	Shirley MOTAUNG	South Africa	Tshwane University of Technology, South Africa	motaungsckm@tut.ac.za
7	Bade OGUNDIPE	Nigeria	University of Ibadan, Nigeria	bade_ogundipe@yahoo.com
8	Iqbal PARKER	South Africa	International Centre for Genetic Engineering and Biotechnology (ICGEB), South Africa	iqbal.parker@icgeb.org
9	Anjali SHIRAS	India	National Centre for Cell Sciences (NCC), India	anjali@nccs.res.in
10	Venant TCHOKONTE-NANA	South Africa	Stellenbosch University, South Africa	venant@sun.ac.za
<b>Other Experts</b>				
11	Kevin DZOBO	South Africa	International Centre for Genetic Engineering and Biotechnology (ICGEB), South Africa	kd.dzobo@uct.ac.za
12	Jacque GREENBERG	South Africa	University of Cape Town, South Africa	Jacque.greenberg@uct.ac.za
13	Marianne MUREITHI	Kenya	KAVI-Institute of Clinical Research, University of Nairobi, Kenya	marianne@uonbi.ac.ke
14	Kathy MYBURGH	South Africa	Stellenbosch University, South Africa	kham@sun.ac.za
15	Atunga NYACHIEO	Kenya	Institute of Primate Research, Kenya	anyachieo@yahoo.com
16	James O. OLOPADE	Nigeria	University of Ibadan, Nigeria	jo.olopade@mail1.ui.edu.ng
17	Marí VAN DE VYVER	South Africa	Stellenbosch University, South Africa	vandevyverm@sun.ac.za
<b>Mentees</b>				
18	Hiba BadrEldin Khalil AHMED	Sudan	Al Neelain University, Sudan	hibabadr@gmail.com
19	Farisai CHIDZWONDO	Zimbabwe	University of Zimbabwe, Zimbabwe	farisaichidzwondo@yahoo.com
20	Clare N. KIMANI	Kenya	Institute of Primate Research, Kenya	njokifora@gmail.com
21	Lucy MACHARIA	Brazil	Universidade Federal do Rio de Janeiro, Brazil	macharialw@gmail.com
22	Caroline W. MURIITHI	Brazil	Universidade Federal do Rio de Janeiro, Brazil	cjshiru@gmail.com
23	Afadhali Denis RUSSA	Tanzania	Muhimbili University of Health and Allied Sciences (MUHAS), Tanzania	adrussa@yahoo.com
24	Dorcas WACHIRA	Kenya	Kenya Medical Research Institute (KEMRI), Kenya	dwachira@kemri.org

	NAME	COUNTRY	INSTITUTION	EMAIL
<b>Scientists from Previous CBRM Workshop</b>				
25	Dimakatso Bertha GUMEDE	South Africa	University of Cape Town, South Africa	gumededimakatso@gmail.com
26	John Muturi KIMANI	Kenya	University of Nairobi, Kenya	jmuturik@gmail.com
27	Mosab Ali Awad E. MOHAMMED	Sudan	Al Neelain University, Sudan	mosb555@gmail.com
<b>AAS Affiliates: 2016 to 2020</b>				
28	Augustina Angelina ANNAN	Ghana	Kumasi Centre For Collaborative Research in Tropical Medicine, Ghana	annan@kccr.de
29	Tobias Obejum APINJOH	Cameroon	University of Buea, Cameroon	apinjohtoby@yahoo.co.uk
30	Denis ZOFOU	Cameroon	University of Buea, Cameroon	zofden@yahoo.com
<b>Selected Applicants</b>				
31	Mustapha Oluwaseun AHMED	Nigeria	Federal University of Agriculture, Nigeria	mustaphaoa@funaab.edu.ng
32	Idowu AIMOLA	Nigeria	Ahmadu Bello University, Nigeria	iaaimola@abu.edu.ng
33	Zohra ALOUI	Tunisia	Institut Pasteur de Tunis, Tunisia	zohra.aloui@pasteur.rns.tn
34	Nkiruka C. AZUBIKE	Nigeria	University of Nigeria, Nigeria	nkiruka.azubike@unn.edu.ng
35	Christine ICHUGU	Kenya	Kenya Medical Research Institute (KEMRI), Kenya	cichugu@kemri.org
36	Bernadette JANI	Zimbabwe	University of Zimbabwe, Zimbabwe	rutendobj20@gmail.com
<b>STIAS</b>				
37	Hendrik GEYER	South Africa	Stellenbosch Institute of Advanced Study (STIAS), South Africa	hbg@sun.ac.za
38	Nel-Mari LOOCK	South Africa	Stellenbosch Institute of Advanced Study (STIAS), South Africa	nelmvdmerwe@sun.ac.za
39	Christoff PAUW	South Africa	Stellenbosch Institute of Advanced Study (STIAS), South Africa	cpauw@sun.ac.za
<b>AAS</b>				
40	Berhanu M. ABEGAZ	Kenya	African Academy of Sciences (AAS), Kenya	b.abegaz@aasciences.ac.ke
41	Janet KARIUKI	Kenya	African Academy of Sciences (AAS), Kenya	j.kariuki@aasciences.ac.ke
42	Deborah-Fay NDHLOVU	Kenya	African Academy of Sciences (AAS), Kenya	d.ndhlovu@aasciences.ac.ke
43	Olivia OSULA	Kenya	African Academy of Sciences (AAS), Kenya	o.osula@aasciences.ac.ke

## ANNEX 3: WORKSHOP PROGRAMME

TIME	EVENT	SPEAKER/FACILITATOR
<b>DAY 1: MONDAY 27 JUNE 2016</b>		
<b>08:10 – 09:00</b>	Registration	STIAS and AAS Staff
<b>09:00 – 09:30</b>	<b>Opening ceremony</b>	<b>Facilitator: Dr Christoff Pauw</b>
	Introductory remarks	<b>Prof. Hendrik Geyer</b> Director, Stellenbosch Institute for Advanced Study (STIAS)
	Welcome remarks	<b>Prof. Berhanu Abegaz</b> Executive Director, African Academy of Sciences (AAS)
	Overview of the workshop programme/long-term objectives	<b>Dr Christoff Pauw</b> Programme Manager, Stellenbosch Institute for Advanced Study (STIAS)
<b>Session 1</b>	<b>Review of stem cell science and potential for applications in Africa</b>	<b>Chair: Prof. Berhanu Abegaz</b>
<b>09:30 – 10:00</b>	Can regenerative medicine make a difference to the management of organ failure in Africa?	<b>Prof. Abdallah Daar</b> University of Toronto
<b>10:00 – 10:30</b>	Stem cell biology and its specific applications in two areas of eye care – the cornea and the retina	<b>Prof. Dorairajan Balasubramanian</b> L. V. Prasad Eye Institute
<b>10:30 – 11:00</b>	Tea break	
<b>Session 2</b>	<b>Review of stem cell science and potential for applications in Africa</b>	<b>Chair: Prof. Abdallah Daar</b>
<b>11:00 – 11:20</b>	Modelling neural degeneration in <i>Xpinocerebellar ataxia</i> Type 7 using iPS cells	<b>Prof. Susan Kidson</b> University of Cape Town
<b>11:20 – 11:40</b>	Lessons from the embryo to cell and regenerative biology	<b>Prof. Fabio Almeida Mendes</b> Universidade Federal do Rio de Janeiro
<b>11:40 – 12:00</b>	Islet cells recovery in STZ-diabetes model: Beta cell regeneration or islet reorganisation?	<b>Dr Venant Tchokonte-Nana</b> Stellenbosch University
<b>12:00 – 12:20</b>	How does the ectoderm decide between neural or epidermis? May the Wnt pathway solve the question	<b>Prof. Jose Garcia Abreu</b> Universidade Federal do Rio de Janeiro
<b>12:20 – 12:40</b>	Adult progenitor cells: in vitro and in vivo	<b>Prof. Kathy Myburgh</b> Stellenbosch University
<b>12:40 – 13:00</b>	<i>Q &amp; A for Sessions 1 and 2</i>	
<b>13:00 – 14:00</b>	Group photo and lunch	
<b>Session 3</b>	<b>Review of stem cell science and potential for applications in Africa</b>	<b>Chair: Prof. Susan Kidson</b>
<b>14:00 – 14:20</b>	Recent advances in stem cell therapy	<b>Prof. Iqbal Parker</b> International Centre for Genetic Engineering and Biotechnology (ICGEB)
<b>14:20 – 14:40</b>	Induction of human pluripotent stem cells and their in vitro differentiation: Looking forward to regenerative medicine	<b>Dr Anjali Shiras</b> National Centre for Cell Science (NCC)
<b>14:40 – 15:00</b>	Dreams for the future of tissue engineering and regenerative medicine on african continent based on medicinal plants	<b>Dr Shirley Motaung</b> Tshwane University of Technology
<b>15:00 – 15:20</b>	Stem cell impairment in chronic inflammatory conditions and its implications for autologous cell therapy	<b>Dr Mari van de Vyver</b> Stellenbosch University
<b>15:20 – 15:50</b>	Refreshments	

TIME	EVENT	SPEAKER/FACILITATOR
<b>Session 4</b>	<b>Aspirations to build competency in stem cell science in Africa</b>	<b>Chair: Prof. Iqbal Parker</b>
<b>15:50 – 16:10</b>	Prospects of ocular stem cell science in Nigeria	<b>Dr Ayobade Ogundipe</b> University of Ibadan
<b>16:10 – 16:30</b>	Establishment of assays and systems for culture and manipulation of haematopoietic stems cells and mesenchymal stem cells	<b>Dr Marianne Mureithi</b> KAVI-Institute of Clinical Research, University of Nairobi
<b>16:30 – 16:50</b>	Stem cells treating myocardial infraction; an experimental study	<b>Dr Hiba BadrEldin Khalil Ahmed</b> Al Neelain University
<b>16:50 – 17:10</b>	Stem cells in regenerative medicine and cancer	<b>Dr Kevin Dzobo</b> International Centre for Genetic Engineering and Biotechnology (ICGEB)
<b>17:10 – 17:30</b>	<i>Q &amp; A for Sessions 3 &amp; 4</i>	
<b>18:30 – 20:00</b>	Welcome reception/dinner	

<b>DAY 2: TUESDAY 28 JUNE 2016</b>		
<b>Session 5</b>	<b>Presentations by young scientists</b>	<b>Chair: Dr Venant Tchokonte-Nana</b>
<b>08:10 – 08:30</b>	The development, production and characterisation of adult neural stem cells from the Greater Cane Rat ( <i>Thryonomys swinderianus Temminck</i> )	<b>Mr Mustapha Oluwaseun Ahmed</b> Federal University of Agriculture
<b>08:30 – 08:50</b>	Pharmacological study of a pro-angiogenic snake venom protein	<b>Dr Zohra Aloui</b> Institut Pasteur de Tunis
<b>08:50 – 09:10</b>	Inflammatory markers as emerging risk factors of cardiovascular diseases in HIV	<b>Ms Bernadette Jani</b> University of Zimbabwe
<b>09:10 – 09:30</b>	Applications of induced pluripotent stem cells: A statement of professional development in stem cell science	<b>Dr Nkiruka C. Azubike</b> University of Nigeria
<b>09:30 – 09:50</b>	Stem cell research: Pathway to sickle cell therapy?	<b>Dr Idowu Aimola</b> Ahmadu Bello University
<b>09:50 – 10:10</b>	Regenerative medicine and severe acute malnutrition	<b>Ms Christine Ichugu</b> Kenya Medical Research Institute (KEMRI)
<b>10:10 – 10:30</b>	<i>Q &amp; A</i>	
<b>10:30 – 11:00</b>	Tea break	
<b>Session 6</b>	<b>Presentations by young scientists</b>	<b>Chair: Dr Anjali Shiras</b>
<b>11:00 – 11:20</b>	Therapeutic efficacy and safety of oogonial stem cells (OSCs) injection into baboon ovary	<b>Dr Atunga Nyachieo</b> Institute of Primate Research
<b>11:20 – 11:40</b>	Origins and reservoirs of zoonotic viruses: Coronaviruses as a paradigm for the transmission interface between wildlife, livestock and humans	<b>Dr Augustina Angelina Sylverken</b> Kumasi Centre for Collaborative Research in Tropical Medicine
<b>11:40 – 12:00</b>	Exploring the African Pharmacopoeia as source of new therapies: Screening efforts at the Biotechnology Unit, University of Buea (Cameroon)	<b>Dr Dennis Zofou</b> University of Buea
<b>12:00 – 12:20</b>	Population genetics and immunology of <i>Plasmodium falciparum</i> in natural populations of Southwestern Cameroon	<b>Dr Tobias Obejum Apinogh</b> University of Buea
<b>12:20 – 12:40</b>	<i>Q &amp; A</i>	
<b>12:40 – 14:00</b>	Lunch	



TIME	EVENT	SPEAKER/FACILITATOR
<b>Session 7</b>	<b>Presentations by young scientists</b>	<b>Chair: Dr Mari van de Vyver</b>
<b>14:00 – 14:20</b>	Investigating the role of a FAM111B mutation in hereditary fibrosing poikiloderma using induced pluripotent stem (iPS) cell models	<b>Ms Dimakatso Gumede</b> University of Cape Town
<b>14:20 – 14:40</b>	Comparative analysis of wound healing and regenerative ability in different mammals	<b>Dr John Muturi Kimani,</b> University of Nairobi
<b>14:40 – 15:00</b>	The stem cell potential of the adult hippocampus	<b>Mr Mosab A A Mohammed</b> Al Neelain University
<b>15:00 – 15:20</b>	Current scientific work	<b>Prof. James Olopade,</b> University of Ibadan
<b>15:20 - 15:40</b>	Q & A	
<b>15:40 – 16:00</b>	Refreshments	
<b>16:00 – 17:00</b>	Interviews with AAS Communications Manager	<b>Ms Deborah-Fay Ndhlovu</b> Communications Manager, AAS

<b>DAY 3: WEDNESDAY 29 JUNE 2016</b>		
<b>Session 8</b>	<b>Presentations young scientists/CBRM mentees</b>	<b>Chair: Dr Ayobade Ogundipe &amp; Prof. Fabio Almeida Mendes</b>
<b>08:10 – 08:30</b>	Applications and new insights of stem cells in the cancer context: A neural point of view	<b>Dr Louis Gustavo Dubois</b> Insituto Estadual do Cerebro Paulo Niemeyer
<b>08:30 – 08:50</b>	Use of skin stem cells in the treatment of wounds	<b>Dr Farisai Chidzwondo</b> University of Zimbabwe
<b>08:50 – 09:10</b>	Stem cell technology: Current status and future trends in Tanzania	<b>Dr Denis Russa</b> Muhimbili University of Health and Allied Sciences (MUHAS)
<b>09:10 – 09:30</b>	My journey as a “mentee in cell biology and regenerative medicine” under The African Academy of Sciences Mentorship Programme	<b>Ms Dorcas Wachira</b> Kenya Medical Research Institute
<b>09:30 – 09:50</b>	Study of tumor stem-like cells from glioblastoma and medulloblastoma: Contributions to diagnostic and therapy	<b>Ms Lucy Macharia</b> Universidade Federal do Rio de Janeiro
<b>09:50 – 10:10</b>	Multi-Drug resistance in glioblastoma: The involvement of ABC transporters in glioblastoma	<b>Ms Caroline Muriithi</b> Universidade Federal do Rio de Janeiro
<b>10:10 – 10:30</b>	Current work and future plans relating to stem cells and regenerative medicine	<b>Ms Clare N. Kimani</b> Institute of Primate Research
<b>10:30 – 11:00</b>	Tea break	
<b>11:10 – 11:40</b>	Q & A	
<b>Session 9</b>	<b>Mentor-mentee session</b>	
<b>11:40 – 13:00</b>	Time for young professionals to meet individually with the Resource Persons	Resource Persons
<b>13:00 – 14:00</b>	Lunch	
<b>Session 10</b>	<b>Discussions</b>	<b>Chair: Prof. Dorairajan Balasubramanian</b>
<b>14:00 – 16:00</b>	Discussions (Resource Persons, other experts & all young scientists)	Roundtable led by <b>Prof. Balasubramanian</b>
<b>16:00 – 16:30</b>	Overview on visit to the laboratories including logistics	<b>Dr Christoff Pauw</b> STIAS
<b>16:30 – 17:00</b>	Tea break	

TIME	EVENT	SPEAKER/FACILITATOR
<b>DAY 4: THURSDAY 30 JUNE 2016</b>		
<b>Session 11</b>	<b>Hands-on sessions at laboratories</b>	
<b>10:30 – 13:00</b>	Hands-on techniques on islet and mesenchymal cells separation, and eventually co-culturing these cells to generate new islet cells	<b>Prof. Susan Kidson</b> University of Cape Town <b>Prof. Iqbal Parker</b> The International Centre for Genetic Engineering and Biotechnology (ICGEB) <b>Prof. Venant Tchokonte-Nana</b> Islet Research Laboratory
<b>13:00 – 14:00</b>	Lunch	
<b>14:00 – 16:00</b>	Lab session continues	

<b>DAY 5: FRIDAY 01 JULY 2016</b>		
<b>Session 12</b>	<b>Feedback on lab sessions (Representatives from each lab group to give a report)</b>	<b>Chair: Prof. Jose Garcia Abreu</b>
<b>08:30 – 08:40</b>	Report from University of Cape Town	Group representative
<b>08:40 – 08:50</b>	Report from ICGEB	Group representative
<b>08:50 – 09:00</b>	Report from Islet Research Laboratory	Group representative
<b>09:00– 10:00</b>	Ethical Issues in stem cell research	<b>Prof. Jacquie Greenberg</b> University of Cape Town
<b>10:00 – 10:30</b>	Q & A	
<b>10:30 – 11:00</b>	Tea break	
<b>Session 13</b>	<b>Closing</b>	<b>Chair: Prof. Susan Kidson</b>
<b>11:00 – 12:00</b>	Next Steps for CBRM programme	<b>Dr Marianne Mureithi,</b> KAVI-ICR, University of Nairobi
<b>12:00 – 12:30</b>	Vote of thanks	STIAS and AAS
<b>12:30 – 14:00</b>	Farewell lunch and departure	

## Rapporteurs

**Chief Rapporteur:** Ms Olivia Osula & Ms Deborah-Fay Ndhlovu

**Opening Ceremony:** Ms Olivia Osula & Ms Janet Kariuki & Ms Deborah-Fay Ndhlovu

**Session 1:** Dr Denis Russa & Prof. James Olopade

**Session 2:** Dr Farisai Chidzwondo & Mr Mustapha O. Mohamed

**Session 3:** Dr Nkiruka C. Azubike & Mr Mosab A A Mohammed

**Session 4:** Dr Tobias Obejumo Apinjo & Ms Lucy Macharia

**Session 5:** Dr John Muturi Kimani & Ms Dimakatso Gumede

**Session 6:** Dr Hiba BadrEldin Khalil & Ms Caroline Muriithi

**Session 7:** Dr Zohra Aloui & Ms Dorcas Wachira

**Session 8:** Ms Christine Ichugu & Dr Idowu Aimola

**Session 9:** N/A

**Session 10:** Dr Kevin Dzobo & Dr Augustine Angelina Sylverken & Dr Marianne Mureithi

**Session 11:** For each lab, the group should select a representative to give a report the next morning

**Session 12:** Ms Bernadette Jani & Ms Clare N. Kimani

**Session 13:** Dr Atunga Nyachio & Dr Mari van de Vyver & Dr Denis Zofou

## ANNEX 4: GROUP PHOTO



