THE CSIR'S OPERATING UNITS, NATIONAL RESEARCH CENTRES AND SERVICES

- **CSIR Biosciences**
  Pretoria 012 841-3260
  Modderfontein 011 605-2544
- **CSIR Built Environment**
  Pretoria 012 841-3871
- **CSIR Defence, Peace, Safety and Security**
  Pretoria 012 841-2780
- **CSIR Materials Science and Manufacturing**
  Pretoria 012 841-4392
  Port Elizabeth 041 508-3200
  Cape Town 021 685-4329
- **CSIR Natural Resources and the Environment**
  Pretoria 012 841-4005
  Johannesburg 011 358-0000
  Stellenbosch 021 888-2400
  Durban 031 242-2300
  Pietermaritzburg 033 260-5446
- **Meraka Institute**
  Pretoria 012 841-3028
- **CSIR National Laser Centre**
  Pretoria 012 841-4188
- **CSIR National Metrology Laboratory**
  Pretoria 012 841-4152
- **CSIR Satellite Applications Centre**
  Hartebeesthoek 012 334-5000
- **CSIR Knowledge Services**
  Pretoria 012 841-2525

Design: Loretta Steyn Graphic Design Studio
Compiled by: CSIR Communication

www.csir.co.za ISSN 1017-4966
Enquiries: (012) 841-2000 query@csir.co.za

our future through science

ScienceScope

Quarterly publication of the CSIR
South Africa's Council for Scientific and Industrial Research

Volume 2 Number 1 April 2007

www.csir.co.za

LIFE SCIENCES

CSIR

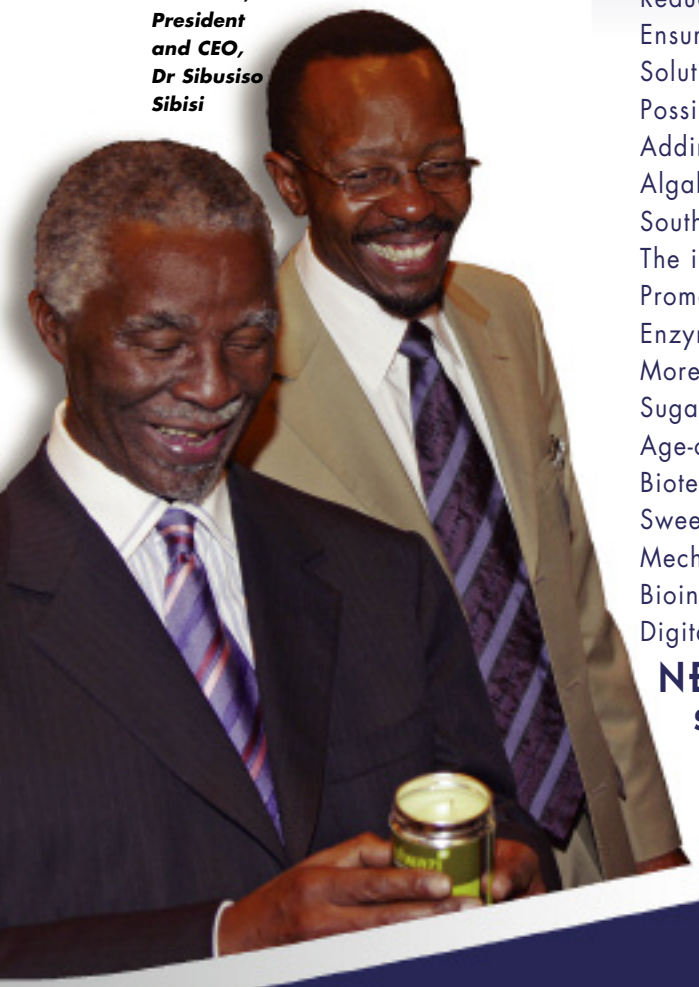
our future through science

Volume 2 Number 1 April 2007

IN THIS ISSUE...

LIFE SCIENCES

NEWS



Taking a closer look at the mosquito repellent candle produced in Limpopo following collaboration by traditional healers and bioscientists from the CSIR and with funding from the Department of Science and Technology – South African President, Mr Thabo Mbeki and CSIR President and CEO, Dr Sibusiso Sibisi

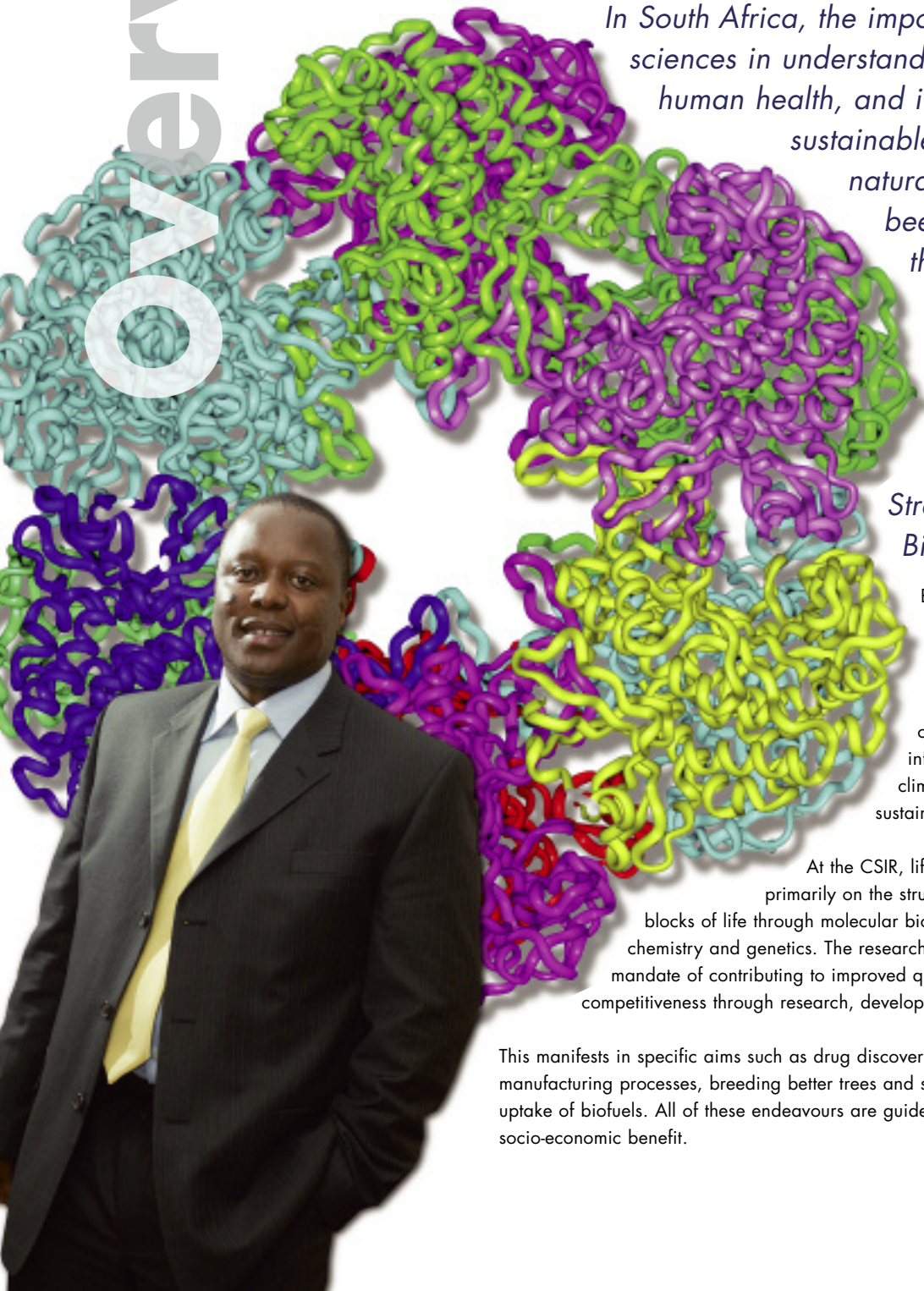
On the cover:
Escherichia coli
glutamine synthetase

overview

Life sciences: studying systems in living organisms

By Dr Gatsha Mazithulela

Life sciences has become a vast research enterprise worldwide and is not regarded as a single discipline. In South Africa, the importance of the life sciences in understanding and improving human health, and in the development of sustainable approaches to our natural environment, has been recognised through the implementation of a number of important government-led initiatives including the National Research and Development Strategy and the National Biotechnology Strategy.



Both of these strategies identify the life sciences, and more specifically biotechnology, as important contributors to overcoming many significant social and economic challenges including liquid fuels, infectious diseases, food security, climate change, job creation and sustainable economic development.

At the CSIR, life sciences research efforts centre primarily on the structure and function of the building blocks of life through molecular biology, cell biology, biochemistry, chemistry and genetics. The research focus is shaped by the CSIR's mandate of contributing to improved quality of life and industrial competitiveness through research, development and innovation.

This manifests in specific aims such as drug discovery, the development of biochemical manufacturing processes, breeding better trees and studying the impact of a significant uptake of biofuels. All of these endeavours are guided by the principle of developing socio-economic benefit.

A new group working in aptamer technology investigates the molecular basis of disease so that new drugs and diagnostics for HIV and TB can be developed.

The biotechnology value chain

The largest single group working on biotechnology within South Africa – and possibly Africa – resides within the CSIR's Biosciences unit and has to demonstrate leadership, relevance and impact in this field. As a core implementor of the National Biotechnology Strategy, the CSIR is continuously realigning its research to national priorities and committing itself in terms of the quantity and quality of its research.

The world of biotechnology is driven by the convergence of various technologies in the chemical, biological, genetic sciences and other fairly established, but related fields. The CSIR's earlier focus to serve the pillars of mature food, biological and chemical industries was changed to concentrate technical expertise on a single value chain in biotechnology, thereby responding to new opportunities as they emerge.

Today, the majority of CSIR Biosciences research is structured in two competence areas: drug and therapeutic discovery; and bioprocessing and product development. Within these areas, the CSIR invests in building skills and infrastructure in highly-specialised research groups.

Bioprospecting aims to add maximum value to South African bio-resources and indigenous knowledge systems (IKS), and is one of the prime research platforms employed in drug and therapeutic discovery. The research focuses on the scientific validation of medicinal plants and includes the elucidation of new molecular scaffolds, lead molecule optimisation and a systems biology approach to drug and target identification and validation. Appropriate bio-assays are sought and accessed to allow a systems-based approach for elucidating the mechanism(s) of action of traditional medicines.

In **discovery chemistry** researchers focus on the application of synthetic and medicinal chemistry to develop drugs for diseases such as HIV/Aids, tuberculosis (TB) and malaria. An understanding of the molecular basis for the treatment of the disease condition forms a core component of the research.

Using **structural biology**, scientists identify, elucidate and validate potential new drug targets and use this knowledge for rational drug design and lead modification, focusing primarily on infectious diseases. To date, research has focused primarily on biological reaction mechanism approaches to the development of enzymes of nitrogen metabolism as new drug targets. Significant intellectual property (IP) has been developed around exploitation of glutamine synthestase as a drug target. This can now be extended, consolidated and exploited.

A new group working in **aptamer technology** investigates the molecular basis of disease so that new drugs and diagnostics for HIV and TB can be developed. Aptamers are nucleic acid ligands that combine the optimal characteristics of antibodies and small molecules.

CSIR **systems biologists** seek explanations of the properties and behaviour of complex biological systems in terms of their molecular components and interactions. Key technologies required to allow a full study of complex systems include cell culturing (to provide model systems), transcriptomics (to investigate global gene expression), proteomics (to investigate global protein synthesis and regulation, and for protein characterisation), metabolomics (broad-based systematic analysis of the small molecules in the cell) and bioinformatics (for integration and processing of the complex data generated). It is clearly impossible to establish a critical mass of capacity within the CSIR in all these technologies, hence a strategy of partnership and collaboration is pursued.

The CSIR houses the high-end analytical expertise and infrastructure required to fulfil research objectives. **The analytical chemistry** group has the role of molecular and bio-molecular structural elucidation required for drug discovery and development and biological target and pathway elucidation.

A major research capability that contributes to bioprocessing and product development in biosciences is **plant biotechnology**. The CSIR has a clear aim of improving the nutritional value of African staple cereals, and using plant systems for production of biopharmaceuticals. The CSIR has built significant capacity in this area in recent times and intends maximising this strength. Successful inclusion in international consortia include the Bill and Melinda Gates Foundation, for nutritional improvement of sorghum, and several European consortia for production of pharmaceuticals. The group is also leading the establishment of a national plant transformation platform initiative, thus acting as an important catalyst for local collaboration with the universities of Cape Town, Pretoria, Stellenbosch and KwaZulu-Natal, among others.

Researchers in the CSIR's **enzyme technology** group are developing proprietary enzyme technology that can be applied to gain a competitive advantage within the emerging South African biosciences industry. This newly created research platform focuses on developing novel biocatalysis processes for chemical synthesis and synthesis of "designer" proteins. Genomics and bioinformatics technologies, together with the use of a meta-genomics library and directed evolution, are facilitating this approach.

A focus on **microbial expression systems** for the expression or production of proteins and peptides has resulted in proprietary IP, using a novel Bacillus host system. The next few years will see the development and validation of processes for synthesis of high value proteins and peptides.

A newly established group of scientists is developing **yeasts as expression systems** for valuable proteins, with an emphasis on biotherapeutics. The current focus is on development of the host *Yarrowia lipolytica*, previously used in the CSIR to produce epoxide hydrolase enzyme.

A **bioprocess development** group focuses on the development and implementation of biological technologies and products to allow manufacturing in South Africa – an important growth opportunity is the expansion into pharmaceutical and biopharmaceutical products and processes. Such a capability will find alignment with the portfolio of products already generated and with South Africa's needs in the health arena. Key initiatives over the following few years include developing the expertise and processes required for exploitation of bacteria and yeast expression systems outlined.

The **agroprocessing and chemical technologies** group focuses on the beneficiation of indigenous biomass resources and the development of chemical technologies and products. The agroprocessing activities of the CSIR are well integrated with national and international research. This expertise forms a core component of the new thrust into biofuels, with substantial involvement in beneficiation of biodiesel byproducts. This role will be expanded to develop bio-ethanol technology suitable for South African feedstocks and conditions.

Impact of biofuels

The CSIR also has a role to play in clarifying and quantifying the impact of biofuels on hydrology, food security, poverty relief and biodiversity conservation. A combination of process-based field measurements and modelling exercises are being undertaken.

Tree genetics

The reality of an ever-growing demand for forest products on the one hand and stringent environmental management constraints on the other result in pressure to produce "better" trees: trees that yield more paper and pulp products off the same land. The CSIR plays a key role in efforts to breed better trees, using modern genetic tools.

Emerging research

A new and exciting development on the CSIR life sciences horizon is an emerging research area in synthetic biology, the design and fabrication of biological components or systems that do not exist in nature. The initial research revolves around two core areas: bio-energetics (developing biophotonic nanodevices); and molecular biomaterials (aimed at developing advanced smart materials). The research will be multidisciplinary and multi-institutional, and contribute to the international development of the field.

Our future through science

With the completion of the elucidation of the human genetic code and other codes for micro-organisms, animals and plants, as well as advances in measurement and analysis of biological phenomena; discoveries in the life sciences in coming decades are predicted to yield the most important industries to date.

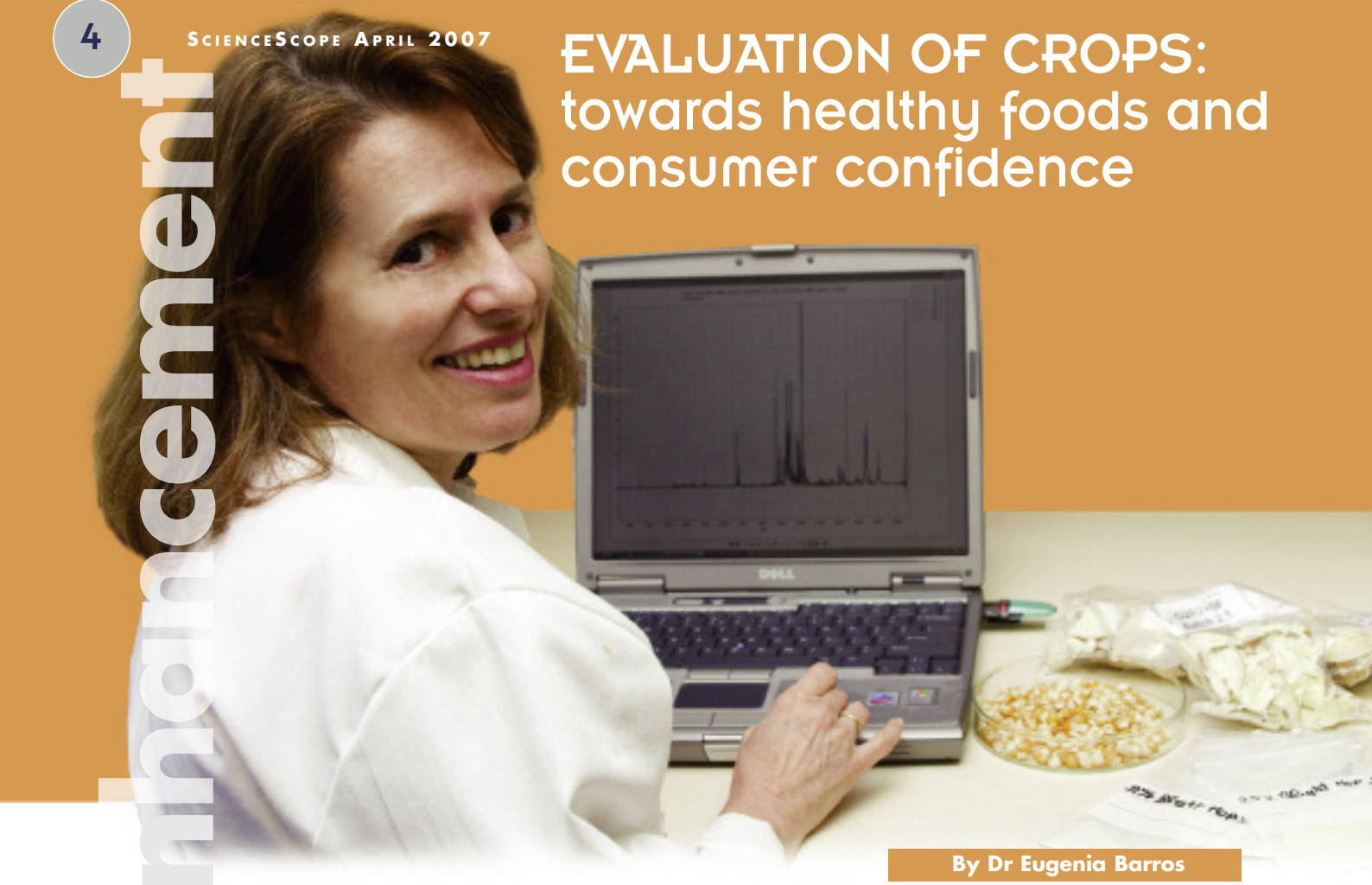
Against this backdrop, the CSIR is geared to play a significant role in addressing the unique challenges of this country and the African continent. Our research will help to ensure that South Africa will develop its indigenous knowledge, apply new knowledge from the life sciences in treating and/or preventing disease, manage our unique and fragile ecosystems, and find more sustainable energy alternatives.

This edition of **ScienceScope** features some CSIR research outcomes in life sciences achieved to date, while outlining current and future objectives.

Enquiries:
Dr Gatsha Mazithulela
CSIR Biosciences Executive Director
Tel 012 841-4616
Email gmazithulela@csir.co.za

Nutritional enhancement

EVALUATION OF CROPS: towards healthy foods and consumer confidence



By Dr Eugenia Barros

Dr Eugenia Barros's research focuses on profiling selected crops to address concerns about the production of higher quality and safer foods. Barros is part of an international team involved in two European Union-funded projects – Safefoods and Develonutri

Increasing and maintaining the nutritive value of staple food crops and products are of increasing importance worldwide. The ability to produce higher quality food in a safe and environmentally-friendly manner has become a top priority for consumers, policymakers and the commercial sector.

Working towards the goal of healthier foods and an integrated risk approach for these foods, scientists taking part in a European Union (EU)-funded research project are using the newest and highly sensitive profiling technologies in combination with the development of sophisticated comparative databases with detailed information of selected crops. This detailed study is the first of its kind, as this is an enormous task that requires a variety of specialised equipment and trained scientists and technicians.

An international team of plant molecular biologists, chemists, biochemists and specialists in bioinformatics – from 35 institutes in 19 countries – joined forces during 2004 to embark on this unique, large-scale comparative safety analysis. Focus is on two crops produced by different agricultural practices, including high- and low-input (organic) agriculture, and through different breeding approaches, including traditional plant breeding, *in vitro* culture and genetic modification. The two crops being studied are potato and maize. Samples of these crops have been collected from all over the world and are currently being evaluated using profiling methods, i.e. transcriptomics, proteomics, and metabolomics.

The data generated are captured in a massive comparative database that will allow for the determination of what compounds, metabolites and nutrients make up crops, which ones remain constant, which ones change, and the production of new ones depending on the specific agricultural practice or breeding approach used in the production of that crop. Information is also being gathered on the type of mycotoxins – a toxin produced by an organism of the fungus family – associated with the crops and the effect of their presence on the normal crop profile.

This comparative analysis of compositional profiles of foods, produced by different agricultural practices, under different

environmental conditions, will provide relevant information for establishing baselines and will document the history of the safe use of foods, which is an important element in the safety and nutritional evaluation of foods.

The CSIR, in collaboration with the Agricultural Research Council and the University of Pretoria, is playing a significant role in this project, called Safefoods. The project entails sample collection, identification and preparation, database construction and also specifically in the metabolic profiling, using nuclear magnetic resonance spectroscopy (NMR). The CSIR has been tasked with the NMR analysis of all the maize and potato samples studied for the duration of the project. Skills development in bioinformatics is an important outcome of this collaborative project.

The first figure shows the effect that growing conditions can have on the amount of certain compounds produced in a potato cultivar. The same potato cultivar was grown under different fertiliser regimens, i.e. organically (with compost fertiliser) and conventional (mineral fertiliser).

The second figure shows the variation found in maize cultivars normally grown in Germany compared to maize cultivars grown in South Africa for a specific metabolite, in this case sugars. These are the kind of results that are being analysed and will be used to design a new integrated risk analysis approach for foods produced by different breeding methods and production practices, which is one of the major outcomes of the Safefoods project.

The databases that are being generated for the design of the improved risk assessment and risk analysis practices are valuable sources of information to plant breeders and primary producers, enabling them to select the nutritional traits that should be improved as well as the optimisation of agricultural practices and storage regimes.

The CSIR participates in a more targeted research project, Develonutri, which is also funded by the EU and consists of 17 international institutes in nine countries. The aim is to develop and validate high throughput profiling technologies for quantification and optimisation of the nutritional value of crops and crops-based foods.

These validated methodologies should be such that they could be deployed at all stages of crop improvement and used to identify post-harvest and processing events that may contribute to nutritional losses. The crops being studied are potato, wheat and tomato. While the Safefoods project aims to understand the sources and extent of variation in potato and maize as well as the compositional changes as a result of the sources and extent of natural variation, the Develonutri project aims to understand the major, minor and key nutrients in potato, wheat and tomato.

Both projects provide valuable information that can be used when dealing with legislation, where the increasing stringent EU legislation on nutritional value and labelling of food crops has led to extra demands on specific nutritional claims on a crop and its derived foodstuff.

FIGURE 1: ORGANIC VERSUS CONVENTIONAL POTATO - NMR

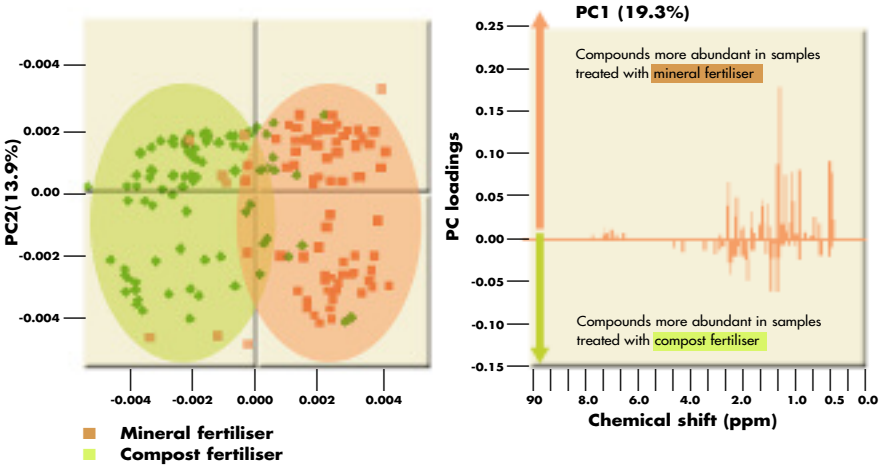
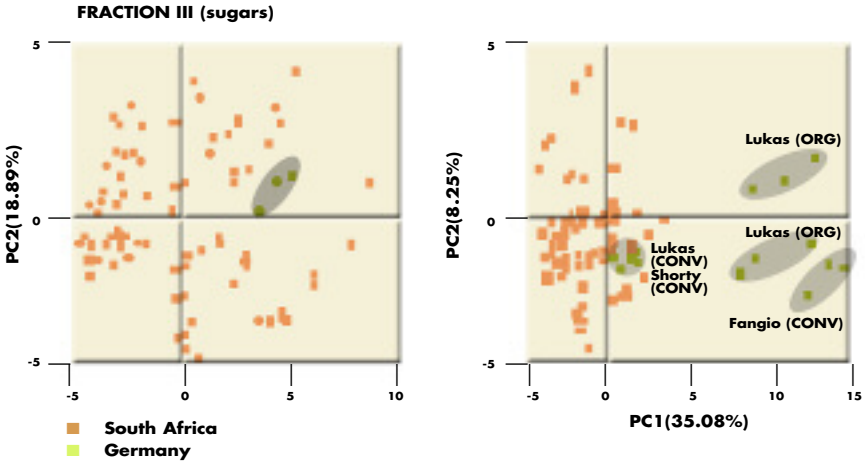


FIGURE 2: SOUTH AFRICAN MAIZE SAMPLES



Enquiries:

Dr Eugenia Barros

Tel 012 841-3221

Email ebarros@csir.co.za

Global effort to enhance nutrition of sorghum

By Dr Rachel Chikwamba
and Dr Maretha O'Kennedy

Poor nutrition is a major global health problem, contributing to more than half of the nearly 11 million deaths that occur each year in children younger than five years. In Africa, thousands die each year from starvation or malnutrition, while millions of people suffer from health problems associated with vitamin and mineral deficiency.

Impaired immune systems, blindness, low birth weights, impaired neuropsychological development and stunted growth are just a few of the problems associated with inadequate intake of essential micronutrients. Bio-available iron, vitamin A, and zinc are mainly provided in the human diet by animal source foods. In the developing world, where poorer individuals consume predominantly plant-based diets, deficiencies of these micronutrients are common. Infants, children, as well as pregnant and lactating women are most at risk because of their additional nutritional needs.

The Bill and Melinda Gates Foundation launched the Grand Challenges in Global Health to improve health in the world's poorest countries through science and technology. Grand Challenge No 9 sets the goal of improving nutrition and promoting health by creating a full range of optimal, bio-available nutrients in a single staple plant species, with a specific focus on banana, cassava, rice and sorghum. The CSIR is involved in research into one of these crops, namely sorghum.

The Africa Biofortified Sorghum (ABS) project seeks to develop a more nutritious and easily digestible sorghum that contains increased levels of essential amino acids, especially lysine, increased levels of pro-vitamin A and vitamin E, and bio-available iron and zinc. The institutional partners in this initiative include the CSIR; Pioneer Hi-Bred International, a subsidiary of DuPont; the Forum for Agricultural Research in Africa (FARA); the Agricultural Research Council (ARC); the African Agricultural Technology Foundation (AATF); the International Crops Research Institute for the Semi-Arid Tropics (ICRISAT); and the universities of Pretoria and California-Berkeley. Africa Harvest, an international non-profit organisation, is coordinating this project.

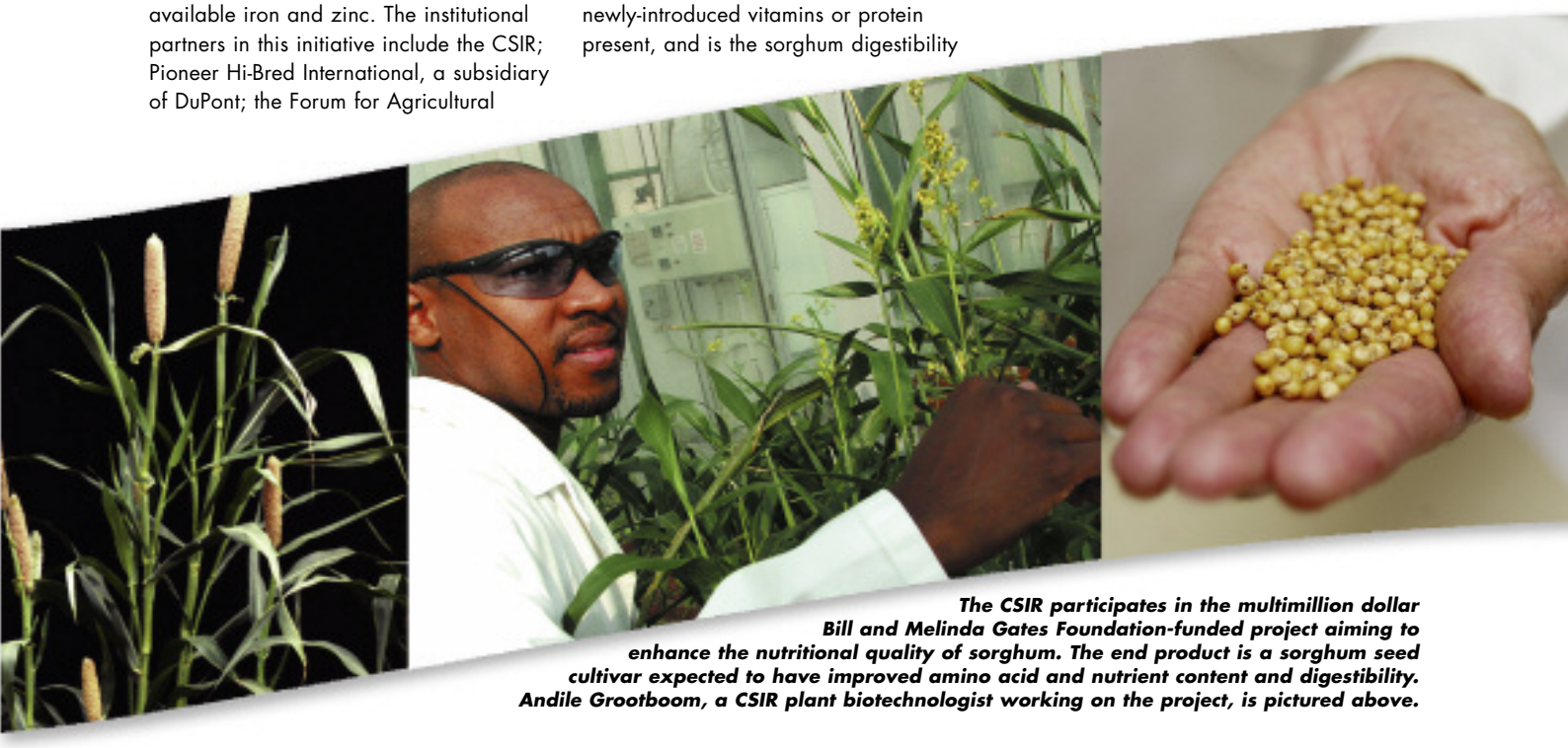
The approach adopted for the ABS project is to introduce – through genetic engineering – selected genes from mainly plant sources into the genome of sorghum. Traditional plant breeding methods continue to make important contributions towards meeting the need for more food, whereas recombinant DNA technology permits a more precise and predictable introduction of a broader array of traits that can help meet the need for nutritionally improved varieties. Using this approach, whole pathways and pathway components can be introduced into crops precisely and in a relatively short space of time, without compromising other attributes of the crop performance.

Other aspects of this work will include molecular analyses of the modified plants and an impact assessment of the grain to determine through biochemical and other techniques whether or not the desired traits have been introduced: are there more of the targeted elements; are the newly-introduced vitamins or protein present, and is the sorghum digestibility enhanced? Further down the line, limited animal and human studies will be carried out with the improved grain to make a full assessment of the nutritional enhancement efforts to human nutrition.

The role of the CSIR in this project centres on technology development. To this end, the CSIR has been working closely with Pioneer Hi-Bred, a world leader in agricultural seed technology in Iowa, USA, to select the genes that are required to introduce specific traits, and to modify the expression of genes that impact on protein quality and macronutrient availability. As part of this endeavour, CSIR scientists have visited and worked at the Pioneer laboratories where they were exposed to cutting edge molecular biology and plant modification techniques.

Upon his return from Iowa, where he spent 18 months working on sorghum transformation and related research, CSIR plant biotechnologist Dr Luke Mehlo, commenced with the process of filing invention disclosures on his work at Pioneer.

His colleague, Andile Grootboom, also worked at Pioneer and is in the process of completing his doctoral research. He is instrumental in the delivery of the CSIR's science obligations to this global initiative. Collaboration is playing a key role in



The CSIR participates in the multimillion dollar Bill and Melinda Gates Foundation-funded project aiming to enhance the nutritional quality of sorghum. The end product is a sorghum seed cultivar expected to have improved amino acid and nutrient content and digestibility. Andile Grootboom, a CSIR plant biotechnologist working on the project, is pictured above.

Dr Maretha O'Kennedy and Dr Rachel Chikwamba view the separation of Kafirins (a specific component in sorghum) on a protein gel

unlocking the potential of scientists and is contributing significantly to human capital development. It is expected that over the next five to 10 years, many scientists will define a career path based on the ABS project. Many postgraduate students at PhD and MSc levels at the three project partners in South Africa (the CSIR, the ARC and the University of Pretoria), will also be trained in various aspects of the value chain; from research in laboratories to product development and processing. The CSIR has upgraded its research infrastructure, notably its greenhouse facilities, which now comply with world-class standards for research involving genetic modification.

The ABS project is a pioneering initiative in the use of genetic modification for the improvement of sorghum, which is an indigenous crop with wild relatives in Africa. The CSIR is therefore taking precautions to ensure that the project is implemented in an environmentally sound way. To this end, only genes for the nutritional attributes will be left in the final product and no antibiotic or herbicide resistance markers will be present. The consortium and the CSIR are working closely with the regulatory authorities in South Africa to determine the regulatory regime that is required for this work.

The CSIR is looking beyond the use of genetic engineering to improve cereal grain nutritional quality. A research consortium led by the CSIR has received a substantial international grant to explore an advanced method of nutritionally enhancing two of Africa's major staple food crops without introducing any foreign genes to these plants. The revolutionary method of altering the plant's own genetic signals without introducing any foreign genes is based on nuclear radiation technology. The grant was awarded by the International Atomic Energy Agency (IAEA), a specialised agency of the United Nations.

Enquiries:

Dr Rachel Chikwamba and
Dr Maretha O'Kennedy
Tel 012 841-2177/2535
rchikwamba@csir.co.za
mokennedy@csir.co.za

Drug discovery for diseases prevalent in Africa – an introduction

By Dr Dusty Gardiner

A major shift in the biotechnology industry has biotechnology companies building small molecule or chemistry expertise and integrating this expertise with existing biology capability. The integration is providing a critical advantage in finding innovative new molecules for the treatment of diseases. In parallel with this shift, big pharmaceutical companies have been expanding into biologics, largely through acquisition of biotechnology companies.

This changing environment finds resonance at CSIR Biosciences, where research groups continue to build multidisciplinary capacity in drug and therapeutic discovery, with a focus on diseases that contribute substantially to the burden of disease on the African continent. HIV/Aids, tuberculosis (TB) and malaria are the key targets of drug discovery research at the CSIR.

Multipronged, yet integrated research approaches, have been implemented to tackle these diseases. Natural products chemistry (taking advantage of South Africa's floral biodiversity coupled with strong indigenous knowledge systems), medicinal chemistry, structural biology and systems biology (including genomics and proteomics) are being applied in the search for new solutions. A rational approach – as opposed to random, high-throughput approaches – is being followed to maximise outputs from available resources. This integrated approach allows CSIR scientists to identify and develop bio-active molecules and to identify their mode of action at a cellular level. Most recently the CSIR has established the capacity to deploy aptamer technology to the search for new therapeutics and to the continuing elucidation of the pathogenesis of these diseases.

South Africa has a relatively well established research capacity in the discovery of new molecules that may be developed into new drugs. A current bottleneck, however, is found in the drug development phase – and most particularly in the pre-clinical drug development stage. CSIR Biosciences is currently working with the Department of Science and Technology, BioPAD and research institutions in the country to assess the current, fragmented capacity in this area and to develop a route map towards building capacity that will expedite the development of new drugs and treatments from South African research and intellectual property.

Enquiries:

Dr Dusty Gardiner

Tel 011 605-2201

Email dgardiner@csir.co.za

Biosciences research re-engineered

By Dr Dalu Mancama

The shift from the single molecule paradigm to an approach characterised by large-scale profiling of living cells, is set to transform the future of biosciences research.

Systems biology is likely to benefit the sectors of drug discovery and development, crop transformation and enhancement, and bioprocessing and fermentation. These represent only the most obvious sectors where benefits from the emerging platform can be applied, and the CSIR is uniquely positioned to maximise the development of growing innovations born out of this technology.

But what is systems biology? Thanks to rapid developments in high-throughput technology, it is becoming possible to profile virtually any cellular system to determine the state of its genes, proteins, metabolites and related constituents. The ability to simultaneously measure all these quantifiable variables negates the prerequisite to develop a prior hypothesis of which constituents are likely to be related to a perturbation of interest. Instead, this new discovery-driven approach enables unbiased decisions to be reached regarding the effects of such phenomena on the entire system.

Systems biology is underpinned by several leading technology platforms that include transcriptomics, proteomics, metabolomics and bioinformatics.

Transcriptomics traditionally employs micro-array technology to exploit the unique hybridising characteristics of nucleic acids on a large scale. It aims to profile the entire set of genes expressed throughout an organism. Recent developments now extend the use of this technology to include identifying *in vivo* DNA sequences bound by transcription factors, and characterising intricate processes that occur at the gene level such as methylation and alternative splicing.

At the protein level, large-scale proteomics profiling is achieved through the mainstay technology of two-dimensional polyacrylamide gel electrophoresis. New applications such as 2-D fluorescence difference gel electrophoresis (2-D DIGE) allow this process to be undertaken simultaneously in different samples. At the same time, similar separation techniques based on liquid chromatography are becoming more commonplace. Coupled with mass spectrometry, these processes provide a powerful means of identifying proteins of interest within complex cellular mixtures.

The central focus of systems biology is the integration of the wealth of data generated from supporting parallel technologies and its interrogation through mathematical modelling and simulation to ultimately obtain the big picture

Metabolomics is the third major technology platform driving development towards large-scale molecular profiling. Using methods in gas and liquid chromatography that incorporate mass spectrometry, metabolomics elucidates the entire set of small molecules within a cell by quantifying the building blocks of anabolism, catabolism and secondary metabolism. Ever increasing demands for complementary technologies and higher resolving capability in this area have led to the more widespread use of nuclear magnetic resonance (NMR) and fourier transform infrared (FTIR) spectroscopy.

The central focus of systems biology is the integration of the wealth of data generated from these supporting parallel technologies and its interrogation through mathematical modelling and simulation to ultimately obtain the big picture - an *in silico* representation of the complexity of living systems. This level of integration and complex understanding is achieved through bioinformatics.

The recent establishment of a systems biology research platform within the CSIR makes it possible to use this emerging technology for developing innovative solutions throughout the biosciences sector.

Globally, the largest immediate beneficiary of the technology will be pharmaceuticals. In South Africa, the impact of systems biology will be felt most keenly in the development of indigenous chemical biodiversity for new drug development.

For centuries pharmaceuticals have remained among the most valuable products to be derived from plants. In the past, a predominantly reductionist approach was used to try to explain activity by studying the effects of plant-derived molecules on known targets. In the majority of cases, no single active compound has been found that sufficiently explains the observed clinical activity, particularly when the mode of action involves synergism, pro-drugs and extrinsic host responses that cannot readily be interpreted by conventional approaches.

In such multicomponent mixtures, systems biology becomes a powerful alternative to demonstrate efficacy by determining the global effects induced by these molecules on the host and identifying primary targets and underlying interactions that elicit drug efficacy.

The systems biology platform works closely with the CSIR's bioprospecting group to expedite the development of plant-derived pharmaceuticals. Current efforts focus on malaria, which remains the most important tropical infectious disease worldwide. Illness is mostly due to infection by *Plasmodium falciparum*.

The present array of drug targets used to treat this parasite represents a significantly small proportion of the enzymes and metabolic processes that could be exploited for the development of new therapeutics. At the same time, through mechanisms borne out of existing targets, the parasite has developed rapidly growing resistance to the current range of drugs available. Coupled with the relatively remote likelihood of attaining a cheap, effective vaccine solution in the near

future, this has led to an urgent need to develop novel drugs and to identify alternative targets that aid drug development.

Using a multidisciplinary approach, the systems biology platform provides innovative solutions to validating anti-malarial compounds derived from indigenous plants. In contrast to the conventional drug discovery paradigm where the approach is to isolate a pathway and target, and use this for drug screening; the systems biology approach studies many cellular pathways in the parasite at once.

Perturbing these pathways with the drug of interest and quantifying these changes provides a deeper insight into those molecular interactions relevant to drug action.

The approach also provides information on potential drug targets in the parasite that can subsequently be used for rational drug design and development. In this area, the platform works closely with synthetic and medicinal chemists in the CSIR's discovery chemistry group to guide the rational design and synthesis of improved anti-malarial leads based on synthetic and naturally-derived chemical scaffolds.

Agrobiotechnology is also expected to benefit from advances in systems biology in the near future. This expectation has initiated close collaborations with plant biotechnology to advance existing methods in crop improvement for nutrition and health. The technology is currently used to obtain a more comprehensive understanding of regionally-relevant crops – such as soya bean – and to develop new varieties that provide enhanced benefit and diet-related health advantages without compromising safety. Systems biology adds significant value to the development of novel plant-based expression systems for the production of therapeutic proteins and peptides, by elucidating key molecular components and interactions in these systems that can subsequently be modified to undertake the process more efficiently. Current application areas include the development of new preventative solutions against rabies infection.

Bioprocessing and expression systems represent further application areas where significant gains are expected in the near future through integrated research strategies that incorporate systems biology. The possibility now exists to comprehensively reveal the molecular functions and interactions that underlie microbial and yeast growth and survival. This has facilitated new opportunities and approaches to re-engineering these micro-organisms to enhance turnover during production.

Enquiries:

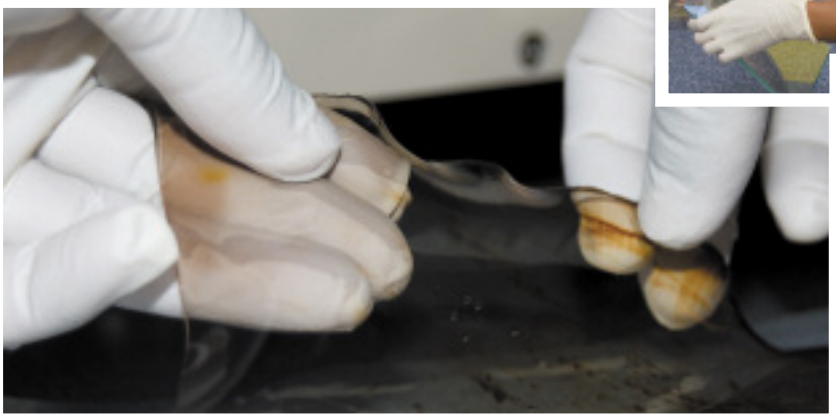
Dr Dalu Mancama

Tel 012 841-4533

Email dmancama@csir.co.za

Dr Dalu Mancama monitors the effect of anti-malarial drugs and drug leads on the morphology of the parasite

The primary focus for the Systems Biology group is to elucidate the mode of action for anti-malarial drugs. The main tool used is a 2-dimensional gel system. Here Dr Linda Mtwisha applies a sample on gel, using an isoelectric focusing system



The second step in the process of elucidating the mode of action for anti-malarial drugs involves imaging of the gel

Ancient knowledge meets modern science for medicinal purposes

By Dr Vinesh Maharaj

Dr Vinesh Maharaj leads the CSIR's bioprospecting research group

South Africa is blessed with a rich plant biodiversity of more than 24 000 indigenous plants, representing about 10% of all higher plants on earth. The country also boasts a long tradition of medicinal use of plants. In marrying this rich heritage with modern science, the scientific validation of traditional medicines is the focus of the bioprospecting research group

The search and sustainable use of chemical and genetic components of biodiversity and indigenous knowledge (IK) can lead to economic and social benefit for South Africa and the region.

The CSIR's bioprospecting group focuses on the transformation of African traditional medicines into minimally-processed, scientifically-validated herbal medicines; the discovery of new pharmaceutical active ingredients; and providing opportunities for establishing community-based agro-processing businesses for producing medicinal crops.

Pharmaceutical formulations, often based on new chemical entities that result from scientific research on traditional medicines, can be patented. Traditional healers currently provide CSIR scientists with IK to stimulate research that eventually allows the filing of patent applications. The right of the providers of IK to share in future financial benefits that might be derived from commercial exploitation of any such future patented inventions, is protected through a memorandum of understanding (September 1999) and a benefit sharing agreement (February 2003) signed between the CSIR and the Traditional Healers Committee.

The CSIR entered into a similar memorandum with the South African San Council during March 2002 and signed an agreement in March 2003.

These IK owners provided their knowledge exclusively to the CSIR because of the organisation's ability to add value through development of scientifically-validated products and to manage confidential information. This work includes the development of a specialised database to capture and safeguard IK of medicinal plant remedies. The collaboration involves the investigation of information on more than 250 claims for cures provided by traditional healers.

The group combines the efforts of a multidisciplinary team within the CSIR in as far as structural biology research identifies the mode of action of the traditional preparations, while medicinal chemists perform synthetic modifications to improve activity and chemical product and processing optimisation of herbal remedies.

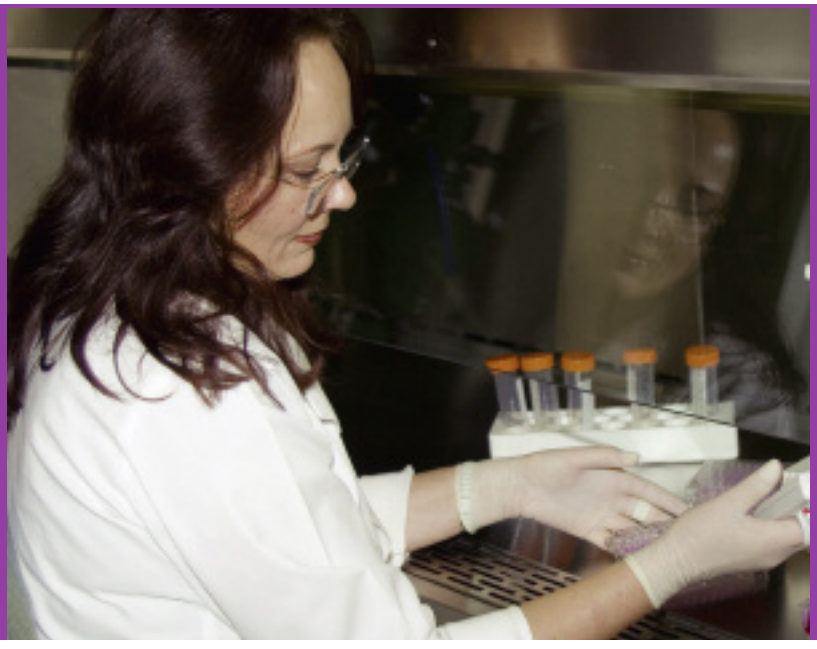
Collaborators include the South African National Biodiversity Institute (SANBI), the Medical Research Council, the University of Cape Town, the University of KwaZulu-Natal and the Traditional Healers Committee. International collaborators include the National Cancer Institute in the United States for research aimed at identifying new anti-cancer drugs, the University of Leuven in Belgium and the Esperenza Foundation in Switzerland for the discovery and development of plant-based treatments for HIV. The partnerships were formed between the various groups to harness the full scientific potential of the country in a coordinated and comprehensive investigation.

The CSIR's bioprospecting activities involve the screening of indigenous plants believed to display anti-cancer properties. The system used was adopted from the National Cancer Institute in the USA

In addition to laboratories dedicated to the isolation and characterisation of pharmacologically-active ingredients in medicinal plants, specialised facilities include Good Manufacturing Practice (GMP) processing facilities for the supply of plant extracts to be tested in clinical trials. The group provides research support to controlled horticulture of medicinal plants in support of its GMP processing facility and runs an information management system for capturing and safeguarding IK of traditional medicines.

Collection, extraction and screening of SA's indigenous plants

To date more than 11 000 indigenous plant species have been collected. SANBI conducts all botanical research on behalf of the CSIR and is responsible for keeping herbarium samples. At least 32 000 corresponding extracts of the collected plants have been prepared, using approved extraction protocols, and are stored in



cold rooms. The repository of extracts serves as an asset to the organisation and allows for the early biological screening in drug discovery based on plants without having to embark on extensive plant collection trips and extraction.

Scientific validation of medicinal properties

The design of experimental protocols aimed at finding scientific evidence of efficacy starts with the method of preparation and administration of medicines used by traditional healers. Extensive interaction with the traditional healers is undertaken to understand the disease being treated and to identify the therapeutic concept.

The CSIR's bioprospecting team has captured more than 250 claims for cures based on medicinal plants and completed desktop and literature studies on at least 50% of these to determine what research is already in the public domain, establishing the therapeutic area and identifying possible biological assays.

At least 72 claims for cures were identified for which the therapeutic concepts were established for different diseases e.g. asthma, arthritis, malaria and HIV. Samples for at least 32 claims were tested for efficacy in suitable biological assays; 15 of these demonstrated positive results and are being developed further.

Scientific evidence of the efficacy of these traditional claims provides data for the process required for further development into validated herbal treatments or prescription drugs.

The 17 claims that did not give a positive result in the chosen biological assays cannot be ruled out as alternative biological assays need to be sought and the possibility of novel mechanisms of action investigated. This supports the holistic approach to testing traditional medicines rather than a reductionist one. Currently, 15 leads are in development for therapeutic areas including mosquito repellency, asthma and allergies, arthritis, anti-inflammatory, wound healing, benign prostatic hyperplasia, malaria, HIV, cancer and erectile dysfunction/libido.

One of the leads being developed is BP4, a novel herbal extract for long-term management of asthma and allergies. The traditional use of the plant is for the treatment of mild asthma, colds, influenza and sinus problems. Literature studies on the specific plant provided anecdotal information but little scientifically-evaluated biological data. Biological assaying of extracts of the plant and a purified non-steroidal metabolite demonstrated efficacy in assays implicated in the asthmatic disease. These included glucocorticoid receptor binding, 5-lipoxygenase and phosphodiesterase-4 inhibition and down regulation of nuclear factor- Kβ. *In vivo* biological assaying of the herbal extract in asthmatic rats demonstrated moderate activity in reducing broncho-constriction, while significantly reducing the pro-inflammatory and inflammatory mediators such as the cytokine Interleukin-8 (IL-8) responsible for the inflammatory pathway. The results have pointed to the mode of action through which this traditional remedy acts and are the first scientific evidence that validates the traditional use of the plant for the treatment of asthma.

BP16, a novel herbal extract for the treatment of inflammation and arthritis, is based on a medicinal plant used for the treatment of this disease. *In vivo* studies of the herbal extract have shown significant reduction in inflammation in arthritic rats, and for the first time demonstrated scientific evidence validating the traditional use of the plant.

Lavendar is known to have medicinal properties. Essential oil extracted from lavendar reportedly has antiseptic and anti-inflammatory properties

Two lead compounds have been isolated and identified from medicinal plants that are traditionally used for the treatment of malaria. The compounds have shown significant anti-plasmodial activity in *in vitro* assays for both the chloroquine sensitive and resistant strains of *Plasmodium falciparum*. These are currently undergoing pre-clinical studies as part of their further development.

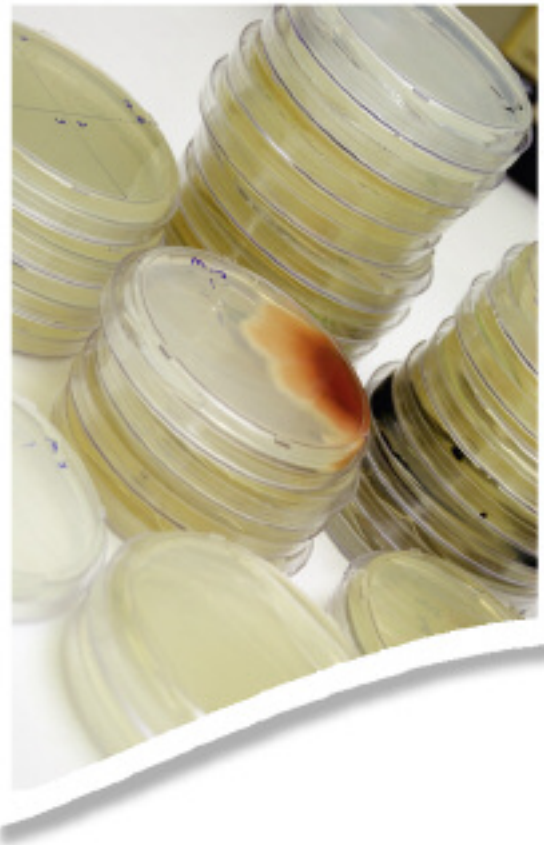
Three herbal remedies based on the traditional use of plants for the treatment of HIV-infected patients - for which the dosage forms have been manufactured in the clinical supplies unit in compliance with GMP - have shown significant anti-viral activity with limited toxicity in an HIV cytoprotection assay conducted both in the United States and in South Africa. These herbal treatments are entering pre-clinical development.

A natural anti-obesity agent based on the Hoodia plant developed by bioprospecting scientists promises to become the first major registered product based on a plant indigenous to the African continent.

The research programme that led to this potential product started at the CSIR in 1963, and today includes major multinational pharmaceutical companies, farmers and communities. An analysis of the key innovative steps in the research programme illustrates the value of combining modern science and ancient knowledge of the use of South Africa's rich biodiversity. Hoodia illustrates the potential of bioprospecting to produce significant economic and social benefits for a nation. The project has led to the creation and protection of intellectual property, licencing to commercial partners and a benefit-sharing agreement with the San, custodians of related indigenous knowledge.

Enquiries:
Dr Vinesh Maharaj
Tel 012 841-3295
Email vmaharaj@csir.co.za

By Dr Colin Kenyon



Identifying novel mechanisms in the fight against diseases of the developing world

A multidisciplinary CSIR research team is involved in a number of projects that use rational drug design techniques for the design and synthesis of molecules for the regulation of specific enzyme reactions. Novel enzyme mechanisms identified may be targeted for combating diseases of the developing world, with the focus on tuberculosis (TB), HIV/Aids and malaria. The research team comprises biochemists, microbiologists, molecular geneticists, organic chemists and clinical biochemists.

Using enzymes and bacteria, for the development of new drugs for treating tuberculosis, HIV/Aids and malaria, are (from left) Dr Robyn Roth, Dr Colin Kenyon and Lyndon Oldfield.

The CSIR's structural biology group has been involved in the clarification of the reaction mechanisms used by the enzyme glutamine synthetase (GS) for a number of years. GS is a central enzyme involved in nitrogen metabolism and catalyses the reversible conversion of L-glutamate, ATP and ammonia into L-glutamine, ADP, and inorganic phosphate. Three distinct forms of GS occur, with GSI found only in bacteria (eubacteria) and archaea (archaebacteria). GSII occurs only in eukaryotes (higher organisms) and GSIII genes have been found only in a few bacterial species.

Two significant bacterial GSI sub-divisions exist: GSI-α and GSI-β. Included in the organisms that have a GSI-β, is the TB-causing organism *Mycobacterium tuberculosis*. The GSI-β enzyme is regulated via a complex adenylylation/deadenylylation cascade.

Work carried out at the CSIR has demonstrated that the adenylylated form of GS enzymes from the GS1-β sub-group, including *Escherichia coli* and *M. tuberculosis*, possesses a novel reaction mechanism for the phosphorylation of glutamate. One of the primary outcomes of this project was the successful demonstration of the selective inhibition of adenylylated GS. In addition, it was demonstrated that the compounds capable of inhibiting adenylylated GS from *E. coli* were also capable of inhibiting the adenylylated form of GS from *M. tuberculosis*. A project has been undertaken in collaboration with Professor Guy Dodson and Dr Lesley Haire of the National Institute of Medical Research (NIMR) in Mill Hill, London, to elucidate the structure of *M. tuberculosis* GS by X-ray crystallography.

In conjunction with Professor Paul van Helden of Medical Research, a number of these adenylylated GS inhibitors have also been found to inhibit the growth of *M. tuberculosis*. This work now forms part of an extended project done in conjunction with the EU 6th Framework New Drugs for Tuberculosis project.

In another collaborative project, the CSIR works with the University of Pretoria, the South African Malaria Initiative and the WISDOM initiative to combine this enzyme-related research with bioinformatics for potential malaria targets.

With regard to HIV/Aids, the CSIR participates in a project with the NIMR and the Great Ormond Street Hospital for Children, University College London, to investigate the role that certain structural motifs of the gp41 surface protein of the HIV virus may play in the apoptosis of CD4 cells.

The immunodeficiency that defines Aids is primarily due to the progressive decline in the number and function of CD4 cells. A number of mechanisms that cause this decline have been investigated and demonstrated. Direct viral destruction of the CD4 cells is not regarded as contributing significantly to the decline in the number of these cells. There are increasing data that, within HIV-infected individuals, the depletion of CD4 cells is secondary to HIV-mediated enhanced lymphocyte apoptosis. The induction of apoptosis by the HIV envelope protein gp120 in CD4 cells has also been demonstrated.

A project is currently being undertaken by the CSIR in conjunction with Professor Guy Dodson and Dr Rod Daniels (NIMR) and Dr Hugh Brady, the Great Ormond Street Hospital for Children, University College London, to investigate the role that certain structural motifs of the gp41 surface protein of the HIV virus may play in the apoptosis of CD4 cells.

Enquiries:
Dr Colin Kenyon
Tel: 011 605-2702
Email: ckenyon@csir.co.za

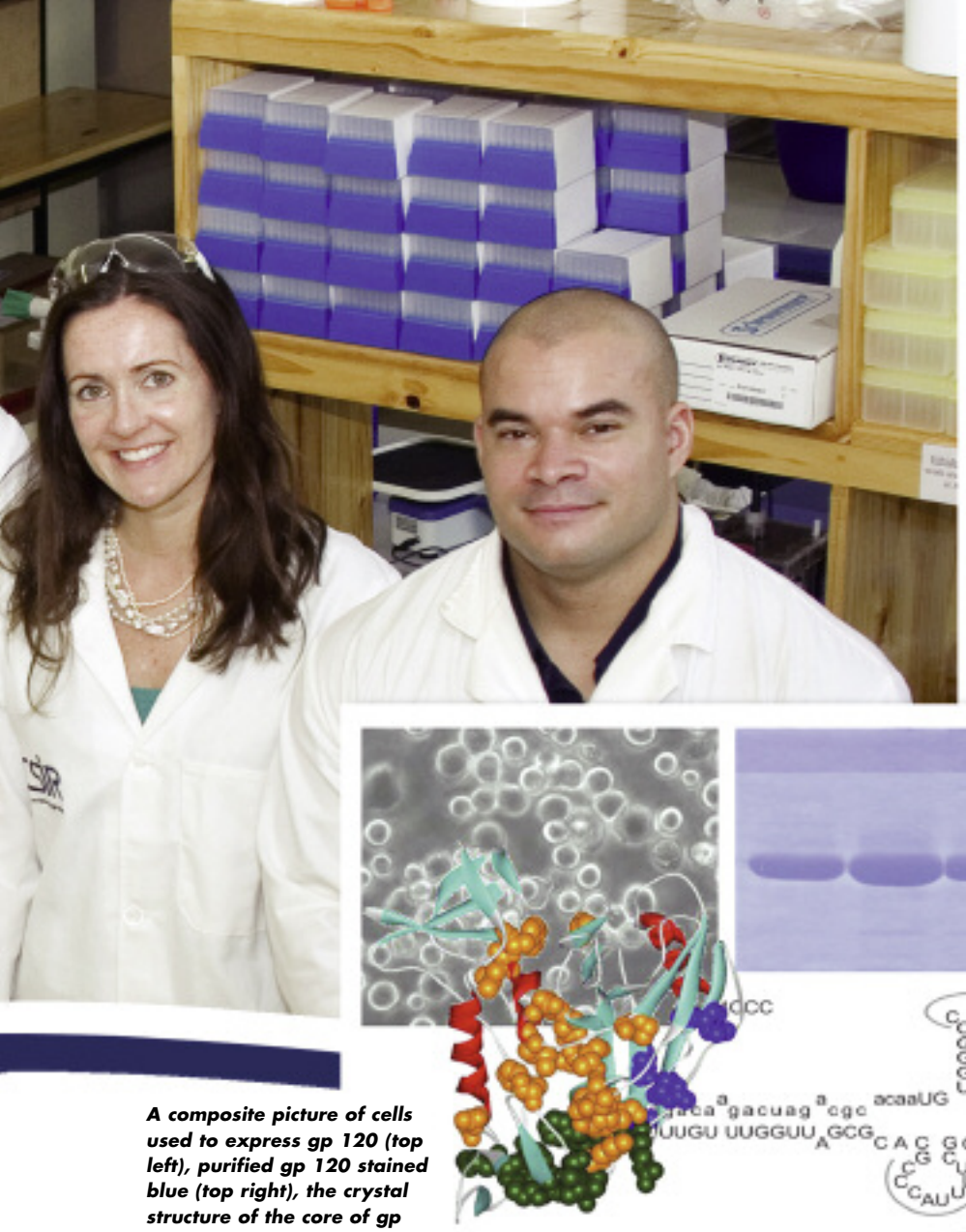
The CSIR's Aptamer research team. Front: Godfrey Sithole, Dayaneethie Coopusamy. Back, left: Dr Jabulani Nhlapo, Hazel Mufhandu, Dr Makobetsa Khati, Dr Marisa Baron and Walter Campos

Aptamers: a new approach to therapeutics and diagnostics

By Dr Makobetsa Khati, Dr Marisa Baron and Dr Jabulani Nhlapo

A new, powerful tool to study, treat and diagnose diseases in the 21st century has emerged in recent years, called aptamer technology. From the Greek word "to fit", aptamers are artificial nucleic acid molecules (RNA or DNA) that are engineered in a test tube for specific binding to various targets such as small molecules, cancer cells, viral and bacterial proteins and whole micro-organisms such as protozoan parasites that cause diseases such as African sleeping sickness or malaria.

Aptamers are emerging as a class of molecules that rival antibodies in both therapeutic and diagnostic applications and they have applications in target validation and drug discovery. The CSIR has a dedicated aptamer research group that investigates biomedical systems and the molecular basis of diseases to provide cutting-edge solutions to major public health problems of our generation, such as HIV/Aids and tuberculosis (TB). The CSIR's research aim in this regard is to bring the people of South Africa, and the continent, improved tools for diagnosis, treatment and prevention of diseases endemic to Africa.



A composite picture of cells used to express gp 120 (top left), purified gp 120 stained blue (top right), the crystal structure of the core of gp 120 [3-4] (bottom left) and the secondary structure of an RNA aptamer that binds and inhibits the function of gp 120 (bottom right). HIV gp 120 plays a vital role in HIV infection and progression to Aids, making it a desirable target in efforts to prevent and treat the disease. Neutralising antibodies bind the green, orange and blue residues on gp 120, which also happen to be specific targets of aptamers.

Aptamers as potential HIV/Aids prophylactics and therapeutics

HIV infection and its associated disease – Aids – remain significant health problems globally. In South Africa alone, a staggering 5,5 million people are estimated to be infected with HIV, over 300 000 of whom die every year, making HIV/Aids the leading cause of morbidity and mortality in South Africa. The epidemic has attained a scale at which the impact on the economy and, even more broadly, on our society, is evident and serious. Over the past 25 years, enormous efforts have been directed at HIV/Aids research – and yet a vaccine has still not been found.

The majority of research to date has focused on approaches such as cellular-based immunity and antibody technology, all promising ideas that have not yet come to fruition. Another challenge is that while current antiretroviral drugs have improved the quality of life of many HIV-positive people, they do not prevent viral infection because they act once the virus has infected target cells. Furthermore, the rapid emergence of drug-resistant HIV strains, side-effects due to toxicity of the drugs and associated costs of treatment with current antiretroviral drugs, mean that the search for alternative new antiretroviral drugs and anti-infectious agents is as pressing as ever. Recently, scientists have turned their attention to the earliest stage of HIV infection – viral entry. This stage of viral pathogenesis is largely attributed to gp120, a virion surface glycoprotein that mediates fusion of the viral membrane with the host plasma membrane to allow viral entry into the host cell.

A CSIR scientist isolated and identified a set of novel RNA aptamers against HIV gp 120 while at the University of Oxford[1], which is one of the CSIR's collaborating institutions. These aptamers against gp 120 were shown to potently inhibit viral entry and hence infectivity of diverse clinical isolates of HIV[2]. To further this research, the CSIR is testing aptamers in blocking entry and infectivity of several endemic South African clinical isolates of HIV from adults and paediatric patients at different stages of the disease. In addition, a structural-based research approach is investigated to elucidate the specific inter-action between gp120 and the aptamers that interrupt its function. This structural information is vital for understanding the mechanism of viral infection and pathogenesis. The results of the research will be used to decipher the molecular explanation of binding of aptamers to gp120 and thus the detailed mechanisms underlying their inhibition of HIV infectivity. Detailed structural information can then be used to design highly efficacious prophylactic drugs that will prevent HIV infection and also new therapeutic drugs that will be combined with existing drugs to treat already infected HIV/Aids patients. This will help maximise suppression of the virus.

Aptamers as rapid and reliable TB diagnostics

The HIV/Aids problem is intrinsically linked to and complicated by TB and poor TB diagnostic tools in general. Diagnosing active TB is a challenge, especially in HIV-positive people. Despite the enormous burden of TB, conventional approaches to diagnosis used today continue to rely on tests that have major drawbacks. Many of these are slow and lack both specificity

Dr Makobetsa Khati leads the CSIR's aptamer technology research group

and sensitivity. For example, sputum smear microscopy is insensitive; the culture method is technically complex and slow; chest radiography is non-specific; and the tuberculin skin test is imprecise and the results non-specific. Clearly the TB diagnostic, especially in the light of the HIV epidemic, needs to be improved. A rapid, more sensitive and specific diagnostic assay needs to be developed because the most powerful tool in any TB control programme is prompt and accurate diagnosis. For this reason, CSIR researchers also focus on exploiting aptamers and their favourable properties to develop rapid and reliable TB diagnostics.

Advantages of aptamers over conventional diagnostics and therapeutics

Aptamers have many advantages over conventional approaches, including the relatively simple techniques and equipment required for their isolation, their chemical simplicity and the large number of combinatorial molecules (up to 10^{15}) that can be screened *en masse*. The molecular recognition properties of aptamers are very similar to antibodies, which recognise a target with high affinity and specificity and in many cases effectively inhibit its function. However, unlike antibodies, aptamers can even discriminate between very subtle structural differences, such as the presence or absence of a hydroxyl group or enantiomers (molecules that have an identical chemical composition but are mirror images of one another). Aptamers also offer other advantages as they can be engineered completely in a test tube, are readily produced by chemical synthesis, elicit no immune response, are not toxic in therapeutic applications and possess desirable storage properties – ideal for resource-poor settings such as many parts of South Africa and the rest of the continent.

Therapeutic aptamers are chemically robust, intrinsically adapted to regain activity following exposure to heat and denaturations, and can be stored for extended periods of more than one year at room temperature as lyophilised powders, which can be readily reconstituted. In addition, due to their small size, aptamers can fit into clefts where bulky molecules such as antibodies would otherwise be excluded. Aptamers can also be modified easily to increase their survival in a biological environment. Unlike therapeutic organic molecules, aptamer flexibility allows them to mold and assume the shape of the binding pocket, thereby maximising surface contact with the target protein.

RNA aptamers against extracellular targets such as those against gp120 can be administered intravenously or subcutaneously. The simplicity of this approach is one of its main advantages because pharmacokinetic studies in humans confirm that RNA molecules delivered by these routes are readily distributed throughout the body and are easily taken up by cells. Another advantage of aptamers, especially as anti-HIV drugs, is that they can be delivered topically to defined anatomical locations such as the vaginal mucosa, to prevent infection. Research is ongoing to express aptamers in cells for delivery which, if successful, will continuously produce the aptamer and conceptually provide a single dose, yet life-long treatment[5]. This aptamer-based innovation could provide another milestone in anti-HIV drug development and delivery, especially from an efficiency and cost-effectiveness perspective.

Key References

1. Khati, M. (2002). Macrophage-HIV interactions: aptamers against gp120 surface envelope glycoprotein of the macrophage tropic strains of HIV-1. *Sir William Dunn School of Pathology*. University of Oxford. **D.Phil Thesis:** 1-237.
2. Khati, M., M. Schuman, et al. (2003). Neutralization of infectivity of diverse R5 clinical isolates of human immunodeficiency virus type 1 by gp120-binding 2'F-RNA aptamers. *J Virol* **77**(23): 12692-8.
3. Kwong, P. D., R. Wyatt, et al. (1998). Structure of an HIV gp120 envelope glycoprotein in complex with the CD4 receptor and a neutralizing human antibody." *Nature* **393**(6686): 648-59.
4. Wyatt, R., Kwong, P. D., Desjardins, E., Sweet, R. W., Robinson, J., Hendrickson, W. A., and Sodroski, J. G. (1998). The antigenic structure of the HIV gp120 envelope glycoprotein [see comments]. *Nature* **393**(6686), 705-11.
5. Bunka, D. H. and P. G. Stockley (2006). Aptamers come of age - at last. *Nat Rev Microbiol* **4**(8): 588-96.

Enquiries:

Dr Makobetsa Khati

Tel 012 841-4770

Email mkhati@csir.co.za

Medicinal chemistry – the missing link

By Dr Chris Parkinson

A robotic synthesiser used in discovery chemistry and in the preparation of analogues to improve activity of the primary compound

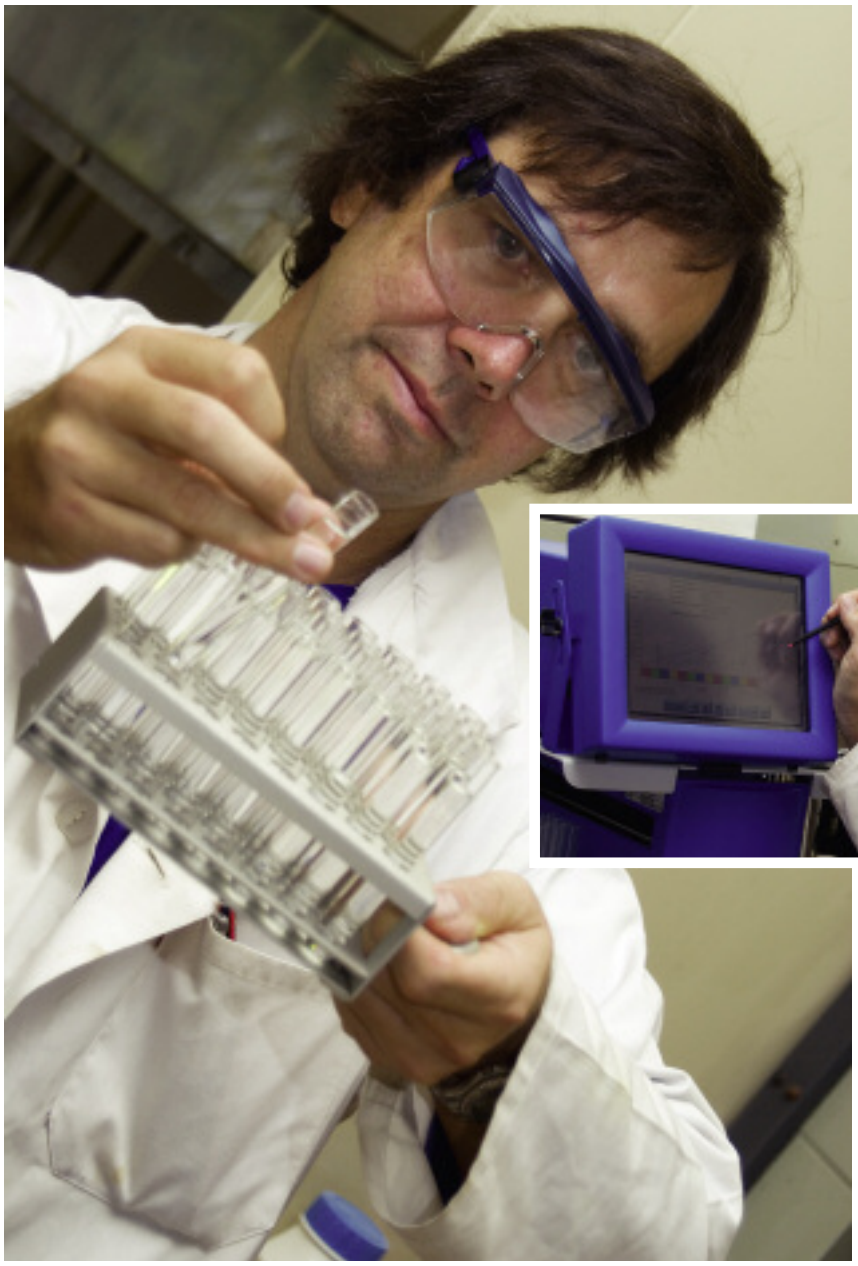
The South African situation is unique when it comes to the discovery of pharmaceuticals or drugs. The region has 12-18% of the world's plant species spread across widely-varied climatic zones, while also having a rich history of traditional medicine.

Although many clinical trials, particularly in the late phase, have been carried out in the region, these have not led to new chemical entities (or active plant metabolites) discovered within the borders, progressing to the point of adoption for development or registration as pharmaceutical agents.

Much of the weakness in the development pipeline appears to be the generation of viable "leads" for pre-clinical development. While many pharmaceutical agents can trace their origins to natural products, less than 10% of agents are the parent natural product. The reasons for this are often undesirable toxicity profile, lack of bio-availability or even insufficient potency of the parent species. All of these aspects must be addressed before a species that is interesting in the laboratory is of interest in the clinic.

It is in this role that medicinal chemists ply their trade.

Medicinal chemistry differs from the classical science in that the researcher seeks to generate properties in a molecule rather than simply synthesising the molecular structure. As such, the science involves synthesis of new structures, examination of



potential interactions with proteins or other targets and assessment of adsorption, distribution, metabolism, excretion (ADME) and potential toxicity in the human body.

Currently, the CSIR focuses on developing new chemotherapeutic agents that may be the drugs of the future in the area of neglected diseases. The therapeutic domains subject to active investigation are tuberculosis (a bacterial disease), HIV (viral) and malarial (protozoal). Due to the highest incidence of these diseases being in developing countries, they are often referred to as the "diseases of poverty" and consequently receive less attention than warranted from the pharmaceutical industry.

Projects at the CSIR include the application of protein kinase inhibitors as agents against tuberculosis, the design of folate antagonists active against the malaria parasite, agents that inhibit reverse transcriptase in HIV, agents active against HIV protease and peroxide antimalarials.

Many of the lead chemical structures are sourced as plant metabolites derived from South African biodiversity. The rationale behind this approach is that plant metabolites have been made by enzymatic synthesis – the result being that these species are designed in such a manner as to interact with enzymes. Consequently, there is a higher probability that a natural product will exhibit biological activity – becoming a useful lead compound in the discovery process.

From the point of discovery of the lead and determining the nature of the biological target, the chemist then attempts to modify, or where possible simplify, the parent structure to ensure that it can accumulate in the correct tissue types in the body, bind more tightly with the target enzyme (often assisted by computational studies), bind less well to similar targets, survive the oxidase enzymes in the liver, and is sufficiently reactive to eventually be metabolised and excreted by the body.

A nuclear magnetic resonance (NMR) spectrometre used in the characterisation and identification of molecular structures

Dr Chris Parkinson

Medicinal chemists have various tools at their disposal: a computational design facility through which interactions between small molecules and proteins can be predicted and visualised; parallel synthesis and robotic synthesis facilities for preparing several variants of a target structure at the same time; automated parallel column chromatography where purity is essential to prevent false positive results; and the more classical synthetic chemistry laboratories. The identity of the molecular species prepared is confirmed through the use of nuclear magnetic resonance spectroscopy (NMR) and mass spectrometry (MS) techniques.

The CSIR's discovery chemistry group collaborates with many researchers employed in other disciplines of the biological and life sciences to progress the goals of generating new small molecule therapeutics.

Enquiries:
Dr Chris Parkinson
Tel 011 605-2601
Email cparkinson@csir.co.za

Product and process innovation

Building the biotechnology industry: an introduction

By Dr Dusty Gardiner

South Africa's National Biotechnology Strategy clearly agrees with the National System of Innovation: innovation is imperative to effect growth. The Department of Science and Technology is the key driver of this strategy, and has secured a significant and growing investment in biotechnology. Biotechnology holds significant promise for South Africa and while this investment is beginning to bear fruit with the creation of new biotechnology SMEs, the sector remains small.

The CSIR has built the capacity to take a lead in developing a national biotechnology industry in partnership with the public and private sectors. The organisation's strategy is clearly aligned with the National Biotechnology Strategy, with a core component focused on innovation to bridge the divide between fundamental research and commercial exploitation. Research activities are focused on creating novel and highly competitive technologies and products that can be developed in South Africa through new start-up ventures or in partnership with existing enterprises.

These technologies are geared to underpin the competitiveness of new biotechnology enterprises, while the products synthesised or produced aim to provide affordable, yet lucrative, solutions to key local challenges

and opportunities. The health sector, in particular, is an area of focus.

The CSIR has been involved in the research and development of novel, "green" technologies that exploit biological mechanisms for synthesis of pharmaceutical ingredients and actives for some time.

A start-up enterprise, Oxyrane, is exploiting novel epoxide hydrolase enzyme technologies. These technologies allow for cheaper synthesis of pharmaceutical chemicals. The CSIR created another start-up company, Arvir, in partnership with LIFE*lab,* to exploit new technologies for biocatalytic synthesis of antiretroviral drugs.

Novel yeast and plant-based expression systems for production of therapeutic proteins are being researched and significant progress is being made towards development of cost-effective production systems.

New bacterial peptide production systems allowing cheaper methods of producing peptide therapeutics are also under development. These technologies will be engineered to allow for production of the new generation biopharmaceuticals that are being developed in the fight against diseases. The new start-up company, Mbuyu Biotech, is exploiting these microbial expression systems. Mbuyu Biotech, created in partnership with BioPAD, includes enzyme self-immobilisation technologies in its intellectual property (IP) portfolio. The immobilisation technologies allow expensive enzymes to be recycled and re-used, and in many instances confer stability to labile enzymes. This technology is currently used in the development of enzyme-mediated processes for the synthesis of pharmaceuticals with other health-related applications at an earlier stage of development. Patents protect all these technologies and provide a key competitive edge to the start-up enterprises created to exploit opportunities.

Integration of scientific disciplines provides a fertile breeding ground for discovery and innovation. The multidisciplinary research approach adopted by CSIR Biosciences challenges scientists to explore and adopt new skills and approaches in their research. A renewed focus on building the scientific capacity of the organisation and instilling a culture of scientific research are now paying dividends. A growing IP portfolio is being exploited through new start-up enterprises, while the CSIR and its scientists are increasingly invited to join international research consortia. In the area of technology and product innovation, invitations include several from European Commission-funded projects such as Pharmaplanta (plant-made pharmaceuticals), NovelQ (novel protein films or coatings) and EMPRO (peptide-based microbicides).

Local partnerships remain important and in the biosciences domain the CSIR collaborates with most local universities and research organisations to optimise the impact of the National System of Innovation in South Africa.

Enquiries:
Dr Dusty Gardiner
Tel 011 605-2201
Email dgardiner@csir.co.za

The Cashew plant is native to north-eastern Brazil, but was spread to other areas of the world by the Portuguese. India, Vietnam and Brazil are the largest growers of the cashew kernel dubbed the "true fruit". The top juicy "pseudo fruit" – the cashew apple – is acidic and used in the production of condiments and beverages

The CSIR has established a pilot plant in rural Manguzi (Kosi Bay), KwaZulu-Natal, where biotechnology is applied to add value to the ilala (palm fruit), marula and cashew apple fruit. Job creation and technology transfer are spin-offs from this project

Biotechnology at work for value addition to raw products: the Kosi Bay cashew apple

By Raj Lalloo and Kgaladi Thema

The Manguzi (Maputaland) area of the north-east coast of South Africa is a rural, impoverished region. This despite being richly endowed with natural resources: the lush plant growth testifies to a high annual rainfall and warm weather throughout the year. The area boasts an abundant supply of natural palm (Ilala), marula and cashew apple – all ingredients with significant potential in the food and beverage domains.

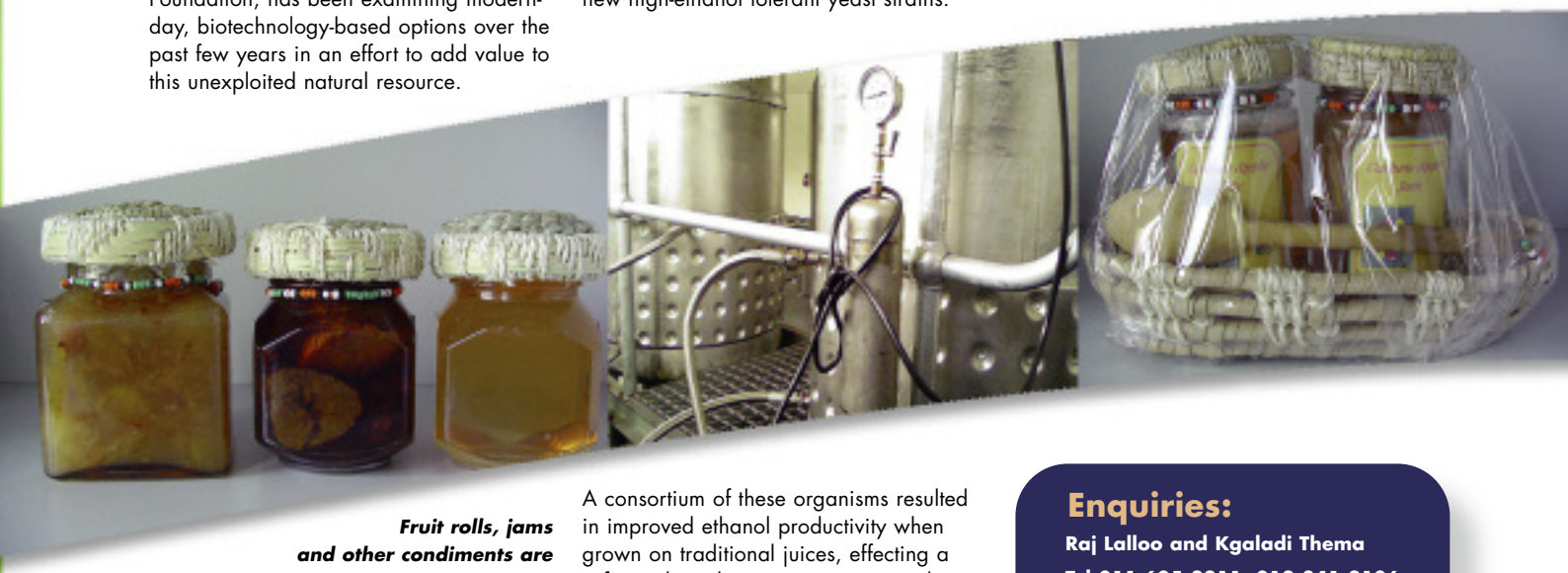
A community-based cashew orchard of 650 hectares is one of the economic pivots in Manguzi. Cashew trees are grown mostly in tropical climates for its cashew nuts, while the tree also carries an accessory fruit, the cashew apple. Cashew apples are usually discarded after the cashew nut harvest.

The CSIR, in partnership with the Maputaland Development and Information Centre (MDIC), the Department of Science and Technology (DST) and the Kellogg Foundation, has been examining modern-day, biotechnology-based options over the past few years in an effort to add value to this unexploited natural resource.

Based on traditional knowledge of indigenous foods and beverages resident in the local community, CSIR food and bioprocessing scientists have developed new and innovative processes for the competitive production of a host of fruit pulp-based products and indigenous alcoholic beverages destined for speciality niche markets. The product range includes dried fruit, jams, fruit juices, spirit coolers and liqueurs. The product needs of the local community were also taken into account and the quality, safety and stability of the indigenous brewed products were improved.

Technology challenges included the requirement for unique media formulations, clarification of the fermented broths and appropriate stabilisation protocols to improve the shelf life and quality of the products.

The project required fermentation process development that led to the isolation of new high-ethanol tolerant yeast strains.



Fruit rolls, jams and other condiments are manufactured at a factory in Manguzi that was established by the CSIR and its partners

A consortium of these organisms resulted in improved ethanol productivity when grown on traditional juices, effecting a safer end product in comparison to the classical uncontrolled fermentation process. CSIR scientists designed, installed and commissioned a fully functional pilot plant, equipped with oven driers, state-of-the-art fermentors, a fruit processing machine, a fruit pulp pasteuriser and juice processor in Manguzi – operated exclusively by members of the community.

Special plant design and implementation expertise was required to overcome the unique challenges of implementing this technology in a region where infrastructure and utility supply are limited. Further expansion of the pilot-scale technology and replication of this type of installation in other parts of Africa will result in job creation and an improved quality of life.

The project included the development of human capacity in biotechnology through studentships at the CSIR and training of people from the community. The project is at the technology validation and finalisation stage, with product prototypes imminent.

Enquiries:
Raj Lalloo and Kgaladi Thema
Tel 011 605-2211; 012 841-2106
Email rlalloo@csir.co.za
kthema@csir.co.za

Combination HIV/Aids treatment strategy brings hope

By Dr Moira Bode

CSIR researchers are using biocatalysis – in which enzymes, nature's own catalysts, perform chemical transformations on organic compounds – to decrease the costs of manufacturing generic antiretrovirals.

Researcher Justice Rashamuse conducting a polymerase chain reaction which is then inserted into a micro-centrifuge for purification

LIFE*lab*, the East Coast Biotechnology Innovation Centre, aims to be a leader in the development of world-class biotechnology innovations, with a special focus on health care and bio-processing.

LIFE*lab* provides venture capital funding to projects that enhance the quality of life of all South Africans through the development of innovative, cost-effective and appropriate health care solutions for key infectious diseases, such as tuberculosis, malaria and HIV/Aids.

A number of antiretroviral drugs have been approved for clinical use in the treatment of HIV/Aids. These drugs fall into different classes, based on their biological target.

To date the approved therapies include nucleoside reverse transcriptase inhibitors (NRTIs); non-nucleoside reverse transcriptase inhibitors (NNRTIs), both acting against the viral enzyme reverse transcriptase; protease inhibitors, acting against the viral enzyme protease; and an entry inhibitor that inhibits fusion of the virus to the mammalian cellular target.

Successful treatment regimens generally comprise a combination of a number of drugs from different classes. This combination strategy, known as HAART (highly active antiretroviral therapy), minimises the risk of resistance to any one of the drugs being developed by the virus. Full compliance to the dosing regimen by the person living with HIV/Aids is also an extremely important factor in minimising resistance. If resistance should develop to a drug combination, or if the particular drug combination causes serious side-effects in a particular individual, then another combination treatment option is chosen.

In South Africa the first-line treatment regimen usually includes a combination of two NRTIs (often stavudine and lamivudine) and one NNRTI (efavirenz or nevirapine). Second-line treatment generally includes two NRTIs (for example AZT or didanosine) and protease inhibitors (such as ritonavir, lopinavir or saquinavir).
Drug resistance in certain cases or the development of serious side-effects in some people can generally be overcome by switching treatment regimens. HAART dramatically improves the quality of life of people living with HIV/Aids, greatly increases their life expectancy and in most cases allows them to lead normal lives.
It is therefore imperative that this treatment be available to all who require it.
One of the factors that contributes to the availability of these drugs is their cost. Cheaper antiretroviral compounds would allow more people to be treated within a given government budget.

A few years ago the CSIR initiated a project to examine ways of reducing the manufacturing costs of generic antiretrovirals. This project currently focuses on reducing the cost of preparing NRTIs by using a biocatalytic step, i.e. where enzymes catalyse a reaction, for preparation of one of the important intermediates in the preparation of drugs such as stavudine and AZT. The biocatalytic step uses two enzymes to convert an inexpensive, relatively abundant nucleoside into a high-value nucleoside, which is used as an intermediate in antiretroviral production.

A nucleoside is a compound that comprises two parts, a sugar portion and a base portion. The first enzyme uncouples the sugar and base and the second enzyme recouples the newly-released sugar to a different base, in this way converting a low-value into a high-value product.
This work is carried out under the auspices of Arvir Technologies (Pty) Ltd, a private start-up biotechnology enterprise, of which the CSIR and LIFE*lab* are equal shareholders. In South Africa the number of people requiring antiretroviral drugs is estimated at more than 500 000.

Economies of scale come into play, making the local manufacturing of these drugs an imperative. One of the major aims of the CSIR's work is to contribute towards this goal.

Enquiries:
Dr Moira Bode
Tel 011 605-2791
Email mbode@csir.co.za

Dr Rachel Chikwamba and the plant biotechnology research team at the CSIR have secured resources from the Department of Science and Technology (DST) to support a plant-based platform for the production of health molecules in plants. Tobacco plants, like this one, are key expression hosts for molecules used to fight transmission of HIV

NOVEL BIOREACTORS: plants and cells as sources of valuable health molecules

By Dr Rachel Chikwamba

Plants are the most efficient producers of proteins on earth. They are similar to human cells and yeasts in many ways – they have similar protein synthesis machinery, they read the same genetic code and they can assemble, fold and secrete complex proteins.

Advances in molecular biology and genetics have created the possibility of using plants as vehicles for producing therapeutics, vaccines, food additives or other valuable products. There are several perceived advantages of using plants as sources of health molecules, including potentially lower production costs, as plants are relatively easy and cheap to grow, and offers the feasibility of large-scale protein production without the immense capital investment required for setting up conventional systems.

Scale-up technology is available for harvesting and processing of plants or plant products on a large scale, even in developing countries. Large amounts of protein that are required for various oral and topical applications can therefore be produced cheaply. This is important in improving the affordability of health care.

Plant products are free of mammalian pathogens such as those associated with manufacture in mammalian cell cultures, or endotoxins associated with expression of health molecules in bacterial fermentation systems. Plant products are thus potentially safer. With such potential benefits, this technology could empower developing countries, making feasible the

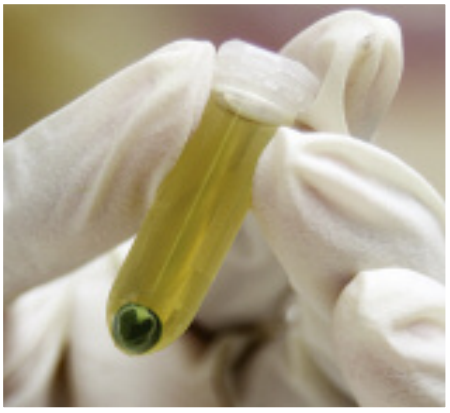
possibility of producing medicines locally, controlling costs and distribution and making health care more affordable.

Functional proteins for use in vaccination, disease diagnostics and therapy for cancers and various immune disorders have already been generated in plants, and the forerunners have progressed to the last stages of human clinical trials.

The CSIR is one of the pioneering local organisations in the establishment of this technology in South Africa. It has selected socially-relevant target molecules including anti-HIV antibodies and anti-HIV peptides, for use in passive immunisation and as microbicides, respectively, for the control of HIV infection. Microbicides are molecules that prevent sexual transmission of HIV through mucosal surfaces during intercourse. The CSIR is also exploring the expression of subunit vaccine candidates against HIV by expressing pieces of the HIV gp120 molecule.

Tobacco is used as a key expression host for these molecules – it is selected as host because it has several unique advantages, including well-established technology for gene transfer and expression, and high biomass yield (up to 100 000 kg/ha). Among the leafy plants, tobacco is the leading host globally used as a host system for biopharmaceutical production. The process entails the introduction of genes encoding the target molecules into plants or plant cells. The plants are then grown to generate bulk biomass expressing these molecules. Fresh leaves are harvested, immediately processed, and crushed in suitable buffering solutions to protect the molecules from degradation by plant enzymes once the tissue is disrupted. The product is then purified away from the "green juice" through a series of steps that removes undesirable compounds such as nicotine, phenolic and various other contaminating plant compounds. After this, the product is concentrated and formulated in a form appropriate for further drug development.

CSIR researchers also explore the production of health molecules in other plants, including maize, which has numerous advantages as a production host. Advantages include that seeds are specialised as protein accumulating organs allowing for long-term storage of final products; drying of grain concentrates the product and because maize is not toxic, protein extraction and purification should be simpler than in tobacco. However, as a staple food crop, the use of maize has biosafety concerns that reduce its attractiveness as a production host.



Advancement in molecular biology and genetics has made it possible to use plants as biological factories for producing therapeutics, vaccines, food additives and other valuable products. Here a tobacco plant is crushed and purified for further drug development

To lead the way with this technology, the CSIR has partnered with world-class institutions in technology development. By collaborating with laboratories in Europe and the United States, the CSIR has access to cutting edge technologies in the identification of lead molecules, expression in plant systems, extraction, purification and formulation of target molecules. These partnerships also provide access to animal and human tissue testing models that are essential for determining safety and efficacy of candidate health molecules. Some of these global partnerships include Pharmaplanta, a European Commission-funded project within the European Union's Sixth Framework Programme (FP6).

This is an initiative involving 39 European research institutes and companies and the CSIR, which works on plant expressed clinical grade pharmaceuticals against various diseases, including HIV and rabies. Another such initiative involving the CSIR, is the European Microbicides Consortium (EMPRO), a research network that investigates and develops new microbicides for the prevention of HIV infection. This initiative is also funded by the European Union.

The CSIR has secured resources from the Department of Science and Technology (DST) to support a plant-based platform for the production of health molecules in plants. The expected outcome of the DST-funded initiative is not only the establishment of technical aspects of health molecule production, but also to work closely with biosafety and drug development authorities in developing policies for regulating the production and use of such molecules. Built into this project is the inclusion of other South African research institutes. To date, the CSIR has participated in the South African Aids Vaccine Initiative (SAAVI), led by the University of Cape Town. In this project, the CSIR produces adjuvants (molecules that make vaccines more potent) and vaccine candidate molecules. The CSIR is also working on establishing collaboration in this field with local partners such as the University of Pretoria, the University of Cape Town and Stellenbosch University.

A major component of this project is human capacity development. It is expected that during the execution of this project, students and scientists at various levels (from BSc to PhD) will be afforded study and training opportunities. At CSIR Biosciences, two PhD candidates – Nosisa Dube and Therese Lotter – and an MSc candidate – Patricia Mathabe – are furthering their studies through this project.

Enquiries:
Dr Rachel Chikwamba
Tel 012 841-2177
Email rchikwamba@csir.co.za

Engineering bacterial cell surfaces for new biotechnology applications

By Dr Maureen Louw

A recent discovery of biology is that peptides of interest can be expressed as fusions to proteins and displayed on the outside of the bacterial cell wall, giving rise to an expression system with many biotechnological and medical applications. An example of this technology is called cell surface display, where the peptide or protein of interest is the passenger protein, which attaches itself to the bacterial cell wall using an anchoring motif as its carrier. In this way the protein of interest is exposed to the outside of the bacterial cell.

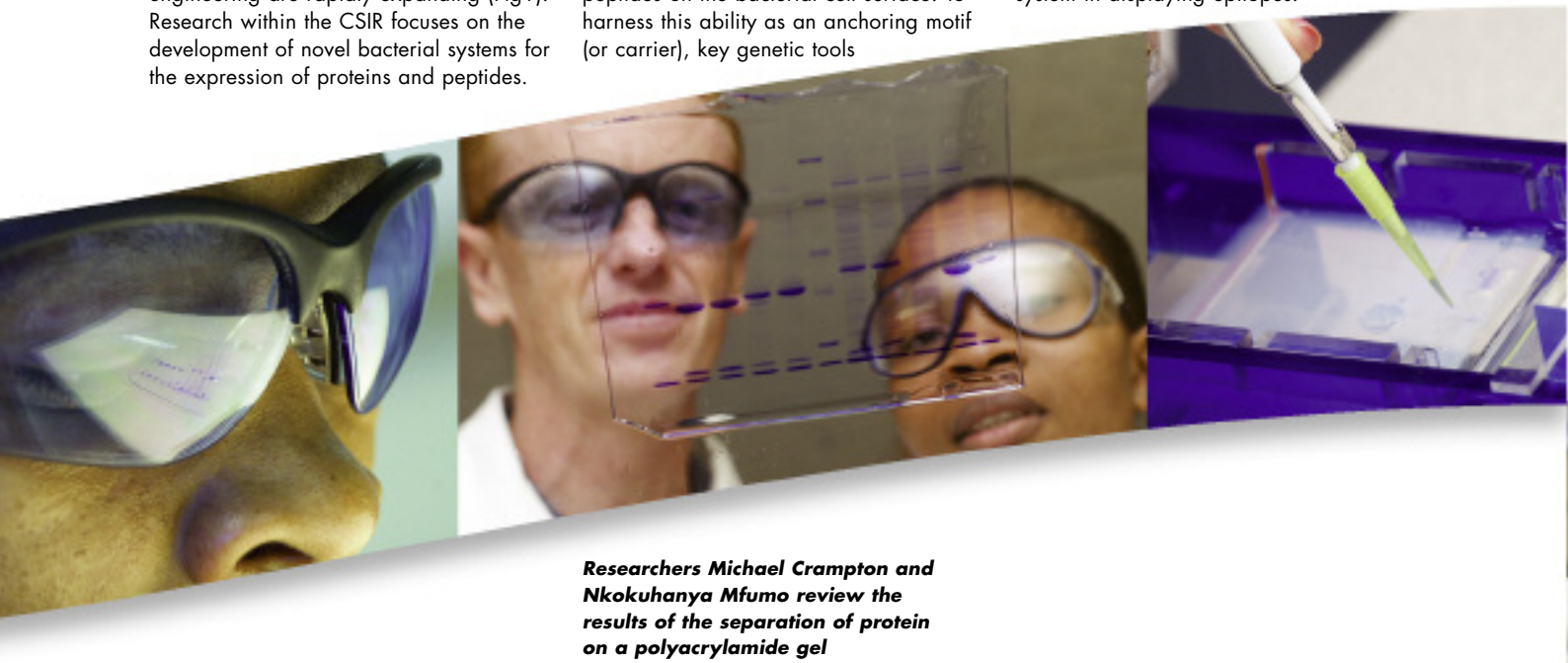
To do this, gene fusions have to be constructed to the gene encoding the surface localised carrier protein of choice. The concept of using naturally occurring surface proteins as a mechanism for targeting foreign molecules to bacterial surfaces has resulted in a broad range of biotechnology applications. Gram positive bacteria are potentially attractive candidates because of their robustness due to the thick cell wall surrounding the cells and lack of an outer membrane.

The opportunities afforded by cell surface engineering are rapidly expanding (Fig1). Research within the CSIR focuses on the development of novel bacterial systems for the expression of proteins and peptides.

The current thrust of research is on the development of a strain of the bacterium *Bacillus halodurans* for the surface display of gene products. This bacterium is able to grow over a wide pH and temperature range and continuously over-produces flagellin.

As each bacterial flagella may be made up of approximately 20 000 flagellin monomers which join together to form functional flagella, this system would enable the highly efficient immobilisation of a significant number of heterologous peptides on the bacterial cell surface. To harness this ability as an anchoring motif (or carrier), key genetic tools such as gene targeted inactivation were developed for this strain. Peptides encoding a poly-histidine peptide and the HIV-1 subtype C gp120 epitope were respectively incorporated into the flagella as in-frame fusions. (An epitope is a site on a large molecule against which an antibody will be produced and to which it will bind.)

These peptides were chosen to evaluate the potential of the strain as a bio-adsorbent in binding metals such as copper and Ni^{2+} as well as a vaccine delivery system in displaying epitopes.



Researchers Michael Crampton and Nkokuhanya Mfumo review the results of the separation of protein on a polyacrylamide gel

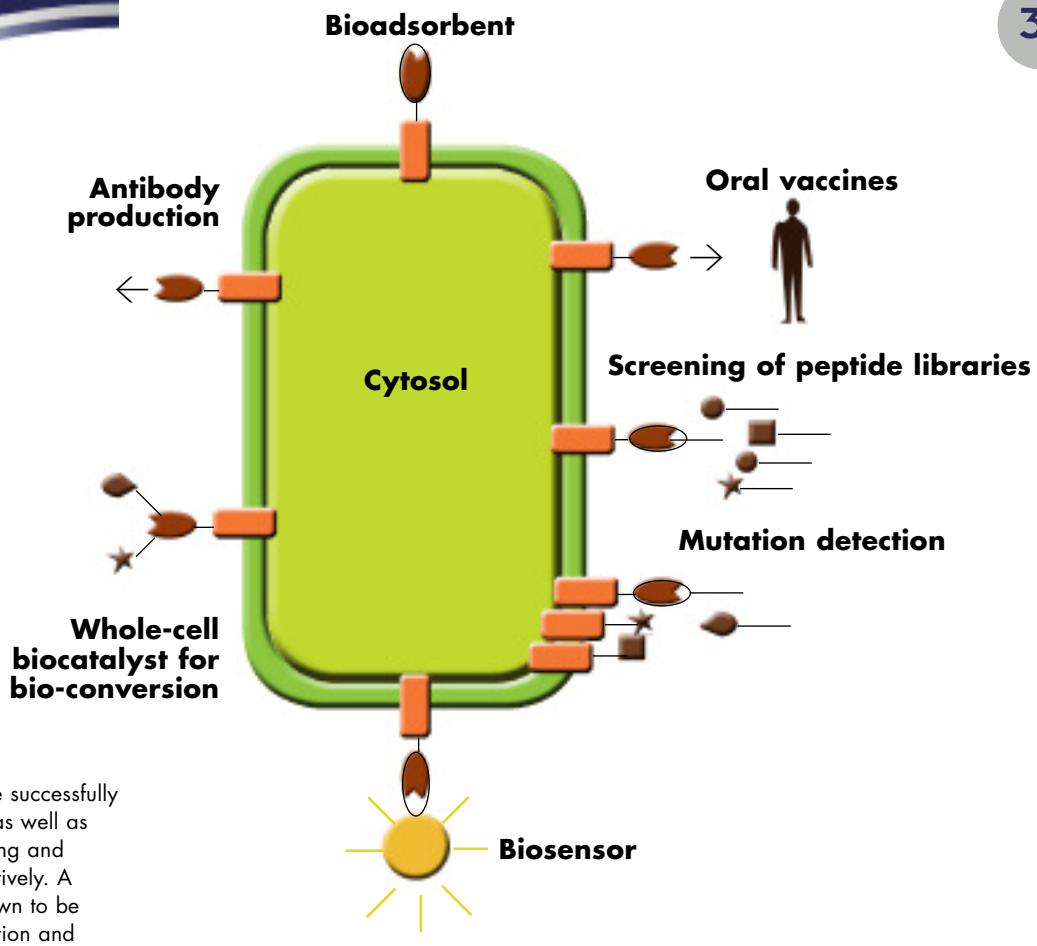


Figure 1
The diagram illustrates examples of surface displayed proteins/ peptides and possible application areas for such recombinant bacteria

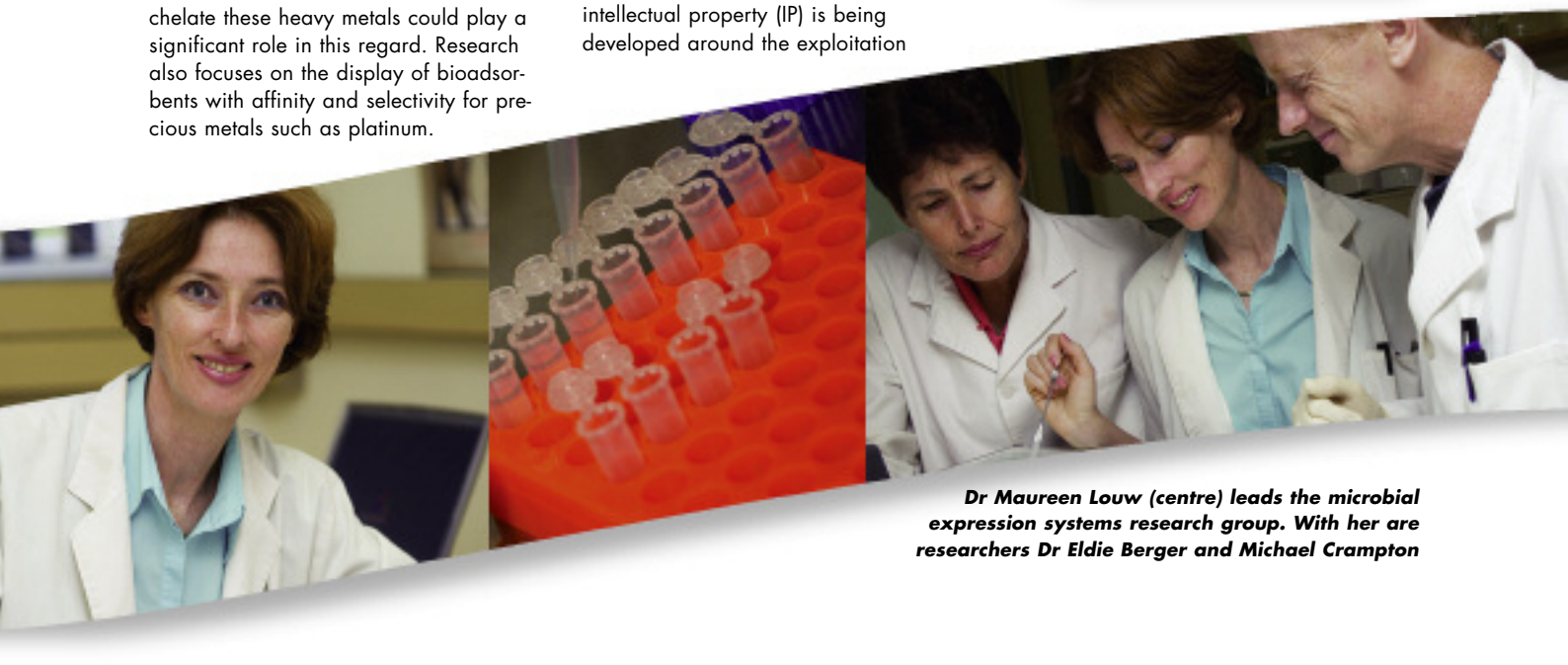
The peptides were found to be successfully displayed on the cell surface as well as functional through metal binding and immunological studies, respectively. A lipase-flagellin fusion was shown to be expressed in the cell wall fraction and enzyme activity confirmed through whole cell bio-assays.

These results are encouraging, as bacteria displaying heterologous enzymes on their surface hold great potential as inexpensive whole cell biocatalysts. The discharge of heavy metals from agricultural and industrial processes has serious adverse effects on the environment and conventional technologies are often inadequate to reduce heavy metal concentrations in wastewater to acceptable regulatory standards. Metal binding peptides displayed on the bacterial cell surface able to chelate these heavy metals could play a significant role in this regard. Research also focuses on the display of bioadsorbents with affinity and selectivity for precious metals such as platinum.

Flagella are potent immunogens and numerous reports show that immunisation with purified hybrid flagella induces cellular and humoral responses in laboratory animals against the chimeric flagellin epitope of choice. The combination of flagella to act as an effective adjuvant and the potential for large scale chimeric flagellin over-production make this a potentially attractive candidate as a vaccine delivery system.

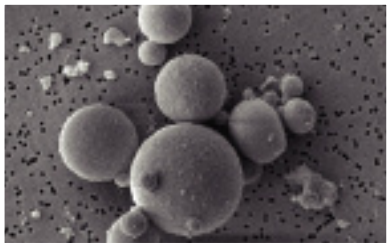
This research is currently being supported by Mbuyu Biotech (Pty) Ltd, a CSIR/BioPAD joint initiative. Significant intellectual property (IP) is being developed around the exploitation of various applications arising from this system and future focus will be on extending, and exploiting the IP portfolio associated with this system.

Enquiries:
Dr Maureen Louw
Tel 012 841-2167
Email melouw@csir.co.za



Dr Maureen Louw (centre) leads the microbial expression systems research group. With her are researchers Dr Eldie Berger and Michael Crampton

Dr Justin Jordaan (right) and Dr Dean Brady have collaborated with colleagues in materials sciences to develop a proprietary enzyme self-immobilisation technology



SphereZymes™: a proprietary protein immobilisation technology

By Dr Justin Jordaan

Enzymes are biological catalysts that offer several advantages over current chemical synthesis methods for the generation of chemicals. Enzymes are of specific importance for their chiral and regio-specificity, properties often not offered by chemical reaction equivalents and of particular importance to the pharmaceutical industry. This reduces unwanted side reactions with a concomitant reduction in waste products when using them for catalysis, termed biocatalysis.

However, these advantages offered by biocatalysts are often hindered by their relative cost as compared to current chemical catalysts. Their immobilisation is of particular interest as it facilitates recovery and recycling. Furthermore, immobilisation stabilises enzymes, making them more amenable to operate in unnatural environments, such as in solvents and at high temperatures – process conditions often required for chemical production.

To meet these challenges, the CSIR's enzyme technologies group and its research colleagues active in polymers, composites and ceramics, have developed a proprietary enzyme self-immobilisation technology. The technology takes advantage of size control offered by emulsification, orientation of molecules at interfaces and high volumetric activities to provide one of the most versatile immobilisation technologies currently available.

Enzyme particles are generated by linking the enzyme units together while in the form of stabilised emulsion droplets. Stabilisation is attained through the formation of chemical covalent linkages between the proteins, brought about by treatment with chemicals having at least two reactive groups. The particles are easily recovered by filtration or centrifugation. The stabilisation is often performed in the presence of a chemical protectant suitable to the enzyme that acts to protect the catalytic site of enzyme during the immobilisation process. The resulting product is spherical immobilised enzyme particles exhibiting a narrow, defined size distribution combined with high volumetric activity and most pertinently, exceptionally good enzyme activity maintenance. These factors contribute to the success of SphereZymes™ as one of the most versatile enzyme immobilisation technologies.

Previous technologies often resulted in the loss of a large proportion of the enzyme activity. In alternative technologies where enzymes are linked to a support or backbone, they exhibit low volumetric activity and low activity recovery and are unaffordable for large-scale applications.

Several advancements have been made while developing this technology, most notably the ability to improve access for substrates to the enzymes catalytic region. This results in doubling of the enzyme activity through the immobilisation process.

Based on these exciting advances, commercial exploitation of the first generation of this technology is being pursued by Mbuyu Biotech (Pty) Ltd, a joint initiative between the CSIR and BioPAD, a biotechnology regional innovation centre.

Enquiries:
Dr Justin Jordaan
Tel 011 605-2739
Email jjordaan@csir.co.za

Dr Corinda Erasmus with Hendrik Nkwana, a technician at CSIR Biosciences, administering a dosage of the soya-derived trial fish food at the fish-feeding pilot plant

International research efforts to reduce food processing waste

By Dr Corinda Erasmus

The CSIR participates in a collaborative research project that looks at the development of novel hybrid processing methods to deconstruct co-products from the food processing industry and then process these into defined and marketable product streams. Bioprocesses are at the centre of these studies.

A group of scientists from 13 internationally acclaimed research institutions from 10 countries has joined forces on this food quality and safety project, awarded by the European Commission under the Sixth Framework Programme. South Africa is the only third world country in this consortium, while the project is being led by Dr Keith Waldron of the Institute of Food Research (IFR) based in Norwich, UK. Work on this project started in February 2005.

Brewers' spent grain and cabbage trimmings

Methods to upgrade waste products are generally poorly addressed and manufacturers do not have many options from which to choose. This results in large quantities of food processing wastes being discarded and used for landfill, or as bulking products with a very low value.

Two waste streams have been selected for this project namely vegetable trimmings – particularly cabbage trimmings – and brewers' spent grain. The grain, produced from the beer brewing industry, consists of the barley husks, protein and fat after the starch is removed during the malting and fermentation stage.

With beer production being such a large industry, spent grain has become one of the biggest sources of food processing wastes in Europe and South Africa.

Brewers' spent grain has a relatively poor energy value and also a low protein value (usually only about 21% protein), making it unsuitable as a food adjunct. Its high fibre content aggravates the situation as food processing wastes are generally high fibre wastes, which consequently flood the market with unwanted fibrous compounds. The nature of the fibre does not lend itself for use in textile or other non-food applications.

New methods for utilising these selected co-products focus largely on integrated procedures for ensuring microbiological safety, stability and traceability, accompanied by the development of tailored bioprocesses for precisely extracting and modifying these waste co-products or components. The new processes are then integrated with advanced extraction, filtration and drying technologies.

New aquaculture feeds

Exploiting the new technologies depends largely on maximising the technological feasibility, economic viability and environmental safety and risk analyses. The CSIR's contribution focuses primarily on the use of some of these new materials in the formulation of new aquaculture feeds, targeting various finfish species. Worldwide, pressure exists to reduce the dependency on fragile natural resources, specifically on the use of marine fish as a source of animal feeds. To produce

farmed fish, for example salmon, protein and highly unsaturated fatty acid sources are needed, which are obtained mostly from fish meal. It is estimated that up to 4 kg of fish-based ingredients are needed to produce 1 kg of farmed fish – an unsustainable situation. There is pressure to replace fish meal, typically used in fish feed formulations, with plant-based ingredients. Plant-based proteins can be used successfully in new feed formulations, but the highly unsaturated fatty acids are found only in marine animal species, and to a limited extent in land-based microbial (fungal) species adapted to very cold climates (Alpine environments). These fungi have developed the ability to produce highly unsaturated fatty acids to prevent solidifying of their cell membranes, especially when having to survive in snow-covered habitats. The unsaturated fatty acids typically include eicosapentaenoic acid and docosahexaenoic acid. Both these highly unsaturated fatty acids are also essential in human nutrition, with specific roles in the cognitive development of young children.

The CSIR is conducting trials of its novel fish meal under controlled conditions on the Mozambique tilapia, an edible fish species endemic to south-eastern Africa

Growing fungi for new fish feed

The CSIR's task in this international project – called REPRO – is to evaluate the production of highly unsaturated fatty acids (specifically targeting Eicosapentaenoic acid) by growing oil-producing fungi of the *Mortierella* species on barley spent grain and spent grain derivatives, for inclusion in novel fish feeds. A second task is to produce a high-protein spent grain stream by incorporating new processing technologies developed by other partners. The CSIR is also responsible for manufacturing prototype fish feeds from these ingredients and compare its nutritional value with existing fish-meal based feeds. Fish feed formulations are developed to be species specific and are tested at facilities in Pretoria and Cape Town. A sensory evaluation of fish flesh targeting the restaurant market will be conducted to compare the flesh quality of fish fed on the newly-developed feed ingredients to fish-meal based fed fish. Specific methods have been developed for the scaled-up production of the fungal material and problem areas for further scale-up have been identified. The specific fungal material has been shown to be non-toxic and is certified for use in human and weaning food applications, thereby making the fish flesh safe for human consumption. Fungi tested were also obtained from South Africa's rich natural environment, specifically the Drakensberg. Various product prototypes are been manufactured and evaluated for suitability as fish feed, and for product stability.

Mortierella growing on brewers' spent grain

Enquiries:
Dr Corinda Erasmus
Tel 012 841-2163
Email cerasmus@csir.co.za

Ensuring biodiesel is green

By Colin Everson

Scientists have shown that over the past century, sea levels have risen by between 10 and 20 cm, ocean heat content has increased, snow cover and ice extent have decreased and the global average surface temperature has increased by about 0,6 °C. It is generally agreed that the 1990s was the warmest decade, and 2006 the warmest year in a millennium. Thus the arguments around the existence of global warming have been settled by science, and the debate is now about how far the effects of global warming will go. Increased levels of CO_2, coupled with ever increasing oil prices, have led to international concern about the global impacts of greenhouse gases and the worldwide consumption of fossil fuels (oil, gas and coal). Some 85% of the world's energy comes from fossil fuels that emit CO_2. Consequently, many countries are considering the possibility of the large-scale production and use of biofuels – such as bio-ethanol and biodiesel – as alternatives to conventional fossil fuels. The Kyoto Protocol commits most industrialised countries to reduce their greenhouse gas emissions by 5% below their 1990 levels, by 2012. The South African White Paper for Renewable Energy Policy gives a 10-year target for replacement of 14% of fossil fuel-based energy sources by renewable energy, such as from biomass. This is equivalent to replacing 1,1 billion litres of diesel (14%) with biodiesel.

Considering the wide range of scientific disciplines effecting energy and climate change, it is not surprising that CSIR scientists are increasingly involved in research on resolving the energy crisis and global climate change.

Optimistic prospects – Colin Everson and Mark Gush of the CSIR inspecting a Jatropha curcas plant. Research is underway to establish whether to use the plant in the large-scale production of biofuels

Biodiesel: the impact on South Africa's scarce water resources

By Colin Everson and Mark Gush

The proposed introduction of bio-energy species for large-scale planting and biofuel production can help reduce net greenhouse gas emissions. *Jatropha curcas* has attracted international and local interest as a drought tolerant, fast growing, bio-energy crop. Other advantages attributed to this species are that it tolerates marginal soils and is unpalatable to livestock, reputedly making it suitable for restoration of degraded land. The South African government has received numerous requests for permission to plant *Jatropha*, but the impacts on hydrology, food security, poverty relief and biodiversity conservation are currently unknown. These uncertainties require clarification through a combination of process-based field measurements and modelling exercises.

The ecophysiology group of the CSIR in Pietermaritzburg forms part of a team tasked by the Water Research Commission to conduct a study into the potential hydrological impacts associated with the large-scale planting of *Jatropha*. The CSIR's task is to conduct studies of *Jatropha's* water use at several sites in KwaZulu-Natal, using site water balance modelling and evapotranspiration measurements. The combination of a *Jatropha* tree and an animal grazing system is suggested to provide flexibility in the cash flow of this agroforestry system, making it more economically viable and sustainable. The possibility for poverty relief through the production of biodiesel is a key driving force in attracting investment by the various provinces in South Africa. These projects aim to contribute to a broader assessment of the species, investigating the feasibility, viability and advisability of the wide-scale introduction of *Jatropha curcas* to South Africa.

Enquiries:

Colin Everson
and Mark Gush
Email ceverson@csir.co.za
mgush@csir.co.za
Tel 033 260-6195
033 260-5783

Biofuel: a solution, or a socio-economic and environmental disaster in the making?

By Graham von Maltitz

Interest in plant-based fuels is skyrocketing all around the world, but the conversion of large areas of land to energy crops raises many social and environmental issues, not all of which are bad. There is, for example, the potential for competition between biofuels and food production from limited arable land; loss of biodiversity if new land is planted; loss of access to alternate natural products; gains of some jobs, but potential losses in others.

Biofuel production from annual crops is being promoted by South Africa's draft Biofuels Industry Strategy as a way to revitalise rural areas, especially in the former homelands. Some bio-energy projects probably have this potential, but others have disadvantages that outweigh their benefits. Some may even make climate change worse rather than better. How are policymakers, developers and energy entrepreneurs to sort the good from the bad in an efficient, but reliable way?

The CSIR is a partner in a large international project (RE-Impact) to develop and test a framework for weighing up the societal costs and benefits of individual bio-energy initiatives. The CSIR's contribution is to adapt the well-regarded South African environmental impact procedures (including the strategic environmental assessment framework developed by the CSIR) to this specific task. The streamlined process will then be field-tested in five environmentally and socially diverse regions around the world, including southern Africa, and modified if necessary. The intended outcome is an agreed methodology that will meet international standards while protecting local livelihoods and environments. The project is funded by the European Union.

Keeping an eye on issues. Graham von Maltitz and the rest of the RE-Impact project will determine the long-term effects of the production of large-scale plant-based fuels

Enquiries:
Graham von Maltitz
Email gvmalt@csir.co.za
Tel 012 841-3640

Mechanisms of photosynthesis may provide solutions to energy crisis

By Dr Raymond Sparrow

The most abundant and environmentally friendly energy source is solar energy. A considerable amount of research exists into the use of solar energy for a variety of applications, mostly in the area of photovoltaic devices, using inorganic materials. With these kinds of systems and materials, the efficiencies are often very low (less than 10%). However, as in many other instances, nature has developed her own solar energy trapping and conversion system, called photosynthesis. Research into this area is therefore of crucial importance, not only from basic scientific interest but also for all our lives, in providing for our future energy needs in an environmentally friendly manner.

Photosynthesis is the fundamental biological process through which ecosystems capture energy from the sun, on which almost all life is dependent. The very initial photochemical reactions of photosynthesis are 95-98% efficient at trapping radiant energy and transporting it to initiate photosynthetic electron transfer. However, once the energy has passed through the enzyme reactions and has been converted to plant biomass, and the biomass to useable energy for humans, the efficiency drops to 1-2%.

A CSIR research project looks at using these very efficient light harvesting and energy transfer processes and materials that are found in higher plants and photosynthetic bacteria, as light (energy) harvesting and energy transfer systems to power and control bio-molecular nanomachines. This marriage of nature and technology, if successful, could help us create a more sustainable future.

The CSIR's Dr Raymond Sparrow focuses on harvesting light from the sun to power and control biomolecular nanomachines

Enquiries:
Dr Raymond Sparrow
Email rsparrow@csir.co.za
Tel 012 841-3741

Adding value to biodiesel by-products

By Dr Corinda Erasmus

Biodiesel is a fatty acid ester derived from fats and oils obtained from biological material. One of the major sources of biodiesel is oils produced from oilseeds such as soya bean and sunflower. The CSIR is conducting an extensive research programme in partnership with the Department of Science and Technology to develop new processes and applications for the soya oilcake – a high-protein by-product stream produced after removal of the oil. The by-product stream typically comprises 60-80% of the total weight of an oilseed, thereby making its sales value critical to ensure the economic viability of such processing plants. Novel applications include the development of new biomaterials; replacement of fish meal in animal feeds; human food applications; use as a fermentation substrate to produce novel products; and the production of oilcake products with low levels of anti-nutrients. Future work will look at expansion into the by-product streams from other feedstocks, such as other kinds of oilseeds and other systems, such as algae.

Food scientist Dr Corinda Erasmus with a De Smet pilot-scale screw press used to extract oil from soya beans. The oil is used to produce biodiesel while the by-products are processed to develop alternative animal feed

Algal biodiesel

By Dheepak Ramduth

A wide range of algae has been shown to produce lipids from solar energy, CO_2 and an appropriate water source such as wastewater. The lipids are stored in lipid vesicles as energy reserves and can comprise up to 60% of the dry weight of the algal cell. The CSIR, in partnership with the Durban University of Technology, does research on the production of biodiesel from algae as a potential alternative energy source for Africa. The project integrates bioremediation possibilities by examining the sequestration of harmful flue gases and the usage of domestic and industrial wastewater as nutrient sources. Researchers have isolated some 3 000 strains of *oleaginous* algae and some of the best strains are undergoing evaluation. Several indigenous isolates capable of hyper producing lipids are also being developed. Research is ongoing to develop novel processes that integrate solutions to national priorities, such as alternative energy, reducing environmental impact and job creation while simultaneously exploiting the ideal environmental and solar radiation advantages of South Africa's climate.

Lipid producing algal culture Cyclotella cryptica

Enquiries:
Dr Corinda Erasmus
Tel 012 841-2163
Email cerasmus@csir.co.za

Adding value to resources

Processes to add value to South African natural resources: an introduction

By Morewane Mampuru, Raj Lalloo and Dr Jozef Dudas

South Africa has an immense wealth of biodiversity and natural resources. Sustainable exploitation of these natural resources through appropriate technology interventions has promise for social and economic growth and can contribute to job creation, skills development and, in some cases, the survival of poor rural households.

Previously, natural products have been harvested for subsistence purposes as direct inputs into rural households, or offered for sale and often exported without appropriate local value addition. The value addition to natural resource products empowers previously marginalised rural communities and makes it easier for them to participate in the market as a means to cope with economic hardship. In some instances in South Africa, trading in natural resource products may be one of the few accessible local income-generating options available to the rural poor, women in particular. High levels of unemployment, a shrinking job market and a scarcity of arable land have driven many households in rural areas to seek alternative means of meeting their livelihood requirements. The appropriate technologies to ensure suitable processes for the production of competitive products from natural resources are however, lacking.

The CSIR, in partnership with the Department of Science and Technology and other funding organisations, has developed some process technologies linked to the South African natural resource endowment in an effort to boost the commercial potential of these resources through value addition and technology transfer.

High on the list of process technologies developed are promotion and commercialisation of indigenous foods, mopani processing beneficiation, traditional fermented beverages, cashew apple processing and producing agave fructans.

Through biotechnology-based interventions, the possibility of commercialisation of natural resource products is increasingly being realised. Government has also introduced intervention programmes primarily targeted at addressing socio-economic challenges.

Indigenous aloes: more than just bitter succulents

Aloe is a succulent plant with many species indigenous to South Africa. Products from aloe have been used in traditional medicine for centuries in the treatment of constipation, burns and skin disorders. In modern therapeutic applications aloe gel is used as an anti-inflammatory, anti-ulcer, anti-diabetic and antioxidant. Aloe products are also used extensively in the cosmetic and health-food industries. The main species of aloe used domestically in pharmaceutical, therapeutic, dermatological or cosmetic applications are obtained from wild harvested Aloe ferox (A. ferox), a species restricted to southern Africa.

By Raj Lalloo and Dr Ingrid Weinert

The products currently manufactured in South Africa and derived from *A. ferox* are based on harvesting of leaves by tapper communities and the supply of either the bitter sap or crystalline bitters to traders. Only some 1% of all harvested leaves are collected and processed. Most of the processing methods employed are fairly harsh, resulting in a change in bio-active composition and consequent uncertainty about product quality and efficacy.

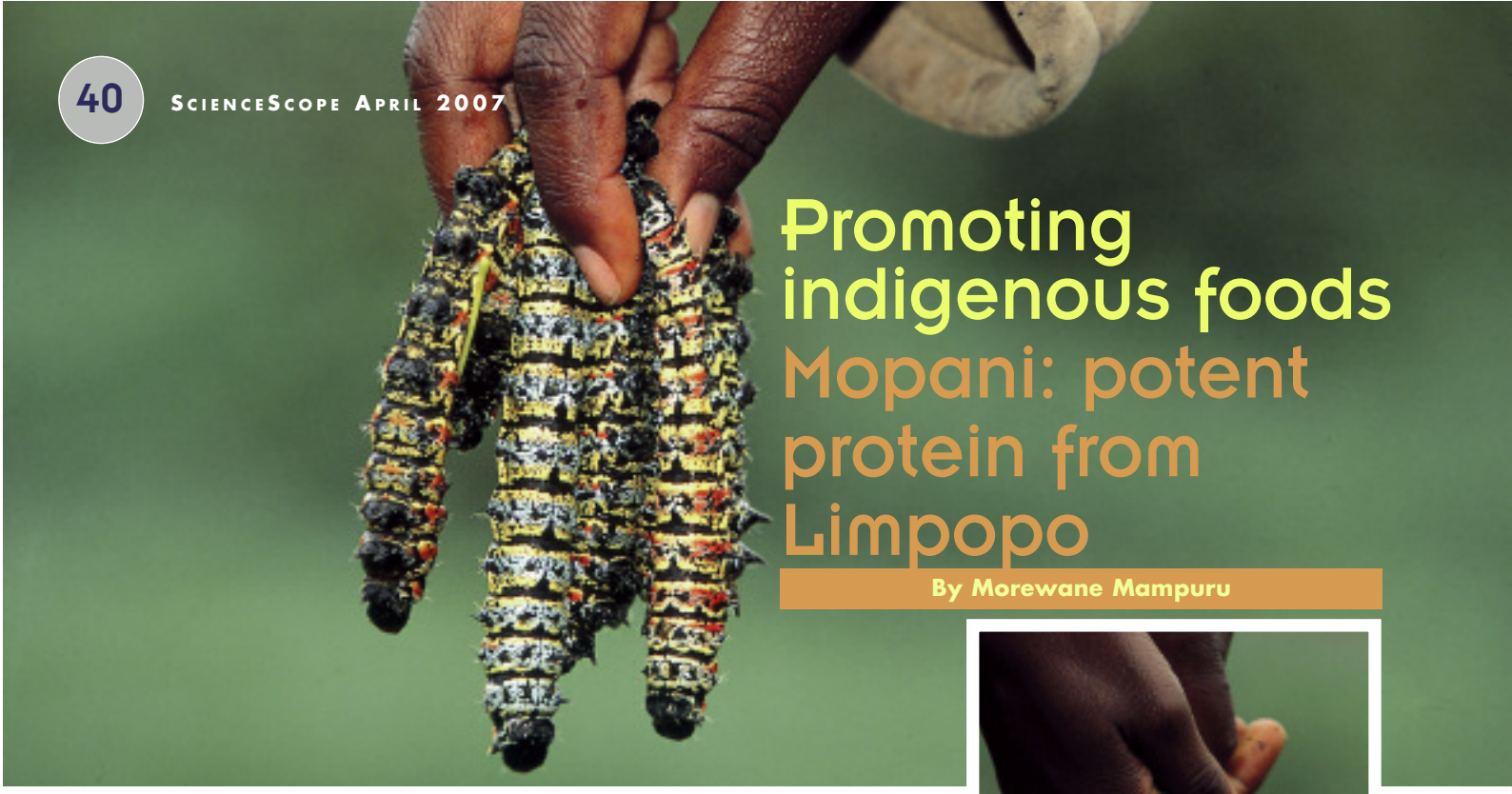
Products from the *Aloe vera* species dominate the international cosmetics market at present, but there is substantial scope for new developments of improved products from local aloes, as the unique composition could be exploited to differentiate the local products. Products of higher quality are likely to command higher prices on the local and international markets.

Another aloe species, *Aloe aborescens* is also under-utilised and very suitable for gel and juice production. The CSIR investigates technology development options for intermediate products (powders and gels) of high quality through innovative new process methods. The selection of these formulations is based on a combination of high market growth potential, knowledge of traditional uses and novel processing methods of indigenous aloes. The CSIR has developed a process to produce a first-ever cold-water, soluble, spray-dried aloe bitters powder, containing 20-22% aloin, utilising extraction, separation, concentration and spray-drying process operations.

These processes are new compared to conventional ones, as they are performed at low temperatures and therefore improve the preservation of bio-active compounds. Such water-soluble aloe bitters allow novel formulations in juices, yoghurts and effervescent tablets for regulated dosage of the pro-drug aloin.

The CSIR has also developed product prototypes of clear, high-quality gels and gel powders and has developed and licensed a production process for aloesin, which is a skin lightener. The commercialisation model being developed by the CSIR includes Black Economic Empowerment small micro and medium enterprises that will obtain raw material and value-added intermediates from the established *A. ferox* tapper communities of the Eastern Cape and the emerging harvesting industry in KwaZulu-Natal.

Enquiries:
Raj Lalloo and Dr Ingrid Weinert
Tel 011 605-2211
012 841-2195
Email rlalloo@csir.co.za
iweinert@csir.co.za



Promoting indigenous foods

Mopani: potent protein from Limpopo

By Morewane Mampuru

Through the promotion and commercialisation of indigenous foods, the CSIR aims to raise awareness of the important role that indigenous food plays, in poverty reduction and the extent to which science and technology (S&T) can unlock sustainable socio-economic development.

The CSIR's indigenous foods project has developed replicable models that can be used to improve the skills, information and economic empowerment of the rural poor. It promotes effective strategies to enhance previously disadvantaged individuals' participation by using S&T.

Collaboration between CSIR Biosciences and the custodians of indigenous knowledge has resulted in the development of a variety of food products from indigenous raw materials and recipes that had been collected from different provinces.

Laboratory-scale trials were performed to create the products. These were tested against information and feedback received from target markets on the acceptability of a product for consumption. New food processing techniques and quality measures were applied to ensure conformity to food standards. After further small-scale trials, scale-up was undertaken to prepare for technology transfer. The scale-up process aimed to optimise the process technology using equipment similar to that which would be used in the final production facility.

The indigenous foods project culminated in the establishment of a Section 21 company, IndiZAfoods, loosely translated as "indigenous South African foods". The company was the result of an initiative implemented by the CSIR on behalf of the Department of Science and Technology.

IndiZAfoods's main business intent is to promote and commercialise indigenous foods produced at manufacturing centres across South Africa. It has four manufacturing centres operating in four provinces: Isintu Foods Enterprise in Richards Bay (KwaZulu-Natal); TsaSetso Foods Enterprise in Mangaung (Free State); Chivirikani Enterprise in Tzaneen (Limpopo); and a centre in Mogwase near Rustenburg (North West). The company is responsible for overall management and marketing of the manufacturing centres.

Mopani worms – local protein source

The people of Limpopo have been eating mopani worms for many years. These worms are in abundance during collection periods in December and April, and form an important part of the culture in most communities in the province. Mopani worms are known to be a very good source of protein and more cost-effective than regular meat. Research indicates that about 100 g of dried mopani worms provides up to 76% of a person's daily protein requirement and offers most of the necessary vitamins and minerals.

CSIR Biosciences has embarked on a mopani processing project as part of the Greater Giyani Natural Resources Development Programme, funded by the Development Bank of Southern Africa to the tune of R11, 6 million.

The goals of the mopani processing project include complementing the indigenous knowledge of people in the region with scientific knowledge. Adding value to the natural resource may lead to job creation and generate income for the local people.

Another intervention aimed at adding value is the development of a variety of new food products. The technology and process for making mopani-flavoured snacks and canned stew have been completed.

Other activities include improving the technology for preparing and drying mopani worms; introducing hygiene and quality controls in the value-addition chain; and transferring skills and technology for mopani processing.

Enquiries:
Morewane Mampuru
Tel 012 841-2356
Email mmampuru@csir.co.za

Pectin: enzymes put citrus waste to good use

By Dr Henry Roman

Lemon producers in the Eastern Cape have a large surplus of lemons from which they can derive no monetary value. Against this backdrop, the 'Beneficiation of Citrus Waste' project was conceived to extract a valuable product from these waste lemons.

Pectin is a water-soluble, colourless, tasteless, odourless and amorphous substance suitable for application as a gelling compound in many processed foods. It is used as a food additive in high-quality jams, jellies and dairy products. Pectin can be found in a variety of sources, but the preferred source is citrus peel (lemon, grapefruit, orange), which contains 30-35% pectin by mass of dried peel (some 2-4% based on wet peel).

The main structure of pectin is a polysaccharide colloid, composed of (1,4)-linked-D-galacturonic acid and methyl esters of galacturonic acid. Pectin is classified into two groups according to the degree of esterification, i.e. a designation referring to the number of methyl esters of carboxylic acids, either as high methoxyl (HM) or low methoxyl (LM) pectin. The degree of esterification determines the physical properties of the gel, gel forming

ability, solubility, and sensitivity to salts. These factors dictate the ultimate use of the pectin. High methoxyl pectins are used in jams and jellies, while low methoxyl pectins are formulated in low calorie, low sugar jams and jellies owing to their unique ionic mechanism of gelation.

Neither HM nor LM pectins are currently produced locally; the entire market requirement is imported, despite local good quality raw material in the form of citrus waste. South Africa is the third largest citrus exporter in the world, after America and Spain. Local citrus by-products are either disposed of as waste, or dried and used as low-value cattle feed.

The CSIR initially developed a laboratory-based HM pectin extraction process. The CSIR optimised the process efficiencies and piloted the process to 1 000 litre scale. Pectin extraction is a physicochemical process in which hydrolysis and extraction of pectin macromolecules from plant tissue and their dissolution take place taking into account various factors.

The principal steps in the preparation of pectin are treatment of raw material; shredding and washing of citrus peel; dissolution of the pectin by heating in acid solution; separation of the pectin solution from plant tissue by filtration; concentration of the pectin extract; precipitation, filtration and drying. This is a relatively easy downstream process that does not need specialised chemicals or equipment. Small business entrepreneurs can carry out the extraction at sites close to major citrus juice producers or near citrus-growing farms. Final purification and further processing of the isolated HM pectin will be conducted at a central facility to be constructed at the Coega Development Zone.

To demonstrate the technology, CSIR Biosciences recently completed the construction of a demonstration unit in Fort Beaufort. The unit will operate for six months and the data collected will be used to design an extraction plant.

LM pectin is produced from HM pectin by de-methoxylation of methyl-galacturonate esters. Chemical methods are unfavourable, being stoichiometric, and result in the degradation of pectin bonds, thereby reducing yield. This project proposes to focus on enzymes for the de-esterification of HM pectin to produce LM pectin of high-quality and consistency. No commercial biotechnology process currently exists to produce LM pectin and this technology is set to lead to new intellectual property. The enzyme process will have several advantages, including selective hydrolysis of the ester bonds, higher pectin yields and quality, and mild reaction conditions. Further advantages lie in the environmentally-friendly technology resulting in minimisation of the salt wastewater streams associated with the chemical processes in LM production.

The project is novel in three respects. Firstly, it remedies the lack of commercial pectin production in South Africa. Secondly, it provides a biochemical route that would be superior to traditional base hydrolysis methods for generation of LM pectin. This process avoids pectin hydrolysis and the generation of alkaline or salt waste streams through a carefully controlled biocatalysis process. Production and marketing costs of additional high value by-products from citrus waste can furthermore be made economical by integrating their extraction process flow sheets with the above processes.

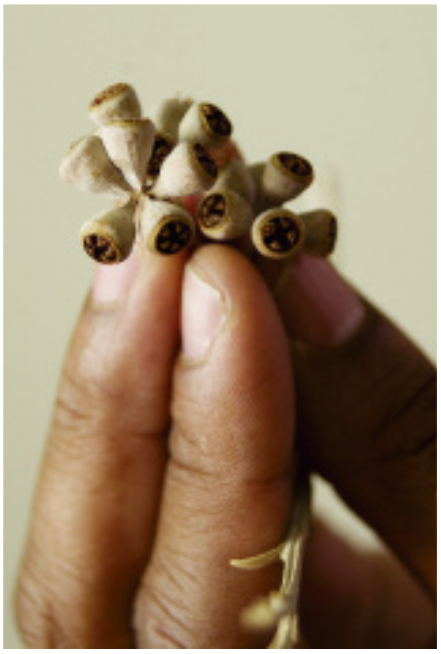
Enquiries:
Dr Henry Roman
Tel 012 841-3614
Email hroman@csir.co.za

Focused research: Amithkumar Sivlal hard at work in the CSIR tree breeding reproductive biology laboratory

Getting more fibre from less land

By Dr Steve Verryn

Modern forest plantation practices are aligned with increasingly stringent environmental management constraints. This has resulted in the withdrawal of the plantation areas from riparian zones and conservation areas, and the consequential reduction in some plantation sizes. In addition, there is a need to limit the extent of afforested land to manage our scarce water resources. On the other hand, there is an ever growing demand for forest products, as with most resources, in particular for pulp and paper. Some 56% of the approximately 1.33 million hectares of South African forestry area are earmarked for the pulp and paper industry, and the value derived from pulp and paper accounts for an even larger percentage of the sector's value.



Dr Steve Verryn displays one of the many wood samples produced using CSIR tree breeding techniques

Historically, the approach towards higher demands has been to expand the plantation area and breed trees suitable for new environments. The alternative is to accept the challenge to breed forest trees that can produce more pulp and paper off the same land base. The CSIR tree improvement research group is developing and testing a series of innovative interspecific hybrids – crosses between different species within the same genus – aimed at transforming the value of our plantations. This research is done in collaboration with the Innovation Fund of the Department of Science and Technology (DST) and NCT Forestry Co-operative Ltd.

Interspecific hybrids tend to present unique challenges and opportunities. Reproductive and various compatibility barriers often exist, which prevent the successful creation of such hybrids. The CSIR has succeeded in producing a number of new hybrids, despite this barrier. Once a promising hybrid has passed the initial trials, one needs to mass produce it, typically through vegetative means, although replication through seed may also be a solution. Further research and development is required to determine the most effective means of production of these hybrids (if at all possible). Some of the new interspecific hybrid types are currently being tested for suitability for mass vegetative replication.

Hybrids between different species provide the unique opportunity of combining desirable attributes of the different – but often related – species. In this instance, the CSIR is looking for a combination of species that display characteristics such as excellent pulp yields and wood densities, together with species well suited to South African growing conditions. This will result in more production of pulp fibre off the same or even a smaller land base than is the current practice.

A first for South African forestry

Most of the best solid wood (e.g. sawtimber) is sourced from natural forests internationally. However, this resource is rapidly being threatened and depleted. An economic substitute for the hardwood saw timber market could be the fast-growing eucalypt tree. However, wood splitting tends to be a problem when this timber is used for solid wood products.

The CSIR and the Innovation Fund have developed and released a novel set of eucalypt clones for the solid wood industry. These clones have the advantage that their wood has significantly reduced splitting or does not split at all, in some cases. More than 60 000 of these trees are already being grown for commercial purposes in South Africa. Commercial production of some of our other sawtimber clones has also commenced in Argentina and Paraguay, after extensive testing in those countries over a five-year period.

Collaboration with Australia in addressing common rural needs

Australia has serious concerns about the large-scale de-afforestation and the resultant rising water table and increased salinity soil in certain areas. In order to redress this, it is important to encourage farmers to plant trees. However, the harsh conditions are not friendly environments for re-establishment of trees, and farmers would like to plant trees which stand to offer some economic return. These farmers often own small farms, and do not have the resources to breed and trial different species and hybrids for their use. In South Africa, over 10 000 small farmers in the forestry sector do not have the resources to develop appropriate

genetically improved trees for their use. They also often farm in harsh environments.

In a partnership between a number of Australian and South African research institutions and companies (principally sponsored by ACIAR), the CSIR has developed a number of promising new hybrids suitable for these farmers. The material is currently being field-trialled on both continents. The research has included collaborative investigations into underpinning reproductive biology (investigating why certain interspecific crosses are successful and whether they will reproduce vegetatively), quantitative genetics (developing the mathematics and statistics behind non-conventional hybrid breeding) and social sciences (understanding farmers' needs and drivers for adoption of new forestry practices) over a period of five years.

CSIR in research on GMOs and the environment

Technology on genetically modified organisms (GMOs) holds tremendous potential for a developing country such as South Africa. With that potential, however, comes a responsibility to heed any potential risks to the natural environment.

In a project funded by the Department of Environmental Affairs and Tourism (DEAT), the CSIR, in consultation with a large number of stakeholders and others, interrogated relevant issues with the aim of developing guidelines around GMOs and the environment.

The CSIR undertook literature studies and provided technical inputs on issues relating to:

- The risk of gene flow into natural populations, especially when dealing with indigenous species
- The risk of transformed plants invading natural habitat
- The impact of the introduced gene(s).

The project is currently entering a research phase, during which research data will be generated.

CSIR researcher Karen Eatwell is the project manager for Project Pulp

Enquiries:

Dr Steve Verryn
Email sverryn@csir.co.za
Tel 012 841-4948

Designing process technologies for sugars from Karoo tequila plant

By Dr Jozef Dudas

Scientists at the CSIR are investigating processing technologies to develop potential fructan products from the *Agave Americana* plant that flourishes in the arid conditions of the Karoo.

Agave Americana, a fibrous plant originally from Mexico and the Caribbean area that has since been naturalised in South Africa, is one of the few species able to survive the harsh arid conditions of the Karoo. Although best known for its use in tequila production, the natural storage fructans found in both the pina – the central core of the plant – and the leaves of the plant are potential commercial products in their own right. At present the local industry harvests the pina for the fermentation, whilst the rest of the plant – mostly leaves and offcuts – is used as fodder or left to decompose in the field. This currently wasted by-product provides opportunity for exploitation of both the fibre and the sugar components.

The target sugars – fructans – comprise molecules of variable length, mainly joined by the specific beta-(2→1) fructosyl-fructose linkage. The degree of polymerisation (DP) has bearing on the functional behaviour of the molecules and determines their end use. The larger molecules are known as inulin and commercial products are generally processed to have an average DP ranging from 14 to 17.

Fructans function as prebiotics due to the inability of the human gut to digest this specific linkage type. The shear characteristics of inulin make it a suitable substitute for fat in various food products and the superior sweetness of the short chains allow them to be used as low calorie (6,3 kJ/g) sweeteners.

Initial work focused on the recovery and characterisation of the agave fructans from the pina and leaf tissue. The pina material contains up to 25% sugars, while the leaf content ranged from 2 to 16%, with the thick leaf base being the richest source. The fructan content has been found to vary according to location, environmental conditions and age of the plant.

Characterisation of extracted fructans from both the heart and the leaf material has shown the average DP of the polymers to be around 10 to 16. The leaf base and pina show higher levels of longer polymers than the rest of the leaf and would be the target material for inulin production. Work on the chemical configuration of the molecules suggested that the structure of the *Agave americana* inulin is a branched polymer and differs from chicory inulin, which is a linear molecule. The branched form may be advantageous as this leads to increased solubility and ease of use.

Processing to develop potential fructan products has shown that agave tissues, especially leaf tissues, are difficult to work with due to the presence of the fibres. Both traditional systems and the use of a novel ultrasound system for the release and recovery of fructans are under investigation. The aim is to develop suitable equipment, specifically for this type of raw material that could result in reduced processing steps and greater yields.

Downstream processing includes removal of co-extracted contaminants and separation of the inulin polymer – suitable as a prebiotic or food ingredient – from short chain material and free sugars that can be marketed as fructose syrups.

This project plans to take the work to a level where commercial products have been identified and processing routes to recover the components have been tested for feasibility.

Provided that the outcome of the research proves positive and viable, development of an industry in the Great Karoo will be undertaken by various funding agencies with technical support from the CSIR. This would be of great value to an impoverished area where employment opportunities are rare.

The Agave plant is commonly found in the arid Karoo region. Its leaves and pina contain natural ingredients that can be developed into potential commercial products. The CSIR's agroprocessing and chemical technology research group conducts studies on the plant

Enquiries:
Dr Jozef Dudas
Tel 011 605-2382
Email jdudas@csir.co.za

Age-old knowledge keeps mosquitoes at bay

By Dr Vinesh Maharaj

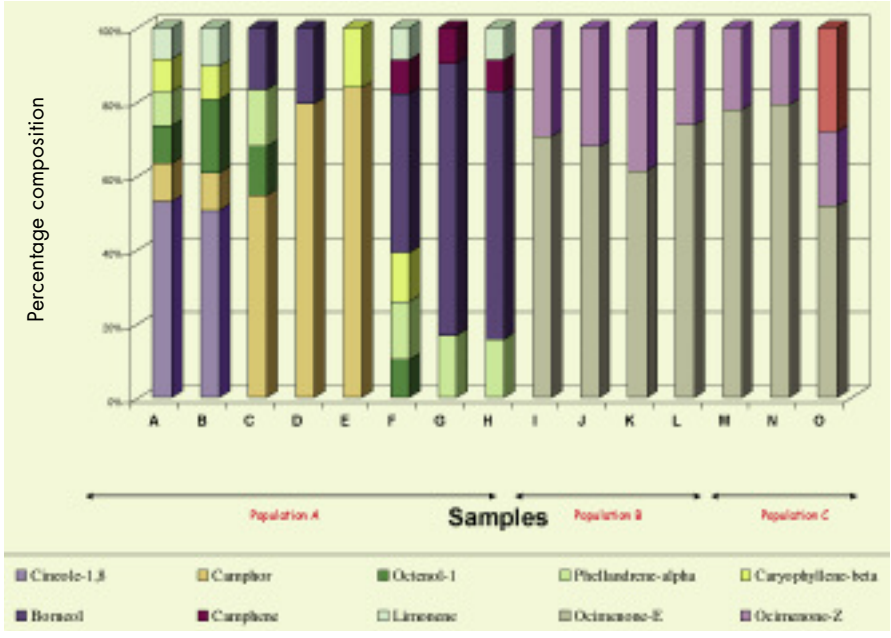
The quest to make humans less attractive to mosquitoes has fuelled decades of scientific research on mosquito behaviour and control.

Worldwide, mosquitoes transmit disease to more than 700 million people. According to the World Health Organization (WHO), approximately 40% of the world population are at risk from malaria. Mosquito bites cause more than 300 million acute illnesses and at least one million deaths each year. Some 90% of deaths due to malaria occur in Africa, with the majority of victims being children under five.

The most widely used mosquito repellent is a by-product of the petrochemical industry, diethyl toluamide (DEET). Increasing consumer demands for natural occurring and environmentally-friendly substances enhance the market potential for alternative mosquito repellents. Repellency is defined as the ability of a product to prevent mosquitoes from entering a non-mosquito contaminated area.

The CSIR's bioprospecting research group collaborated with traditional healers in an area of South Africa where malaria is endemic, to develop a novel, natural method of repelling mosquitoes. This product, patented by the CSIR, not only repels mosquitoes more effectively than similar products based on established essential oils, but also has the remarkable ability to expel mosquitoes from a contaminated area.

Figure 1: Chemical profiles of Pentane extracts from fresh leaf samples



The phytochemical analysis research in combination with biological assaying led to the identification of a chemotype that the essential oil consists of: 14 major and several minor secondary metabolites. The chemical profile obtained through gas chromatography of the essential oil produced from the selected chemotype of the plant is used as a quality control measure

The project demonstrates how ancient indigenous knowledge about the use of medicinal plants and scientific research can be harnessed and lead to new innovative products.

Traditional use and preparation of essential oils for scientific validation

Local populations in various regions of South Africa have traditionally used the indigenous plant, *Lippia javanica*, as a mosquito repellent. The cut branches are wiped on the skin, hung around the entrances to dwellings or thrown on an open fire at night. The traditional method of use and preparation led the scientists to research the volatile components of the plant for mosquito repellency properties.

An essential oil (BP1) was prepared through steam distillation of the plant and a combination of specialised analytical techniques such as head space volatiles analysis, gas chromatography-mass spectrometry (GC-MS) in combination with biological assays were used to identify the biologically-active constituents in the oil. However, GC and GC-MS analyses of essential oils produced from plant samples collected in one season, from four different geographical areas, indicated that the chemical profile of each of the oil samples was substantially different.

The variation in the chemical profiles produced irregularity in the biological assay results. This led to further investigations into the possibility that different chemotypes are present in *Lippia javanica*. Plant samples were harvested from various regions in the Mpumalanga lowveld and processed using standardised protocols.

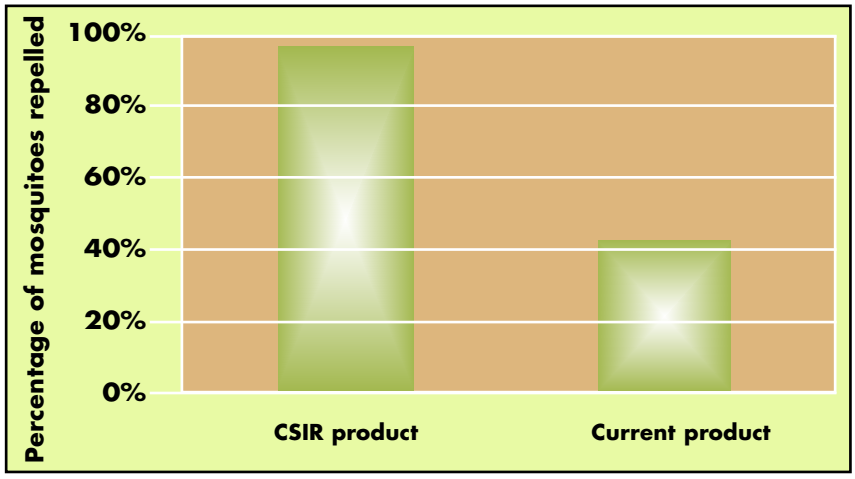
Variations in the chemical profiles were observed for extracts produced from plants of different localities. Furthermore, various plants from the same population and location (Figure 1) also showed different chemical compositions, which demonstrated that different chemotypes are present in *Lippia javanica*.

Biological assaying

The efficacy of the essential oil against mosquitoes was evaluated at the South African Bureau of Standards (SABS), using olfactometer assays. A standard protocol was followed using 30 yellow fever mosquitoes, *Aedes aegypti*. The results showed that the essential oil is significantly more efficient at repelling mosquitoes compared to current products on the market.

Suitable candle formulations of the essential oil were prepared and biologically assayed for their mosquito repellency properties. The results illustrated in Figure 2 show superior repellency properties for the BP1 candles when compared to citronella candles.

Figure 2

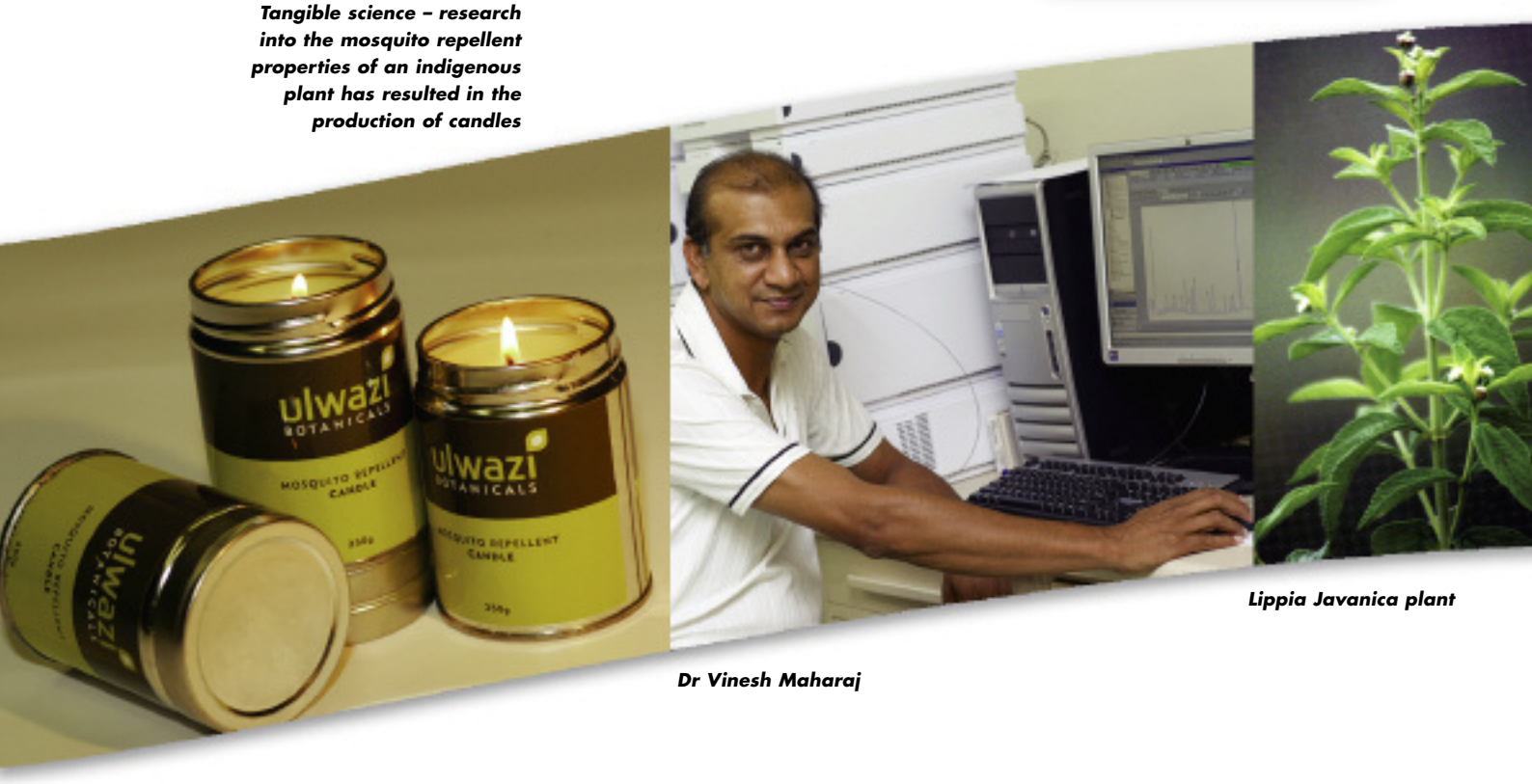


Benefit-sharing and commercialisation

A benefit-sharing agreement was signed with the holders of related indigenous knowledge and future benefits that lead from this research will be channelled through a Trust. The product has been registered for use under Act 36 of the Department of Agriculture and the registration certificate is held by a wholly-owned CSIR subsidiary, Ulwazi Botanicals (Pty) Ltd. Ulwazi Botanicals will facilitate the commercialisation of the products.

Enquiries:
Dr Vinesh Maharaj
Tel 012 841-3295
Email vmaharaj@csir.co.za

Tangible science – research into the mosquito repellent properties of an indigenous plant has resulted in the production of candles



Dr Vinesh Maharaj

Lippia Javanica plant

A Northern Cape biotech success story unfolds: beta-carotene from algae

By Dr Dusty Gardiner and Raj Lalloo

Beta-carotene is an important source of vitamin A in the diet. This vitamin plays a key role in vision and has also been reported to act as an antioxidant with beneficial effects in the prevention of cancer, arthritis and cystic fibrosis. As a safe source of vitamin A, beta-carotene is widely used as a vitamin supplement and food colourant in margarine, butter, juices and ice cream. Production of synthetic beta-carotene is undertaken by chemical synthesis, while natural beta-carotene is extracted from carrots and palm oil or produced through the use of algae and, more recently, fungal fermentation.

During the 1980s and 1990s, the South African chemical industry diversification strategy included investment into high value, small volume fine chemicals. Beta-carotene can be categorised as a fine chemical. From the late 1990s, a renewed focus on core business saw most of the large chemical players divesting of their fine chemicals interests. In partnership with AECI, the CSIR developed a technology for production of beta-carotene using the halotolerant algae *Dunaliella salina*. While the commercial cultivation of *Dunaliella* for the production of beta-carotene is undertaken throughout the world, different technologies are used.

In this case, the technology was developed for site-specific implementation in Upington in the Northern Cape to take advantage of high levels of solar radiation, high average temperature and adequate supply of water from the Orange River. The technology comprises an algal growth module in shallow saline ponds that optimise the solar radiation and temperature benefits of the Upington site, followed by extraction and purification of the beta-carotene and final product formulation. During this joint development, a pilot plant was built in Upington and staffed by CSIR employees. Design of a large-scale production plant was also completed.

When AECI divested of its interests in beta-carotene, the CSIR undertook a strategic redesign of the technology to facilitate exploitation of the technology through the creation of a start-up enterprise. The creation of Natural Carotenoids SA (NCSA) resulted, with funding from Bioventures, a South African-based venture capital company and CapeBio, the Cape Town-based biotechnology regional innovation centre, established by the Department of Science and Technology under the umbrella of the National Biotechnology Strategy.

A modular, phased, roll-out strategy was adopted to reduce risk and manage affordability. Phase one of the production plant has been completed and NCSA is currently selling its product to buyers from Europe. The quality of the product has resulted in a rapidly growing order book, and planning for phase two is in progress. The CSIR continues to partner with NCSA by undertaking product purification at the CSIR-owned Imbiza pilot facility in Johannesburg.

These activities will be transferred to the Upington site when the business has reached a critical size that will allow further investment in Upington. The NCSA manufacturing plant in Upington provides employment opportunities for technically-skilled people in a part of the country where new employment opportunities are scarce.

The exploitation of this technology provides an excellent example where government instruments, the private sector and public research organisations (such as the CSIR) partner to create new biotechnology-based SMEs in South Africa. Opportunities for expansion of the Upington site to create an algal biotechnology hub are being investigated, with CapeBio currently providing seed investment for the development of an algal astaxanthin technology.

Enquiries:
Raj Lalloo
Tel 011 605-2211
Email rlalloo@csir.co.za

An aerial view of the algal production ponds in Upington, where natural carotenoids are cultivated, harvested and extracted. The pilot plant is seen in the bottom left

Emerging research

Dr Bethuel Nthangeni is leading the CSIR's yeast expression systems research group in the application of glycobiology, an emerging research field with potential for therapeutic uses

The sweet promises of glycobiology for better therapeutic products

By Dr Bethuel Nthangeni

CSIR scientists are using glyco-engineering technologies to introduce genes involved in the incorporation of human polysaccharides into unicellular organisms to produce pre-determined proteins with therapeutic uses.

Glycobiology, the study of carbohydrates and carbohydrate complexes, is an emerging field of research with enormous potential for the development of glycan-based drugs. Glycans are complex carbohydrates made of monosaccharides or simple sugars such as glucose, fructose and mannose. The sugars and the bonds between the different monosaccharides in a glycan constitute a code.

The capacity of the code by far exceeds the coding capacity of nucleic acids or proteins. The sequence and type of monosaccharide bonds in glycans are regulated indirectly through the genome, through the expression of certain enzymes in glycobiosynthesis, which are often organ and tissue specific. Glycans play a central role in vitally important biological processes, as they are constituents of glycolipids and glycoproteins in cells, in the connective tissue matrix and in human body fluids. Glycans mediate cell-cell recognition and the binding of cells to the extracellular connective tissue matrix; and regulate the migration of cells within the organism during embryonic development, repair processes and immune responses. The structural diversity of glycans makes this wide range of functions possible.

Human proteins are produced in large amounts and the number of human therapeutic products increases each year. The demand for recombinantly-produced proteins is mainly governed by their medicinal need such as for antibodies, growth factors and cytokines. The endogenous counterparts of most human therapeutic proteins contain a glycan component attached to the protein to form glycoproteins. The glycan portion determines specific physical, biochemical and biological properties of the glycoconjugates, and missing glycans can result in a total loss of function. The type of glycosylation is crucial for a number of things, e.g. the half life of the protein in serum; the immunogenecity of a protein; the ability of the glycoconjugate to serve as the receptor for other proteins or molecules; directing antibodies to their targeted cells during detoxifications; and for communication between cells or targeting the glycoconjugate to specific organs or cells.

The uses of glycans

Glycan-based therapeutic drugs on the market include erythropoietin, which is

used to treat anaemia associated with chronic renal failure; granulocyte colony-stimulating for the treatment of neutropenia – a haematological malignancy condition; follicle-stimulating hormone used to treat infertility; granulocyte macrophage colony stimulating factor for treatment of leukaemia; and therapeutic antibodies for treating cancer, auto-immune and inflammatory diseases.

Genetic glycosylation defects are associated with severe clinical consequences such as lysosomal storage diseases, the carbohydrate-deficient syndrome and the leukocyte adhesion deficiency. Changes in the glycan portion of glycolipids and glycoproteins accompany commonly found diseases such as rheumatoid arthritis, acute and chronic inflammation and alcoholism. Knowledge of the clinical significance of glycans leads to the more frequent use of modified glycan epitopes in clinical diagnostics, in particular cancer medicine and in the development of new anti-inflammatory and anti-infectious therapeutics.

Producing glycans

Production systems that have been used in the production of therapeutic proteins include bacteria, yeast cells, and Chinese hamster ovary (CHO) cells. Bacteria and yeast cells have been the preferred host for the production of therapeutic proteins mainly due to the relatively cheap and easy culturing and production processes with high yields of recombinant therapeutic proteins. The major drawbacks of the two systems include difficulties of purification and refolding recombinant proteins and the inability to incorporate required human glycans.

In cases where glycan components were desired, CHO cells were selected for expression of glycoproteins. Although CHO cells are capable of incorporating glycans in the complex manner of mammalian cells, the complex mammalian glycosylation machinery is made up of more than 200 glycosylation enzymes and related proteins differ from cell type to cell type. Moreover, CHOs are not of human origin, and glycoproteins produced in CHO are differentially glycosylated compared to their native human counterparts.

Current research activities

Glyco-engineering technologies are used to develop new products with higher activity, longer serum half life and lower immunogenecity. Glyco-engineering strives for a correct human glycosylation, and more importantly, for an optimised glycosylation with the highest therapeutic efficiencies. The CSIR uses glyco-engineering technologies where genes involved in the incorporation of human glycans are introduced into unicellular organisms for production of proteins with pre-specified and defined human glycan side chains.

The ultimate objective is to have a collection of unicellular organism strains capable of producing glycoproteins with any desired glycoform for therapeutic applications. Research activities are being initiated to look at the development of production proteins of glycosylated therapeutic proteins and at the elucidation of structure-function relationships of glycoproteins.

Research teams and collaborations

The CSIR team consists of six senior research scientists with postdoctoral experience and skills ranging from genetic engineering, fermentation, protein biochemistry and expression, to glycoprotein analyses. Five research scientists on the team are studying towards their PhD and MSc degrees and a number of technicians are also working on the project. The team has well-established, existing collaborations with the Labaratoire de Microbiologie et Génétique Moléculaire, CNRS-INRA, Paris-Grignon in France and the Institute of Chemistry, Universitaet fuer Bodenkultur in Austria. The research group is also collaborating with the universities of the Free State and Stellenbosch.

Enquiries:
Dr Bethuel Nthangeni
Tel 012 894-3981
Email bnthangeni@csir.co.za

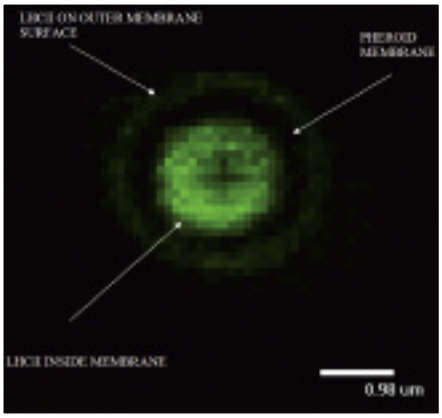


Figure 1 Confocal microscope image of pheroid LHC II (1cm3 2.8:2 pheroid preparation + 5 l LHC II) showing chlorophyll autofluorescence

Synthetic biology – mechanical engineering meets biology

By Dr Raymond Sparrow and Dr Dean Brady

The scientific knowledge base and understanding of biological materials has reached a critical point, allowing for the development of exciting new fields of science and technology. Over the past decade, interdisciplinary research has created opportunities at the interface of biology and physics. As it started becoming evident that the principles of mechanical engineering can be applied to biology, the new field of synthetic biology emerged.

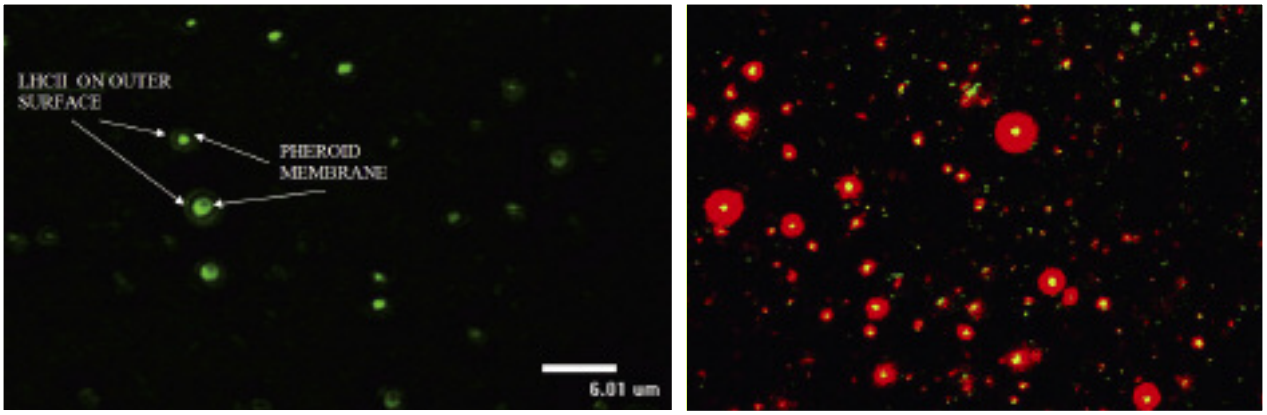


Figure 2a + b Confocal microscope image of pheroid LHC II (1cm3 2.8:1 pheroid preparation + 20 l LHC II) showing chlorophyll autofluorescence and pheroids labelled with Nile Red Data collected in collaboration with the North-West University (Potchefstroom)

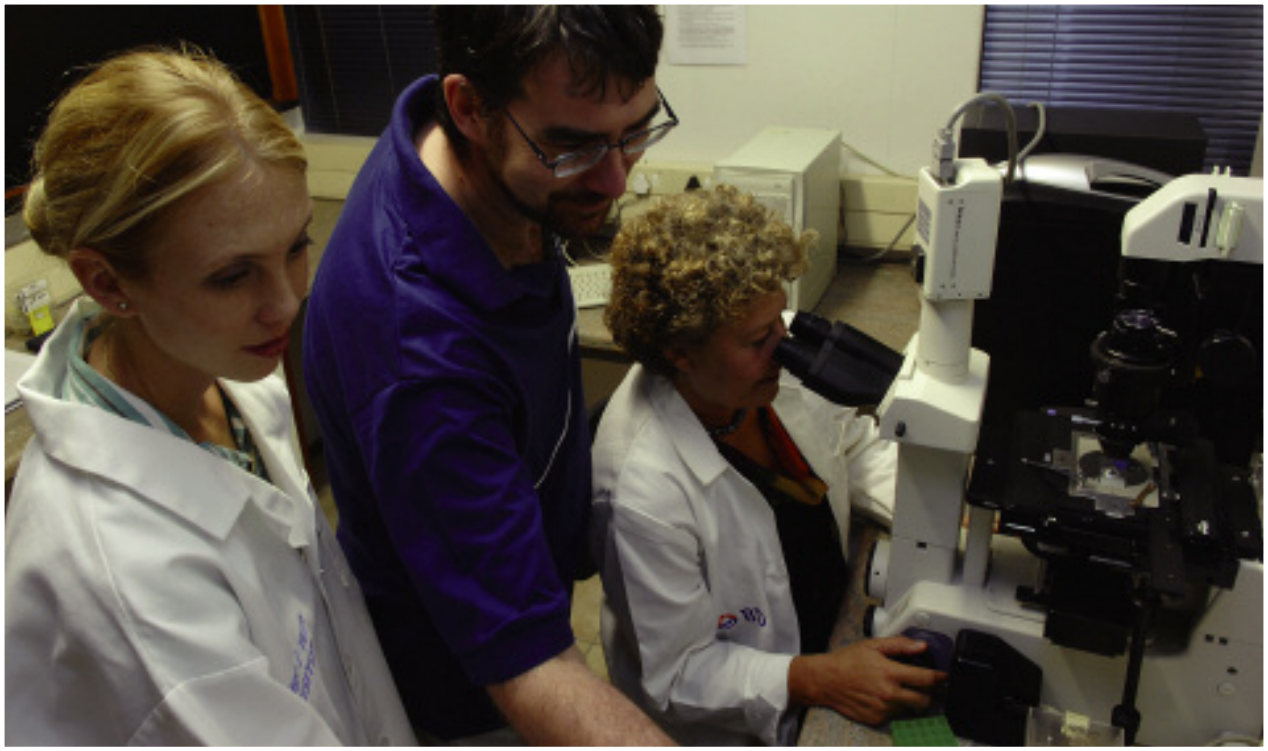
This area of research investigates how to build artificial, biological machines using engineering principles and procedures by taking parts (molecular and sub-cellular) and principles of naturally occuring biological systems, characterising and simplifying them. These components can then be used to engineer essentially artificial (synthetic) biological materials, devices, machines and systems for application in medicine, energy, the environment and industry.

Working at the molecular scale represents a considerable challenge. Fortunately, nano-imaging and manipulation technologies for biological samples have progressed in the last decade and one can now image, characterise and manipulate biological molecules from the macro down to the nano-scale. Their behaviour can be predicted, quantified and utilised in ways not possible before. These advanced techniques make synthetic biology possible. Internationally, synthetic biology is in an embryonic stage of development. South Africa intends to achieve international recognition in this field within the next five years by setting up synthetic biology emerging research area (ERA) laboratories at CSIR Biosciences. This initiative is supported by the Department of Science and Technology and other partners. The challenge is to integrate biological molecular components with each other and with non-biological components to yield new technologies. The initial focus will be on biophotonic bionanodevices and molecular biomaterials.

Biophotonic bionanodevices

The biophotonic bionanodevices platform will focus on the development of biologically-based machines that use light as energy source and as the on/off control

Dr Raymond Sparrow (left) of the CSIR National Laser Centre and Dr Dean Brady of CSIR Biosciences are marrying engineering principles with biology to produce artificial biological devices for use in the fields of medicine, energy, the environment and industry



mechanism. For any device to operate and perform, a controllable energy supply and transducer are needed.

A number of energy forms can be used for nanodevices, including chemical, electrical and light (photonic) energy. Light energy has many advantages over other forms of energy, including:

- High precision and controllability in delivery regarding spatial, temporal and quantity of energy delivered
- High degree of diversity and discrimination. Light energy comes in a vast range or spectrum of wavelength and specific wavelengths of light are very easy to select
- Light is available in a huge range of sources, from natural sunlight to lasers
- The light source does not have to be in direct physical contact with the device it is powering
- Light energy is an environmentally-clean energy source.

The CSIR intends to build a modular light-powered motor, with three sections:

Light harvesting: Chlorophylls absorb light and the excitation energy is transferred by light harvesting complexes for transporting onto an adenosine triphosphate (ATP) generating system.

Energy transfer: An ATP-synthase complex and photosynthetic reaction centre(s) incorporated into a lipid vesicle (called a pheroid). This component generates the ATP energy enabling Kinesin to move the microtubulin.

The motor component: such as Kinesin and associated microtubulin.

Preliminary experiments have been conducted in collaboration with Dr Anne Grobler and her group at the Department of Pharmaceutical Science, North-West University (Potchefstroom campus), illustrating the incorporation of photosynthetic material into pheroids (see figures1and 2).

Molecular biomaterials

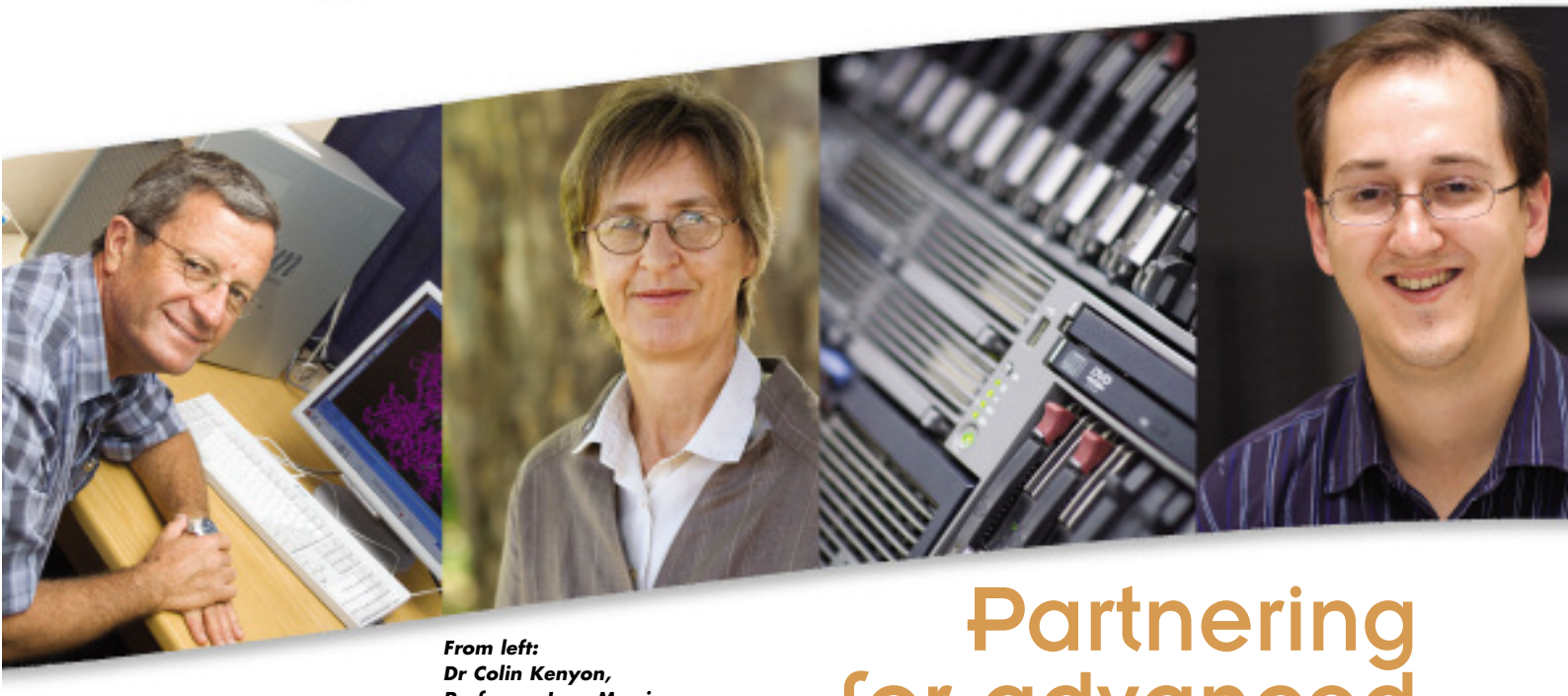
The molecular biomaterials platform will focus on the design and synthesis of new biologically-based materials (e.g. proteins/nucleic acids) that have predetermined properties and characteristics. Although these materials are biologically based, engineering through synthetic biology can extend the range of materials beyond that which nature has provided. For example, protein-based materials could include those amino acids that do not occur in natural proteins or include molecules such as protein-nucleic acid hybrids.

Initially, the CSIR will produce components that can be used to synthesise the biophotonic machinery and other small devices, as well as generating self-contained metabolic units at the micro-scale.

Two additional platforms have been identified for subsequent scientific investigation, namely bionics and biocomputers.

It can be expected that synthetic biology will consolidate current expertise and create new technology capabilities that will be applicable in industry and hence have economic benefits. South Africa needs to invest in these developments to build the necessary intellectual and physical infrastructures for this industry. Areas of application could include diagnostic technologies and intelligent drug delivery systems for HIV, tuberculosis or cancer; tissue micro-engineering and minimally-invasive nanosurgical devices; ultra-efficient light powered systems; and environmental reclamation.

Enquiries:
Dr Raymond Sparrow
Email rsparrow@csir.co.za
Tel 012 841-3741
Dr Dean Brady
dbrady@csir.co.za
Tel 011 605-2711



From left:
Dr Colin Kenyon,
Professor Jane Morris
and Albert Gazendam

Partnering for advanced bioinformatics, computational biology and chemistry

By Dr Colin Kenyon, Uli Horn, Dr Jane Morris and Dr Christopher Parkinson

Bioinformatics and computational biology are fields where close collaboration exists between the CSIR and the University of Pretoria (UP). The Pretoria node of the National Bioinformatics Network is hosted by the university and also involves the University of Limpopo and the Agricultural Research Centre at Onderstepoort. This relationship is facilitated through the African Centre for Gene Technologies (ACGT), a partnership between the CSIR, the University of Pretoria and the University of the Witwatersrand.

Local partners in rational drug design initiatives

Researchers at the CSIR and the UP currently work on a number of rational drug design projects, using the Accelrys Inc suite of protein molecular modelling and rational drug design software. Most of the computational work is therefore applications based, and these computational techniques are absolutely necessary for the rational drug design initiative. Theoretical modelling is applications based with the prime objective of using the modelling techniques to manage research projects to solve specific biological problems. The computational work runs in parallel with the associated molecular biology, biochemistry, microbiology and organic chemistry.

A number of rational drug design initiatives are currently in progress. One major project, funded by the Innovation Fund, aims to produce novel antibiotics for the treatment of tuberculosis. Protein homology modelling has been used to produce structures of a number of the potential drug target molecules. Target-based rational drug design protocols are used to build potential functional inhibitors to the target proteins. The structures of a number of ligands have also been defined using molecular spectroscopy techniques.

A significant amount of structural data – indicating potential transition state intermediate structures – have been obtained from the molecular spectroscopy data, thus allowing ligand-based drug design to be used. Inhibitor/activity data exist for a range of effector molecules acting on the target molecule. Quantitative structure activity relationships are therefore being used in the rational drug design programme.

As a result of the homology modelling, key amino acid side-chains have been identified in the protein target.

An extensive site-directed mutagenesis programme was undertaken to try and define the role of these amino acid side-chains in the reaction mechanism. In conjunction with the molecular spectroscopy, the modelling and the molecular biology have all contributed to understanding the reaction mechanisms involved. The organic chemists are currently trying to produce molecules that not only inhibit the protein by competition with the substrates, but also disrupt the reaction mechanism.

Malaria protein as model in virtual screening of compound library

As a result of collaboration between Professor Fourie Joubert (UP), the South African Malaria Initiative and the WISDOM initiative (led by Professor Vincent Breton of the Laboratoire de Physique Corpusculaire, Universite Blaise Pascal, Claremont-Ferrand, France), the malaria protein glutathione-S-transferase (GST) is being used as a model system for the virtual screening of a 4,6 million compound library, using grid computing. GST was one of the subjects of a collaborative rational inhibitor design project between the Department of Biochemistry at the UP, the CSIR structural biology group and the group of Professor Rolf Walter at the Bernard Nocht Institute for Tropical Medicine.

This new project uses a grid-enabled virtual screening pipeline to create *in silico* data for the definition of pharmacophores and their subsequent synthesis and biological testing. The current FlexX screening programme is based on the curation of the target active site as a rigid body. It does, however, allow for ligand conformational flexibility. Breton's team is trying to implement the use of the AMBER forcefield in conjunction with the FlexX docking protocol. This will allow for molecular dynamics to be done in conjunction with the docking.

Digital health technology expands possibilities for South Africans

By Albert Gazendam

Two high-performance computer clusters housed at the Meraka Institute in Pretoria provide a world-class resource for South Africa's bio- and medical informatics research community. Created by Intel and HP, donated by Intel Corporation and managed by the Meraka Institute (a national research centre of the CSIR), these supercomputers will initially be used for research on HIV vaccine definitions, process analyses of health-related data and perform protein structure modelling.

The supercomputers consist of a cluster of 32 dual-processor servers powered by Intel® Itanium® 2 processors, and a cluster of 32 dual-processor servers with Intel® Xeon® processors. The systems' combined performance is at a theoretical peak of 870 billion floating point operations per second (gigaFLOP/s).

Intel Corporation Chairman Craig Barrett and the Deputy Minister of Science and Technology, Mr Derek Hanekom, inaugurated the supercomputers in December 2006. "Intel, together with its partners, has donated technology that can make a huge difference to the important work of the South African bio- and medical informatics community," Hanekom commented. "This supercomputer provides a scalable solution that can help accelerate finding a cure for harsh diseases by handling complex data-intensive processing for experiments measuring tens of thousands of data points in hundreds of thousands of samples."

Barrett noted, "The increasing spread of communicable diseases threatens South Africa's livelihood and economy. This high-performance computing system will push the limits of scientific discovery to accelerate the creation of treatments and cures."

Enquiries:
Albert Gazendam
Tel 012 841-4820
Email agazendam@csir.co.za

Enquiries:

Dr Colin Kenyon	**Tel 011 605-2702**	**Email ckenyon@cisr.co.za**
Uli Horn	**Tel 011 605-2815**	**Email uhorn@csir.co.za**
Dr Jane Morris	**Tel 012 420-6007**	**Email jmorris@csir.co.za**
Dr Christopher Parkinson	**Tel 011 605-2601**	**Email cparkinson@csir.co.za**

Dr Sharon Biermann of CSIR Built Environment explained to the President and Mr Mosibudi Mangena (centre), Minister of Science and Technology, how advanced planning technology support spatial development that allows for efficient service delivery and shared growth. She also showed them the Housing Atlas 2005, which provides a spatial interpretation of current policy as it relates to human settlement and housing locality on a national scale

CSIR research and development endeavours impress SA President

When visiting the CSIR in March 2007, South Africa's President, Mr Thabo Mbeki, received a hands-on demonstration of CSIR research that improves the quality of life of South Africans.

Visit to CSIR by SA President

A statement issued by The Presidency stated that "the CSIR visit provides a platform to showcase extraordinary work achieved through joint initiatives with the Department of Science and Technology (DST) and private sector companies, as part of the national effort of achieving sustainable socio-economic development."

In a meeting at the DST preceding the visit, Mr Mbeki was informed of the improvements the science sector required to ensure that it contributed to the socio-economic development of South Africa. Afterwards, Mr Mosibudi Mangena, Minister of Science and Technology, said these improvements included the need to double the number in the next five years. He said for that to be realised, more bursaries had to be made available and that tertiary education institutions had to be more aggressive in recruiting Honours, Masters and PhD students.

A major testing facility at the CSIR, the medium speed wind tunnel is one of the best equipped and most sophisticated tunnels of its kind in the country and was selected as the venue for Mr Mbeki's on-site visit. The wind tunnel is a research tool developed to assist with studying the effects of air moving over or around solid objects moving at speeds of between Mach 0.2 to Mach 1.4. Air is blown through a duct equipped with instrumentation where models or geometrical shapes are mounted for study. Various tests are conducted, including force measurement, pressure measurement, flutter and dynamic stability, flow visualisation, two-dimensional aerofoil tests, and high angle of attack tests.

CSIR projects showcased included the application of human language technologies, nanotechnology, building and construction, preserving natural resources and the environment, mining, the hydrogen economy and fuel cells, biosciences, materials and manufacturing and laser technology.

The CSIR Satellite Applications Centre prepared two framed satellite images for Mr Mbeki as a souvenir. The one is an image of the Union Buildings taken by a Quickbird satellite, procured as part of a data set for the Gauteng Department of Housing to monitor and evaluate informal settlements in this province. The other image is a 2001 Ortho photo showing his place of birth, Mbewuleni in the Eastern Cape.

Above:
The Meraka Institute's Dr Quentin Williams and Willem van der Walt (seated) demonstrated how an information and communications technology (ICT) device, Notetaker for the blind, uses built-in speech technologies to allow the visually-impaired to benefit from ICT. The notebook allows them access to email, an electronic calculator and audio books

Taking a closer look at the mosquito repellent candle produced in Limpopo following collaboration by traditional healers and bioscientists from the CSIR and with funding from the Department of Science and Technology – Mr Mbeki; CSIR President and CEO Dr Sibusiso Sibisi; and Dr Gatsha Mazithulela (far right), Executive Director of CSIR Biosciences

Mandate

The CSIR's mandate is as stipulated in the Scientific Research Council Act
(Act 46 of 1988, as amended by Act 71 of 1990), section 3: Objects of the CSIR:

"The objects of the CSIR are, through directed and particularly multi-disciplinary research and technological innovation, to foster, in the national interest and in fields which in its opinion should receive preference, industrial and scientific development, either by itself or in co-operation with principals from the private or public sectors, and thereby to contribute to the improvement of the quality of life of the people of the Republic, and to perform any other functions that may be assigned to the CSIR by or under this Act."

The CSIR's shareholder is the South African Parliament,
held in proxy by the Minister of Science and Technology.

CSIR

our future through science