



Inqaba Biotechnical Industries (Pty) Ltd, trading as inqaba biotec, is South Africa's first, private genomic service company (www.inqababiotec.co.za). The company, based in Sunnyside, Pretoria was co-founded in 2002 by Dr Oliver Preisig and started with four staff members. After six years the team has grown to fourteen full time staff members, several part-time staff members and internship students.

inqaba biotec started producing oligonucleotides and rendering a DNA sequencing service in 2002. These services were later supplemented with the exclusive distributorships of Fermentas Life Science, Lucigen and Nanodrop Technologies. As the company has grown inqaba biotec has added several different services including Gene Synthesis, genomic DNA extraction, PCR amplification, PCR product cloning, RNAi synthesis and phylogenetic analysis. The dynamic distributorship portfolio has also increased with the products of Clare Chemicals Research, MiVac, Zymo Research, CLC Bio, PolyPlus Transfection and Seegene, Inc.

In November 2005, Dr Preisig welcomed BioPAD as a shareholder and a strategic partner, a biotechnology trust funded by the South African Department of Science and Technology. A recent highlight in the company's development was the installation of BioPAD's infrastructure investment, the Roche GS 20 in February 2007. The Roche GS 20, used for Africa's first high throughput sequencing service, is available to all Life Scientists world-wide. The service was launched in March 2007 and was upgraded to the new GS FLX system in August 2007. The GS FLX sequencer has longer reads (± 250 bases) and generates up to 100 Mb of data in a single run. GS technology has many different applications and is set to revolutionize genomics. The inqaba biotec team often helps customers to customise the technology to suit their applications. After fourteen months in operation, our GS sequencing service has attracted a wide range of local and international projects.

An example of such projects is the formation of a TB consortium in October 2007. This group including the Chris Hani Baragwanath business unit of the National Health Laboratory Services, the Respiratory and Meningeal Pathogens Research Unit at the University of the Witwatersrand and inqaba biotec, are working together to find the genetic differences between XDR (Extreme Drug Resistant), MDR (Multi Drug Resistant) and wildtype strains of *Mycobacterium tuberculosis* in South Africa.

Several Mtb genomes will be sequenced. Read more on Page 4.

On a more traditional side, our DNA sequencing lab was recently upgraded as well, with the purchase of the ABI 16 capillary 3130 XL sequencer. This coupled with a web based sequencing tracking and retrieval system from Geospiza has increased our efficiency and has allowed us to offer our clients an even better pricing structure.

inqaba biotec is looking forward to a successful future together with its valued customers: Breaking Biotech Boundaries! We not only serve customers in South Africa... we work with the whole of Africa.

Our partners:

- Fermentas LIFE SCIENCES
- Lucigen
- NanoDrop Technologies
- ZYMO RESEARCH
The Beauty of Science is in Making Things Simple
- Seegene
- CLC bio
- miVac Concentrator range
- Polyplus transfection.
- Clare Chemicals Research



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South Africa's

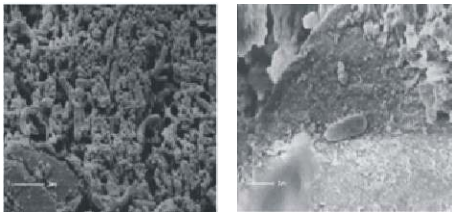
inqaba biotec offers services and products to a diverse customer base in South Africa and Africa. On the following two pages, four of our customers, by coincidence all female, give us a glimpse of their research aims.

Environmental Bioremediation SRK Consulting

Industrial and technological progress made during the last century has led to some amazing discoveries and technological developments. Progress in mining and development often disregarded environmental consequence. Global awareness of the effects industrial activities has on the environment, has resulted in an international tendency toward environmentally friendly processes and remediation of contaminated environments. Remediation of historically contaminated sites is often complex due to recalcitrant nature of chemical contaminants and geological setting. Advances in molecular DNA methods have allowed us a glimpse into the unseen realm of micro life in these manmade extreme environments.



Relatively little is known about the majority of environmental microorganisms due to their resistance to culture under standard laboratory conditions. Alternative approaches are necessary to allow the assessment of the environmental metagenome directly from the environment without the need of culturing in a laboratory. As such, environmental sequencing projects will provide valuable insights into the microbial diversity of microorganisms occupying various environmental niches. Environmental sequencing efforts include the extraction of genomic DNA directly from environmental samples, amplification using conserved 16S rDNA primers, followed by high-throughput 16S rDNA sequencing.



Electron micrographs of Bacillus shaped bacteria present in chlorinated solvent contaminated groundwater that was previously thought to be sterile and only undergoing abiotic degradation. Molecular and microbiological methods were used to prove and optimise in situ bioremediation strategy.

Natural attenuation and bioremediation of metals and organic contaminants can only be effectively applied at many sites after assessment of the physiology, ecology, and phylogeny of microbial communities at contaminated sites. Molecular site characterization is done to assess the sites potential to undergo biological remediation. The presence of key microbial populations is determined using high throughput 16S rDNA GS FLX sequencing. The second step is the identification of key genes associated with the degradation of specific contaminants. This gives us valuable information that can be correlated to

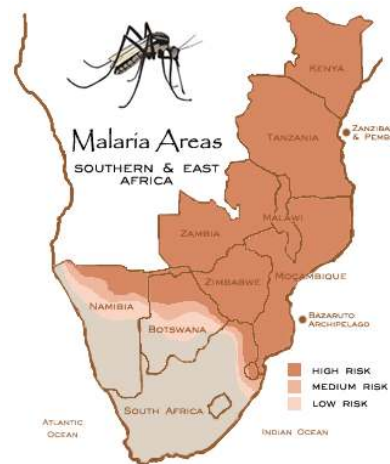
geochemical analysis and isotopic fractionation analysis to allow an overall look at the sites bioremediation potential. These answers are also valuable for proving that monitored natural attenuation is taking place at sites.

Applying molecular methods with geohydrological characterisation techniques allows for better in sight of process active in subsurface environments and allows for better optimisation and applications of *in situ* bioremediation strategies.

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Malaria Research Medical Research Council

As the emergence and spread of resistance to both insecticides and antimalarials have been identified as major stumbling blocks in the attempts to control the burden of malaria, the search for a solution to this problem forms the core of our research. To this end the molecular laboratory is involved in the routine surveillance for molecular markers (single nucleotide polymorphisms, gene copy number changes, changes in certain metabolic enzyme activities, etc) associated with either insecticide or antimalarial drug resistance in Anopheles vector species and Plasmodium isolates, respectively, collected as part of the monitoring and evaluation arm of our malaria control interventions implemented in various African countries.



Molecular marker surveillance is conducted using PCR (nested and qPCR) and ELISA driven technologies. Information derived from this surveillance has been utilised to inform both antimalarial drug and insecticide policy in South Africa, Mozambique and Bioko Island, Equatorial Guinea.

With our collaborators at the London School of Tropical Medicine and Hygiene we are currently attempting to trace and map the spread of resistance to sulfadoxine-pyrimethamine through Africa using microsatellite data. We hope this data will be used to inform drug policy as well as predict the spread of resistance to new antimalarials.

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Flower Power ...



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Hepatitis Virus Diversity Research Programme University of the Witwatersrand

Hepatitis B virus (HBV) is estimated to infect one billion humans and it is second only to cigarette smoking as a human carcinogen. Over 350 million individuals, of which 65 million reside in Africa, are chronically infected with the virus and about 300 000 per annum will develop liver cancer. Although an effective vaccine against this virus is currently available, inoculation will not help those already infected. No really effective anti-viral drugs are available to use against HBV and it is essential that such drugs be developed. In order to develop such drugs, a detailed knowledge of the viral strains, the mechanisms by which they replicate and useful animal model systems are needed.

This is clearly important at an international level but also at a national level because approximately 1% of the carriers of the world reside in South Africa. Moreover, the strains that infect this population are different to subgenotypes found in other hyperendemic regions of the world. It is therefore of paramount importance that we study the unique subgenotypes, which are of direct relevance to South Africa and its people. It has become increasingly evident that the heterogeneity in the global distribution of HBV genotypes may be responsible for differences in the clinical outcomes of HBV infections and the response to antiviral treatment and vaccination. However, there are a limited number of studies relating genotypes to clinical outcomes from African countries and most observations are anecdotal. Therefore it is important that the strains circulating in a particular geographical region should be studied and characterized because results and observations from other regions can strictly speaking not be extrapolated from one locale to another.

Professor Anna Kramvis, Reader in Molecular Virology, heads the Hepatitis Virus Diversity Research Programme in the Department of Internal Medicine, University of the Witwatersrand, Johannesburg. The major objective of the research undertaken by Professor Kramvis and her team of staff and postgraduate students is to study of hepadnaviral sequence variation, its functional characterization and role in the clinical manifestation of liver disease. This research is undertaken in close collaboration with laboratories in South Africa, Ghana, Zimbabwe, the Gambia, USA, Japan, China, Sweden, Belgium, Germany, Greece and Australia.

Professor Anna Kramvis with Professor Sydney Brenner, 2002 Nobel Laureate in Physiology or Medicine and University of the Witwatersrand Alumnus, during his recent visit to South Africa



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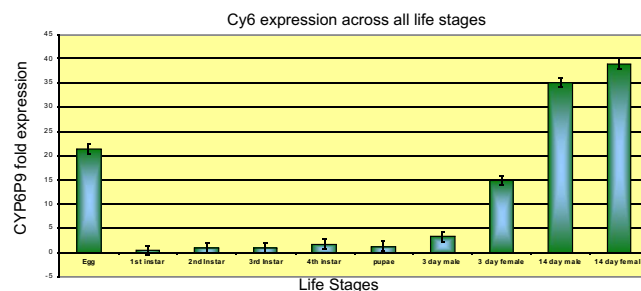
Vector Control Reference Unit National Institute of Communicable Diseases

The VCRU provides an identification service of medically important arthropods for entomologists, medical practitioners and health inspectors. Malaria vector mosquitoes are routinely identified using the latest PCR technology for the South African Malaria Control Programmes, as well as neighbouring countries. Our research is mainly based on different aspects of insecticide resistance in the major African malaria mosquitoes.



Our molecular research on insecticide resistance predominantly focusses on two main African vector species: *Anopheles funestus* (from Mozambique and Angola) and *Anopheles arabiensis* (from Sudan and Zimbabwe). We aim to characterize the metabolic mechanisms involved in these populations. The newest technologies including microarrays and quantitative Real-Time PCR are used to advance our knowledge in this field.

The development of new assays has been initiated to either replace or improve existing assay for the screening of target site mediated insecticide resistance.



Quantification of a major gene (CYP6P9) upregulated in pyrethroid resistant *An. funestus*. RNA extracted from eggs, larval stages (4 instars), pupae, 3 day old adults (males and females) and 14 day old adults were used. This gene was found to be highly over-expressed in insecticide resistant mosquitoes following microarray analysis.

The unit is also collaborating on investigations into the effect of entomopathogenic fungi on various insecticide resistant vector colonies housed at the VCRU. During these investigations, mosquitoes are exposed to two different entomopathogenic fungal species (commonly found in soils worldwide): *Beauveria bassiana* and *Metarhizium anisopliae*, and are analysed for survival and fungal infection.

We have active research collaborations with research groups in the UK, USA, Netherlands as well as African countries such as Nigeria, Gambia, Ghana, Ethiopia, Sudan, Zimbabwe, Namibia and Uganda.

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African TB Project

CLC bio tests Next Generation Sequencing solution on African tuberculosis data

Aarhus, Denmark and Pretoria, South Africa -- February 12, 2008

The world's leading bioinformatics solution provider, CLC bio, has joined forces with the first center for High Throughput DNA Sequencing in Africa, Inqaba Biotechnical Industries (Pty) Ltd., in an effort to help fight tuberculosis on the African continent. Together CLC bio and inqaba biotec will assemble and analyze data from multiple tuberculosis strains, sequenced on inqaba biotec's Genome Sequencer FLX system.

CLC bio, is in the final stage of development of their upcoming CLC Genomics Workbench, which is a new workbench aimed at next generation sequencing and whole genome assembly. The new workbench will support all next generation sequencing platforms, such as Roche GS FLX (454), Illumina Gene Analyzer System (Solexa), and SOLiD Analyzer from Applied Biosystems from the start - with Helicos and others to be included in the near future.

Dr. Oliver Preisig, Executive Director at Inqaba Biotechnical Industries, states:

'The consortium's goal is to find the genetic differences between different strains of Mycobacterium tuberculosis. We target our genome sequencing on XDR (Extreme Drug Resistant) and MDR (Multi Drug Resistant) strains of the bacterium. Having assembled the genomes of these strains we can find the strains' specific markers and develop a PCR test that could bring much faster diagnosis for proper treatment. This means we have an urgent need for whole genome sequencing, and look forward to CLC bio's upcoming workbench, which will provide an intuitive and fast solution.'

Senior Scientific Officer at CLC bio, Dr. Roald Forsberg, continues:

'We are really excited to join forces with inqaba biotec in their Tuberculosis research program. The large amount of genomic data inqaba biotec produces offers us an exciting opportunity to test and fine tune our algorithms on real and challenging data - and at the same time it allows us to contribute to the ongoing fight against Tuberculosis. This is a great motivation to our developer team.'

The South African *Mycobacterium tuberculosis* genome sequencing project is funded by BioPAD, a biotechnology investment trust funded by the Department of Science and Technology of South Africa and includes as consortium members the Chris Hani Baragwanath business unit of the National Health Laboratory Services, the Respiratory and Meningeal Pathogens Research Unit at the University of Witwatersrand and inqaba biotec.

The upcoming CLC Genomics Workbench will among other

things feature an SIMD accelerated genome assembler, and will take full advantage of "paired ends" data. CLC bio will release CLC Genomics Workbench in the spring.

About CLC Bio:

CLC bio is the world's leading full-service bioinformatics solution provider, solely focusing on the development of bioinformatics: software, hardware, data analysis, and custom-designed bioinformatics algorithms. CLC bio is an Apple solution provider and value added reseller. CLC bio's mission is to be among the most innovative bioinformatics companies in the 21st century.

This is realized through:

- ↳ Development of bioinformatics software and hardware based on the latest scientific findings
- ↳ User-friendly, integrated and intuitive cross-platform software solutions
- ↳ Continuous focus on customer needs and superior customer service
- ↳ Frequent product updates including the latest IT technologies and bioinformatics algorithms
- ↳ A flexible IT architecture, enabling customers to buy or develop individualized solutions at a reasonable price

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The GS 20 Training Team with the GS 20 Sequencer. From Left to Right: Dr Oliver Preisig (inqaba biotec); Dr Inga Böll (Roche Molecular Diagnostics, Germany) and Dr Arshad Ismail (inqaba biotec)