twas

Centre of Biotechnology of Sfax

SFAX, TUNISIA

CBS

EXCELLENCE IN SCIENCE

Profiles of Research Institutions in Developing Countries

PUBLISHED WITH THE SUPPORT OF
the David & Lucile Packard Foundation

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Published by TWAS, the academy of sciences for the developing world,
with the support of the David and Lucile Packard Foundation

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Foreword

Founded in 1983 and officially launched in 1985 in Trieste, Italy, by the secretary-general of the United Nations, TWAS, the academy of sciences for the developing world, is dedicated to the promotion of scientific excellence and research capacity in developing countries.

With an initial membership of 42 'Founding Fellows', TWAS now counts 880 eminent scientists in 90 countries among its members. More than 85 percent of these scientists live and work in developing countries. This membership not only gives the Academy insight into the state of science in developing countries, but also provides a unique network of individuals and institutions through which the Academy can coordinate its activities.

Among these activities are the annual TWAS Prizes, designed to honour scientists in the South for their outstanding work in the fields of agriculture, biology, chemistry, earth sciences, engineering sciences, mathematics, medical sciences and physics. TWAS Prizes help bring the achievements of scientists working in the South to the attention of their national governments, providing them with a rare opportunity for recognition in their home countries. TWAS also offers research grants to individual scientists working in developing countries, as well as to research groups based in the world's least developed countries (LDCs). In addition, in collaboration with the governments of Brazil,

China, India and Pakistan, TWAS oversees the world's largest South-South fellowship programme. Under this scheme, young scientists from one developing country visit participating institutions in another developing country – particularly those mentioned above – to further their research, often by having access to equipment and materials not available at their home institution.

Institutions of scientific exellence in the developing world are included in a unique resource book, *Profiles of Institutions for Scientific Exchange and Training in the South*, produced jointly by TWAS and the Commission on Science and Technology for Sustainable Development in the South (COMSATS), based in Islamabad, Pakistan. The fourth edition of this book, published in 2007, lists 485 such institutions located in 65 different countries in the South, and outlines their main scientific achievements, facilities and future plans.

Despite the perception that science in the South is lagging behind science being carried out in laboratories in the North, these 485 institutions provide evidence that top-quality research can be carried out in developing countries. And with a growing consensus that indigenous capacity in science and technology drives sustainable economic development, there is a need for more countries in the South to build their own scientific infrastructure – in terms of both human and institutional resources.

The purpose of this series of TWAS publications, which has been generously funded by the Packard Foundation, is to provide more details about individual 'centres of excellence', including how they developed, how their research programmes are organized, their achievements, their strengths and weaknesses, and – most important – how they

can act as a model that other governments and organizations can follow when considering building scientific capacity. In this way, we hope the series will form a 'blueprint for a centre of excellence' that can be used by policy makers and those involved in the administration of national science policies.

The choice of which institutions to include in the series was difficult. However, it was felt that if the selected institutions all focused on a similar research area, then comparisons between institutions and countries would be simplified, making it easier to draw valid conclusions once several institutions have been studied. We have therefore taken advantage of the existence of a network of institutions created thanks to a programme originally operated by the Third World Network of Scientific Organizations (TWNSO), a TWAS-affiliated organization also based in Trieste and recently transformed into the Consortium on Science, Technology and Conservation for the South (COSTIS), which focuses on the development of pharmaceutical products from medicinal plants. Despite the common theme, the institutions profiled in this series cover a wide range of activities, from the scientific validation of traditional medicines to the use of modern biotechnology. Taken together, however, these institutions are representative of a cross-section of countries in the South. They have also been instrumental in taking indigenous resources – in terms of local biodiversity – and transforming them into profitable commercial products available on local and international markets. In this way, these institutions are excellent examples of how capacity in science and technology can lead to innovation and socio-economic development.

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Introduction and History

When asked whether the Centre of Biotechnology of Sfax (CBS) is a success, director-general Hammadi Ayadi answers with an emphatic "yes". In fact, it would be hard to find anyone who would answer differently among the centre's 200-plus staff of scientists, engineers, technicians and students. The staff's commitment to their organization is unwavering, their enthusiasm infectious, their confidence well founded.

On a continent that has yet to fully embrace the so-called biotechnology 'revolution', and where such research is lagging, CBS is certainly ahead of the game.

While elsewhere in Africa the often-heated biotechnology debate continues to unfold, largely focused on genetically modified crops, CBS researchers are busy exploring biotechnology's wider applications – in particular, seeking practical solutions to local and regional problems in agriculture, industry, health and the environment.

Then and now

CBS began in 1983 in a small corner of the University of Sfax's School of Engineering. Today the institute sits at the centre of its own campus, a tangible reflection of a US$10-million investment. The campus will soon cover eight hectares, once the two new wings currently under construction are complete.

When discussing the history of the centre, one name constantly crops up: Radhouane Ellouz, CBS's founding director. Ellouz is widely considered – not just in Tunisia, but

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throughout the continent – as the father of biotechnology in Africa. Initially a lecturer of biochemistry, Ellouz was the first dean of the Faculty of Science at the University of Tunis. Ali Gargouri, head of the CBS Laboratory of Eukaryotes, remembers: "When he took charge of the faculty, he changed many programmes and introduced genetic engineering, which people found very strange at the time".

Ellouz began to think seriously about biotechnology and the possibility of establishing a dedicated research centre in the early 1970s. "It took almost a decade and a half to put it together. As often happens when you start something new, there were many challenges and difficulties along the way. You have to go step by step", says Ellouz.

Ellouz's first step was to nurture the necessary human resources. He achieved this by identifying promising science undergraduates in Tunisia and arranging for them to continue their studies in Europe, mainly France because of the common language. The risk was that many students would not come back. In Africa, no one can ignore the threat posed by 'brain drain'. After all, more African scientists work outside Africa than on the continent.

How did Ellouz ensure that his young charges would return home? "I had to keep in constant touch with them", he recalls. "I would even travel to Europe to talk to them. We would discuss what they would do when they returned to Tunisia. That was the biggest challenge – making work available and assuring them that there would be research projects for them when they came back. At that point, we could not even discuss money".

Ellouz's devotion and human touch paid off. Today, the majority of scientists at CBS are, in his words, his 'academic grandchildren'.

The next obstacle standing in the way of success was a resistance to using biotechnology techniques. "Many people, still today, are wary of biotechnology", explains director-general Ayadi, "because, even if they understand its benefits, they fear it won't be used well or equitably. And so, they think it would be better not to use it at all."

> *"Radhouane Ellouz, CBS's founding director, is widely considered as the father of biotechnology in Africa."*

Confronted with such resistance, Ellouz needed to convince decision-makers, both of biotechnology's usefulness and that it could be used fairly and for solving regional problems affecting everyone. He arranged a series of conferences and meetings. His efforts culminated in the Tunisian government's decision to implement a 'biotechnology plan'. This led to the creation of CBS in late autumn 1983, under the auspices of the National Institute of Scientific Research.

Between 1983 and 1987, the centre operated largely within the University of Sfax's School of Engineering. A turn toward independence came in 1987, when the United Nations Industrial Development Organization (UNIDO), through a contract with the Tunisian government, awarded the centre a US$1.5 million grant to develop research

projects with Tunisian priorities, in particular the research and production of enzymes with industrial applications. Ellouz explains, "UNIDO gave the money on the condition that CBS commission senior researchers to work on the project." Ellouz did this by calling on Tunisian scientists working in France.

Since then, various government decrees – for example, the finance laws of 1988 and 1989, which spelled out the centre's organization, and the prime minister's decree of 1998, concerning the creation of CBS's research laboratories – led to the institute's current structure. CBS became an independent institution in January 1989 when its budget became officially integrated into the state budget. In 2001, the Tunisian Ministry of Science and Technology announced the creation and composition of CBS's board of directors and scientific council.

CBS at Work

For the past 15 years, CBS has been exploring biotechnological solutions to some of Tunisia's more pressing problems in four key areas: agriculture, industry, health and the environment.

Agriculture plays a vital role in the Tunisian economy and way of life. Where the land is suitable for cultivation, Tunisians grow barley, citrus, dates, olives and wheat. The livestock industry produces beef, dairy products and poultry. Agriculture accounts for less than 13 percent of Tunisia's GDP but employs 55 percent of the work force.

In addition to crop pests and diseases, Tunisian farmers must deal with problems related to desertification – including water scarcity and soil salinization – which reduce crop yields and the amount of arable land. CBS researchers are working on developing drought- and salt-resistant varieties of wheat, biological pest controls, and other ways of increasing production and food security in the region.

Industry makes a larger contribution to the country's GDP (31 percent) and employs nearly a quarter of the work force. Main industries include phosphate and iron ore mining, petroleum and textiles. CBS researchers are seeking ways to help Tunisian industries enhance manufacturing processes to improve productivity. At the same time, they are working on new solutions to the ineffective disposal of toxic and hazardous industrial wastes that pose serious environmental and public health risks.

In the area of health, CBS scientists are researching potential therapies for three types of cancer. They are also developing ways of extracting biophenols – a source of natural antioxidants – from olive processing wastes.

Solutions for agriculture

Olive cultivation and production

As is true of many Mediterranean countries, Tunisia – with its hot, dry summers and warm, wet winters – enjoys an ideal climate for olive cultivation. Indeed a third of the country's arable land is devoted to olive cultivation – 1.6 million hectares. Tunisia is second only to Spain in olive production, and its 60 million olive trees represent 19 percent of the world's olive orchards.

The 'immortal' olive tree – believed to have been cultivated in the region since the 7th century BCE – continues to play a vital role in the Tunisian economy. Today most olives in Tunisia are grown for their oil. Not only is olive oil a staple of the famous Mediterranean diet, but it is also an important export product. The country is the world's fourth-largest producer of olive oil, producing some 170,000 tonnes a year, and the second-largest exporter.

But the nearly one million Tunisians for whom the olive oil industry provides an income are not the only ones living off the olive tree. *Prays oleae*, the olive moth, is a major pest in the region. In a typical year, three generations of this moth plague the orchards, each associated in its larval stage with different parts of the tree. First-generation larvae, for example, feed on the flower buds, while third-generation larvae feed on the leaves. But it is the second generation – when larvae grow inside the olive kernels, before emerging to pupate – that has proven the most harmful. Their destructive force often causes massive fruit drop, as well as damaging the remaining fruit for oil making. Oil from olives affected by the moth has an oxidized, rancid or 'dirty' taste.

BIOTECH SOLUTIONS FOR INCREASING OLIVE OIL PRODUCTION

• Tunisia's adherence to the General Agreement on Tariffs and Trade (GATT) in 1990 opened new markets for its olive oil, notably in Australia, Canada and Japan. And, now, there is a great potential to increase exports to the United States. The Tunisian government hopes to boost production, while improving quality and increasing the share of premium virgin oil.

Indeed, CBS's Laboratory of Molecular Genetics of Eukaryotes may have found a viable way of increasing production. It has carried out research on pectinases – a class of enzymes that break down pectin, the jelly-like matrix that glues plant cells together. Pectin is also the matrix in which other cell wall components, such as cellulose fibrils, are embedded. Working with these enzymes, they have improved processes for degrading plant materials. This, in turn, has facilitated the extraction of fruit and vegetable juices.

Ali Gargouri, director of the laboratory, explains: "Ordinarily, olives are ground, mixed and then pressed to give two separate products: oil, plus water and pulp. We found that if we add pectinase enzymes between the grinding and mixing stages, the cell walls become degraded. As a result, some 10 percent more oil is extracted and less electrical energy is required". Gargouri notes that conventional methods allow "20 kilogrammes of oil to be obtained for every 100 kilogrammes of olives extracted. When enzymes are added, it is possible to obtain 2 kilogrammes more oil from the same amount of extract".

SNAPSHOTS

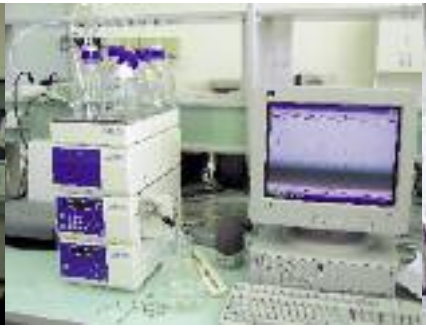
Second-generation olive moths are currently controlled by the application of chemical insecticides. The CBS Laboratory of Biopesticides has conducted successful research on a potentially more effective method of combating this major pest – applying new biological pesticides to first-generation olive moths when females lay their eggs on the blossoms.

These new bio-insecticides are based on *Bacillus thuringiensis (Bt)*, a naturally occurring, soil-dwelling bacterium. "Some *Bt* strains have proven very effective against this pest", says laboratory director, Samir Jaoua. "In collaboration with the national Olive Tree Institute in Sfax, strains obtained were successfully tested on 39 olive trees". Test results were then handed over to the Olive Tree Institute for wider application.

Transgenic crops

Drought and soil salinity are the two main challenges for agriculture in Tunisia, as well as in other Middle Eastern and North African countries.

Tunisia is an arid to semi-arid country. Northern Tunisia, with its moderate annual rainfall of about 800 millimetres, should be an ideal wheat-growing area. Yields, however, are often reduced due to the stress caused by soil salinity. Central Tunisia, where rainfall averages 200 millimetres a year, and southern Tunisia, where there is hardly any rainfall at all, have to contend with soil salinization and water scarcity. These two factors not only cause major yield losses and threaten food security but also restrict the expansion of agricultural land.


CBS's Plant Molecular Genetics Unit is working to enhance drought and salinity tolerance in wheat varieties indigenous to northern Africa by developing transgenic wheat plants with increased expressions of certain genes (for example, dehydrin) that enhance the osmoregulatory capability of the cells, allowing the wheat to adapt to the lack of water and the salinity of the soil.

The unit's studies are based on the understanding that plants develop different physiological and biochemical strategies to adapt to stress. These adaptations are manifested in changes in gene expression. "Plants develop their own mechanisms to react to water deficits", explains Khaled Masmoudi, head of the unit. "In this regard, much of our attention is focused on identifying the genes and proteins induced in response to environmental stress".

To examine the correlation between phenotypic adaptation to stress limitation and induced gene expression, the unit examined a model system consisting of a salt-tolerant line and a salt-sensitive line of durum wheat under abiotic stress and variable environmental conditions.

"Drought and soil salinity are the two main challenges for agriculture in Tunisia, as well as in other Middle Eastern and North African countries."

"We have identified a wheat dehydrin (DHN-5) that is accumulated differently in two Tunisian durum wheat varieties with marked differences in salt and drought tolerance", continues Masmoudi. "The tolerant variety has a greater accumulation of a phosphorylated form of DHN-5 than does the sensitive variety. This suggests that the phosphorylated DHN-5 plays a role in the preservation of cell integrity in conditions of drought and salinity. Thus it could be used as a basis for a molecular screen of tolerance/sensitivity to drought and salt stresses in wheat".

"We have been granted a Tunisian patent on methods of regeneration and genetic transformation of durum wheat genotypes adapted to the Mediterranean conditions", Masmoudi adds.

Biological pest and disease control and fertilizer

In addition to developing new bio-insecticides, based on *Bt* δ-endotoxins, to control the olive moth, the Laboratory of Biopesticides has also produced biological fungicides for the control of plant pathogenic fungi, as well as antibiotics used to control pathogenic bacteria that infect both seeds and plants.

The laboratory is in the process of researching and developing the production of inoculants, or biofertilizer, based on *Rhizobia* (a nitrogen-fixing bacteria). The aim is to reduce the amount of synthetic nitrogen used in agriculture, a source of surface and groundwater pollution.

Human health

Mosquito control

The Laboratory of Biopesticides has also been working on combating mosquitoes resistant to chemical insecticides – such as the *Culex pipiens*, a vector for more than 600 human diseases (including malaria, filariasis, leishmaniasis, trypanosomiasis and encephalitis B). CBS researchers have found several strains of *Bacillus thuringiensis* subsp. *israelensis* – which could be sprayed into breeding sites – to be highly effective against the *Culex* larvae.

Cancer

The 'tumour suppressor' gene called 'p53' – known as the 'guardian of the integrity of our genome' because of its ability to stop the formation of tumours – is the object of intense research by the scientists in CBS's Laboratory of Molecular Genetics of Eukaryotes.

They, along with their colleagues in the Laboratory of Enzymes and Metabolites of Prokaryotes, are working on potential therapies for three different types of cancer: nasopharyngeal cancer, breast cancer and bladder cancer.

"The p53 gene has been implicated in more than half of all sporadic human cancers", explains Ali Gargouri, head of the Laboratory of Eukaryotes. "If a person inherits only one functional copy of p53 from their parents, they are predisposed to cancer and usually develop several independent tumours in a variety of tissues in early adulthood".

CBS has been working on a project in collaboration with a group headed by Mehmet Öztürk, at Bilkent University in Ankara, Turkey. The Turkish colleagues produce p53 in bacteria, while CBS researchers produce it in yeast. "Surprisingly, we discovered that when p53 is produced at a high level in yeast it makes the cells grow very slowly. We are now studying this negative effect by selecting mutant yeasts that escape this effect", Gargouri says.

At the same time, the laboratory has studied the molecular nature of p53 mutations in tumour DNA in breast cancer among women in the Sfax region and from bladder cancer patients in the Sousse region (midway between Sfax and Tunis). In cooperation with doctors from Sfax Hospital, they have investigated whether p53 – and the behaviour and interaction of other proteins – would help in understanding tumour progression and the outcome of patient therapies.

The laboratory, along with Sfax Hospital, is also studying nasopharyngeal cancer. "There is an interesting aspect for us in nasopharyngeal cancer", explains Gargouri. "Unlike the rest of the world, where this cancer mainly affects elderly people, in the Maghreb region, there are two peaks – in young people and in adults".

Environmental solutions

Treatment of olive mill wastewater

As the world's fourth-largest producer of olive oil, Tunisia is also the fourth-largest producer of olive mill wastewater. The process of extracting oil from what Tunisians used to call 'black pearls' – because of the profitability of olives – leaves behind an equally black and toxic aqueous liquid. Disposing of this liquid poses a significant environmental problem.

Untreated olive mill wastewater is ordinarily pumped into shallow pools and left to evaporate. But Tunisia produces as much as 600,000 cubic metres of this highly polluting wastewater each year.

CBS's Laboratory of Bioprocesses, as part of its strategy to treat and add value to agro-industrial wastes, has been studying ways of using micro-organisms to degrade these effluents. In collaboration with the Université Libre de Bruxelles in Belgium, it has developed an olive mill wastewater treatment plant. "Using different reactors, we have taken the effluent through various stages of treatment and recovered some compounds that may be valuable for other uses", explains laboratory director Sami Sayadi.

Treatment results in a solid and a liquid waste, as well as energy – biogas. The latter is achieved through a process of biomethanization. After additional

> *As the world's fourth-largest producer of olive oil, Tunisia is also the fourth-largest producer of olive mill wastewater.*

EXTRACTING BIOPHENOLS FROM OLIVE PROCESSING WASTES

• There is a growing interest in phenolic compounds, owing to their antioxidant and health-enhancing properties. CBS's Laboratory of Bioprocesses has developed a process to extract high added-value bioactive molecules (biophenols) from olive processing wastes and olive by-products.

The interest in this technology began with the environmental problems posed by the huge amounts of olive processing wastes and by-products in Tunisia. Each year the country produces 600,000 cubic metres of olive mill wastewater, 100,000 cubic metres of olive brine wastewater, 265,000 tonnes of olive cake (the residue remaining after olive pressing) and 1.5 million tonnes of olive leaves and branches.

Biophenols are a promising alternative source of natural antioxidants. They are considered completely safe compared to such synthetic antioxidants as butylated-hydroxyanisole (BHA) and butylatedhydroxytoluene (BHT), compounds widely used in the food industry but which have potentially undesirable effects on the functioning of human organs.

SNAPSHOTS

> *"The Laboratory of Bioprocesses is studying ways of extracting natural antioxidants from both the wastewater and olive by-products."*

treatment to eliminate toxic compounds, the solid waste can be used as agricultural compost. The remaining liquid – still rich in nutrients – can be used for fertigation, the addition of fertilizer to crops during irrigation.

"Given the growing demand for energy in Africa and elsewhere, the biogas potential in these by-products is of great interest. In fact, examining the potential of biogas is now part of a study supported by the United Nations Development Programme (UNDP)", explains Sayadi.

Just as olives before pressing contain many nutrients, so too does the olive mill wastewater. Thus, the Laboratory of Bioprocesses is studying ways of extracting natural antioxidants from both the wastewater and olive by-products. In particular, olives are rich in phenolic compounds – natural antioxidants believed to help prevent heart disease, cancers and other ailments. Because the polyphenols are soluble in both oil and water, most are lost into the wastewater.

"We have assessed the biological activities of the major compounds and extracts to evaluate their potential use as food additives and in stabilizing refined husk oil", says Sayadi. "We have identified 11 compounds, with the antioxidant activities of hydroxytyrosol and dihydroxyphenylglycol among the highest".

Sayadi explains that "with doubts concerning the safety of synthetic antioxidants – especially those being used as preservatives in many food products – olive mill wastewater, olives and olive leaves represent potential natural sources of antioxidants. The

laboratory is studying the development of effective procedures for recovering phenolics from the olive mill wastewater".

Treatment of other industrial and urban wastewater

Each year, more than 100,000 cubic metres of surfactant-rich wastewaters are released by cosmetic and detergent industries in Tunisia. As a major industrial centre, Sfax suffers from the environmental hazards posed by such effluents.

"In the past 15 years, the city's wastewater has become highly contaminated with surfactants", says Sayadi, referring to the compounds commonly used in making such products as laundry detergent, shampoos and cosmetics. "Tunisian regulations stipulate that an industry should not generate wastewater with concentrations of surfactants higher than 5 milligrammes per litre. Yet some industries in Sfax exceed 2,000 milligrammes per litre".

> *"Sfax is the capital of the Tunisian pastry, and manufacturers there have been wondering what to do with 'spoiled' sweets."*

The CBS Laboratory of Bioprocesses is working on ways to treat such anionic surfactant-rich industrial wastewater. To counter this problem, the laboratory has:

- selected a powerful strain of *Citrobacter braakii* capable of degrading a wide range of anionic surfactants;
- developed a biological treatment system for these industrial wastewaters based on the use of this bacterial strain in a membrane bioreactor; and
- applied this process at an industrial scale in two large cosmetic factories in Sfax.

The Unit of Valorization of Research Results is working on a similar problem for local olive oil refineries, which generate a wastewater resistant to biological treatment. Unit head Nabil Zouari explains: "Many refineries have been cleaning their production facilities by washing them with soapy hot water. This produces additional wastewater. We have developed a more efficient industrial process for treating such effluents, largely based on separating the soap from the oil". In addition, under an agreement with the Agro-Zitex company in Sfax, which produces edible fats and oils, Zouari notes that the unit has developed an industrial process for the physicochemical treatment, and reuse, of these oil refinery emissions.

Industrial technologies

Enhancing manufacturing processes

A highlight of Tunisian cuisine are its delicious sweets and pastries, based on wholesome ingredients such as almond paste, pistachios, flour, honey, sugar and butter, and coming in a delightful variety of shapes and colours.

Sfax is the capital of the Tunisian pastry, and manufacturers there have been wondering what to do with 'spoiled' sweets. Every day, a typical factory may produce more than 5,000 kilogrammes of pastries that are judged to be unsuitable for the market and therefore need to be recycled.

However, the delicate pinks, greens and yellows that colour the sweets, when mixed together, result in an unattractive dark hue. So, batches need to be discoloured before being reused. "To solve this problem, we developed an industrial process of decolourization", says Zouari. "We also created chemical techniques adapted for the proportioning of sugars in confectionery products".

One popular treat in the region is halva, which is made from ground sesame seeds (or tahini). The tahini and sesame oil in such products easily separates and is also relatively unstable due to oxidation. Halva manufacturers would like to stabilize the oils so they would not separate between the oil and solid phases.

CBS's Unit of Valorization of Research Results has found a solution by using biotechnology processes to extract alimentary fibres from the husks of the sesame seeds. "By incorporating fibres into the products, you get both good texture and stability", explains Zouari. "Such alimentary fibres are technologically interesting and could be added to more oil-rich foods to improve their stability and texture".

"Aside from acting as stabilizers," continues Zouari, "fibres have many other interesting characteristics". For instance, they retain water. "They are very good for you, because they aid the passage of food through the intestine and help prevent colon diseases. And the sesame fibres, found in the husks, also contain antioxidants – mainly hydroxytyrosol, which is believed to be the antioxidant with the highest free-radical scavenging capacity". Medical researchers believe hydroxytyrosol may help combat cardiovascular diseases. To allow these 'fibre' benefits, Zouari's unit has developed sweets that are 50 percent sesame-based.

'BIO-STONING' BLUE JEANS

• In its research on industrial applications of enzymes, the Laboratory of Molecular Genetics of Eukaryotes has selected some local fungal strains that produce alkalophilic cellulases and xylanases – that is, which act as alkaline pH.

Such enzymes can be used in the 'bio-stoning' – rather than 'stone-washing' – of denim fabrics, to give blue jeans a faded, worn-out look and soft worn-in feel. "These enzymes can replace the pumice stones ordinarily used, which Tunisia imports from Turkey", Nabil Zouari says. "One cup of enzymes produces the same results as 50 to 70 kilogrammes of stones".

Bio-stoning results in a much more uniform fading (as the enzymes can reach deep into the pockets and seams) and – not surprisingly – is much gentler on the material than pumice stones, thus reducing the number of defective garments.

"Since enzymes are biodegradable, their use also greatly reduces pollution", Zouari adds. "In addition, using enzymes can lower costs, especially if we lower the cost of their production by selecting mutant strains of bacteria that over-produce these enzymes".

"*Bio-stoning results in a much more uniform fading and – not surprisingly – is much gentler on the material than pumice stones.*"

How CBS Works

The work of the centre is carried out through its four laboratories, three units and four service departments.

Laboratories

Laboratories must receive the approval of the Comité National d'Evaluation des Activités de Recherche Scientifique (CNEAR), which is part of the President of Tunisia's office. To be classified as a national laboratory, a laboratory must have at least six senior researchers, with two having the grade of professor, and four to six students. Above all, the proposed research must be in line with national objectives.

The criteria for setting up units are not as stringent: only two senior researchers and two students are required. Laboratories and units are financed yearly and evaluated every four years.

ORGANIZATION OF CBS

CBS is organized into four laboratories, three units and four service departments:

Laboratories:

- *Laboratory of Molecular Genetics of Eukaryotes*
- *Laboratory of Enzymes and Metabolites of Prokaryotes*
- *Laboratory of Bioprocesses*
- *Laboratory of Biopesticides*

Units:

- *Unit of Plant Molecular Genetics*
- *Unit of Valorization of Research Results*
- *Unit of Information and Scientific Documentation*

Service Departments:

- *Informatics and Bioinformatics Service*
- *Analysis Service*
- *Culture Collection Maintenance Service*
- *Maintenance Service*

Laboratory of Molecular Genetics of Eukaryotes

Ali Gargouri, head of the Laboratory of Molecular Genetics of Eukaryotes, has a dream. "One day", he says, "I hope to find a yeast-based medical protein that can be used to treat the sick".

The name of Gargouri's laboratory refers to the so-called higher organisms (or eukaryotes) – which include fungi, plants and animals – in which the genetic material of the cells is organized into membrane-bound nuclei. Gargouri's team, consisting of some 30 people, focuses on fungi and human beings. The team searches for proteins that might have medical value for humans and fungal enzymes with potential industrial uses.

"Among the illnesses we hope to treat with proteins expressed in yeast is hepatitis, for which we are developing new vaccines", Gargouri says. "The gene coding for the surface protein of a local strain of the hepatitis B virus was successfully expressed in yeast, and its protein is now being purified for use as a vaccine for humans".

"Another strategy in this field has also been developed: the expression in yeast of a protein, p53, which is very important in cancer genesis", Gargouri continues. "In this case, the recombinant yeast would become a useful tool to search for novel drugs acting on this protein".

As for industrial applications of enzymes, the team is looking at the production, purification and biochemical studies of hydrolases. "We are interested in fungal enzymes that can degrade plant material", says Gargouri. "These enzymes could prove very important in industrial applications that require the complete or partial degradation of plant fibres, such as in agro-food, paper pulp, textiles and detergents".

"An application of fungal enzymes has been successfully tested in collaboration with the Olive Institute in Sfax to improve oil extraction from olives. The addition of pectinases, produced in our laboratory by an improved fungal strain, significantly enhanced the oil yield".

Encouraged by these successes, Gargouri hopes that he can soon produce new drugs using modified yeast – *Saccharomyces cerevisiae*, the classic baker's variety, or *Pichia pastoris*, an alternative widely used in laboratory studies. Though he is not yet satisfied with the number of publications and patent applications his work has achieved, he has no doubts his dream will become a reality. And much progress has been made. "Today we have a few excellent collaborations that did not exist 10 years ago, mainly with French but also Tunisian partners".

KEY PERSONNEL

ALI FAOUZI GARGOURI, director of the Laboratory of Molecular Genetics of Eukaryotes

• Ali Gargouri, professor of molecular genetics, was among the first generation of eight students sent to France by Radhouane Ellouz, CBS's founding director. Gargouri has spent most of his career working on yeast, having studied the mitochondrial introns of the organism for his PhD thesis. After completing his undergraduate studies at the University of Sfax in 1979, he left for France to obtain his master's and doctorate degrees from the University of Paris XI and Paris VI, France, in 1980 and 1989, respectively. He then returned to Tunisia to join the centre as director of the Laboratory of Cellulose, which was renamed the Laboratory of Molecular Genetics of Eukaryotes in 1998.

We are interested in fungal enzymes that can degrade plant material.

Laboratory of Enzymes and Metabolites of Prokaryotes

The Laboratory of Enzymes and Metabolites of Prokaryotes has a dual role: to study and produce microbial enzymes that can be used in industrial processes, and to develop biologically active metabolites that can be used as pharmaceuticals, agricultural compounds and food additives.

'Prokaryotes' is the name given to the group of organisms, mostly unicellular, that lack nuclei and in which the genetic material is not membrane-bound (the majority of prokaryotes are bacteria). The laboratory operates with an annual budget of $80,000 derived from Tunisian government funding and grants from such organizations as the International Centre for Genetic Engineering and Biotechnology (ICGEB) based in Trieste, Italy.

"The overall strategy", explains laboratory head Samir Bejar, "is to screen and isolate bacteria from Tunisian habitats in search of enzymes that are stable and interesting – from the biochemical, physiological and molecular points of view. Once defined, these enzymes are cloned and their genes sequenced to identify structural and functional relationships".

The laboratory concentrates on enzymes that can be used in food production. Thus far, it has studied:

- amylolytic enzymes (α-amylases, pullulanases and amyloglucosidases) – with applications in starch bioconversion, commercial baking, detergents, maltodextrin production and animal nutrition;
- isomerases – with applications in the confectionery and carbonated drinks industries;
- glucanases – with applications in animal feedstuffs and brewing industries.

SAMIR BEJAR, director of the Laboratory of Enzymes and Metabolites of Prokaryotes

• Founding member and head of the Tunisian Association of Biotechnology, Bejar is also a 'decorated citizen' of Tunisia, an honour accorded him in 2000. In the same year he also won a Scientific Award from the Arab League Educational, Cultural and Scientific Organization (ALESCO). Knowledgeable in applied microbiology, genetic engineering and biotechnology processes, Bejar obtained his bachelor of science degree from the University of Sfax, in 1979, and his master's degree in molecular biology from Université Paul Sabatier, Toulouse, France, in 1980, where he also completed doctorate studies in 1983. He has served as the director of the Laboratory of Enzymes and Metabolites of Prokaryotes since 1998.

Lofti Mallouli focuses on the other main aspect of the laboratory's research – determining the structure of secondary metabolites and their biological activities. Such compounds can have antibiotic and antifungal activities with applications in healthcare and agriculture. The research involves screening, selecting and identifying bacterial strains that produce the desired metabolites, which are then extracted and purified prior to determining the structure of the active molecules. The final step is to clone and express the genes implicated in the biosynthesis pathways of the interesting active molecules.

This laboratory counts among its achievements the publication of some 40 articles in such international journals as the *Journal of Bacteriology*, *Biochemical Engineering Journal, Enzyme and Microbial Technology, Journal of Biomedicine and Biotechnology,* and *Process Biochemistry*.

Laboratory of Bioprocesses

"We study biosystems – cells, resting cells, enzymes, micro-organisms and plants, in fact anything living – for possible solutions to the biological treatment of compounds that are difficult to degrade, such as industrial wastewater, surfactants and other urban effluents", explains Sami Sayadi. "We also explore possibilities for cleaning gases, solids and liquids".

Sayadi heads the CBS Laboratory of Bioprocesses, which has a budget of US$154,000, derived from the Tunisian government and European Union. The laboratory's expertise includes:

- isolation and characterization of new strains of fungi and bacteria from local habitats;
- production of laccases and peroxidases from fungi;
- bio-reactor conception;
- advanced technologies for the treatment and reuse of urban and industrial wastewaters.

The laboratory is also capable of converting aromatic compounds (such as hydroxytyrosol) using biological rather than chemical processes, for antioxidant production, and can bio-transform liquid and solid residues by using a mixture of microbes in anaerobic digestion and composting systems. In addition, it conducts environmental impact studies, designs industrial wastewater treatment plants, prepares standardized microbial inocula, and develops evaluations and prototype systems for industrial companies in the country.

The laboratory is investigating the potential of using anaerobic processes (i.e., that can occur in an environment without oxygen) to allow slow net growth of bacteria in the treatment of both low-strength domestic and industrial wastewater. A pilot project on anaerobic treatment of industrial wastewaters is underway. Bench-scale anaerobic

KEY PERSONNEL

SAMI SAYADI, director of the Laboratory of Bioprocesses

• Sami Sayadi, head of the Laboratory of Bioprocesses since 2002, is a principal investigator of several international projects for technology transfer. Sayadi obtained his PhD at the University of Picardy in Amiens, France, in 1994. He did his thesis at the University of Compiegne in France in 1988, and earned an engineering degree from the University of Sfax in 1985. He has been at CBS since 1985, first as head of the Bioenergy Unit and then as head of the Valorization Unit.

reactors, which can be operated in combination with membrane filtration devices to achieve low and germ-free effluent concentrations, have also been developed.

The laboratory, Sayadi explains, devotes 50 percent of its time to academic research. The other 50 percent is dedicated to the development of applicable technologies with projects that respond directly to requests from Tunisian companies and other organizations.

Because of its ability to respond directly to the country's needs – and especially its shared objective with the Tunisian government to promote technology application in Tunisia – the laboratory received the Award of Merit from the President of Tunisia.

> *"Samir Jaoua, director of the Laboratory of Biopesticides, has a passion for soils."*

Laboratory of Biopesticides

Samir Jaoua, director of the Laboratory of Biopesticides, has a passion for soils. On a visit to Togo, for instance, he brought back some soil from which he isolated some "very interesting strains of bacteria".

Such bacteria are analysed to fulfil the laboratory's mandate: to research and develop microbial biopesticides used to control insects, fungi, bacteria, and other parasites harmful to plants or humans.

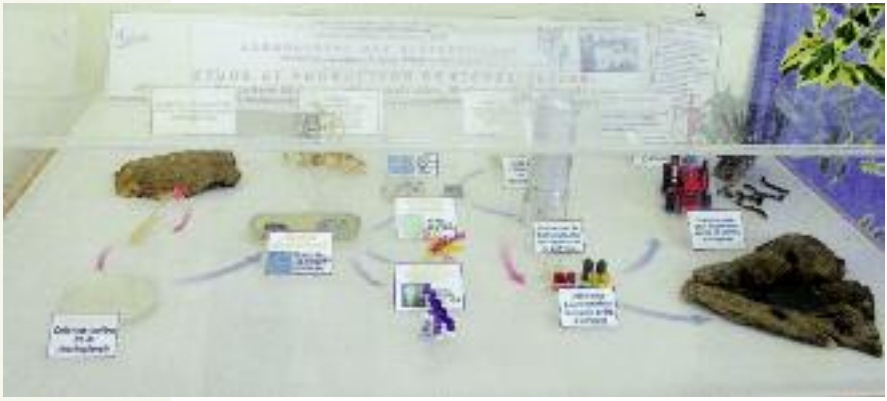
Once samples are collected, Jaoua and his team isolate and identify micro-organisms of interest. These are then studied to identify genes responsible for the interesting traits.

"The Laboratory of Biopesticides is extracting biomolecules – from plants and macroalgae – that have different biological activities, such as insecticidal, antifungal, antibiotic, antioxidant or anti-tumour", Jaoua explains. "Several active molecules, acting efficiently on micro-organisms pathogenic to humans and plants, have been extracted and purified in collaboration with other Tunisian and foreign laboratories".

"Part of our work is to show that the strains we have obtained are original", he continues. "We sequence key areas of their genomes and compare them with published sequences to determine if we have isolated novel organisms".

The laboratory, which began as a unit just six years ago, is already achieving results. Jaoua confidently says, "We have found strains of insects, bacteria and fungi that may be able to control most families of pest insects found in Tunisia".

To date, some 500 strains of micro-organisms have been uncovered, a number of which have been tested in the field and proven effective. The laboratory has produced



new bioinsecticides based on VIP proteins, on the toxic complexes of *Photorhabdus luminescens*, and on δ-endotoxins of *Bacillus thuringiensis (Bt)*. Indeed it has become recognized as one of the major research centres for *Bt*, a naturally occurring, soil-dwelling bacterium widely used for fighting insects implicated as plant pests and human disease vectors. It has isolated some 500 strains of *Bt*, many from soils in Tunisia, some from other African countries, and others from even farther afield.

The laboratory works in collaboration with institutions in Canada, Egypt, France, and Japan, as well as Morocco, where it is involved in searching for a solution to a fungal disease affecting palm trees. To date, several samples of antifungal compounds have been tested. Some have been found to be efficient biofungicides.

The Laboratory of Biopesticides has published 34 articles in international journals, including *FEMS Microbiology Letters, International Journal of Medical Microbiology, Journal of Applied Microbiology* and *Plant Science*. Among the six national patents it has obtained are those for new *Bt* strains with very high insecticidal activities, a new process for producing bioinsecticides by scaled-up fermentation, and a more economical fermentation process.

KEY PERSONNEL

SAMIR JAOUA, director of the Laboratory of Biopesticides

• Samir Jaoua studied biology at the University of Sfax, obtaining a bachelor's degree in 1982. Two years later, he added engineering to his studies before proceeding to the University of Technology of Compiègne, France, for a master's degree, which he completed in 1984. He earned a doctorate in microbial engineering and bioconversion in 1986 from Compiègne and was awarded a doctor of science degree at the University of Tunis in 1991. Jaoua began his career as a lecturer in Rouen, France, in 1987, before assuming a post-doctoral position at Ciba-Geigy Ltd., in Basel, Switzerland, from 1989 to 1991. He joined CBS in 1992 as an associate professor, becoming full professor in 1996. From 1993 to 1998 he directed the research Unit for the Production of Metabolites before becoming director of the Laboratory of Biopesticides in 2002. He has taught at the University of Sfax and has been a visiting professor at Qatar University. He spends two weeks each year teaching microbiology and molecular genetics at the University of Saint Joseph, Lebanon.

Units

Unit of Plant Molecular Genetics

"Our goal is to engineer drought and salinity tolerance in an important cereal crop – wheat", notes Khaled Masmoudi, director of the Unit of Plant Molecular Genetics. The unit is a recent addition to the centre, having been approved by the Comité National d'Evaluation des Activités de Recherche Scientifique (CNEAR) in 2002 to develop research projects dealing with abiotic stress in plants.

"To understand the molecular mechanism of tolerance to abiotic stress in plants, we have chosen to study the functional basis of the response to osmotic and ionic stresses", explains Masmoudi. The unit is studying candidate genes isolated from wheat and involved in the tolerance to abiotic stress. A variety of potentially useful genes have already been identified.

In the areas of genomics and proteomics, the unit is trying to isolate the genes in the halophyte *Aeluropus littoralis* plant that allow it to tolerate water deficits and soil salinity. The goal is to develop drought- and salt-tolerant varieties of wheat and other crops either through plant-breeding or genetic modification.

"We know that the genetic transformation of wheat is not easy", Masmoudi says. "We also know that we are dealing with difficult traits – drought and salinity. Yet we believe we have the strengths and expertise to succeed. I believe we will create a drought- and salt-tolerant wheat variety that will thrive in the climatic and soil conditions found in North Africa and the Middle East".

The unit receives funding from the Tunisian Ministry of Science and Technology, US Department of Agriculture, the European Union and International Atomic Energy Agency (IAEA). It collaborates with organizations in Tunisia, France and Spain, as well as with the International Centre for Genetic Engineering and Biotechnology (ICGEB) and TWAS, in Trieste, Italy.

"I believe we will create a drought- and salt-tolerant wheat variety that will thrive in the climatic and soil conditions found in North Africa and the Middle East."

KHALED MASMOUDI, director of the Unit of Plant Molecular Genetics

• Khaled Masmoudi is a Fulbright Fellow and a visiting scientist at the University of Connecticut, USA. He studied genetics in Tunisia and did his PhD thesis in 1993 at Pierre & Marie Curie University, Paris VI, France. He joined CBS in 1994 as an assistant professor. He was appointed head of the Plant Molecular Genetics Unit in 2003.

Unit of Valorization of Research Results

"When a new product or gene has been sufficiently studied, well characterized and patented, it needs to be developed for industrial production", says Nabil Zouari, head of the Unit of Valorization of Research Results.

Zouari understands this is the final step – which should provide the interface between research and industry. He also understands that this step is often the weak link for institutions such as CBS, which obtain excellent results from fundamental research but have often stumbled when trying to transfer such technologies into new products, processes and services.

The centre "has all the necessary equipment to develop pilot- and semi-industrial scale production plants", Zouari says. For instance, CBS scientists can carry out fermentation procedures followed by the conditioning of cells or biomolecules – steps that are prerequisites for industrial-scale applications. Its equipment can also process three types of products: antibiotics; biopesticides; and enzymes, such as amalyse (used in bread making) and cellulases and pectinases (used for breaking down plant cell walls).

In addition, the centre recognizes a great need to integrate its research laboratories and their outputs, not just with other national research and development agencies, but also within the nation's socio-economic fabric, including the private sector.

In 1998, these principles led CBS to create its Unit of Valorization of Research Results. The unit remains the only facility of its kind in Tunisia. Its mandate is to follow up on research results, develop and finalize integrated processes, and scale them up to pilot and industrial levels. At the same time, the unit assists researchers in the use of technologies, while transferring and exchanging knowledge with both other national centres and the industrial sector.

"We provide solutions for particular problems, for instance to help industries improve their production processes by incorporating new technologies", explains Zouari. "Our approach is to identify the problems and needs of the industrial sector. We then suggest and develop integrated processes as solutions. In cases where companies need additional research and development, the unit turns to other CBS laboratories and staff. We not only offer the industrial sector new processes and products but also scientific competency".

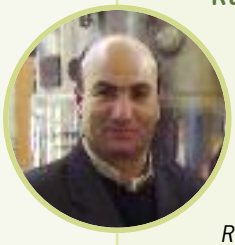
These broad guidelines permit the unit, which works closely with other national organizations specialized in technology transfer, to partner with industries as diverse as confectionery and cosmetics, and with olive oil refineries. Twelve projects are currently in place.

The unit also assists researchers in CBS laboratories and other national research institutions in transferring results either by helping them improve their processes and products or by fostering project innovation.

Although it is currently based at the University of Sfax, the unit's importance to CBS is well recognized. It will move to the CBS campus once the construction of the new wing is complete.

KEY PERSONNEL

NABIL ZOUARI, director of the Unit of Valorization of Research Results



- *Nabil Zouari studied biological engineering at the University of Sfax and holds a doctorate from the University of Compiegne, France. He has been a researcher at CBS since 1998. In addition to steering the activities of the Unit of Valorization of Research Results, he is also a member of the Laboratory of Biopesticides. He was appointed head of the Unit of Valorization of Research Results in 2003.*

Unit of Information and Scientific Documentation

The Information and Scientific Documentation Unit helps keep CBS staff well informed, mostly by maintaining a well-stocked library and by providing access to scientific information online. The unit alerts CBS scientists to new publications of potential interest and conducts surveys of new databases. By negotiating waivers on access to scientific information, especially online editions of journals, the unit has managed to keep costs to a minimum.

Service Departments

Informatics and Bioinformatics Service

The Informatics and Bioinformatics Service manages and maintains CBS's computer facilities as part of its informatics mandate. The department is also responsible for protecting the local data processing network and administering the centre's biological databases. Three major servers are designated for scientific, administrative and security use.

As with all scientific institutions in Tunisia, CBS's activities are monitored by the Ministry of Scientific Research, Technology and Competency Development, which ensures that its research meets required standards. Because the centre receives most of its funding from the government, it must obtain authorization for all its expenditures. For this purpose, the administration servers are networked through a node at the National Centre of Informatics (CNI) to the servers in different ministries, including the Ministry of Finance, which checks that the funding provided to CBS is being used for the intended purposes.

"The security server basically deals with issues of internet access", explains Ahmed Rebai, the department head. "The Centre has a network of 85 PCs, most of which are connected to the internet through a two-megabit-per-second connection, probably four times faster than systems in similar institutes in Tunisia and elsewhere in Africa".

THE GROWING ROLE OF BIOINFORMATICS

• "When I joined CBS in 1999", recalls Ahmed Rebai, head of the Informatics and Bioinformatics Service, "the department was struggling. The use of computer science in biology was still in its infancy. Even buying a basic computer was a major headache. Back then, we didn't have our own funding. The department relied on the centre's core budget. Every time we needed a piece of equipment, we had to convince management it was worth buying".

Things started to change in 2002 when the department secured its own annual budget of about US$7,500. The amount has since doubled. In addition, the Tunisian government recently made improving computing resources a national priority.

The department has also seen an encouraging evolution in its other mandates: to provide statistical and bioinformatic analyses of biological data for CBS scientists and to organize practical courses in bioinformatics.

As recently as seven years ago, few people – CBS management and ministry personnel included – were aware of how bioinformatics could improve their work. For instance, common experiments in biology, such as cloning genes, can be made much easier by using computer programs that predict, based on the sequence of the gene to be cloned, the most appropriate enzymes. "This", says Rebai, "can save both time and money.

It took a lot of time and persuasion to convince our researchers that this science could actually work. Younger scientists were the first to use these services, but now senior researchers invest in the system too".

In addition to providing bioinformatics services to CBS researchers, the members of the department teach biostatistics and bioinformatics at five different institutions throughout Tunisia. Since 2001, the department has offered courses – four or five one-week sessions per year – to students across the country. This was expanded in 2005, when, for the first time, it organized an international course, with participants from ten countries and four continents. Building on that success, the department is currently preparing an international workshop on bioinformatics.

The Informatics and Bioinformatics Service also conducts its own research in bioinformatics, including the development of computer programs that address specific topics in genome data analysis. Examples are programs that identify, with great accuracy, charge cluster segments in proteins, hormone receptor response elements in DNA sequences of mammalian genomes, and promoter sites in prokaryotic genomes.

The department has also developed a database of single exonic human genes and a database of microsatellite variations and single nucleotide polymorphin (SNP) markers in Arab populations. These databases and computer programs will eventually be made available on the CBS website.

KEY PERSONNEL

AHMED REBAI, head of the Informatics and Bioinformatics Service

• *Ahmed Rebai studied in France, obtaining his bachelor's degree in agricultural engineering sciences and his master's in quantitative genetics and biostatistics at the Institute of Agronomy of Paris in 1991. He earned his PhD at the French National Institute of Agricultural Research (INRA), Paris, where he developed new methods and computer programs for analyses of complex genetic data. He also holds a certificate for supervising research, obtained from the University of Paris in 2002. Rebai's areas of interest include bioinformatics and sequence analysis, computational biology, biostatistics, gene mapping and computer programming. He has published more than 50 papers in peer-reviewed international journals. He is also a reviewer for such international journals as* Biometrics, Genetical Research, Genetics *and* Heredity. *Rebai was appointed head of the Informatics and Bioinformatics Service in 2003.*

Analysis Service

The laboratories of the Analysis Service are packed with sophisticated equipment. Indeed, the department provides techniques and services to CBS researchers, allowing them to separate mixtures of chemicals using a variety of chromatographic methods and to determine the identity of separated compounds using mass spectrometry.

"We carry out qualitative as well as quantitative analyses using various chromatographic techniques", says engineer Hedi Aouissaoui. "Our expertise includes such processes as the separation and purification of proteins and other bioactive molecules, determination of the exact mass of pure molecules, confirmation of the presence or absence of compounds in very low concentrations in complex mixtures, and automatic sequencing of DNA".

For these purposes, the department is equipped with:

- four high-performance liquid chromatographs (HPLC), with UV-visible detectors and refraction index;
- fast-phase liquid chromatograph (FPLC);
- gas-phase chromatograph equipped with a flame ionization detector (FID);
- mass spectrometer linked to a capillary liquid chromatograph;
- automated DNA sequencer;
- thermal cycler for carrying out quantitative PCR (polymerase chain reaction) in real time;
- computer-assisted UV-visible spectrophotometer.

"The laboratory", Aouissaoui notes, "has managed to establish many collaborations with the academic and industrial world".

"Our goal is to meet the needs not just of CBS staff but those from other organizations in Tunisia in such diverse fields such as pharmacology, the environment, petrochemistry, cosmetics and food", he adds.

CULTURE COLLECTION MAINTENANCE SERVICE

• The Culture Collection Maintenance Service has collected and maintains more than 1,000 strains of micro-organisms, including 600 bacteria, 400 fungi and 100 yeasts. It is the department's task to isolate, identify and conserve these strains. As such, it works closely with all CBS laboratories.

Each of the strains has been catalogued, and information regarding them is made readily available to CBS researchers. The department also develops new techniques to isolate, identify and process strains of micro-organisms.

"Our objective is to develop in Tunisia the infrastructure of a collection of living micro-organisms with possible biotechnological, industrial and other scientific applications", says department head Abdelhafidh Dhouib. "We are a relatively young outfit, but both our collection and our expertise are growing rapidly".

SNAPSHOTS

Maintenance Service

In addition to installing, maintaining, and making any necessary modifications to the centre's research and other heavy equipment, this department participates in the technological development of projects by assisting with necessary studies on, and the design and realization of, control systems for the valorization of research projects.

Reasons for Success

CBS is located in Tunisia's second-largest city, on the country's east coast, midway between the northern shores and southern border with Libya.

Sfax lacks the glamour of Tunis, the country's cosmopolitan capital, which lies 270 kilometres to the north, and the tourist appeal that has made other Tunisian cities, such as Hammammet and Sousse, famous.

One reason for this is that its coastline does not have an attractive beach. Sfax is also living with the legacy of a former industrial zone, which created an out-and-out barrier separating the city from the Mediterranean Sea.

Researchers at CBS stand firm by their city and suggest that a major reason for the success of the institute lies in its location. It is widely held that the people of Sfax are the most hardworking and enterprising in Tunisia. Indeed, Sfax remains the heartbeat of the Tunisia's industrial sector; it is the country's largest economic centre and the main

source of industrial employment in southern Tunisia. In addition, its educational system and universities are rated higher than even those of Tunis.

One does indeed notice a certain sense of seriousness behind the doors of the centre. But, in addition to the researchers' hard work, skill and dedication, there is another important factor in CBS's success – the Tunisian government's growing commitment to science and research.

"Biotechnology is one of the three major science issues – the others being water and information and communication technologies – that the Ministry of Science and Technology focuses on", explains Rebai. The Tunisian government also pays a great deal of attention to science and research in general. "Currently nearly one percent of the gross domestic product is invested in science and technology, and this figure has been rising steadily", says director-general Hammadi Ayadi.

All this means that institutions like CBS have adequate funding. The centre receives up to 70 percent of its annual budget – including money for research projects and core activities – from national funding. Counterparts in other developing countries constantly complain about a lack of funds and government support. But not CBS. "We have enough funding," confirms Ayadi "not a lot, but sufficient for our activities".

This allows the centre to enjoy sophisticated equipment and infrastructure and it allows scientists to focus on their research rather than spending excessive amounts of time seeking external funds. It also means the centre can conduct research that is relevant to the nation's needs. Indeed research at CBS is largely commissioned by the government in alignment with national priorities.

> *"CBS is one of the first institutes in Africa or the Arab region to bridge the gap between research and industry."*

At the same time, the Ministry of Higher Education, Scientific Research and Technology has set standards that both scientific institutes and research projects must meet to ensure that their results are of a high quality and are conducted in the interest of the international scientific community. This is clearly demonstrated by what the centre considers one of its key measures of success: "We are very well known in international networks", notes Ayadi. "We are, in fact, part of three European networks: medical genetics on hereditary hearing loss; devolution of water and soil; and plant agriculture".

Samir Jaoua, head of the Laboratory of Biopesticides, adds: "One of the easiest ways to measure international success is to look at the number of publications in reputable journals. The centre publishes about 45 such papers a year. That is commendable given our size, and it is particularly good for an institute in a developing country".

CBS also makes the grade for another international yardstick of scientific success – the creation of intellectual property – and it boasts several national and international patents.

In addition, the centre counts the creation of a critical mass of technological expertise among its successes. "In this institute you will find scientists from all fields. You will also find that advanced technologies, such as genetic modification, are routinely carried out in our laboratories", Ayadi points out.

Owing largely to guaranteed government funds and the centre's scientific expertise, CBS has been able to do more than fundamental research. It has managed to weave its results into the socio-economic fabric of Tunisia. Indeed CBS is one of the first institutes in either Africa or the Arab region to bridge the gap between research and industry, neatly combining the core issues of research, innovation, intellectual property and patenting along the way.

Strengths and Weaknesses

Radhouane Ellouz, CBS's founding director, is well aware of both the centre's achievements and what it still has to accomplish. "We have achieved a great deal in the laboratory. Our research activities show that we have the structure to develop technology", he says. "Now we need to strengthen our connections with industry even more. We have begun this process, but we need to take additional steps to exert greater impact".

The centre's success has also brought new challenges. While praising CBS's ability to build capacity by training young Tunisian scientists, senior researchers say the number of students is growing more quickly than expected. "Perhaps we have too many students for our size", says Gargouri, head of the Laboratory of Molecular Genetics. "If you have more than 30 students in your lab, they all require projects and supervision. It is difficult to give enough time to them all. In the future, we need to focus on fewer students while maintaining or even improving the quality of our research".

We need to strengthen our connections with industry even more. We have begun this process, but we need to take additional steps to exert greater impact.

Another challenge lies in Tunisia's geographical location, which makes it difficult to obtain equipment or research material as quickly as is desirable. "We don't receive reagents or chemical products as soon as we would like", admits director-general Ayadi. "When I was working in Paris, I would pick up a phone, call and have the item I needed within hours. Here, you can wait days". Gargouri gives an example of a case where one of his students needed to obtain an antibody from Europe. It arrived a year and a half later – too late for the student, who had already written and defended his thesis.

As a beacon of biotechnology in the developing world, CBS's accomplishments could be replicated in other countries, especially in sub-Saharan Africa and the Middle East. Yet, so far there is little success in this area. "It's a mixture of logistics and funding", explains Ayadi. "Most organizations in Africa don't have enough funding. It's also a lot easier for us to work with Europe, with most countries being just a few hours' flight away. This is not the case with sub-Saharan Africa, where flight connections are often difficult and time-consuming".

But the centre is not giving up and is committed to continue working on paths that might lead to partnerships with other developing countries – partnerships that will put the benefits of research in biotechnology to work for economic development in the world's financially poor, but biodiversity-rich, countries. "This", concludes Ayadi, "is our challenge and our dream".

Conclusion

CBS's organization into laboratories, units and services allows researchers to concentrate on their particular fields of interest, while also creating a collegial atmosphere where they can share knowledge and ideas, thus stimulating creativity. And, with the assistance of the Unit of Valorization Results, researchers can expect their discoveries to be transferred to industry.

Guaranteed government support means scientists need not worry about funding. It also encourages a 'culture of results', focused on national priorities – seeking solutions to local problems, working with industry to increase productivity while reducing harmful wastes, and collaborating with the international scientific community – in which research projects must meet government standards.

The researchers at CBS are enthusiastic with good reason. They know they've got the knowledge, skills and support necessary for success. They also know that whatever they are working on – extracting biophenols from olive processing wastes, combating crop pests with biopesticides, seeking yeast-based proteins with medicinal properties or enzymes with industrial applications, or working to develop drought- and salt-tolerant wheat varieties – success means improving the lives of the people around them.

CBS – a centre run by an all-African staff – can, indeed, be said to be an excellent example of how advances in biotechnology can tap Africa's rich biodiversity to improve agricultural productivity and to develop products of benefit to human health and the creation of wealth.

Acknowledgements

The authors, Liz Nganga and Brian Smith, would like to thank everyone at CBS for their hospitality and helpfulness in researching and preparing this report. We would especially like to thank the director-general, Hammadi Ayadi, and Khaled Masmoudi, director of the Unit of Plant Molecular Genetics, for their kind and generous assistance.

TWAS

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TWAS

TWAS, the academy of sciences for the developing world, is an autonomous international organization that promotes scientific capacity and excellence in the South. Founded in 1983 by a group of eminent scientists under the leadership of the late Nobel Laureate Abdus Salam, of Pakistan, TWAS was officially launched in Trieste, Italy, in 1985, by the secretary-general of the United Nations.

TWAS has nearly 900 members from 90 countries, over 85 percent of whom live and work in developing countries. A Council of 13 members is responsible for supervising all Academy affairs. It is assisted in the administration and coordination of programmes by a small secretariat, headed by the Executive Director. The secretariat is located on the premises of the Abdus Salam International Centre for Theoretical Physics (ICTP) in Trieste, Italy. UNESCO is responsible for the administration of TWAS funds and staff. A major portion of TWAS funding is provided by the Ministry of Foreign Affairs of the government of Italy.
The main objectives of TWAS are to:

- recognize, support and promote excellence in scientific research in the South;
- provide promising scientists in the South with research facilities necessary for the advancement of their work;
- facilitate contacts between individual scientists and institutions in the South;
- encourage South-North cooperation between individuals and centres of scholarship.

To achieve these objectives, TWAS is involved in various activities and collaborates with a number of organizations, especially UNESCO, ICTP and the International Council for Science (ICSU). For additional information, see www.twas.org.

THE DAVID AND LUCILE PACKARD FOUNDATION

The David and Lucile Packard Foundation was created in 1964 by David Packard (1912–1996), co-founder of the Hewlett-Packard Company, and his wife, Lucile Salter Packard (1914–1987). Throughout their lives in business and philanthropy, the Packards sought to use private funds for public good.

Guided by the founders' values, the David and Lucile Packard Foundation supports both people and organizations with the aim of enabling the creative pursuit of science; conserving and restoring the Earth's natural systems; improving the lives of children; and advancing reproductive health.

For additional information, see www.packard.org.

EXCELLENCE IN SCIENCE

This series of booklets – published by TWAS, the academy of sciences for the developing world – highlights successful scientific institutions in the South and explains how their research has both been sustained over a number of years and is helping their host nations achieve sustainable economic development.

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