



Emphasizing the importance of quality: Algis Markauskas, a Lithuanian biochemist, is the new Chief Executive of Fermentas, Vilnius.



The coat of arms of Lithuania, entitled *Vytis* ('the chaser'), is one of the oldest national coats of arms in Europe.

Making restriction enzymes in Lithuania: Fermentas, Vilnius

Baltic Boom

Fermentas, the Lithuanian supplier of molecular biology reagents, is at least as well known for its restriction enzymes as it is clouded in secrecy for its hidden history. *Lab Times* met up with Algis Markauskas, who became CEO this year, and learned how a formerly Soviet academic institute adapted to capitalism and is now the world's second biggest provider of restriction enzymes.

Possibly, they should thank Leonid Brezhnev. After his takeover in 1964, the then political leader of the Soviet Union made a clever move by ending the disastrous era of Lysenkoism. Brezhnev thus stopped the decade-long absurdity of Soviet life 'science' that had declared genetics a pseudoscience and caused nearly irreparable damage to the Union's biology and agriculture. The relief was enormous, in Russia and the so-called 'satellite nations' at Russia's European border.

Meanwhile, in Western countries, the era of molecular biology had started. Swiss microbiologist, Werner Arber, discovered DNA restriction enzymes in Basle, while at the same time Hamilton Smith succeeded in Baltimore, USA, in purifying "molecular scissors". Soon afterwards another scientist from Baltimore, Dan Nathans, used restriction enzymes for a specific fragmentation of the SV40 virus genome.

Just a few years later, the new method was a state-of-the-art technique, crowning restriction enzymes the work horses of the emerging molecular biology. In 1978, only seven years after their discoveries, the three scientists were awarded Nobel Prizes in Stockholm. The life sciences revolution was under way.

Missed the boat?

However, this particular revolution passed the Eastern bloc by. In the Soviet Union and its satellites (such as the Baltic states of Estonia, Latvia and Lithuania), biological sciences were still suffering in the 1960s and 1970s under Lysenkoism. To catch the life science train and to achieve anything in the emerging discipline – cutting DNA strands and cloning them, proceeding with the resulting constructs to express proteins, and so on – Soviet scientists needed one thing. They needed restriction enzymes.

But there were no Soviet producers of the desired enzymes. To buy them from

western countries was too expensive for a federation that had military power but was economically weak. Thus, the Soviet government decided in 1975 that their scientists should create their molecular scissors themselves. They established an institute to develop and produce tools for molecular biology. Its location was not in the Rus-

ing enzymes, DNA/RNA and protein markers and various reagent kits.

Lucky satellite catches up

Why was it luck?

"The newly-founded Lithuanian Institute of Applied Enzymology (IAE) was under the direct umbrella of the Academy of Science



Photo: Wójcyl

It's not convenient for former communist dictators, such as Joseph Stalin (above), to live in Lithuania today. They are exiled to *Gruto Parkas* (unofficially called 'Stalin World'), a sculpture garden of Soviet-era statues, about 130 km southeast of Vilnius. By the way, its founder, the Lithuanian entrepreneur Viliumas Malinauskas, won the 2001 Ig Nobel Peace Prize.

sian centres of science such as Moscow or Novosibirsk, but in the Lithuanian capital, Vilnius.

"That was luck", says Algis Markauskas, 46, a biochemist and since 2008 Chief Executive of Fermentas UAB, a Vilnius-based biotech company that sells tools for molecular biology as DNA restriction and modify-

of Lithuania, which was ruled and funded directly from Moscow", Markauskas explains. That was uncommon and meant one thing, "The institute had significantly better funding than scientific facilities in the rest of Lithuania." In other words, they could do academic research on DNA and enzymes at the IAE on an almost level playing field with



Photo: Fermentas

Fermentas has new established state-of-the-art facilities in Vilnius, to produce restriction enzymes and other molecular biology products under clean room conditions.

capitalist Western nations such as Switzerland, the United Kingdom and the USA.

Markauskas, then an adolescent from the countryside with a strong interest in science, became in the 1980s, as a student at the IAE, one of Vilnius' 550,000 inhabitants. At that time, the institute's director was Arvydas Janulaitis, a PhD specialising in restriction enzymes and recombinant human proteins for pharmaceutical use.

"Janulaitis was a kind of nucleus for the beginning of this research," says Markauskas, who worked from the 1980s onwards in Janulaitis' group to develop technologies for the production of enzymes for molecular biology. Later, Markauskas became a group leader at the IAE, and today, the student and his professor are long standing colleagues at Fermentas – Markauskas as the newly appointed CEO, Janulaitis as Director for Research.

Perestroika heralds new era

For nearly 15 years, the daily grind for the about 50 researchers at the Institute of Applied Enzymology was research, development and production for the good of the Soviet Union. Obviously it was unthinkable for communist scientists in the 1980s to found a private company or to do business with anyone from beyond the border. However, the IAE scientists had better working conditions than their Soviet colleagues. They got in touch with "capitalist" scientists from foreign countries periodically and therefore didn't lose touch with the front line of current research.

This mostly academic life drew to a close, step by step, when in 1988, during Mikhail Gorbachev's programme of *per-*

estroika, the LIAE was allowed to sell enzymes to Western countries. The newcomers from Lithuania tried hard but nevertheless made almost every business mistake a newcomer can make. But they learned quickly. Then came the Act of 11th March. On the 11th of March, 1990, Lithuania became the first Soviet republic to declare its renewed independence. A year of anxiety followed that included an economic blockade, Soviet forces storming the Parliament building in Vilnius and various protest marches, accompanied by the injury and death of numerous protesters. Then, in 1991, Lithuanian independence was recognised throughout the world. Trading conditions immediately changed for the better and Baltic companies entered a new world: that of big business. A few years later, in 1995, the Institute of Applied Enzymology began operating as an independent entity under the name Fermentas (derived from the old German word *Ferment*, meaning enzyme).

They started with 60 people.

Lithuania's undersized biotech sector

Let's make a leap in time. Today, the biotech sector, while small, is still regarded as one of the most promising sectors in Lithuania, far ahead of other former Soviet satellites. Biotechnology is actually part of the Lithuanian Government's long-term strategy, referred to as the "High Technology Development

Lithuania's main capital Vilnius has a picturesque (though small) Old Town, whereas the suburban quarters (right) are run-down and inappropriate for postcards.

Programme", launched "to increase competitiveness by attracting investments, improving education and establishing a biotechnology science park," spoken in official terminology. The nation has three passably known biotech companies – Fermentas, Biocentras and Sicor Biotech, that generate 80 percent of the biotech industry's income. However, Fermentas with its 400 employees is by far the biggest.

Biocentras, founded in 1988, is a small company with 28 employees that produce microbial strains for remediation of soil polluted by oil and oil products and for the treatment of slaughterhouse wastewater.

Sicor Biotech, another prominent Lithuanian biotech firm, has similar roots as Fermentas at the Institute of Applied Enzymology in Vilnius. With 150 employees, Sicor develops techniques for genetic engineering. The company was acquired in 2004 by the Israeli generics producer, Teva Pharmaceuticals. Apart from these three, there are only a handful of other small biotech companies in Lithuania.

"We'd like to have much more biotech start-ups here in Lithuania," Markauskas laments. However, that could take a long time, despite political efforts.

New England Biolabs: the main rival

Fermentas didn't need any development programmes. The enzyme cut its business teeth selling enzymes to Japan. In 1993, Fermentas founded an office in St. Leon-Rot, Germany, as its first international distributor (St. Leon-Rot is now the main office for Europe). Three years later, a US office followed.

At present, Fermentas is the worldwide number two restriction enzyme supplier after New England Biolabs (NEB) from Ipswich, Massachusetts. The Americans have



Photo: Florian Fischer

secured themselves 50 percent of the global market, Fermentas an additional 25 percent.

Established in the mid-1970s as a cooperative laboratory of experienced scientists, world market leader NEB has very similar roots and similar principles to the Lithuanians. NEB offers the largest selection of recombinant and native enzymes for genomic research. In addition, the Americans claim the, "highest standards for quality and value".

Entering a crowded market

This sounds very familiar. Fermentas claims that its scientists have discovered "more than 30 percent of all known restriction enzymes" and during his conversation with *Lab Times*, Algis Markauskas repeatedly emphasised that the motto of Fermentas was quality. One could dismiss such a statement as hollow marketing speak, or as a desperate bid to catch up with NEB. In fact, the Lithuanians didn't have any other choice but to focus on quality, Markauskas says.

"When we started our business, we didn't have extra cash for aggressive marketing. But the market was crowded, nobody waited for us," Markauskas laughs. "Therefore we decided to focus on quality – on good products, good service, convenient manuals, and good support. In this way we grew slower than we could have made by aggressive marketing, but our customers trusted us and so we got loyal customers and long relationships to them."

It's an interesting fact that for several years, even NEB sold enzymes that were produced by Fermentas – and was not cagey about it.

ISO certification and top secret finance

In addition, Fermentas quickly upgraded its internal standards. In 1996 already, one year after the former academic lab became an independent entity, Fermentas acquired ISO certification (as the world's first company producing enzymes for molecular biology). Today, the firm produces more than 600 molecular biology products under ISO 9001 and ISO 14001 quality and environmental management systems.

Not unusual for a private company, Fermentas is secretive about its financial figures. Revenue in 2007 was, "considera-



(above) Trakai Island Castle, located 28 km west of Vilnius, is the most outstanding defensive complex in Lithuania. Between the 13th and the 15th century, the castle was nearly impregnable for invaders.



(left) A tough nut to crack as well: At the U19 World Championships in 2007, the US basketball boys nearly shipwrecked on their Lithuanian rivals (at the end the US boys won 90-81). Quite possible that world market leader New England Biolabs will soon be forced to struggle in a similar manner against its Lithuanian competitor Fermentas.

bly more than 10 million euros," Markauskas says, with a growth rate of "considerably more than the 8 percent" at which the Lithuanian mother country is growing. The company was profitable all the time, he adds. "We hadn't any year with a loss, and we always reinvested all the profit." With no opportunity to verify his statements, one has to believe them.

Fermentas was always majority-owned by its founders and workers. In the last years, some private shareholders from Germany and Canada came along, and in October 2007 an institutional investor, Summit Partners from Boston, USA, came into play as a significant minority shareholder. "We believe that will strengthen us and allow us to grow faster – much faster than we grow by investing our profits alone," Markauskas comments.

Is he thinking about going public or about merging with a competitor?

"I don't want to disclose any plans for the future – but we are open! We are open to any business decision that will be necessary in future. We are not restricted to something," Markauskas answers.

Proud to be Lithuanian

The biochemist, whose parents were deported by Stalin's regime to Siberia in the 1940s, has retained a certain patriotic pride in his company, that is, since 2003 – at least on paper – Canadian.

"Fermentas International Inc. is for financial reasons located in Ontario, Canada, but our main activities are located in Lithuania, of course. However, we are proud of Lithuania and that we are Lithuanians. We feel responsibility for our community and therefore we sponsor numerous cultural projects, for example the building of modern sculptures in the European park (Europos Parkas) in Vilnius." W. KOEPELLE