

Evaluation report

Evaluated point	Grade	Comments
Scientific impact of research	Good	<p>Protobios is a privately-owned biotech company situated in the Technopol. In 08-09, the company was at level of independence. We had an opportunity to meet with the CEO (Dr Kaia Palm) and the CSO (Dr Toomas Neuman). We met research scientists and had free access to interview researchers with no interruptions or interferences. The previous day, we met with Professor Tõnis Timmusk, Scientific Advisor and Founder of the company. We met research staff and students during our visit. Research scientists publish in middle to high impact journals, and papers by CEOs had over 500 citations. Protobios does frontline research both on methods and topics (primarily cancer, and “immunprofiling” diagnostics) that are currently the subject of high levels of scientific interest. The self-reported number of major projects in the period 2010-15 was 8. It was stated that some of the project lines had been scaled down (RNA array, stem cells) whereas others were regarded as high priorities, especially the immunoprofiling avenue. We got the impression of many ongoing projects: in-house, at TTU and in Protobios’ subsidiaries and spin-offs that comprised vaccines, immunoprofiling of autoimmunity conditions, stem cells, biomarkers, and food analysis.</p> <p>The company is clearly commercially-driven, but it is engaged in innovative and high-quality research, with a substantial academic output completed in parallel with their commercial activities. Several published papers have achieved very high citation rates and have had a significant impact on the development of the field. While there was the potential for exploitation of the commercial opportunities presented by manufacturing, these were not being pursued: rather the strategy was focused on innovative research and the translation of this research to commercially-viable products that could be licensed to others.</p> <p>Clearly, there was a scientific focus and desire to publish and an expressed incentive to collaborate with international and TTU partners. Protobios provided structured training opportunities for 11 students in the period 10-16, including 3 PhDs. The laboratory is well equipped with core facilities and equipment for their research. Further, they have a contract with TTU allowing Protobios access to the equipment present there.</p> <p>Protobios produces highly cited, high-impact scientific articles. The number of publications listed in the years 2010-15 were 13, which is not impressive considering the presence of PhD and MSc students in addition to core staff.</p>

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		<p>This yields about one paper per 5 years per employee which should be regarded in the context of a private enterprise. However, the obtained scientific results led to applications (patents) that form the basis for spin-off companies: Fibrotex, Cellin Tech and more. The research environment consisted of enthusiastic researchers working in a positive atmosphere having a flat managerial structure.</p> <p>We conclude that the scientific impact of research is good.</p>
Sustainability and potential of research	Good	<p>We were shown the premises including biobanks and cell culturing facilities. The predominant part of the organization with labs, offices and IT support was together on one floor with shared offices and easy accessibility. We gained the impression of an open and collegial working environment and a non-hierarchical structure that is conducive to both professional and personal development. Protobios perceives itself as being part of the “personalized medicine” national program of Estonia. Multiple collaborative agreements assured full access to technical equipment at the Tallinn Technical University. Laboratory equipment was up to date and lab space was ample. The department hosted an IT unit and integrated IT experts for data storage, handling and analysis. There were solid connections with the Technical University. Kaia Palm was teaching 25% of her time at TTU and thus exposed to the student mass with access to recruit students.</p> <p>Funding derived from domestic R&D contracts and “international” contracts and grants with 3-500.000 EURO per year. Protobios employ between 10-15 research staff on average in the period 2010-16. The staff and generated income from R&D contracts, grants and commercial activities seems stable based of the number of staff over the years. The richness of ideas present will generate new opportunities when needed.</p> <p>The great international collaboration network is considered to assure access to resources. Especially the scientific accreditation by Estonian state, the support and supervision of PhD students and the contract with TTU on access to special equipment are good examples of Public/Private Partnerships. Extensive exchange of PhD students with Technical University and with foreign labs – a post-doc from Belgium just started and an Italian post-doc left on the day of the visit. The accreditation from 2010 allowing Protobios to supervise PhD student had led to 9 PhD’s.</p> <p>It is critical to Protobios to be successful in national and EU granting programs for “smart specialization”. Planning beyond a horizon of a few years is not possible. Few data were presented to us to support the immunoprofiling as a new breakthrough. It is clear that Protobios is a fast mover</p>

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		<p>to use modern high throughput techniques and apply well known phage display techniques in new and ingenious ways. Moreover, Protobios engaged external partners whenever necessary to accomplish project needs.</p> <p>There was strong evidence of commercial success with spin-off companies in diverse scientific areas. Some of the areas were more in the cosmetics and well-being industry and thus had a commercial focus rather than a strict health science focus. Retention of ownership of Intellectual Property (IP) rights opens the prospect of an income stream to fund further developments. The commercial success of some of these (specifically FibroTx) seems not to be based on sound science (as admitted by Dr Neuman).</p> <p>Sustainability and potential of research is considered good.</p>
Societal importance of research	Good	<p>The potential of the research and commercial direction for societal impact is clearly high. Immunomics and immunoprofiling may prove to be a major tool in the analysis of health status, and may have a strong potential to influence not only the use of biomarkers for diagnostic and monitoring purposes but also the development of new therapeutic interventions. However, at present this is potential and not proven. There was also mention in our discussions of a wide array of further potential applications, including quality control, forensic science, environmental monitoring and systems biology. The commercial potential in terms of company growth is impressive. Protobios may have further impact on society by creating highly specialized biotechnology job platforms within Estonian Society. The generation of commercial business, patents, teaching of students, generation of work places through of spin-off and hopefully a widespread use of diagnostic and therapeutic agents that improves health for patients, all in all prove importance of such start-up companies for the Estonian knowledge society. It is a prime example of successful Public-Private-partnerships.</p>
Scientific basis in the field is sufficient to conduct doctoral studies. (This question should be answered only if: a) institution being evaluated is conducting doctoral studies and; b) The field being evaluated is proposed to grant		<p>The company is built on a sound scientific base, with one foot in industry and the commercial exploitation of ideas and the other in research and early-stage product development. There is a good mentoring program for students at all levels, though the former reliance on undergraduate students seems to have been replaced by an increased number of PhD students and post-doctoral workers. Good mentorship and close supervision seem to have resulted in successful completions on a laudable timescale. These graduates should be highly employable, with a range of transferable skills that will make them attractive to both academia and industry. The challenge will be to ensure that there are opportunities for them to remain</p>

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positive evaluation. If these conditions are met then: a) If the level of scientific basis is sufficient for conducting doctoral studies in every structural unit being evaluated, then the answer should be „yes“; b) If the scientific basis is not sufficient in some structural units, then those units should be listed.)		in Estonia. Protobios represents a top class environment for conduct of PhD studies due to the presence of excellent supervisors, free flow of ideas, access to good scientific equipment, well sourced research budgets and a fruitful research environment and thus the basis is regarded as very good

Summary assessment

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Areas of special note as appropriate (Where necessary indicate sub-fields, assessment criteria, and/or structural units which, in the committee's opinion, were of a notably high level.)		Notably high level: The short distance from basic science to applied science and further to commercialisation. It is a showcase for university people how to generate business and work places.
Areas in need of improvement as appropriate (Where necessary indicate sub-fields of the field being evaluated, assessment criteria, and/or structural units which, in the committee's opinion, revealed significant shortcomings.)		Suggestion for improvement: The company should have more focus on possible freezer breakdown by installing alarms.
Assessment proposal to the Minister of Education and Research	To grant positive evaluation	The committee suggests positive evaluation

Feedback

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Feedback for institution (This question should be answered only if the institution asked for feedback from the evaluation committee in the self-report (about up to three specific areas of R&D which it finds to be currently important, e.g., related to its development plan).)	In response to the question of a wider implementation of immunoprofiling in EU Healthcare we cannot give advice as we were not presented with findings in detail. One way is to publish many good papers on the subject, establish collaborations with leading public laboratories (e.g. State Serum Institute in Copenhagen, run by Niels Heegaard) and give many but cheaper licenses.
Suggestions for unit, institution, state etc (As appropriate, committee can give additional feedback for the structural unit, the institution, or the State (please specify whom feedback is directed to) according to the directive assessment criteria for regular evaluation (article 7).	Protobios insists on maintaining its own biobanks, which is ambitious but also risky since critical mass is not easily achieved. However, if focus is maintained on selected cases this could be a sustainable approach. There appeared not to be collaboration with the nationwide Genome Centre at Tartu University that hosts 5% of the Estonian population. It is highly recommended to continue this accreditation with PhD student supervision on basis of the high scientific activity in the laboratory and as a living example on how good science and commercialisation goes hand in hand. We saw evidence of a strong pipeline of ideas, suggestive of a bright future. Development of these ideas into solid research and commercial success seems to be limited rather by resource than by ideas and industry on the part of the CEO, the CSO and the whole R&D team. The laboratories were well-equipped, with access to further research and analytical facilities within Tallinn University of Technology laboratories: this provides resources that complement the facilities available within the company itself. An international, rather than purely local, perspective was obvious, with other European nationals (Italy, Belgium) represented in the research team: contacts with Japan were also in existence. There is clearly an open and collegial working environment with good inter-personal relationships: this is crucial for success.