

Estonian Higher Education Accreditation Center

## **Joint Final Report**

### **Research Evaluation on Genetics, Physiology, Microbiology and Molecular Biology**

Institutes evaluated:

National Institute of Chemical Physics and Biophysics (NICPB) Laboratory of Molecular Genetics/Gene Technology Center, Tallinn Technical University;

NICPB Laboratory of Bioenergetics;

Estonian Biocentre, Institute of Molecular and Cell Biology, Tartu University and Center of Technological Competence of Tartu University;

Institute of Exercise Biology, Tartu University

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## **1. Organizational Arrangements and General Comments**

The task of the panel was to review research conducted between 1996 and 2000 at the four research units. Self-assessment reports were provided to the Panel prior to the evaluation. The Panel discussed potential conflicts of interest in an organizational meeting. Dr. Stuerzbecher informed that he has a joint EU grant with Dr. Maimets of Tartu University/Estonian Biocentre. The Panel visited the respective research units in Tallinn and Tartu, and also visited two Tartu University biotechnology spin-off companies, QuattroMed and Asper Biotech.

The Panel was surprised that the Medical Faculty of Tartu University (Biomedikum) targeted on research in the fields of genetics, physiology, microbiology and molecular biology were not included in the present evaluation. The Panel would have been well qualified to do it, and collaborative research arrangements exist between Biomedikum and some of the four research units now evaluated.

The Self-assessment reports provided to the reviewers were generally adequate, but could have been better organized to facilitate the reviewing process; several

sections e.g. the lists of grants with publications were redundant. The oral presentations, interviews and tours were informative. They largely confirmed the impressions the Panel had developed on the basis of the written material but also brought out more distinctly some of the quality differences, in research resources and research abilities among the research units and their individual programs.

## **2. General Recommendations**

Some of the general impressions and recommendations of the Panel are:

- Estonian research in the units evaluated is performing quite well, especially considering the limited resources currently available for most of the research units. This is largely due to the traditions, human resources and enthusiasm that survived during the difficult periods in the past.
- The Estonian government should realize that now it has a golden opportunity to invest in biotechnology and molecular biology to fertilize the development of also the commercial aspects of this field. At present only very few biotechnology companies exist, but with proper investments in basic and applied research and more organized teaching the development will pay excellent dividends.
- The Panel also felt that Estonia could well have two national centers in the field of biotechnology and molecular biology, Tartu and Tallinn. In addition to the promotion of research at Tartu University, also investments to develop the research infrastructure within and around Tallinn Technical University should be made. Moreover, the undeveloped transportation connections between these two centers (road and railroad, lack of airport in Tartu) clearly hamper development.
- The government should expand a repatriation program to recruit the excellent Estonian scientists now working abroad.

## **3. National Institute of chemical Physics and Biophysics and centre for Gene technology**

### **3. 1. General comments**

The institute was founded in 1979 as an independent research institute.

The name stems from the Soviet time, which explains its choice of name. The institute is practically divided into several separate units. The Laboratory of Molecular Genetics (LMG) and Laboratory of Bioenergetics are meant to be exclusively dedicated to research while the centre for Gene technology (SCG) is primarily a teaching institution. There is a near 100% overlap between the personnel of the LMG and SCG.

National Institute of chemical Physics and Biophysics and centre for Gene technology now operate at two locations. The administration and heavy computing is down-town in the city and the laboratory work is carried out at the Mustamäe campus which, creates great administrative difficulties for the everyday research projects.

At present the institute functions without a director. The institute is *de facto* run by the chairman of the Scientific Council whose background is in physics. The deputy chairman has a molecular genetics background but is operating mainly as a director of the Helsinki Biocentre. There seems to be no external advisory board for the activity. Also, a functioning internal scientific board dealing with the organization of molecular genetics and microbiology is lacking.

### **3. 2. Evaluation of the activity**

We were impressed by the enthusiasm and high quality of research in spite of the extremely difficult working conditions. This of course means that a lot of the scientific work still needs to be carried out outside of Tallinn. Thus we have to rate the institute as **satisfactory**.

The institute has made excellent repatriation and has been able to recruit high quality research scientists. The publication record contains many articles of high-ranked peer-reviewed international journals. The work is being carried out on important and interesting topics.

The most prominent problem of the institute is the uncertainty of the future of the leadership. The present situation with the leadership is that the institute is in fact run by the chairman of the scientific council is unfortunate for the molecular genetics section which should have more possibilities to influence its own activities. We were concerned by the lack of strategic planning and coordination and collaboration.

The research groups are small and there are too many diverse research projects with little methodological overlap or cooperation. There are many diverse

topics under investigation, some of which do not belong to a Molecular Genetics unit.

The deteriorated building and even probably unhealthy conditions are of major concern. Without facelift the institute is unable to perform its function and to attract prominent scientists from outside.

Much of the laboratory equipment is outdated. There is lack of animal facilities that would be urgently needed for the projects. This is especially the case because the institute is in the fortunate position to have expertise for handling transgenic and knockout animals.

The excellent facilities of the physics unit have not been exploited in the biological research. We were impressed by the competence and resources of the physics unit and these could be exploited in activities such as computing and molecular modeling.

The current relation between the institute and the teaching unit of Tallinn Technical University seems uncoordinated. Teaching biosciences is expensive and the University should really allocate resources to ensure development of these fields.

### **3. 3. Evaluation of research groups**

Of the projects implementing modern techniques the Panel was most impressed by the Molecular Oncology and Neurobiology units. Concerning their publication record these groups are **good** and could in a better research environment reach excellence. The Molecular Plant Virology/Biology units is carrying out solid basic research reaches nearly the same level (**good/satisfactory**).

The Cell Physiology and Biotechnology groups including the Toxicology are professionally competent and unique but they are on the other hand using standard technology. Their line of research is **satisfactory**. We were impressed by the drive and productivity of Dr. Anne Kahru who is taking a more modern approach. However, most of the research in the Biotechnology unit is primarily at an applied level. Therefore these programs do not fit very well at present within the molecular genetic programs.

The protein chemistry group (**satisfactory/good**) dealing with snake venoms also appears competent. This group suffers from the lack of modern instrumentation. They could benefit from extending their research in enzymes

and production of diagnostic reagents into other areas of general interest such as the recent anticancer angiogenesis-related program at the institute. They have, however, been able to induce collaboration with the mass spectrometry group, which integrates biophysics and molecular biology.

The group working on developmental aspects of the interferon/2-5A system and DNA diagnostics is not making enough progress (**satisfactory**).

The NICPB laboratory of bioenergetics headed by Dr. Saks is highly productive, publishing about 5-10 articles per year in high-quality journals reaching occasionally the Journal of Biological Chemistry level. We rank this laboratory as **good**. Yet much of the significant results are achieved abroad. Dr. Saks is holding another position in Grenoble. Considering the resources available the group is unusually efficient with a well-established collaborative network coordinated in Tallinn. The group suffers from outdated ancient equipment, which is nevertheless maintained functional. Also this group suffers from lack of animal facilities as the transgenic and knock-out animals have to be kept in Grenoble. This group is already establishing itself in proteomics and could gain from setting up a proteomics core facility. This group has also utilizes the NMR facility of the institute. The expertise of the group could well be applied to medical problems like mitochondrial diseases.

### **3. 4. Recommendations**

#### **3.4.1. General recommendations for the institute**

- It would be advisable to include *molecular genetics* in the name of the institute to underline the importance of this field. This discipline has a great growth potential in the capital area of Estonia.
- Immediate steps should be taken to identify new directions for leadership either in the form of a democratic organ or a strong successor of the present leadership.
- The organization of the institute needs revision. There is an overall lack of strategic planning. The institute should probably be divided into two autonomous units: a Chemical Physics Unit and a Molecular Genetics Unit. The applied biotechnology groups should be affiliated more closely with the Technical University.

- There should be a contract outlining the position and financing of teaching between Tallinn Technical University and the institute. This is the only way to ensure development of productive and innovative biotechnology industry for the benefit of the Estonian people and would bring resources to the institute. It is urgent that the Technical University develops a program of educating biotechnologists with competence in molecular genetics.
- Of all the units we evaluated this institute suffers most from lack of resources. Thus we recommend that the administration building downtown could be leased and the funds used to renovate and equip the facilities of the Mustamäe site. Several of the groups deserve and badly need more modern instrumentation. The administration should be transferred to the Mustamäe site.
- The institute with its competence in biophysics and molecular genetics could with rather small investments be developed into a National Structural Biology Centre.
- The protein chemistry expertise should be better utilized within the molecular genetics program and this would be important in the research in proteomics. The group has already utilized mass spectrometry for protein analysis. This type of methodology may be essential for structural determination of proteins. The unique combination with biophysics gives the institute an unusual opportunity to develop new approaches and be developed to a National Proteomics Centre. The Institute has in fact the potential to develop proteomics technology further (higher sensitivity and resolution). An essential prerequisite for this would be a strategic plan and exact time-table of the necessary steps to be taken.
- An animal facility should urgently be established to meet the needs of several groups (Kogerman, Metsis, Saks).

#### **3.4.2. Recommendations concerning individual groups**

- The University should take financial and administrative responsibility for the Cell Physiology and Biotechnology units. The group would be important for teaching and its competence should be used in the development of biotechnical industry around the university.
- The group of Dr. Merike Kelve may wish to consider a new direction in its research where its experience is used better.
- The group of Dr. Jüri Siigur could be central in the setting up of the proteomics facility. It should focus his research on projects more related

to the molecular genetics groups such as his emerging work on disintegrins.

#### **4. Institute of Molecular and Cell Biology of Tartu University (IMCB), Estonian Biocentre (EBC) and Centre of Technical Competence (CTC)**

##### **4. 1. General comments**

EBC was founded in 1985 as an independent research unit as a joint venture between Tartu University and Estonian Academy of Sciences, IMCB was founded by The Tartu University Council in 1990 and CTC in 1997 as a branch of Tartu University to develop technologies. The three independent units form a functionally integrated entity and were formed to represent the different financing sources. The three units (collectively called as Consortium below) function largely in the same building, composed of an old part owned by Tartu University (Faculty of Biology) and a new part opened in December 1997 and owned by the English charity "Citrina Foundation UK". Both parts of the building are quite functional and well maintained. Some sections are getting quite crowded and demand for new space exists. The spin-off companies (see below) are located quite far from the premises of the Consortium.

##### **4. 2. Evaluation of the activity**

The Consortium researchers (**good**) represent the elite of molecular and cell biology in Estonia and have been quite successful, e.g. compared to Tartu Medical Faculty researchers, in obtaining external international (EU, Soros Foundation, Howard Hughes) and national funding on which the Consortium largely operates. This is an indication of their professional capacity. The International Advisory Board is important in guiding and directing the research in the Consortium. The quality and quantity of research output by the various groups/departments varies; some are close to excellent, some are good and some merely satisfactory. Notably, within 1996-2000 only one of the researchers reached the very top-level journals (Cell, Nature, Science, EMBO J.) with a full article.

##### **4. 3. Evaluation of research groups**

###### **4.3.1. Department of Biochemistry**

The chair of biochemistry is not filled at present. Therefore it is not relevant for this evaluation. Dr. Sedman who is taking care of the teaching duties of this department, will be subject to our evaluation as included in the Department of Molecular Biology. The facilities are split into two different places. This setting is not ideal for the functioning of this department. The research is hampered by the heavy teaching load, which is by far too much for a single person to cope with. People who could share teaching responsibilities are not available at the department.

#### **4.3.2. Department of Biotechnology**

This is a large and productive unit, which has built up a lot of expertise in large-scale gene screening technology. This technology will be essential for future DNA diagnostics as well as research on the human genome. The research is unfocused and publications are numerous but seldom reach top level. Therefore, in spite of their intensive activity we rate them at present as **satisfactory/good**. This group has been instrumental in launching of the array biotechnology spin-off company Asper Biotech. This innovative company, we predict, will be one of the major biotech companies in Estonia.

#### **4.3.3. Department of Cell Biology**

The laboratory with 17 people (research and teaching) has been able to acquire EU funding, works on a competitive field (p53 tumor suppressor protein), is engaged in international and in-house collaboration. The laboratory still lacks profile in p53 research and is **good** but not as yet at the cutting edge. The laboratory is doing good solid work in several aspects of p53 research but could be more original by focusing its activities. During 1996-2000 one PhD and less than 10 original publications were generated. Of these two, driven by Dr. T. Maimets, appeared in a high-class journal, Oncogene.

#### **4.3.4. Department of Evolutionary Biology**

The department (**satisfactory/good**) seems to function in a very organized fashion. Laboratory space and equipment are very satisfactory and of technically high standard. The expertise is profound and the results are of general interest and appeal to a wider audience of the non/professional public. However, the scientific approach taken is undemanding and merely a descriptive collection of data. Although there are some publications in highly ranked journals, scientists from this department are not listed as main authors of these papers. The main scientific contribution of this department clearly lies

in deepening the understanding of human genetic inheritance and diversity of different genetic pools, which might be of interest to the Estonian society.

#### **4.3.5. Department of Genetics**

The projects of the department of genetics (**good**) are devoted towards different aspects of microbiology and environmental research. Their studies on the genetics of xenobiotic metabolic regulation are exciting. The latter are of high importance for Estonia in terms of dealing with toxic waste. The project of biodegradable polymers is very promising and has a good potential to be exploited in a spin-off company. First steps in this direction have already been taken. We were especially impressed by the scientific output of Dr. Maia Kivisaar. The protein expression project by Dr. Tiina Alamäe is still in its infant state. Nevertheless, the results so far look promising.

#### **4.3.6. Department of Microbiology and Virology**

This is a fairly large laboratory with 6 senior researchers holding *e.g.* doctoral degrees, 6 PhD students. The laboratory has (had) several international grants (Howard Hughes, EC Copernicus) as well as abundant national funding (Estonian Science Foundation, Estonian Innovation Foundation). The basic projects center around papilloma virus research in which the laboratory is clearly one of the international leaders. During 1996-2000 the laboratory generated 3 PhDs and 16 original publications, of which 9 appeared in high-class journals (EMBO J., J. Virol., J. Bacteriol., Molec. Microbiol.). Dr. Mart Ustav also takes a keen interest in business-oriented biotechnology and was a key figure in the establishment of the spin-off company, QuattroMed. The laboratory is undoubtedly one of the most dynamic and productive units in the consortium (**good/excellent**).

#### **4.3.7. Department of Molecular Biology**

This department (**satisfactory**) is mainly devoted to understanding ribosomal RNA structure and functional mechanisms of ribosomes. The quality of the projects is good. However, the productivity is lacking behind. There are only few publications in highly ranked journals.

#### **4.3.8. Centre of Technological Competence**

The main achievement of this unit (**good**) has been setting up and running the transgenic & knock/out mouse facility. This unit appears to be in a good shape and functions very well. Although many of the projects run in the institute

would benefit from including transgenics in their research programs, there are apparently only very few collaborations. On the other hand, the demand for transgenic animals from outside the institute and even from abroad is excellent. For that reason, Dr. Alar Karis has set up a spin-off company for transgenic mice, which produces animals mainly for customers recruited by a German company. In collaboration with his Dutch colleagues, Dr. Karis has recently published a number of papers in highly ranked journals. It is expected that he will successfully continue with his productive work. The collaboration with the Physiology Department of the Medical Faculty appears highly interesting.

#### **4. 4. Recommendations**

##### **4.4.1. General recommendations for the Consortium**

- The Consortium composed of three units may need to be restructured to a more coherent entity. The third unit (CTC) now appears to represent partly a core facility, partly a unit designed to assist development of commercial biotechnology and partly a appealing target for external funding. The Panel recommends that this type of confusion should be terminated.
- The Consortium should develop its core facilities such as DNA sequencing, amino acid sequencing, confocal microscopy, FISH, FACS, large-scale cell culture, cDNA arrays, yeast-two-hybrid systems, and especially bioinformatics. Admittedly most of these facilities are available but they have not been organized to a user-friendly core service maintained by the overhead charges taken from the grants. This would be an essential attraction when the Consortium tries to recruit/repatriate top-class scientists. On the other hand the in-house transgenic mouse unit is not utilized effectively.
- We agree with the leadership that the Consortium should make intensive efforts to generate additional space to accommodate/repatriate talented scientists from abroad.
- In the present state the Consortium in a way is too local (“boiling in its own soup”) and efforts should be made to attract scientists e.g. from neighboring countries to create a more international scientific environment which helps to generate networks of excellence.
- Teaching appears to be quite unevenly divided. For some IMCB departments, such as Department of Biochemistry, the teaching burden is just too much. All researchers, including graduate students, should contribute to teaching. This would be like a compensation for the privilege to carry out research within the Consortium.

- The Consortium needs to develop more organized research training and create Tartu University Graduate Schools.

#### **4.4.2. Recommendations concerning individual groups**

- The institute should reconsider whether a department of Biochemistry should be re-instated in the present setting of the institution or whether it would be better to find some other arrangement. If a decision is made that there should be such a department, then appointment of a new Head of Biochemistry should urgently be undertaken. The assets for this department should be made more attractive in order to be able to recruit a competent leader who should fit into the overall programmatic setting of the institute. The teaching load of this department should be rationalized and divided between several scientists. The facilities of this department should be brought into close proximity of the Biocentre.
- The Department of Biotechnology should make use of their technology also in scientifically more fundamental projects.
- The Department of Cell Biology needs to focus and make use of the transgenic core facility.
- The excellent facilities, talents and scientific expertise of the Department of Evolutionary Biology should be diverted to cover also scientifically more challenging problems.
- The Department of Microbiology and Virology should not devote too much of their capacity in applied research.
- The already very well established transgenic facility should be exploited further and developed towards an independent spin-off company, capable of recruiting directly its own customers.

### **5. Institute of Exercise Biology, University of tartu**

#### **5.1. General comments**

The Institute is a major part of a relatively small Faculty of Exercise and Sports Sciences whose main objective is training of teachers and coaches. There are four main lines of research namely functional morphology, exercise physiology, exercise biochemistry and nutrition, kinesiology and biomechanics. The teaching seems to be well organized and is probably of high quality. The staff is very up to date concerning developments in muscle physiology. The institute operates at three locations.

#### **5.2. Evaluation of the activity**

The institute appears to be very isolated from the research community in Tartu. The senior research staff of the institute suffers from heavy administration. One is at present Vice Rector and one is serving as Dean. There has also been a considerable reduction in teaching staff, resulting in a heavy teaching load for the remaining staff. Most of the research is carried out in the old building at 5 Jakobi Street which is in urgent need of renovation and most likely unhealthy and unsuitable for physiological research.

Quantitatively the Institute has a high productivity. Except for the functional morphology most of the activity is concerned with human subjects. For the latter activities the competence and resources are adequate. This research seems very productive but superficial and applied. When compared to international physiological research the quality applied research can only be evaluated as **satisfactory**. Yet, the Panel appreciated the overall organization and structure of the research.

The research is however important nationally. However when judged as compared to other applied exercise biology units the activity would probably be satisfactory/good. The basic research deals with many interesting projects on physiological aspects of exercise myopathy, but suffers from lack of resources and do not fit in very well in the general setting. The projects themselves are good, but the quality and productivity of the present research is only satisfactory. They could in another environment produce very important international results. Dr. Teet Seene has a good collaboration with Dr. Saks in Tallin.

### **5.3. Recommendations**

- The isolation of the institute should be dealt with. The studies on human subjects and administration could probably be moved to the Sports Centre where the facilities seem much better. The basic research of the institute could be improved by moving into another location at least partially in close contact with Biomedikum where it could make use the core facilities of the biomedical center.
- Another improvement would be to include more international research programs and to publish less on superficial studies. There would be

- several important basic problems, which could be investigated more in detail.
- Fusion of the Institute with the medical faculty would help the administrative and teaching load. We feel that the Institute is too small to have such a heavy administration. The Panel supports the idea to reestablish a specialty of Sports Medicine. The institute could then form the nucleus of teaching within this discipline. We understand very well that due to the present education organization and research in Kinesiology and Biomechanics there are limitations concerning the localization of the different activities.
  - We also recommend that the research should in the future include more modern methodology for instance the transgenic facilities. An overall increase in basic research on exercise and myopathy is highly recommended.
  - The international contacts of the research could also be improved and the institute should have a program for postdoctoral training in foreign institutions.

Tallinn, December 2, 2000

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