SAMBIO Core Facilities at the University of Gothenburg

CORE FACILITIES

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GENOMICS
MAMMALIAN PROTEIN EXPRESSION
PROTEOMICS
CENTRE FOR CELLULAR IMAGING
THE ELECTRON MICROSCOPY UNIT
SWEDISH NMR CENTRE
TRANSGENIC CORE FACILITY
CENTER FOR MOUSE PHYSIOLOGY AND BIO-IMAGING
LABORATORY FOR EXPERIMENTAL BIOMEDICINE

GÖTEBORGS UNIVERSITET

Scientific Background

Health care in a global perspective is much recognized as a matter of inequity among different populations around the world but also among different citizens within single nations. A marshal plan has been formulated under the sticker “Closing the gap in a generation” in order to focus on how health equity can be obtained through multilateral collaborations. The contributions of Gothenburg and Sweden in such collaborations will not be dealt with specifically in this presentation. A Centre for Global Health at the Sahlgrenska Academy was opened in February 2009 to specifically address such issues.

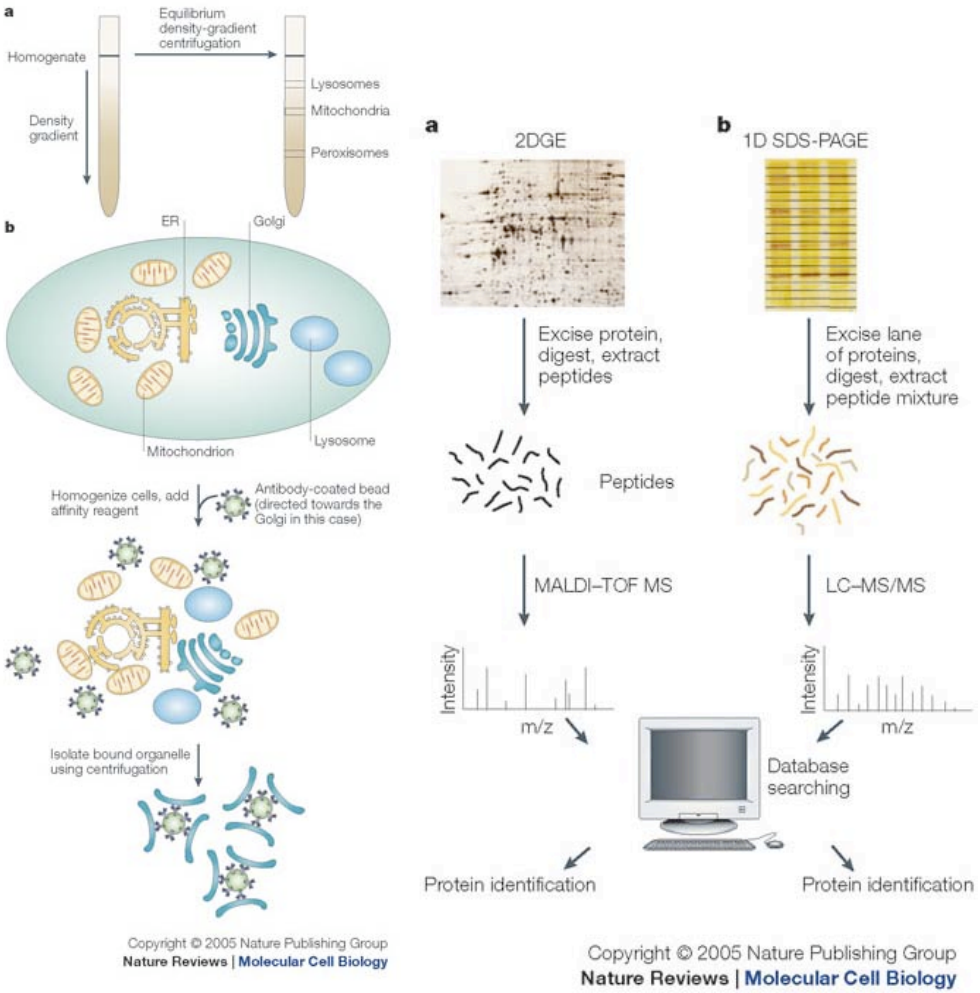
Modern medicine is increasingly becoming dependant on finding diagnostic and prognostic biomarkers as well as explanations to the exact molecular pathogeneses underlying common diseases in populations and in single individuals. With such new knowledge there will be new conceptual strategies for developing new tools for diagnosis and follow-up, new therapeutic agents, new regimens for prevention and treatment, and new ways of identifying individualized therapy to avoid unnecessary, ineffective or even harmful high numbers of patients being treated (avoiding preventable side effects).

For the physician, being responsible for the medical care of individual patients, decision making is becoming increasingly demanding both in terms of expected knowledge and in terms of shrinking timeframe for each patient. It may be estimated that >90% of the data on which the physicians make decisions is based on information from analyses performed by laboratory medicine, radiology, nuclear medicine and physiology. The primary data from such analyses are becoming increasingly larger and more complex since at the molecular and cellular level the resolution is increasing and thus the need for development of supportive transdisciplinary information systems for correct decision making is becoming obvious.

With the introduction of automated instrumentation for high-throughput molecular analyses (“-omics”) for genome sequencing, for gene and protein, lipid and carbohydrate expression an immense amount of molecular data may be obtained from single individuals, single organs, single cell types or even from single subcellular compartments. These techniques are of course not applicable only for samples of human individuals but are particularly well suited for comparisons with other animals and organisms, occurring naturally or as gene modified strains to test a particular hypothesis or treatment regimen. This kind of migration from the patient to the laboratory organisms and back is often referred to as translational research or translational medicine (see figures below).

Basic science is founded on the exchange of data and open access to public databases is a hallmark of modern research but such information is yet not made public from patient data neither from clinical tests of new drugs nor from the daily work with individual patients. Thus, there is an immense reduction or even waste of clinical and laboratory data from the clinics which might be overcome if the tools for protection of patient integrity and the safe handling of medical data sets could be made available on-line to the clinicians as well as to the researchers. Bringing such data together in a meaningful context will need the expertise of the medical profession, the university and the industry in diverse areas e.g. evidence based medicine, laboratory medicine, radiology and physiology, systems biology, biostatistics, bioinformatics, e-science, computer technology, biochemistry, pharmacology and toxicology. In a broad sense these concerted actions could be named Systems Medicine.

In Gothenburg we have a unique opportunity to realise Systems Medicine into a functional entity since we have, within a very limited geographic area, all the competence that is needed for such an enterprise; Sahlgrenska University Hospital, University of Gothenburg, Chalmers University of technology and both large, small and medium sized companies in the biotech and biomedical sphere. Such a constellation is also strengthened by the permanent establishment, by the government, of the Västra Götaland Region, responsible for sustainable development, good conditions for a flourishing industry and good health care in all parts of the region.



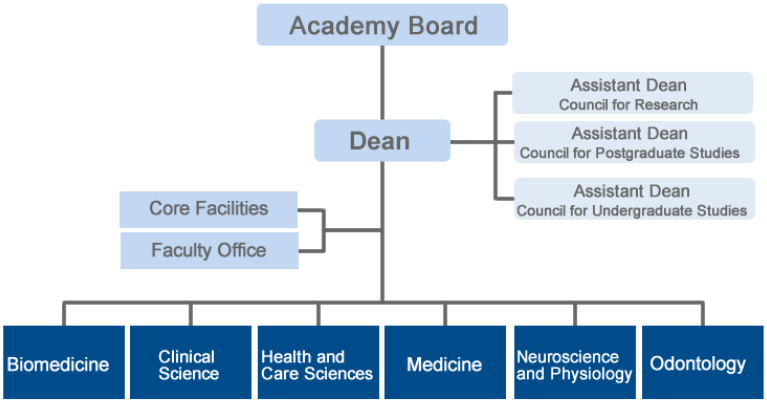
by courtesy of prof. Tommy Nilsson, GU

Administrative background and financing

The University of Gothenburg has for the last decade worked systematically to establish open access core facilities in the areas of natural sciences and biomedicine. The concept for these facilities was already from the start a strategy to strengthen the quality of research and education to the highest international standards. Additionally, by establishing open access core facilities not only the top five, often senior, researchers or research groups at each faculty would have access to such facilities but also younger researchers and students which otherwise would not be able to afford such techniques. The realization of these ideas was only possible through the visionary and generous donations given by major private funds (e.g. Wallenberg, Hasselblad and Lundberg) enabling investments in state-of the art equipment. In most cases the funding was based on research programs and scientific collaborations between several universities in Sweden (SWEGENE, Swedish NMR Centre etc.).

The outcome of the SAMBIO Core Facilities in Gothenburg has been evaluated several times during the last few years both locally and at the national level. A general conclusion is that the establishment of these facilities has been a significant accomplishment giving a scientific boost to the universities involved. The administrative routines, the employed personal, the researchers, the technological platforms and the funding situation has evolved considerably during the last few years and the facilities are now well recognized and well established parts of the university core activities.

On the administrative level the universities of Gothenburg have established SAMBIO as a reference group dedicated to stream-line applications for equipment, running costs, quality assurance, education, updating and development of facilities of common interest to all parties. The SAMBIO group is constituted by representatives from the Sahlgrenska Academy, the faculty of Natural sciences, Chalmers university of technology and the Sahlgrenska University Hospital, and has the vice chancellors´ expectation to override traditional faculty and university borders on infrastructural issues.



The formulation of scientific hypotheses, both in a biological/biomedical context but also in a biotechnological context, is critical for success at each core facility. The concepts of various applications in the strategic areas of research, defined by the Swedish government in “Forskningspropositionen 2008”, will be dealt with separately. Here, the facilities will be described as to their present characteristics and future needs. These open core facilities now cover the areas of genomics, proteomics, mammalian protein expression, cellular imaging, mouse physiology and bio-imaging as well as the handling of animals at the experimental biomedicine facility.

The SAMBIO Core Facilities has a yearly budget of about 80 MKr, has 60 persons employed (about 40 in EBM), has contributed to more than 900 projects/studies and is yearly contributing to about 100 scientific publications. The staff is heterogeneous as to academic degrees but, apart from those of the EBM facility, contains mainly PhDs. Scientific advisors are recruited from faculty staff (professors) to strengthen the link to research groups with high demands on services and expert knowledge in the various technological platforms. Reference groups are established to discuss and communicate activities within each of the facilities.

There are some areas of competence and infrastructural facilities that are still under development within the SAMBIO Core Facilities e.g. molecular bioinformatics and systems biology. However, there is an on going collaboration between researchers from different faculties within the universities of Gothenburg in these areas and a new Centre for Systems Biology and Medicine is now being established in Gothenburg. Another area of competence is handling of samples as well as clinical and research data from biobanked material. This has so far been handled appropriately and efficiently in collaboration with the Sahlgrenska University Hospital and the Västra Götaland Region. The Sahlgrenska academy is also engaged as an active part in the national collaborative efforts in biobanking within Sveriges Kommuner och Landsting (SKL).

Technical facilities and competence centres

CCI - Centre for Cellular Imaging
Confocal microscopy is provided for living cells and fixed tissues or cells. Spinning disc-microscopy is used for studies of faster cellular processes. Multiphoton techniques are used for deeper penetration into tissues. FCS, FRAP and FRET are being used for mobility and interaction studies. LM-EM correlative microscopy is being used for ultra high resolution.
Manager; Julia Fernandez-Rodriguez, PhD

CPI - Centre for Mouse Physiology and Bio-imaging
This centre deals with gene modified animals and animal disease models which are being characterized with modern physiological and bio-imaging methods. The primary areas of analyses are behaviour (basic behaviour, feeding habits, activity, memory and learning), metabolism (energy demand, training, body composition, glucose metabolism), cardiovascular characteristics (blood pressure, ECG, endothelial function, heart function) as well as bio-imaging methods (ultrasound, MRI (7 tesla instrument), DEXA, SPECT, CT).
Manager Anna Wickman, PhD

EBM – Laboratory for Experimental Biomedicine
This facility is housed within a separate building and holds all necessary equipment for handling and treatment of experimental animals in biomedical research. The building contains a large number of laboratories with direct access to stabling facilities of both smaller (rats and mice) and larger animals (eg. pigs and sheep). EBM contains high technology operating theatres for both research and education with possibilities for video conferences and auscultations. Complete equipment for training of physicians for laparoscopy, open surgery, radiology, orthopaedics and anaesthesia is available. Two university veterinaries at EBM are responsible for veterinary medical control of all animals within the facility, yearly give courses in experimental animal sciences and assist researchers in applications to ethical committees and in planning for experiments.
Manager Ulf Nannmark, MD PhD

Genomics CF
This facility is equipped with 2nd generation instrumentation for sequencing, genotyping and gene expression. The facility offers identification of genes coding for defective proteins in specific inherited diseases or identification of genetic risk factors for disease. A series of software programs are used to enable interpretations of large data sets.
Manager Tommy Martinsson, prof

MPE - Mammalian protein expression
This facility offers large scale production of recombinant proteins for research purposes. Specific focus is given to post-translational modifications e.g. glycosylation. In addition cell cultivation and assistance with construction of expression vectors are offered as specific services.
Manager Malin Bäckström, PhD

Proteomics CF
This facility is equipped with MALDI-TOF, Q-TOF and LTQ-FTICR MS instrumentation and is specifically focused on identification characterization and quantification of proteins in biological samples. The centre gives advice for protein purification and mass spectrometric analyses but also offers help in data interpretation as well as image analyses of 2-D gels for identification of biomarkers.
Manager Elisabet Carlsohn, PhD

Electron microscopy and TOF-SIMS molecular imaging
These facilities are not formally incorporated into the responsibilities of SAMBIO Core Facilities but are open access facilities to academic researchers and private enterprises. The EM unit is fully equipped for various preparation (standard, immuno- or cryo-) techniques and offers scanning or transmission EM analyses including digitalized data handling. The TOF-SIMS equipment is a unique facility, financed by grants from the Committee for Infrastructure, and was installed in 2009 for imaging and molecular analyses of biological samples. The tissue preparation techniques are critical also for this technique. Managers (corr.) Bengt R Johansson prof., Håkan Nygren prof.

The Swedish NMR Centre
This facility is a joint effort between the Natural Science faculty and the Sahlgrenska Academy at the University of Gothenburg and gives access to competence and instrumentation for elucidating structures of and interactions between proteins and low molecular weight compounds. The equipment includes several NMR-instruments in the range from 500 MHz up to 900 MHz.
Manager Göran Karlsson, prof

Visions for future

As the scientific achievements and technological innovations progress there will in the future undoubtedly be a need for changes in the repertoire and services given by the Core facilities; new techniques will be launched some of which will replace older techniques due to lower costs, others due to better (molecular, spatial or temporal) resolution or sensitivity and some will be better evolved for human studies. The need for novel instrumentation will come both from researchers but also from the facilities themselves and will - in mutual discussion and concerted actions - be applied for from both private and public funds. In addition, there will

be a continuous need for upgrading advanced equipments that are getting old and where spare parts or running costs, e.g. due to outdated guarantee and service agreements, are becoming increasingly expensive. At the other end of the spectrum, some services or instrumentations will become so mandatory to most research group that they no longer fit as a service in a core facility. For SAMBIO Core facilities it is up to the Board of the Sahlgrenska Academy to finally decide upon which facilities should be established and which should eventually be closed down.

Relations to 2009 strategic applications from the University of Gothenburg

During the processing of this document, as well as the writing of applications to research areas of strategic importance for the University of Gothenburg, straight forward coordination between the applicant parties was guaranteed through the office of the vice-chancellor.

Major investments for a continued advance in SAMBIO Core Facilities

The added cost for fulfilled investments in equipment within the SAMBIO Core Facilities was in 2007 about 76 MKr (equipment from 10 KKr to 15 MKr), service costs per year around 1.5 MKr (ranging from 15 to 500 KKr) and the estimated needs for reinvestment and upgrading of instrumentation for the period 2008-2015 was estimated to be around 50 Mkr (60 items ranging from 5 KKr to 20 MKR). Due to the dramatic drop in the Swedish currency this figure for major investments has now been updated (See Table I).

Table 1

Investment requirements for the Sambio Core facilities 2009-2012					
		Amounts in MKr.			
Centre	Priority order	Equipment/methodolgy	2009-2010	2010-2011	2011-2012
Genomics	1	"3rd gen Sequencing"	7,5		
	2	SNP detektion	2,5		
	3	LIMS (IS-support) and software	1,0	0,5	
	4	DNA Extraction (upgraded)		2,0	
	5	RNA extraction (inclusive)		1,0	
	6	Stand alone TaqMan		2,0	
	7	Stand alone Beckman FX		2,0	
Proteomics	1	2-D gel equipment	1,0		
	2	MALDI-TOF/TOF MS	3,5		
	3	Triple Q LC/MS		3,5	
	4	HPLC		0,2	
	5	CTC-PAL sampler		0,5	
Cellular Imaging	1	Laser Scanning Mikroskop LSM 700	1,8		
	2	Upgrading of VisiTech Spinning disc	0,6		
	3	Upgrade of lasers (514, 491, 561 nm)	0,4		
	4	Upgrades of emission filters	0,2		
	5	Laser Scanning Microscope LSM 710		4,5	
	6	Uppgradering Bio-Rad Multiphoton		0,4	
Mouse Physiology and BioImaging	1	Microsurgery microscopy with camera and minor eqipment	0,5		
	2	Low molecular MRS	1,2		
	3	Videocamera SMART		0,2	
	4	Ultrasound equipment		3,0	
	5	Startle and fear box		0,2	
	6	Replacement Biospec 70/20			20,0
Mammalian Protein Expression	1	Incubator	0,2		
Experimental BioMedicin	1	Racks for mice stalling	1,5		
	2	Ventilated changing stations	1,2		
	3	LAF-benches	2,0		
	4	Surgery surveillance system	0,3		
		SUM (MKr)	25,4	20,0	20,0