

STRATEGISK INNOVATIONSAGENDA

PERSONALIZED MEDICINE – from invention to innovation



Vision

Together we will join forces and make Sweden the first country ever offering a health care system based on the concept of Personalized medicine.

The consensus could not be clearer – the concept of Personalized Medicine opens up for opportunities we cannot afford to neglect. Not only will it offer better healthcare to a lower cost but it will also stimulate research, invention and innovation. Even though there is a national consensus on the importance of the Personalized Medicine-concept, little has happened that actually benefits patients. The concept of Personalized Medicine poses a multitude of challenges when it comes to multidisciplinary collaboration, logistic and economical issues. However, this agenda describes a vision shared by academia, industry and healthcare system - a prerequisite for a successful implementation of a national programme for implementing Personalized Medicine.

True creativity requires collaboration and international competition

Aim

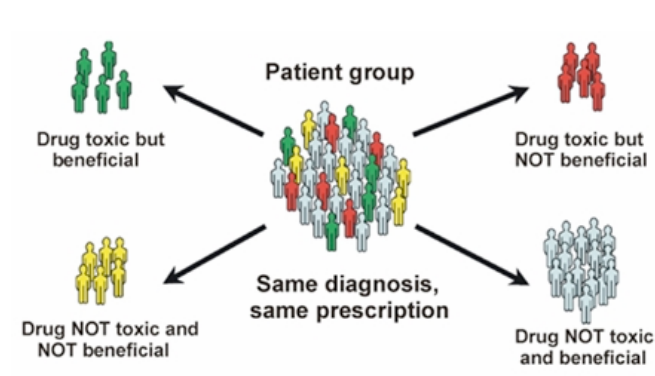
The aim of this agenda is to develop a triple-helix approach, leading to innovative products and processes, better use of drugs, health economy benefits, improved survival figures for patients, and instituting Sweden as a continuous leading force in the development of Personalized Medicine in cancer.

Background

Cancer as a single entity is now the world's leading cause of death with 8,2 million deaths a year according to World Cancer Report 2014 (1). For years it has been obvious that the alarming rise in cancer burden globally has to be met not only with better therapies but with a truly dedicated focus on prevention, early detection, better education and of course refinement of the whole therapeutic armamentarium. In this context the concept of Personalized Medicine, also called *Stratified* or *Precise Medicine*, has a major role to play.

The European Alliance for Personalized Medicine defines the concept of Personalized Medicine as "a targeted approach to the prevention, diagnosis and treatment of disease based on an individual's specific profile" – or in short "the right treatment to the right patient at the right time", (Figure 1) thereby helping not only the patient but also the health care providers to get more value for taxpayers money. Furthermore, Personalized Medicine will make use of new scientific understanding and new technologies to adapt prevention, diagnosis and treatment of the disease to the specific profile of the individual.

In the report "*Personalized Medicine, a new era for healthcare and industry*", presented by Life Science Foresight Institute in Lund (2), the importance of Personalized Medicine is described as "*one of the most exciting topics in medicine today. Although it initially may be difficult to understand the underlying principles of Personalized Medicine, it is a concept that has the potential to transform medical interventions by providing effective, tailored therapies*



based on the genetic profile of an individual. Personalized Medicine represents a new approach to therapy, utilizing the vast wealth of information inherent in our genetic code".

Figure 1. Schematic picture of Personalized Medicine (source: www.tedxvienna.at/blog/personalize-this/)

To date, the impact and implementation of the Personalized Medicine approach has varied depending upon specialty and focus area. It is relatively easy to point out the impact of Personalized Medicine in the regulatory arena. The FDA in the US was quick to establish a regulatory procedure, e.g. if use/prescription of a drug can be linked to a gene mutation that informs about how a patient cohort will or will not benefit, such diagnostic information must

be a part of the documentation submitted for registration of the drug. FDA has approved several drugs under these conditions over the last 15 years. In EU, EMA does not have the "legal" requirement to pursue a similar regulatory process for drug approvals, i.e. linking a diagnostic method to the use of a drug. However, health care payers can, nevertheless take cost/benefit ratios for new drugs based on what is known about patient treatment outcomes, into account when they decide on reimbursement.

In the biomedical field, the attention given to Personalized Medicine spans from research initiatives to dedicated efforts to introduce gene medicine in clinical practice. Examples of research related initiatives are the allocation of resources by NIH in the US into the area of biomarkers and the ambition expressed by the British Government to make the UK the No 1 country in practicing Personalized Medicine, inspired by gene medicine. NIH considers biomarker research a key activity in order to improve disease diagnostics, which in turn facilitates the clinical options regarding treatment decisions. This R&D focus is also in line with regulatory efforts in FDA of joint registration of a drug together with a diagnostic test for the indication or disease in question. As regards the British Government the interesting point is that the "gene medicine" initiative is the first politically expressed national ambition to make use of the R&D deliverables, and among them the Personalized Medicine approach. The British Government also actively promote the conversion of R&D deliverables into clinical practice at the nationally controlled hospitals, as well as business opportunities for the British industry. As an example, Cancer Research UK has and will invest heavily in their cancer centers, as world class competitive and innovative networking organizations, for "*the translation of cancer research for patients benefit*". An important player in this vision is a number of Experimental Cancer Medicine Centre (ECMC), where each ECMC is a partnership between an NHS Trust or Board and a university, which enables the best health researchers and clinicians to work together to generate novel approaches and ensure close collaboration with big pharma. An outstanding example is the collaboration between Cancer Research UK and AstraZeneca with the goal to repropose an experimental drug that was originally designed for asthma into development to a clinical trial for kidney cancer treatment. The collaboration is part of an agreement where the partners want to develop promising anti-cancer agents which the pharmaceutical companies have not selected to further development and where the development is better placed to progress through early phase clinical trials in collaboration with the health care system (3).

Personalized Medicine and Sweden

In Sweden, the Personalized Medicine approach is gradually becoming a consideration for the biomedical community, but so far primarily in academic research and/or development projects and not in the health care system as a consequence of decisions taken by politicians and administrators. It is also difficult to assess to what extent the Swedish medical industry has taken on Personalized Medicine compared to industry initiatives in the US and UK. Compared with the British Government, the Swedish Government has not outlined a

national ambition to further the implementation of gene medicine or Personalized Medicine, which may be understandable given the regionalized decision-making in the Swedish healthcare sector. The importance of Personalized Medicine has also been identified by the European commission thus several programs in the Horizon 2020 has a focus towards Personalized medicine. Several of the proposed projects within the research area associated to this agenda can well be funded within such a program.

It is increasingly clear that the concept of “one size/medicine fits all” is no longer state of the art for optimal medical treatment. In this context, cancer is not one disease, but it is hundreds. The large, and to a great extent unknown, heterogeneity of several cancers leads to the fact that treatment protocols are often shared for patients with diverse tumour subtypes. The consequence is overall lower efficacy and over-treatment, generating unnecessary and severe side effects for the patients, as well as high costs for the society. Thus, while Personalized Medicine can and should be applied to the majority of therapeutic areas, cancer is in the forefront of due to recent years discoveries and inventions on the cellular level. Cancer is therefore the most obvious candidate for this agenda.

In recent years, the rate of improvement in survival for cancer patients has decreased in Sweden compared to other western countries. Further, until around ten years ago Swedish cancer research - both clinical and experimental - was ranked among the top five countries in the world. It was recently made public (4) that since year 2000 the number of the clinical trials in Sweden has decreased from 500 to around 300. Our previous leading position therefore seems to have weakened over the years and the current situation is unsatisfactory for patients, health care providers, the scientific community and the medical industry. As already proposed the creation of a central authority (“Starka tillsammans”) can partly help solve the problem. On the other hand it seems necessary to create a strong milieu within the oncological and haematological departments where patients meet their doctors and nurses and where the recruitment into studies actually takes place.

Furthermore, in the coming years one in two Swedes will get cancer during their lifetime and one in three will die of their cancer provided unchanged treatment efficacy (5). In addition, Sweden is currently spending 60 billion SEK yearly on cancer care in total and it has been calculated that this figures will increase to 70 - 360 billion SEK in the year 2030 depending on which costs are included. It is therefore not only for the benefit of the individual patient but also for the benefit of the Swedish society that we need more efficacious cancer care. In this context the concept of PM must be considered mandatory.

As a first attempt to counteract this negative development a new national strategy for Swedish cancer care and research was formulated in 2009 and led to the creation of six Regional Cancer Centers (RCCs) in Sweden, all coordinated through “RCC i Samverkan” under the auspices of SKL. The aim for the RCCs is to take into account all aspects of the cancer challenge, including research and education with a strong focus on translational cancer

research and development of treatment strategies for the several hundreds of different cancer diagnoses.

A next logical step is to gather all stakeholders (Figure 2) to accelerate a positive and innovative development in order to bring about a change. Only by research-based profiling of the different subtypes in cancer can we assure optimal therapy for the patients as well as assuring the lowest cost for society. This can be obtained if we implement an organization, which can facilitate unprecedented collaboration with all the players outlined in Figure 2. Sweden performs already world-class “omics research”, but we must establish a national framework, which can ensure optimal utilization of the current health care system, university based research facilities in order to meet the industry’s requirements for fast drug development.

The agenda process

Because the objective of this innovation agenda for Personalized Medicine is to initiate a cross-disciplinary dialogue, we started by creating a shared vision of how we can develop the area of Personalized Medicine in cancer in Sweden. The initial working group for this agenda harbors extended clinical, academic and business development experience. Central to this vision is therefore to outline the most important needs for the main players in the arena of Personalized Medicine. The main players are research institutions within academia, the health cancer system in total, the medical/biomedical/biotech industry, institutes with an interest in health economy/sociology/communication, patients and their organizations and the so called “payers” (Figure 2).

Mandatory to the process was upfront full support from various partners within these areas in order to be able to apply for money to develop the agenda for Personalized Medicine in cancer. A logical step was therefore to obtain mainly local support. Hence we worked closely together with the Foresight Institute and the Institute of Health Economics in Lund. Furthermore we got an explicit commitment from the director of Skåne University Hospital and the department heads of Oncology, Hematology, Surgical Oncology and Pathology, in addition we got support from translational cancer platforms like BioCARE, CREATE Health and the Kamprad Lab. In order to have national commitment from hospital departments taking part in cancer care, upcoming meetings with a multitude of departments are already in the planning phase.

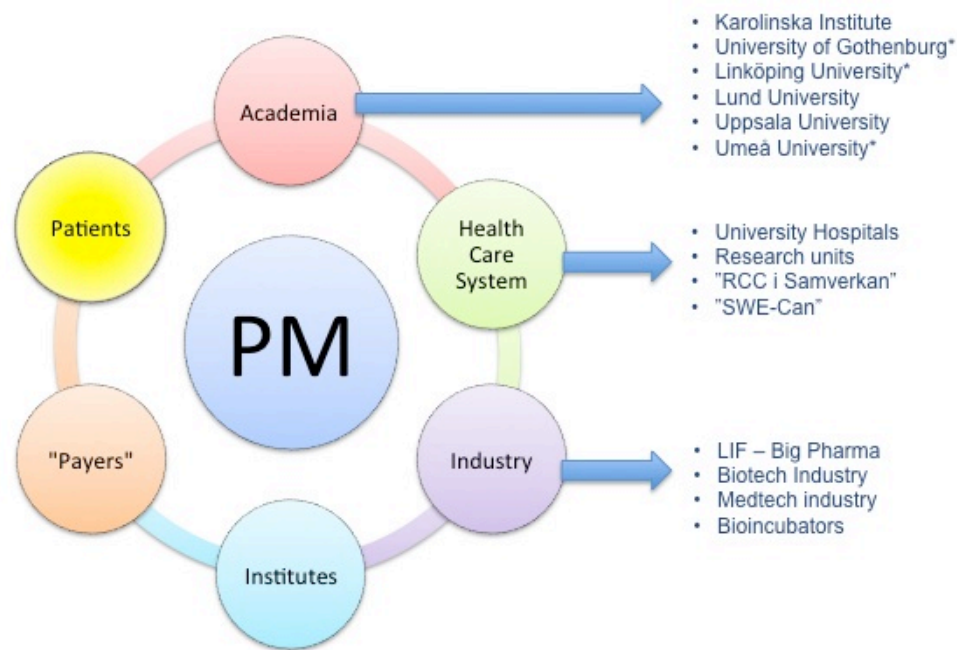


Figure 2. *Partners and stakeholders in the agenda.* The work with this agenda is done in collaboration with different partners and stakeholder as Patient representatives (i.e. RCC), Institutes (Foresight Institute, Institute of Health Economics) and through discussions with Payers (TLV, EMA). The triple helix is formed by Academia, Health Care system and Industry and for those we have exemplified some organizations (* to be involved in the future SIO program together with upcoming stakeholders).

To emphasize the importance of a national implementation we intend to include partners from all over Sweden as seen in “The agenda process”, Figure 2. Already now we have acceptance from the Karma project headed from Karolinska Institute. As an umbrella organization for process oriented cancer care and a link to the various patient organizations, the full support from RCC South was of utmost importance, we are now discussing with the other RCCs as well through “RCC i Samverkan”.

We have had in depth discussions with pharmaceutical companies like Bristol-Myers Squibb (BMS) and Merck, but it soon became evident that the umbrella organization for the research oriented medical companies, Läkemedelsindustriföreningen (LIF), was the natural partner for further discussions. In total we have had four meetings with LIF. At the last meeting (April 7, 2014) with LIF and representatives from 13 major medical companies, they all expressed their support of the vision and that they are willing to actively participate in the vision of taking this agenda further to a SIO program for Personalized Medicine in cancer. During these meetings with the medical industry it was obvious that there was a common goal for true **national** collaboration and the necessity for full commitment from the six regional cancer centers, the university departments of Oncology and Hematology, the Biobanks and the Swedish bioincubators.

The “RCC i Samverkan” has scheduled a comprehensive discussion of the vision at their upcoming meeting on the 27th of May. On the 16th of May, “RCC I Samverkan” together

with LIF and other main players, Biobanks, U-Can, SWE-Can, CREATE Health and Karma study were active in the discussions concerning the agenda.

A national gathering for implementation of Personalized Medicine must furthermore have the full support from a majority of the counties and regions in Sweden. Further, we aim to involve, the biotech industry, the biomedical industry and the universities cancer research in future discussions about the proposed SIO program. To do this we have the unconditioned support from the political and administrative system in the Region of Skåne. Of note, we have already obtained full backing and commitment from all the Swedish bioincubators, which will be indispensable in the maturation of new companies as a result of the focus on Personalized Medicine.

In addition, the following projects/initiatives are examples of Personalized Medicine supportive structures that are important stakeholders in building a Swedish national program in Personalized Medicine:

- **SciLifeLab**, a collaboration between Karolinska Institutet, KTH Royal Institute of Technology, Stockholm University and Uppsala University, building a national resource infrastructure offering technology-driven molecular bioscience and translational medicine
- **LifeGene**, hosted by Karolinska Institutet, aiming at building a Biobank containing data from 200 000 individuals
- The National Cancer Strategy, pointing to the creation of six **Regional Cancer Centers (RCC)** coordinated by “RCC I Samverkan”.
- The National Initiative, BioBanking and Molecular Resource Infrastructure (**BBMRI**), hosted by Karolinska Institutet, for coordination of Swedish Biobank infrastructure
- **The Karma Study**, at Karolinska Institutet, the world’s best characterized breast cancer cohort and developing a risk prediction score and prognostic index for use in future prospective studies
- **SCAN-B** at Lund University, large scale breast cancer biobank aiming at the development of predictive tests used for the optimizing of treatment for breast cancer. Karma is one of several partners to SCAN-B.
- The **BioCARE** strategic research program at University of Gothenburg and Lund University, focusing on the identification and validation of new biomarkers
- **CREATE Health, the Translational Cancer Center** at Lund University, to propel the advancement and coordination of cancer diagnostics and therapies

- **U-CAN** at Uppsala University. U-CAN is a collaboration between Uppsala, Umeå and Stockholm University aiming at optimizing therapy for individual cancer patients by collecting and organizing patient samples that are taken before, during and after cancer therapy.
- **Medetect** at Lund Life Science Incubator; just one example of a small CRO and innovation company aiming at Additive Multiple Labeling Cytochemistry which provided facilitation and collaboration can lead to a paradigm shift in tissue based immunochemistry.

Unfortunately, despite several Swedish Personalized Medicine initiatives mainly in academia (above), and partly in medical industry, policymakers and administrators have not yet actively taken positions or outlined comprehensive strategies.

International collaborations are of course of utmost importance. As examples we list some of the partners for the above mentioned stakeholders in performing concrete research projects: Oxford University, Memorial Sloan Kettering Cancer Center, Stanford University, Oslo Cancer Cluster and Tianjin Medical University Cancer Institute & Hospital.

Future steps

LIFs and LU's project leaders for the SIO Agenda have at the 16th of May invited representatives from a number of important players within the field of Personalized Medicine, i.e. U-Can, Swe-Can, RCC i Samverkan, KI, Onkologen Uppsala and LIF (with representatives for the pharmaceutical companies in Sweden with oncology research e.g. Merck-Serono, Roche, AZ, Pfizer, Lilly, BMS, MSD, Celgene) for a 1-day workshop. The goal for this workshop is to inform and obtain acceptance for a continued, collaborative work with a shared national vision for Personalized Medicine in Sweden.

The strategy - "From Invention to Innovation"

Concept

The overall concept with the establishment of a strategic innovation program within the area of Personalized Medicine is to facilitate, implement and evaluate the different steps summarized in Figure 3.

Facilitate. A facilitation of the execution of clinical research, both pre and post marketing approval, in connection with our high quality population based registers, well organized biobanks and supportive biomedical industry, will increase Sweden's competitiveness and also give important insight to academia and industry how the treatment works in real life.

Implement. A faster and quality assured translation of experimental achievements to clinical implementation, for the benefit of both patients and society, will catalyze novel opportunities both in the therapeutic and diagnostic market place.

Evaluate. A faster evaluation of new therapies and drugs in stratified patient cohort will eventually lead to lower costs for the health care providers.

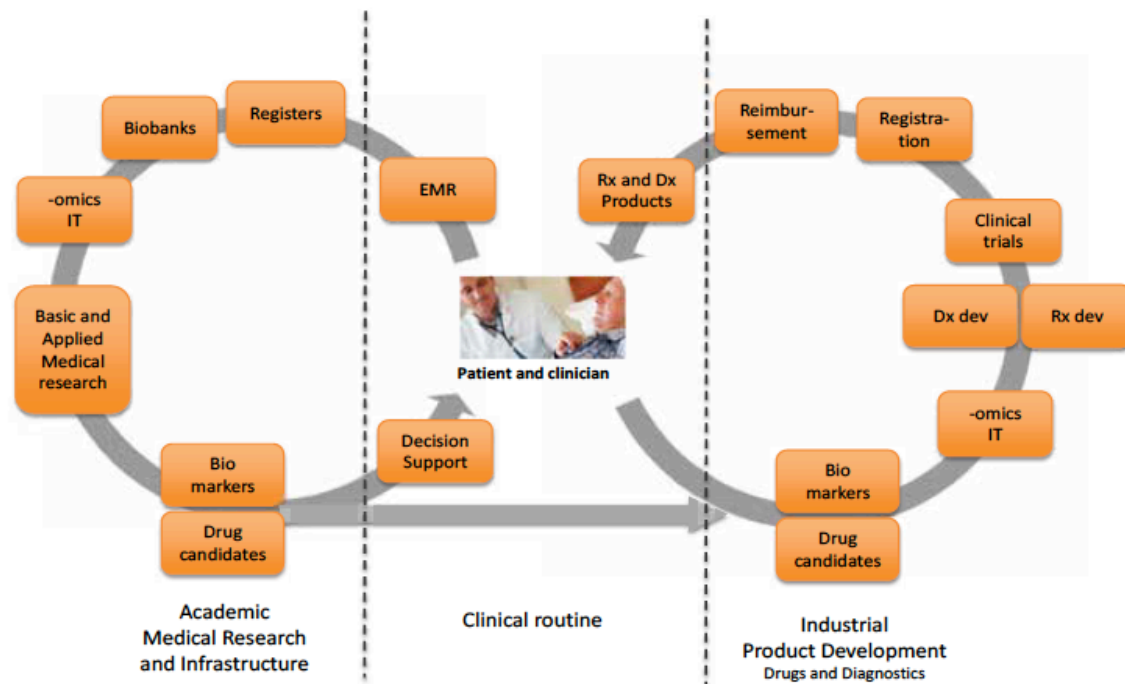


Figure 3 *The important steps in Personalized Medicine, courtesy of Paula Zeilon, Life Science Foresight Institute.* In Personalized Medicine the patient is in focus; it all starts and end with the patient. Registers of all patients and biopsies and other patient samples stored in biobanks is the start for basic or more specific medical research to identify new biomarkers or drugs of benefit for the patients. The identified drug/diagnostic candidates are tested in prospective clinical trials which provides the documentation needed for registration and reimbursement.

We foresee that a successful implementation of Personalized Medicine will generate a new market for e.g. diagnostics, since the use of biomarkers will be a prerequisite for correct stratification of patients for treatment decisions. This is supported by a report by PricewaterhouseCoopers (6), which calculated that the Personalized Medicine market would be worth USD 42 billion in 2014. Molecular diagnostics is an important part of Personalized Medicine, and it has been estimated to grow from USD 3 billion in 2009 to 6 billion in 2015. A substantial part of this growth is attributed to growth of cancer companion diagnostics (7). In addition, IT will be an increasingly important instrument for storage and handling of large data. This poses employment and market opportunities for new companies both within diagnostics and IT. However, it also requires the health care sector to be educated about these possibilities and be committed as well as willing to implement these innovations in their daily practice. A good dialogue with the regulatory agencies to facilitate the approval of drugs and the accompanying companion diagnostics is self-evident!

As previously stated, Swedish cancer care is still in the forefront worldwide when it comes to patient care, survival figures and experimental research. If we want to continue to be in the forefront it is, however, clear that an improved and rapid *implementation* of the concept of Personalized Medicine in cancer is absolutely necessary. Therefore it is a prerequisite that we succeed to implement true national collaboration to meet the need of the patients, the society, the research community and the biomedical industries.

Development of new cancer drugs is worldwide the fastest growing area within the biomedical industry and this innovation process is in Sweden entirely dependent upon smaller biotech companies whereas the larger medical companies mainly pursue their innovative goals outside Sweden. This calls for a structured approach for better clinical testing and concurrent development of accompanying diagnostics within the Swedish cancer community in order to meet the challenges for the entire industry

We therefore aim to facilitate and ensure close collaboration between smaller biotech companies, big pharma, the healthcare system and the university based cancer research as visualized in Figure 4.

Triple Helix collaborations

The proposed structure for this Personalized Medicine Agenda aims to facilitate the national collaboration between the industry, academia and health care providers. The health care system needs to have a confident and long-term relationship to both the medical industry and the university based research. Policy makers and administrators must ensure fast and efficacious regulatory processes and through the regional cancer centers ensure compatible and high quality patient databases in order to find suitable patients for clinical research, access to state-of-the-art biobank material and to ensure thorough quality registers. This also requires sophisticated, widespread and interactive IT solutions. National coordination of clinical trials and collaborative based access to patient cohorts with a coordinated utilization of patient registers is mandatory if the big pharmaceutical companies represented in Sweden should participate in large scale phase III/IV clinical studies. We aim to facilitate such collaborations, being a prerequisite for increased access to cutting edge research for diagnostic test and patient stratification for improved clinical efficacy. Sweden already has some ongoing initiatives, such as BBMRI and SWE-CAN, important parties for the implementation of this agenda.

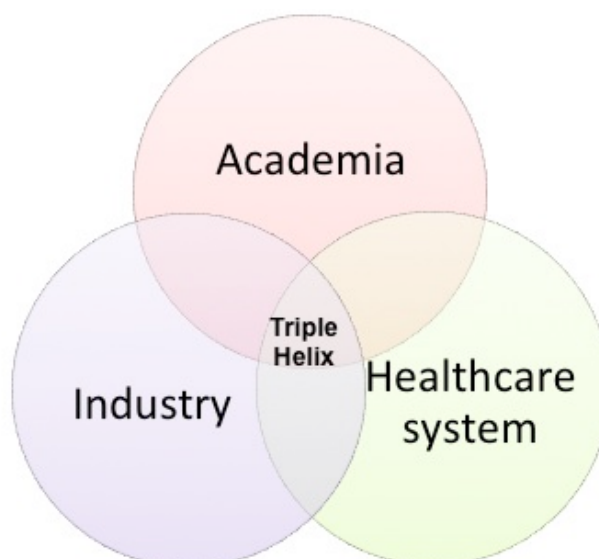


Figure 4. *The Triple Helix formation.* Collaboration between different partners (Academia, Healthcare and Industry) is mandatory for the implementation of Personalized Medicine.

To ensure that new and innovative therapies and concepts reach the clinic, within a short time, a constant dialogue between pharmaceutical companies, smaller biotech companies and the university based cancer researcher is necessary. For example, an interface between academia and the industry could facilitate the exchange of strategies, competences and target product profiles. To achieve those collaborations regular “Round table discussions” allowing for a dialog between translational- and clinical cancer researchers and the research oriented medical industry/biotech companies to identify areas of common interest, goals for collaborations and state of the art clinical cancer research will be made possible. The possibility for academia in participating in clinical studies with development of accompanying diagnostics is of course a prerequisite if we wish to attract international funding for major parts of the academic research. We propose that these meetings are done with one industrial partner at a time. In addition yearly conferences, such Cancer Crosslink, where academia, healthcare system and industry meet for 1-2 days to present the latest data, discuss new ideas and collaborations, will also be arranged.

One problem today is the large amount of projects ending up in the “Valley of Death”, i.e. early projects from academia that are not mature enough to be financed by risk capitalists or big pharma and where the academic researcher lacks expertise and funding in developing these projects further. To avoid this “Valley of Death” and to facilitate clinical use of the multitude of inventions stemming from basic and translational academic research, a Foundation where the different parties (companies, clinicians and researchers) would bridge early inventions to mature innovations should be established. This would increase the industry’s involvement in external innovative projects at an early development stage of benefit for patients and companies. The Foundation could also be used to finance projects in

early phase of development that are decided by the steering group reflecting the needs of the clinic and the companies. A stronger clinical focus of how to utilize the multitude of inventions coming out from these research milieus together with stronger ties to the clinical research units is an essential for the full utilization of the biobanking system and population based patient registers in Sweden.

Industry & Healthcare collaborations

Today, only a minority of cancer patients participates in clinical studies. The current numbers are actually not known, but seem to be in the order of 15 - 20 %. If Swedish clinical cancer research wants to be competitive internationally these figures must raise to a minimum of 25 % and at best 50 %. This requires close collaboration, education and a virtual cancer portal with a registry of all ongoing clinical studies in Sweden, under the auspices of "RCC i samverkan". In collaboration with patient organizations, specific educational programs, both for patients and patients to be, are needed. As outlined above, this calls for innovative IT-based educational programs.

In addition, an expansion of the numbers of drugs that are conditionally approved will allow for a greater number of authorized new drugs on the market. This in combination with better opportunities to integrate adaptive licensing, providing pharmaceutical companies access to clinical data for not only national but also global use, would tremendously shorten the time for new drugs to reach the clinic. Of great importance for the pharmaceutical companies is that access and compilation of all post marketing data is made available for the industry. This should be the case both for existing and new drugs to allow the companies to evolve their drug design and evaluate the best responders and stratification. In addition there is an imperative need to clarify pathways on how new diagnostic tests, which are used to stratify patients (in clinical trials and in praxis) can be implemented and used in the clinic.

Healthcare

Implementation of proper education of doctors and nurses in Good Clinical Practice (GCP) together with continuous training programs for specialty trained pathologists, radiologists, surgeons and oncologists/haematologists will be needed to successfully enroll more patients to state-of-the-art clinical trials. To be able to do this, the following resources will be needed. To be able to do this the following resources will be needed for at least six clinical trial units (CTU).

- Physicians at the clinical dept's. (2/CTU – 12 in total)
- Research nurses at the clinical dept's. (2/CTU – 12 in total)
- Data management
- Translational research schools and cross-disciplinary education for clinicians and scientists.

Industry

Implementation of Personalized Medicine, as foreseen in this Agenda, will lead to more and improved commercial opportunities for small companies, such as biotech/medtech's, CRO's and IT-companies. The already established engagement from BioIncubators at all swedish universities will facilitate this.

Governance structure

To fulfill the needs and coordinate the infrastructures described in this Agenda requires a clear Governance structure. A tentative proposal of the organizational structure of the SIO program can be comprised by the following bodies (Figure 5):

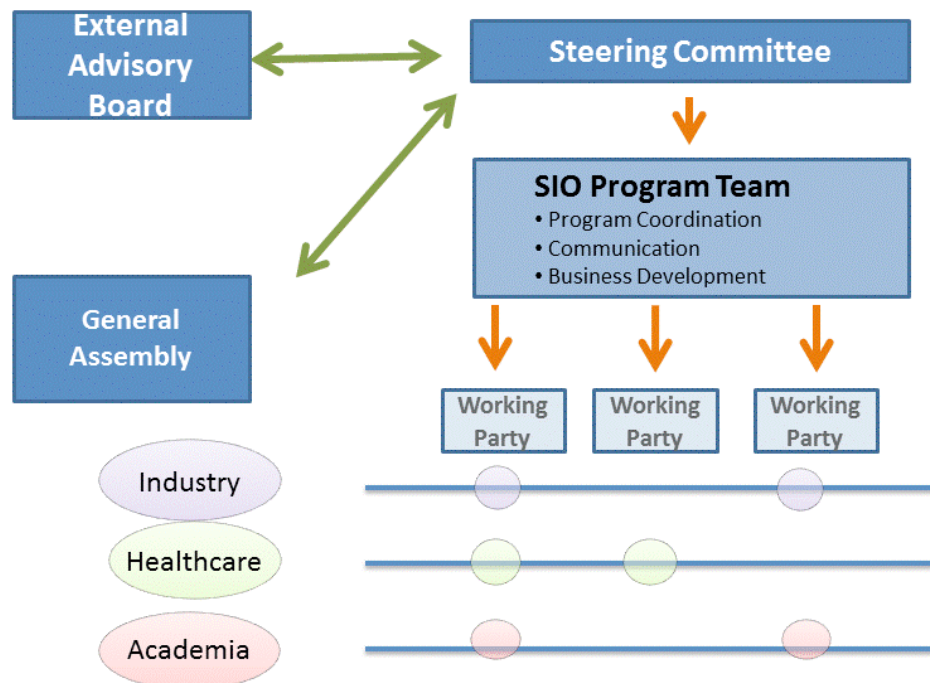


Figure 5. The Governance structure for a SIO program in Personalized Medicine - from invention to innovation. Red arrows indicate decision and green arrows indicate feedback/advice.

The **Steering Committee** with national representatives from academia, LIF, health care sector, RCC and will meet regularly. The role of the Steering Committee will be to provide advice and support to the program coordinator in governing the project groups. The Steering Committee will serve as the main forum for strategic review, and decision-making, enabling efficient discussions and exchange on issues. The program coordinator is a member of the Steering Committee.

The **SIO Program team** shall consist of a program coordinator, a business development manager and a communicator and have secretarial assistance. The team shall be responsible for organizing all necessary activities to ensure operational implementation of the SIO Program at the scientific-technical, and general operational level;

- Defining, dividing and developing individual tasks
- Coordinating the activity of the parties
- Coordinating the preparation of the project reports and communication
- Keeping the parties up to date and notified of developments within the Program
- Overseeing the scientific progress of the Program.

The **External Advisory Board** is aimed at providing recommendations before critical decisions are taken by the Steering Committee, in particular those which result in funds (re)assignments to subprojects and project partners, as well to avoid any conflict of interest. They will also assist in the annual monitoring of the projects from the different Working Parties and help to avoid/solve conflicts between parties. The External Advisory Board will consist of outstanding academic scientists and clinicians with relevant experience in the field, representatives from the biotech and pharmaceutical industry, as well as including representatives of patients associations and regulatory institutions. External Advisory Board recommendations will in most cases be the consensual opinion of the External Advisory Board members, or else a simple majority of member opinions results in the formal External Advisory Board opinion with diverging views being recorded.

All Parties shall be members of the **General Assembly**. The authorized representative of the Coordinator shall chair all meetings of the General Assembly. The General Assembly shall have an annual meeting for reviewing and monitoring the progress of the project as well as identifying appropriate actions for the successful performance of the project groups.


Strategic fit with other Agenda/ Programs

In proposing this strategic agenda, *Personalized medicine – from invention to innovation*, we are well aware of other strategic efforts within Life Science. In addition to this agenda, Lund University is involved in the recently approved SIO program “Chronic Diseases – A proposal to establish a program for a strategic innovation area”. This program describes a program for better health focusing on chronic diseases where diabetes is suggested as the pilot project. However, it is not *diabetes per se* that is the focus, but rather the **innovation processes**. In the present agenda, we describe the importance of implementing Personalized Medicine by involvement of the healthcare system, the industry and the academic research. To implement this concept, cancer is suggested as a target project. Consequently, both these

SIO projects can and will work in parallel and are significant complements to each other, aiming at implementing Personalized Medicine in cancer as well as the innovative processes for the ultimate benefit of chronic patients.

Key success factors

The progress of successfully implementing Personalized Medicine into Swedish health care will actively be monitored and evaluated by the Steering Committee in dialogue with the External Advisory Board. By **yearly** evaluation of our strategy we make sure that our goals will be met and provide opportunities to fine-tune our approaches and focus areas. In addition to these assessments, **every third year**, the Steering Committee will make an in-depth assessment of how well the outlined objectives have been met. We have therefore listed a number of Key Success Factors in Figure 6 below which can be used as **quantitative** measures of progress. In addition, the waiting times for initiation of both treatment and clinical studies will also be closely evaluated and accordingly adjusted. Finally, new companies being formed as a consequence of the Personalized Medicine program will generate more tax revenue and employment opportunities. These societal benefits will also be evaluated.



	Academia	Healthcare system	Industry
Clinical studies based on Personalized Medicine:	X	X	X
Patients included in clinical trials:		X	X
Progression Free Survival:	X	X	X
Companion diagnostics Developed & Implemented:	X	X	X
New companies/IPR:	X		X
PostDocs combining basic and clinical research:	X	X	
Bibliometric methods:	X	X	X

Figure 6. Key Success Factors for three important stakeholders. “X” represents stakeholders working to improve the specified key success factor.

Concluding remarks

Like all patients, cancer patients deserve fast access to reliable and evidence based therapy with as few side effects as possible. The fast development of Personalized Medicine marks the shift from *reactive* medicine to *proactive* and preventive health care, which will lead to fewer side effects and improved survival for the patients. Prerequisite is engagements of patients and patients organizations, not only in clinical research but also in the development of new screening and diagnostic procedures. In view of the recent report from the Union for International Cancer Control (1), prevention is crucial in order to stem “the tidal wave of cancer”. However the development of preventive strategies takes many years and even at the highest rate of success only 30-50 % of all cancers can be prevented according to our current knowledge. It can be argued that the main focus of Personalized Medicine is on high quality treatment and accompanying diagnostics. As an important illustration of this, the large national breast cancer study Karma in Sweden demonstrates that gathering of thorough information about the risk of getting breast cancer can lead to optimizing of not only better and maybe preventive therapies but also optimizing of secondary prevention by mammography screening. So far, more than 70 000 women have had mammography screening and have given information about their life style, delivered blood samples and is currently followed for up to ten years after the first mammography. This large cohort of women between 40 and 74 years of age and at risk for breast cancer provide the basis for improvement of the technique behind mammography screening. Liquid biopsies from these women can be further examined for other blood based prognostic factors such as plasma proteins, and possibly ensure higher specificity and sensitivity in testing for the development of breast cancer. Using extracted DNA, the Karma participants have already contributed to the identification of ≈ 90 genetic markers of breast cancer risk. By defining a group of women with a very high risk of getting breast cancer over the years, preventive studies where for example Tamoxifen is compared to other medical approaches reveal a multitude of possibilities for developing predictive tests and accompanying diagnostics.

This study is an outstanding example on how invention and innovation – screening techniques, digital mammography, development of prognostic and predictive factors, tertiary prevention etc. – can go hand in hand in a Triple Helix structure. Furthermore, it is hard to believe that knowledge from the Karma study, can be obtained from anywhere else than in a society like Sweden.

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