Idéskiss för Ett Strategiskt Innovations Program inom

Personalized Medicine

1 Strategic Innovation Area

1.1 Definition of the strategic innovation area

In 2012, 3.7 million Europeans were diagnosed with cancer and 1.9 million died from the disease. Using the European breast cancer burden as an example, every minute a woman is diagnosed with breast cancer and every fourth minute a woman dies from the disease. Survival rates are going up for some cancers but for most cancers the therapeutic improvements have been few and metastatic disease is still considered incurable. This is where *Personalized Medicine* will make a difference with improved diagnostic abilities and more individualized therapy strategies.

Clinicians are today mainly deciding on therapy based on tumor characteristics and spread of the disease. Few markers, like the estrogen receptor for breast cancer, are therapy predictive indicating how the tumor will respond to therapy. Current markers are few and imprecise and it can be difficult to tell if a patient is struck with an aggressive cancer or not. In breast cancer again, approximately 75% of the patients survive their disease meaning that 25% received ineffective therapy. For the majority of survivors, surgery alone would have been enough but they still received aggressive cytotoxic treatments. Patients thus face a dual risk, i.e. both over- and under treatment.

Novel technologies make it possible to elucidate the complex biology of a cancer leading to novel therapeutic possibility, such as immune checkpoint inhibitors. Furthermore, by analyzing the function and behavior of many thousand genes or proteins, better prognostic and predictive factors will be generated. *Personalized Medicine* aims at identifying the therapy that targets a particular tumor in a particular patient at a particular time. A prerequisite for *Personalized Medicine* to be successful is access to large number of patients to identify clinically relevant biomarkers of response to therapy. Consequently, clinical informatics encompassing tumor and blood samples, pathology reports, diagnostic tests, information on therapy and its outcome, are needed. This puts Sweden in a unique position due to a coherent health care information system that identifies eligible patients, nation-wide registers of high quality to follow patients prospectively at low cost, as well as highly curated biobanks.

By a national hexa-helix approach (Figure 1) we will meet the challenges described above and although *Personalized Medicine* can be applied to all diseases, cancer is in the forefront due to the complexity of this disease and its kaleidoscope of therapeutic possibilities. Cancer is therefore the most obvious and challenging candidate for a Strategic Innovation Programme (SIP) in *Personalized Medicine*. This strategic area will deliver improved survival figures for patients, fewer side-effects from treatment, evidence-based use of drugs, health economic benefits by omitting ineffective treatments and implementation of new innovative products and processes.

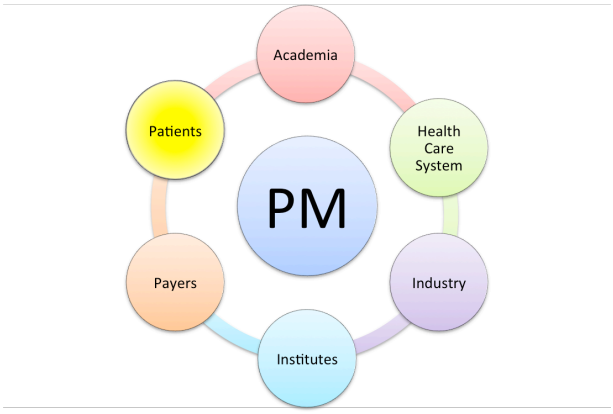

Figure 1. The hexa-helix showing the main actors in this Strategic Innovation Program - *Personalized Medicine*. Further details are shown in 3.2.

1.2 The innovation area in facts and figures

Cancer is today a leading cause of morbidity and mortality, and its prevalence is expected to increase significantly over the coming decades, mainly due to an ageing population:

- 2014 one in three get cancer during their lifetime and one in four will die of their cancer
- 2020 one in two will get cancer during their lifetime and one in three will die of their cancer (*En Nationell Cancerstrategi För Framtiden, SOU2009*).

Until around ten years ago Swedish cancer research - both clinical and experimental - was ranked among the top five countries in the world. However , since year 2000 the number of clinical trials in Sweden has decreased from 500 to around 300 (www.mpa.se). Thus, Sweden's previous leading position has weakened and the current situation is unsatisfactory for patients, health care providers, the scientific community and the medical industry. To tackle the growing burden of cancer and to reduce regional differences in cancer care, the Swedish Government launched the "National Cancer Strategy for the Future" in 2009. This led to the creation of six Regional Cancer Centers (RCCs) in Sweden, all coordinated through "RCC i Samverkan", now a stakeholder in the present *Personalized Medicine - SIP*

New *Personalized Medicine* therapies also constitute a growing part of the over 1000 cancer treatments that are currently in the global drug industry's development pipeline. *Personalized Medicine* will therefore play a crucial role in achieving the goals of the National Cancer Strategy. However, successful implementation of *Personalized Medicine* will require efficient, clinically validated diagnostic testing at Swedish hospital labs, and comprehensive information exchange between the lab and the clinician. Today, great differences in the time needed to establish a diagnosis are seen across regions (County Councils) in Sweden. Furthermore, since *Personalized Medicine* relies on the combination of exact tumor characterization followed by optimal therapy selection by the treating physicians, any attempt to implement *Personalized Medicine* in clinical practice must start with improving the diagnostic work-up of patients and the information exchange between labs and clinicians. If the right infrastructure of testing facilities in labs and clinical information transfer is successfully put in place, patient outcomes can be expected to improve. Moreover, investment in clinical trials, with novel *targeted* therapies by global drug companies will be allocated to Sweden and research into new potential therapies can thereby be facilitated and stimulated.

Sweden is currently spending 60 billion SEK yearly on cancer care in total (Cancerfonden/National strategy for Cancer) with an increase of 9-14% per year (McKinsey), resulting >>100 billion SEK in 2020. It is therefore not only for the benefit of the individual patient but also for the benefit of the Swedish society that we need a more individualized and efficacious cancer care.

In brief, based on the fact and figures above there is a global consensus today that *Personalized Medicine* is highly needed to turn the trends outlined above, and a Strategic innovation Program focusing on *Personalized Medicine* would be an important asset in this endeavor.

1.3 International position and competition

In the rapidly expanding field of immuno-oncology, that recently has changed the course of pharmaceutical development, the attention given to *Personalized Medicine* is immense and spans from cross-disciplinary research initiatives to dedicated efforts on introducing novel treatment options into clinical practice. Swedish medical industry has taken on *Personalized Medicine*, although to somehow minor extent in comparison with international initiatives. The Swedish Government has not outlined a national ambition to further the implementation of

Personalized Medicine, which can be explained by the regionalized (County Councils) decision-making in the Swedish healthcare sector.

In comparison, the British Government has an expressed ambition to make UK the No 1 country in practicing *Personalized Medicine* and has also allocated significant resources in the area of biomarkers to UK. As an example, Cancer Research UK (CRUK) will invest heavily in their cancer centers as world class competitive and innovative networking organizations, for "*the translation of cancer research for patients benefit*". This R&D focus is also in line with regulatory efforts in the US Food and Drug Administration of joint registration of a drug together with a diagnostic test for the indication or disease in question. Biomarker research is again a key activity in order to improve disease diagnostics, which in turn facilitates the clinical options regarding treatment decisions. We cannot treat what we cannot measure!

The importance of *Personalized Medicine* within Cancer is also shown by the European initiative "Piloting Personalized Patient Care" (PPPC), within Horizon 2020. Our SIP-team has been invited to take part in PPPC due to our highly rated cancer research and our initiative and focus of the present SIP. PPPC is aiming to put forward a validated model(s) for the organization and implementation of personalized cancer care in Europe, encompassing prevention, diagnosis, and care and integrate innovative technologies in routine care. Consequently, an important player for this *Personalized Medicine - SIP*.

Discussions are currently underway between Oslo Cancer Cluster (OCC) and the Norwegian government for the development of a plan that also focuses on the *Personalized Medicine* concept (personal communication Ketil Widerberg, CEO). Our team is also involved in these discussions trying to evaluate possibilities for a common test-bed in *Personalized Medicine* between Sweden and Norway. The Future Nordic Co-operation on Health is a recent initiative from the Nordic Council of Ministers that aligns well with *Personalized Medicine* in cancer.

In this competitive and innovative area, Sweden has a long tradition in world-class research and competence, as well is in cancer care. The Nordic countries are unique in integrating medical and radiation oncology and we are in the top of cancer epidemiology due to our registries. We have the National Cancer Strategy and the Regional Cancer Centers that can support innovative projects, both nationally and regionally. Taken our biobanks and mature IT structure into consideration, we can now form a powerful *Personalized Medicine - SIP*, using the Swedish personal identification numbers as a basis to support clinics and research.

2 Potential for the strategic innovation programme

2.1 Visions and goals for the strategic innovation programme

Vision: *The stakeholders will join forces and make Sweden one of the first countries in Europe offering a national health care system based on the concept of Personalized Medicine, using cancer as a model because of its complexity and societal significance.*

The tools for an advanced *Personalized Medicine* are predictive biomarker tests, biobanks and our population based registers, pharmaceuticals and IT solutions but also novel forms of collaboration and developed processes and organizations. A national multidisciplinary initiative is consequently mandatory.

Importantly, we have already managed to gather most of hexa-helix players outlined in Figure 1, to enhance and strengthen collaboration concerning care and research of cancer. The main goals with this proposed SIP in *Personalized Medicine* are:

- *Personalized Medicine* implemented nationally in clinical practice
- Facilitated development, introduction and evaluation of novel cancer treatments based on advanced clinical informatics

- Established an attractive test-bed for predictive biomarkers in clinics treating cancer
- Increased number of patients in current and novel treatment protocols
- Clinical decision support implemented
- Swedish biobank's full potential used for academic and industry-based research

During the work with the previous SIO-Agenda and this SIP proposal, a national framework has started to be formed. Regularly meetings are held with the General Assembly (see below), including members from RCC, academia, clinical health care, LIF, industry, etc. In addition 5 actively working key action groups have been established, with the following focus:

1. **Clinical Informatics** – Create an evidence-based decision support to physicians for optimal treatment strategies
2. **Predictive biomarker testing** - Implement national test-beds to improve the quality of diagnosis and to facilitate patients availability to new techniques and treatment protocols
3. **Strengthening of Clinical Research Units** in oncology and hematology – more *Personalized Medicine* personnel, education and coordination of clinical trials.
4. **Facilitating the hexa-helix** – On a national basis, strengthen the collaboration between the different stakeholders
5. **Increased Competence and Education** – IT-based education of doctors and nurses in GCP and Clinical Trial methodology as well as continued education of specialists in Radiology, Pathology, Surgery and Oncology/ Hematology, dealing with cancer

The deliverables from the working groups already indicate that these key actions are a successful working strategy to deliver the goals shown above. The individuals in each working group are shown below.

2.2 The most important challenges/needs and why public intervention is needed

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

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 and result in increased industrial growth.

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

Oncology is facing major challenges in the future. Recent years progress within novel therapies and technology needs to be implemented in the healthcare organizations and delivered to patients to be able to deliver the right treatment to the right patient at the right time. In order to realize the potential of *Personalized Medicine,* the gaps between the clinic/patient care and the technology will be bridged in a nationally structured way.

Today, molecular techniques are only partly used for *Personalized Medicine.* Therefore, the Swedish health care system faces a major challenge, since the flow between the laboratory, clinic, doctor and patient is suboptimal. In addition, while the patient's needs increases the amount of scientific data is soaring, which is a challenge only solved by improved clinical informatics, leading to improved evidence-based decisions by physicians. This creates entirely new demands, i.e. to manage and draw conclusions from ***all*** the information that is obtained, which is a challenge and a focus of the present SIP- *Personalized Medicine*.

A public funding is the only realistic way forward to establish the success of a proposal aiming at creating a real and national change in how *Personalized Medicine* is implemented and foremost practiced. Based on the challenges discussed above no individual region or organization have the power to act alone – this is truly a national endeavor.

2.3 Renewal of the innovation area by the innovation programme

The proposed structure for the *Personalized Medicine* in cancer aims to facilitate, implement and evaluate the national collaboration between the industry, academia and health care providers. This is an entirely novel and needed implementation of *Personalized Medicine* and requires fast and efficacious regulatory processes, ensured by policy makers and administrators. In this process, the six RCC´s will ensure the necessary compatible and high quality patient databases in order to find suitable patients for clinical research, access to state-of-the-art biobank material and provide thorough quality registers.

A successful implementation of *Personalized Medicine* will generate solutions that will decrease time to diagnosis and treatment for patients thanks to more efficient diagnostic procedures and better information exchange between the laboratory and the clinic. It will also create a new market for biotech companies involved in e.g. diagnostics, since the use of biomarkers will be a prerequisite for up-front and correct stratification of patients before treatment decisions. This is a trend seen all over the world today, and one where our SIP-*Personalized Medicine* will take a natural lead. According to a report from PricewaterhouseCoopers, *Personalized Medicine* market would be worth USD 42 billion in 2014 and Molecular diagnostics itself has been estimated to grow from USD 3 billion in 2009 to over 6 billion in 2015. A substantial part of this growth is attributed to growth of cancer companion diagnostics.

The renewal power of the proposed SIP- *Personalized Medicine* will encompass the entire society, since cancer affects such a large part of the population, health organizational budgets and industrial/pharmaceutical development. From an industrial point of view, unprecedented national access to clinical collaborations, biobanks (including clinical documentation), advanced biomarker technologies and clinical informatics will boost and facilitate clinical trials and development of novel therapies.

2.4 Contribution to the addressed impact goals

2.4.1 Strengthen sustainable growth

The total concept of *Personalized Medicine* opens up for opportunities we cannot afford to neglect and will lead to better healthcare to a lower cost and at the same time stimulate research, invention and innovation. First, the use of biomarkers will be a prerequisite for correct stratification. Novel and powerful clinical test possibilities will be made more standardized and comprehensive, which will shorten time to diagnosis and treatment initiation. This has the potential to not only shorten lead times but also to improve patient outcomes. Introduction of new biomarkers will also open up for a new market for e.g. diagnostics and lead to improved commercial opportunities for small companies. The potential benefits and value from high quality cancer care improves the patient quality of life, enable participation in daily activities and enable work performance, this must be recognized and supported. Consequently, successful implementation of *Personalized Medicine* will contribute and strengthen the sustainable growth in Sweden.

Secondly, the clinical informatics will be strengthen and developed into the potential powerful decision tool it could be, initially in a pilot project managed by SIP-*Personalized Medicine*. With the insight that medical information - such as e.g. novel treatments strategies, experience derived from utilization of novel pharmaceutical and biomarker signatures associated with different stages of disease - will double at least every 5 years in the coming decades will

create a completely novel opportunity and growth potential for most of the stakeholders in this proposal. Consequently, to manage and draw conclusions from all available information that, as such, will have the power to increase the frequency of evidenced-based medical decisions from todays' 20% (www.ibm.com/watson)) will have a significant impact on industry, health organizations and society as a whole.

2.4.2 Strengthening competition and export for the industrial sector

Swedish biotech companies get early experiences to test their techniques in clinical praxis together with large companies and large costumers. This "early use" in clinical practice is a clear competitive advantage for example when applying for reimbursement at international markets, such as US.

2.4.3 Sweden is an attractive country to conduct business and investing in

Globalization can be described as a worldwide movement toward economic, financial, trade, and communications integration. Around the world, large centers compete to collaborate with pharma in research and development. Comparatively, Sweden is a small player in this arena. The big innovation currently taking place in oncology is the changing view of cancer from being an organ disease to a systemic disease. This new molecular pathway has led to more than 1000 new substances with new mechanisms of action that are under development.

Sweden has the infrastructure for population-based research thanks to registries, biobanks and our personal identification numbers. This information has been collected over a long time, and often covers the entire population. Sweden still has an advantage compared to other countries in this respect. Implementation of *Personalized Medicine* will create prerequisites to attract large R&D-projects from global companies within Life Science. We can foresee an increase in the number of clinical studies in oncology, as well as follow-up on individual patient level and thereby help to increase the competitiveness of pharma business in Sweden.

3 Actors

3.1 Coordinator (programme office)

The **Programme Office** will be hosted by Lund University, which also creates synergistic effects with the SIP Folksjukdomar, such as knowledge sharing, coaching, as well as a sharing certain back office functions.

The **Programme Office:** A Programme director, with experience in leadership, managing complex organizations, and knowledge in basic and clinical cancer research will be appointed. Positions encompassing business development, data managing, communication and secretarial assistance will also be needed. The Programme director will work in close relation with the national key action leaders forming the Programme Team. The **Programme Team** will be responsible for organizing all necessary activities to ensure operational implementation of the SIP at the scientific-technical, and general operational level.

The **Steering Committee (SC)** will be headed by Prof. Per Hall (KI) and consists of national representatives from industry (pharma, medtech and biotech), the health care sector, academia, RCC, patient associations, biobanks, and bioincubators. The SC will serve as the main forum for strategic review, and decision-making, enabling efficient discussions and exchange on issues.

The **External Advisory Board (EAB)** will provide recommendations before critical decisions are taken by the SC. The EAB will consist of experienced academic scientists, clinicians, representatives from the biotech and pharmaceutical industry, as well as representatives from patients associations and regulatory institutions.

All Parties shall be members of the **General Assembly (GA).** GA shall have at least one annual meeting/conference for spreading of all result from the SIP as well as reviewing, monitoring and discussing the progress of the SIP. In addition the members of GA have continuous dialogues with international actors through personal contacts and regular scientific meetings.

The Steering Committee members have all long-standing experience in managing complex projects on national as well as on an international level, i.e. the proposed organizational structure is well tested before, with a good track record.

3.2 Main actors supporting the programme

The challenges in implementing *Personalized Medicine* are not possible to solve for the individual actors alone. To succeed, the implementation needs to be based on a national strategy.

Industry: Pfizer, Merck, BMS, Roche Diagnostics, Roche Pharma, AstraZeneca, Celgene, Novartis, Immunovia, Bioincubators and LIF. *Involvement* - taking an active part chairing or participating in different key action groups or as a part of GA.

Academia: Karolinska Institute, Uppsala University, Umeå University, University of Gotenburgh, Lund University, Linköping University (The KICancer - Personalized cancer medicine Program, BioCare, SWE-CAN, UCAN and CREATE Health). *Involvement* - taking an active part in chairing or participating in different key action groups.

Health Care System: Clinical Research Units at Departments of Oncology: Uppsala, Lund, Göteborg, Stockholm, Umeå and Linköping, Nationella biobanksrådet, Biobanks, Swedish Association of Local Authorities and Regions through "RCC i Samverkan". *Involvement* - taking an active part participating in different key action groups and/or active in GA.

Patients: Through RCC. *Involvement* - taking an active part participating in different key action groups.

Institutes: Foresight Institute, The Swedish Institute for Health Economics. *Involvement* **-** Members of GA.

3.3 Important actors that will be invited

Patients: Patient associations through RCC /RCC in "Samverkan"
Payers: Medical Products Agency ("Läkemedelsverket"), European Medicines Agency
Health Care system: Additional Oncology and Hematology clinics

3.4 Actors that will benefit from the programme

Personalized Medicine brings the patient in focus, i.e. it starts and ends with the patients. Registers of all patients and biosamples stored in biobanks are the starting point for basic and targeted medical research to identify new biomarkers and/or drugs for the benefit of the patients. The identified drug/diagnostic candidates tested in prospective clinical trials for efficacy/side-effects will provide the documentation needed for registration and reimbursement. By implementing and evaluating better treatment and diagnostic tools for patients all parties such as Patients, RCC, Health care providers, Health care producers (Pharma industry, MedTech industry, Biotech Industry, Start-up companies, Bioincubators), Biobanks, Institutes, Payers and Academia will benefit from this programme by collaboration and continued facilitation of the process from bench to bedside. Finally, since the economic impact of *Personalized Medicine* is significant, Society will benefit tremendously due to a lower increase in health care costs and improved health care status due to accurate diagnosis and efficacious therapies.

Contact table

Name	Organization	E-mail	Role in the programme
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Carsten Rose	LU	Carsten.rose@immun.lth.se	Chairing "Strengthening of Clinical Research units" and "Increased Competence and Education"
Daniel Brattström	Uppsala University Hospital	daniel.brattstrom@akademiska.se	Deputy Chairing: "Strengthening of Clinical Research units"
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Key action groups consists of:

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Strengthening of Clinical Research units: Carsten Rose (LU), Daniel Brattström (UppsalaUniversity Hospital), Eva Eliasson (Pfizer/LIF),Ulrika Brunell Abrahamsson (BMS/LIF)
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