



Understanding Life! – Program Plan

In memory of those who died too young of cancer and to inspire those who are fighting it

This document describes the program of the Inspire2Live initiative entitled Understanding Life! The objective of Understanding Life! is to get cancer under control. The program was launched with a conference in Amsterdam (12-14 January 2011), during which the world's leading cancer experts prioritized a number of bottlenecks that needed to be resolved to get cancer under control. The basis of the program is found in the Inspire2Live Scientific vision.

Understanding Life! is a patient initiative. It is committed to delivering exceptional results and lasting research and treatment infrastructures to people and patients. The present program involves the best scientists and best cancer centers across the globe to accomplish our goals, working in cooperation with patient advocates.

Our main objective is to ensure that becomes a disease which people die with and not die from. Of course, it's always better to prevent cancer than to recover from cancer. It's probably this path which proves most essential in getting cancer under control' as Arnold Levine stated in his discussions with us.

To meet the goal of getting cancer under control, the question that has to be answered is 'How can we generate knowledge about cancer as a disease in a faster way?' The second question is 'How do we get this knowledge from the laboratory to (all) the clinics faster whilst feeding results back to the laboratory?' We want to be able to tell any patient who is diagnosed with cancer that, in the worst-case scenario, their disease will be chronic rather than life-threatening.

The approach that we advocate is based on informed boldness and countless discussions we have had with experienced patient advocates, scientists and clinicians in the field of cancer research, cancer treatment and drug development. In all these discussions, three questions were continuously put forward:

- Given the social, technical and medical developments of today, how should we proceed with cancer research and treatment?
- How can we improve research and treatment? In the discussions, it became clear that many innovations in the field are infrastructural in character. Improvement not only depends upon changing the science, but also changing the way science is done: in terms of sharing data, actively exchanging findings and results, informing the public etc.
- What should we aim for in terms of treatment and care? Just about all engaged scientists, researchers and clinicians alike noted that cancer is a complex disease.

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It is multifaceted and constantly interacting with its environment, changing its shape as our biological biographies change over the course of time. Therefore, a 'once and for all' cure for is very unlikely. However, an approach that turns the illness into a chronic affliction is not beyond the capacity of science and its infrastructures.

Based on the answers we received from the most renowned scientists and institutions, we drafted our principles, philosophy and approach and their input forms the basis of our plan.

It is important to mention that, based on these responses, an understanding developed that our mission was fully achievable i.e., the international cancer research, development and treatment practices show so many opportunities for fundamental improvement that our mission proves to be much more realistic than most people tend to think. This is also the main conclusion drawn by many renowned scientists and the reason why they decided to put their name and fame on the line to work with us.

Our mission is 'We are the patient's voice in cancer'. We advocate, based on science, knowledge and facts to get cancer under control. And we dream: Our dream is for cancer to evolve from a deadly disease into a chronic illness.

Inspire2Live is founded on the absolute belief that you can attain the greatest possible satisfaction if you put your heart and soul into helping others. Inspire2Live was created with the aim of empowering people to convert the sense of powerlessness caused by cancer into a strength. That strength comes from working together and supporting each other and we know that we need to continue inspiring, motivating and connecting patients, scientists, clinicians and their institutions so much more effectively and efficiently to achieve our goals. In short, we want to mobilize everyone!

The scientific program plan

The crucial question that was brought forward was 'How can we get cancer under control faster?' This conference prioritized some of the most important obstacles that currently slow down our progress in controlling cancer. The conference also made recommendations on how these obstacles could best be tackle and these recommendations form the basis of our basic scientific program plan.

Based on these key questions, five topics have been identified as primary objectives to make cancer a chronic illness, rather than a deadly disease:

1. Improvement of disease and drug response models;
2. Improvement of clinical practice;
3. Improvement of storage, retrieval and exchange of disease-related patient data;
4. Reduction of the incidence of cancer;

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5. Execution of plans for changes and improvements.

Research and development is translational in character. The program focusses on organizing human capital, providing incentives to work together, creating and maintaining infrastructures that support translational medicine within and between laboratories and clinics, and connecting communication infrastructures that support information exchange among the cooperating centers.

The program also focusses on mobilizing the interest of the patient and strongly improving the patient-centric approach. It is obviously in the interest of the patient that cancer therapy becomes more personalized. Cancer must be taken personally. People have learned to avoid infectious diseases as much as possible, through day-to-day habits, various medical means and intuition. This should also be the case for cancer.

Inspire2Live will not set up projects by itself. Across the world there is a variety of potentially very good scientists and institutes that can implement the best projects in the interest of patients. However, every now and then, Inspire2Live can take the initiative to set up small pilots with the best of the best for very innovative projects to minimize the risks and maximize the benefits for patients. And in cases where these innovative pilots work well, we will urge the more conventional institutes to implement them on a larger scale.

Improvement of disease and drug response models

This objective can be summarized under the theme of cancer systems biology. Systems biologists are individuals trained in physics, computer sciences, applied mathematics and other quantitative disciplines, who apply their skills to new challenges in the field of medical biology. Systems biologists are needed to explore the genetic and environmental factors that are involved in cancer treatment and control.

The goal of this theme is to take full advantage of new technologies, data analysis and the ability to assess clear conclusions from the large, complex genomic, structural, and clinical databases that are available. By collecting and analyzing data across experimental and clinical settings, we expect to learn how individual genetic profiles can lead to different treatment responses and the development of preventive approaches.

All projects within this objective must have a realistic chance to deliver substantive improvements in clinical disease management and will be highly translational in character with frequent communication between laboratory and clinic.

Projects will include (but not limited to):

- Development of state-of-the-art models for human cancer treatment, including “omics” analysis of tumors to develop biomarkers that can predict drug sensitivity or resistance.

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- The use of “omics” technologies on in-vitro cell line models to identify drug sensitivity or resistance mechanisms and development of interventions to eliminate or reduce resistance with existing drugs.

Improvement of clinical practice

A central goal will be to expedite and optimize the selection of patients that are likely to benefit from ‘personalized’ drugs. While we expect that the majority of the drugs evaluated in this program will be the new generation of targeted therapies, we will not exclude the identification of predictive biomarkers in response to the more conventional (chemo) therapies. Nor will we exclude the implementation of generics that have never been used in cancer therapies: ‘Drug repositioning’. This objective will also focus on changing the mindset of both clinicians and researchers by aiming to set up a network of clinical research sites, where a new generation of clinical researchers will be trained.

Projects within this objective will be hypothesis and biomarker driven. The use of adaptive trial designs will be used where appropriate e.g., for the rapid validation of new biomarkers and drug screening is also an important part of our activities. Finally, projects should aim to educate a new generation of clinical researchers oriented towards translational research.

Projects will include (but not limited to):

- The development and actual implementation of infrastructures to enable innovative omics-based diagnostics in clinical trials. These technologies include genome sequencing, imaging and the development of these techniques into a ‘toolbox’ for the clinician to improve treatment.
- Innovative (neo-adjuvant) “adaptive” clinical trials that use candidate biomarkers of drug response. The aim of these projects will be to rapidly validate or reject candidate biomarkers of drug response. Biomarkers that graduate from these projects will be tested further in subsequent studies.

Improvement of storage, retrieval and exchange of disease-related patient data

Biobanks should function as an open-source work environment for researchers and clinicians. We will seek collaboration with large international bio banking and data sharing consortia to avoid reinventing the wheel. Bio-banking includes storing and sharing data and knowledge with all stakeholders and will serve as a major infrastructure to drive translational research by connecting researchers, clinicians and patients. Training of a new breed of bio-informaticians will also be a major goal of this program.

We aim to get patients involved in accelerating the cancer R&D process “from the bench to the bed and back again” and to get them to work with us to close the gaps within that same project chain. They are both the patients and the beneficiaries and, as such, they should demand a faster and better outcome of cancer R&D.

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This objective focuses on creating an interconnected network of open-source biobanks to support projects with state-of-the-art patient stratification. The projects within this objective should enable open sharing and mining of data.

Additionally, patients should be encouraged to participate in the process of sharing their data and initiatives should consider topics such as patient consent and participation incentivization.

Projects will include (but not limited to):

- The integration of the biobank material consisting of biological specimens collected under program 2 in existing international bio-banking initiatives.
- The development of an open-access database of data sets in the public domain having a variety of omics data, where possible linked to disease outcome.
- International exchange between key cancer centres of trainees in data mining of large omics data sets. Coordination of clinical and genomics data platforms used in industry and clinical care.

Reducing the incidence of cancer

The incidence of cancer is biologically anchored but is also a function of societal facets such as lifestyle, ageing, persistence of unhealthy habits such as smoking etc. Cancer is also a societal problem that requires a systemic outlook.

This objective requires a bottom-up approach, with a focus on the experience, activities and values of actual people to increase personal control over the disease in its more chronic forms and foster a problem-solving attitude. Considerations for lowering the costs of treatment and prevention programs that reduce the onset and incidence of cancer are important. This is similar to the tiered costing models used in vaccination programs in low- income regions, where vaccines are provided at a cost that is affordable depending on the income of each country.

Projects will include (but not limited to):

- Health education
- Low-cost wide reach approaches
- Importance of fostering a trial mentality

We will promote projects to develop health literacy among youngsters, so they will make better, more informed judgments and decisions about their lifestyle and health practices.

Execution of plans for changes and improvements

The expression 'to execute what we already know' was used by David Lane to give voice to his discomfort about the fact that either we treat or withhold treatment, while the information is often available to come to better decisions regarding a treatment plan. This objective is deliberately activist in nature and, perhaps more importantly, this part of

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the program can (but need not) be carried out without a budget. All that it may require is keen knowledge on what can be done better and how to activate people's will to get it done.

This objective focuses on identifying the knowledge gaps, determining how this knowledge will benefit the patient and setting up permanent trials to increasingly close the gap between new insights regarding treatments and knowledge application.

Projects will include (but not limited to):

- Improving the patient-doctor interaction, with an eye on applying the most up-to-date treatment information.
- Breaking open protocols, which are known to lead to sub-optimal treatments.
- Justifying the cases in which more personalized treatment would benefit the patient, even when this means a breach of accepted standards.
- Empowering the doctor and the patient to act with more confidence based on heuristics and relevant information at the time of planning and implementing treatment.

Program infrastructure

In cooperation with patients, researchers and clinicians, we will establish a mechanism that identifies the most innovative programs by the best specialists and scientists from centers of excellence to tackle the above-mentioned primary objectives.

Congresses and discovery networks

A number of top patient advocates, scientists, clinicians, regulators, industry representatives and funders who are part of various congresses and discovery networks will join forces to significantly increase the speed of disease modelling, drug screening and treatment discovery. These congresses and discovery networks are formed around specific themes such as Targeted Medicine, Intervention Oncology, Immunology and so on. One example is the use of organoids by the Clevers group at the Hubrecht Institute in the Netherlands, that enable highly-sensitive disease modelling and massive drug screening. The massive data that will result from this program will be disseminated into the scientific and medical society, to inspire and motivate brilliant scientists to join the quest for new drug combinations and treatments.

The Implementation projects

Under this scope we aim to get patients involved in accelerating the cancer R&D process "from the bench to the bed and back again" and to get them to work with us to close the gaps within that same project chain. They are both the patients and the beneficiaries and they should demand a faster and better outcome of cancer R&D. In these we identified three projects:

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- Construct an informed patient consent form in which patients request their medical data from institutions and publish these in the cancer commons we wish to establish.
- Construct a data-sharing platform, where patients, scientists and clinicians can publish and scrutinize open data in a true data-sharing environment and venture.
- Set up a number of incentive and reward programs that initiate, promote and demonstrate the successes to be gained from successful data-sharing campaigns.

Reducing incidence

Under this theme, we focus mainly on the role of governments to improve quality of life through lifestyle interventions and regulation of unhealthy products. By way of example, we are in discussion with the College for Human Rights in the Netherlands and in Strasbourg (France) to forbid tobacco sales rather than banning smoking. In this way, we will go after the real criminals and not the victims of the industry. Other initiatives are planned around the topics of food, exercise and obesity.

Activating Patients

This program will stem from the fruits of the Implementation Projects and will be activist by nature. We will mobilise more patient advocates and more patient groups to take up an active role in the cancer R&D and treatment fields. As part of this project, we need to inform, educate, empower and mobilize people to become the active patients we need them to be. In this program, we are taking the first steps to mobilize a brute force patient advocacy.

Activating Knowledge

Within Inspire2Live we are swiftly building an enormous amount of patient knowledge and experience about the differences between treatments, institutions and doctors which is increasing exponentially with the growth of our network. As David Lane put it, it is ethically essential for humans to execute what we already know. A number of international support requests are currently being translated into possible projects and they will eventually be incorporated into this plan as part of our well-guided and -governed efforts.

Dynamics, coherence and stability

There is no single predictive program for the route to get cancer under control. This plan is intrinsically dynamic and high-level, developed and implemented globally taking into account different perspectives, means and cultures. It may look like there is no director and no direction. In a way this is indeed the case and that's good. However; it is always based on fundamental science and pragmatically implemented with respect to the local situation, possibilities and means e.g., while rich countries can afford high-tech forms of diagnosing cervical cancer, low- and middle-income countries are using vinegar.

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Governance

For more information about the governance of all Inspire2Live activities, we refer you to our website: <http://inspire2live.org/about-inspire2live/board-members/>

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