Kræftens Bekæmpelse

Danish Cancer Society Research Center
Strategy 2017–2019

September 2016
PREAMBLE

In 1942, the Danish Cancer Society granted financial support to Dr. Johannes Clemmesen to establish the **Danish Cancer Registry**, the world’s first national cancer registry. Soon after this milestone initiative, cancer epidemiology, a new research discipline in Denmark, grew, and gradually, both cancer registration and the results of a rising number of epidemiological studies attracted widespread international attention and placed Denmark in the forefront of this field of research. In 1949, the Cancer Society likewise provided financial support to Dr. Julius Engelbrecht Holm to establish an institute of biological cancer research, which later became internationally renowned under the name the **Fibiger Institute**. Since establishment of the two institutes, cancer research has been a key component of the Cancer Society’s work.

RECENT DEVELOPMENTS

The two institutes grew strong in their respective fields and, over the years, both contributed significantly to the international body of evidence on the aetiology and mechanisms of cancer, but with no significant internal collaboration. In order to create a critical mass and research synergy, in late 2010, the Danish Cancer Society decided to fuse the two institutes into one research centre.

*Research collaboration within the Cancer Society*

In late 2011, the governing bodies of the Cancer Society approved the new organizational set up for the Society’s research, and the **Danish Cancer Society Research Center (DCRC)** was launched on 1 January 2012. It is now composed of six large units, each headed by an experienced, internationally renowned research leader:

- **Unit of Diet, Genes and Environment (DGE)**, headed by Anne Tjønneland;
- **Unit of Cell Death and Metabolism (CDM)**, headed by Marja Jäättelä;
- **Unit of Virus, Lifestyle and Genes (VLG)**, headed by Susanne Krüger Kjær;
- **Unit of Genome Integrity (GIG)**, headed by Jiri Bartek;
- **Unit of Survivorship (SVP)**, headed by Christoffer Johansen; and
- **Unit of Statistics, Bioinformatics and Registry (SBR)**, headed by Klaus Kaae Andersen.

To expand the research portfolio of the DCRC and to facilitate the transfer of the findings of DCRC researchers into clinical use, the Center was supplemented during 2013 with

- the **Unit of Translational Cancer Research (TCR)**, headed by Nils Brünner, and
- the **Unit of Cell Stress and Survival (CSS)**, headed by Francesco Cecconi.

To ensure representation of the next generation of research leaders in the management of DCRC, two talented, promising young researchers were recruited during 2013 and 2015 and offered resources and manpower to develop their best research ideas, resulting in:
• the Brain Tumour Biology Junior Group, headed by Petra Hamerlik, and
• the Cell Division Laboratory Junior Group, headed by Marin Barisic.

In 2015, the management of DCRC significantly upgraded bioinformatics support and research at the Center by adding a bioinformatics group (Computational Biology Laboratory) headed by Elena Papaleo to the SBR unit.

DCRC as integrated part of the Danish Cancer Society
When the Research Center was established in 2012, it was considered a vital part of The Danish Cancer Society with a set of long-term commitments. Accordingly, the main purpose of the Center was to:

• Ensure that research conducted in all parts of the DCRC maintains a high international standard and that the Center ranks top among comparable research institutes at international level;
• Ensures that the Danish Cancer Society’s research across departments meets uniform requirements for quality and is published in respected international, specialist journals;
• Ensures that the results of the Danish Cancer Society’s research are communicated effectively to the international scientific community at the same level as in the best cancer research institutes and that the results are also communicated to the public and used by Danish stakeholders to the greatest extent possible;
• Ensure that the Danish Cancer Society is at all times up to date about and is engaged in the latest advances in cancer prevention, treatment and prognosis;
• Ensures that the Danish Cancer Society is a visible, natural participant in the public debate about cancer at an informed, well-documented basis and functions as a driver of new initiatives on the cancer agenda in Denmark;
• Ensures uniform, result-oriented working conditions for employees with research positions in the Danish Cancer Society; and
• Ensures public respect for the Danish Cancer Society’s activities in cancer research.

Research collaboration on an international level
Ever since establishment of the two research institutes by the Cancer Society, both national and especially international engagement has been a key component of the daily work of the institutes’ researchers. Currently, more than 65% of the Center’s output – in the form of approximately 250 peer-reviewed scientific publications annually – is produced in collaboration with major research institutions abroad, a principle of operation that the Center is intent on keeping as a vital part of its on-going strategy.

A major organizational initiative on national level
During 2014, the Cancer Society and its Research Center invited leading cancer researchers, key clinicians and representatives from the Danish Multidisciplinary Cancer Groups to participate in a working group to establish a national Danish Comprehensive Cancer Center (DCCC) and thus pave the way for a national cancer research strategy. During 2015, the working group finalized a model for a DCCC, and, presently, in summer 2016, negotiations for a final DCCC model are under way with the ‘Danish Regions’. The Danish Cancer Society and its Research Center will play a key role in this national initiative.
2017–2019 STRATEGIC RESEARCH PLAN FOR THE DCRC

Overview
The figure below illustrates the complex interplay among different research disciplines required to advance the fight against cancer. The core alliance is a fundamental interaction between epidemiology and molecular biology, the two major research areas represented by the units at the DCRC. This collaboration is key to the development of better diagnostics and cancer treatment and personalized prevention and early detection, as also presented in our strategic research plan, outlined below. Our strategy is very ambitious, yet it reflects the recognized level of excellence of the DCRC research teams. This is reflected in the excellent publication profile of the Center, the ranking of the Center among the top-100 research institutions worldwide (on the basis of the publication quality indicators of the Scimago Institutions Ranking System), the excellent citation scores (h-indexes) of the research leaders, and the frequent calls upon DCRC’s leading scientists as invited speakers globally (see also Annex 1).

Thus, in the context of the timeliest, most innovative global challenges in cancer research and considering our own strengths and collaborative links in both epidemiology and biological cancer research, we have conceived the Strategic Research Plan for the DCRC for the next three years (2017–2019), illustrated in the figure and described in more details below. The two main components of the research strategy are:

- to further reinforce cross-disciplinary collaboration between epidemiology and molecular biology, initiated at the establishment of the DCRC in 2012, and
- to reach out for collaboration with external researchers and professionals engaged in cancer treatment and prevention.

EPI, epidemiology; BIO, molecular biology

Cross-disciplinary collaboration between epidemiology and molecular biology is unique to the DCRC and is the most important basis for the Center’s research strategy. Thus, the
national initiative to create a Danish Comprehensive Cancer Center is not a condition for the research strategy described below, as the strategy is based on our own priorities and strengths, however, the principle of cross-disciplinary collaboration is similar, and it will offer highly interesting possibilities for the DCRC in particular and for Danish health care research in general.

**Important components of the strategy plan**

The DCRC staff has a unique combination of expertise, ranging from epidemiology, biostatistics/bioinformatics and psychology to cellular and molecular biology.

- **Understanding cancer initiation**: Our epidemiology units, supported by our Biostatistics/Bioinformatics Unit (termed EPI), can provide the biology units (termed BIO) with top-quality data on all residents of the country as well as personal data and biological samples from large in-house cohorts of Danes with and without cancer and in all age groups. Proper analyses of such data create ample opportunities for the laboratories to unravel the cellular processes and identify the molecules responsible for the cellular and tissue responses to a diversity of external conditions, from environmental insults (such as tobacco smoke and pollution) to specific diet regimens and life styles. Molecules of interest to BIO are those related to the cellular response to stress, such as lipids, DNA repair enzymes, and organelle regulators, as well as factors related to autophagy, cell death and oxidative stress. Such information will be key to a deeper understanding of cancer initiation and consequently to the development of personalized cancer prevention.

- **Cancer prevention**: In turn, BIO will support EPI studies in continuous cross-talk and synergy, which has the vision to reduce cancer incidence by introducing medical cancer prevention initiatives for cohorts of ‘high-risk’ individuals in the Danish population. This will be done by identifying novel methods for detecting pre-cancerous lesions, identifying novel and ‘old’ drugs for chemical cancer prevention, performing preclinical studies in experimental animals followed by studies in large clinical cohorts, and finally initiating prospective clinical trials on medical cancer prevention.

- **Early detection**: Further, as for the EPI-monitored seemingly healthy populations, BIO will aim at identifying crucial and easily measurable biomarkers for early detection of asymptomatic cancer. Such biomarkers could be investigated routinely in appropriate populations defined as being at high risk in EPI studies.

- **Late effects**: Within the intimate EPI-BIO collaboration, innovative previously undetected biomarkers of physical or psychological late effects will be studied in cancer survivors. These biomarkers could then be sought routinely to determine which cancer survivors are at high risk for late effects, i.e. survivors who may need particular advice in order to take appropriate preventive actions or who may benefit by inclusion in suitable medical surveillance programmes.
• **Cancer vulnerability and novel treatment targets**: Given the major work of the **BIO** laboratories in cellular signaling and the molecular pathways that regulate cell growth, response to diverse stresses, autophagy and cell death in normal versus cancer cells, we will identify any vulnerability of tumour cells that can be targeted in future innovative and personalized treatments. These candidate novel molecular targets will be characterized in terms of their chemical structure, their biochemical modifications and their functions in cellular regulatory networks by **BIO**. These targets will also be validated and further analysed in biological materials obtained from **EPI** cohorts, clinical materials from collaborating health centres and oncology departments in Denmark, the other Nordic countries and beyond as well as by use of the abundant information available in international cancer-related databases. Notably, the targets will provide inspiration for the next step: developing ‘innovative therapeutic strategies’ (see next bullet point).

• **Innovative therapies**: In collaboration with appropriate external research teams with complementary expertise and with facilities in Denmark and abroad, we will establish a forward-flow approach to new cancer therapies. Many potential partners in such efforts will certainly be part of the future **DCCC**. The above-mentioned outcome of the joint effort of **EPI** and **BIO** to identify novel molecular targets for cancer treatments will be further exploited in drug development pipelines or in drug repurposing approaches. ‘Repurposing’ is alternative use of, or indication for, a drug originally developed and licensed for a different disease (such as the painkiller aspirin, which has been shown to reduce the risk for gastrointestinal cancer significantly). These joint efforts will also require preclinical studies and parallel development of biomarkers to select the subset of patients who might most benefit from such treatment strategies.

The setup described above will provide the basis for novel prospective **intervention trials**, probably synchronized with innovative nutraceutical approaches, to reduce the ever-increasing cancer incidence. In addition, in collaboration with clinical research environments, we will initiate **clinical trials** to treat individuals at high risk for cancer and thereby prevent the progression towards malignancy and treat already established cancers. In the meantime, the continuous flow of information from such activities will generate new cellular and animal models for testing the molecular mechanisms identified by **BIO**.

In sum, our **cross-disciplinary competence**, which is the main strength and asset of the DCRC, is fundamental for competitive advancement of research in the years to come and will also represent an important element in the success of the **DCCC** initiative. Many approaches, such as chemical research in drug development and repurposing, may contribute to create novel therapeutic avenues. As one of **DCCC** assets, this will help complete our drive towards developing novel clinical approaches to fight cancer.

**OPERATIONAL NEEDS**

To implement the plan in the coming three years, the DCRC will have to increase the capacity of its researchers and its laboratory equipment and facilities, by:
- intensifying cross-disciplinary collaboration between epidemiology and molecular biology;
- greatly increasing its repertoire of large strategic infrastructures;
- devising clear career paths for young and creative scientists, in line with the recent postdoctoral challenge programme;
- and, most importantly,
- including clinicians both nationally and internationally in the DCRC constellation of collaborators, a campaign that will both help us to achieve our **strategic research plans** and increase the multidisciplinary offer of our **educational programmes**.
Among the world's approximately 5,000 research institutions, the DCRC ranks among the top-100 using publication quality indicators of the SCIMAGO Institutions Ranking system.

The H-index is a measure of the amount and quality of research made by individual researchers. The H-index represents the number of papers that have been cited at least that number of times – an H-index of 15 means an author has 15 papers that have been cited at least 15 times each. A high H-index means that the author has a relatively high number of highly cited papers.
Chair of the SAB

• Professor Ulrik Ringborg, Karolinska University Hospital, Stockholm, Sweden

### Units

<table>
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<tr>
<th>Units</th>
<th>Core budget (Mio. DKK)</th>
<th>External grants (Mio. DKK)</th>
</tr>
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<tbody>
<tr>
<td>Diet, Genes &amp; Environment</td>
<td>10.4 (33%)</td>
<td>20.8 (67%)</td>
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<tr>
<td>Virus, Lifestyle &amp; Genes</td>
<td>5.1 (34%)</td>
<td>9.8 (66%)</td>
</tr>
<tr>
<td>Cell Deaths &amp; Metabolism</td>
<td>7.3 (31%)</td>
<td>15.9 (69%)</td>
</tr>
<tr>
<td>Cell Stress &amp; Survival</td>
<td>4.6 (56%)</td>
<td>3.6 (44%)</td>
</tr>
<tr>
<td>Genome Integrity</td>
<td>9.1 (57%)</td>
<td>6.7 (43%)</td>
</tr>
<tr>
<td>Survivorship</td>
<td>5.3 (31%)</td>
<td>12.0 (69%)</td>
</tr>
<tr>
<td>Statistics, Bioinformatics &amp; Registry</td>
<td>5.3 (71%)</td>
<td>2.2 (29%)</td>
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### Center

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<th>Core budget in addition to the above</th>
<th>36.1 (100%)</th>
<th>0 (0%)</th>
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<tr>
<td>Total center budget 2016</td>
<td>83.2 (54%)</td>
<td>71.0 (46%)</td>
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### Scientists with expertise in population-based cancer research

- Professor Cornelia Ulrich, Huntsman Cancer Institute, Salt Lake City, Utah, USA
- Professor Jan-Willem Coebergh, Retired from Erasmus University Medical Center, The Netherlands

### Scientists with expertise in biological cancer research

- Professor Varda Rotter, Weizmann Institute of Science, Rehovot, Israel
- Professor Kevin Ryan, Cancer Research UK Beatson Institute, Glasgow, UK

### OTHER ASSETS

Access to animal facility
Other core facilities, incl. a metabolomics facility
Bioinformatics
Large cohorts collections including biobanking

### CENTER STAFF 2016*

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<th>On core budget</th>
<th>On grants</th>
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<tbody>
<tr>
<td>Technical &amp; administrative staff</td>
<td>32</td>
<td>17</td>
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<tr>
<td>Researchers</td>
<td>45</td>
<td>91</td>
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<tr>
<td>Total</td>
<td>77</td>
<td>108</td>
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* plus 109 guest researchers in 2016

### SCIENTIFIC ADVISORY BOARD (SAB)