

THEME FOR INNOVATION CANCER

1. Introduction and background.

Within the strategic goal to belong to the top 10 academic medical centers in Europe, the LUMC has chosen “Oncology” as one of three strategic areas to prove relevance for society through innovation and valorization. The LUMC has a long track record of excellence in cancer research. Moreover, it hosts world-leading researchers in its ranks, provides top-referral patient care, and has an extensive international network. Nevertheless, there is a general consensus that, as an institute, it has not yet realized its full potential in cancer research. Historically, research groups and expertise have generally been contained within local structures such as departments. Synergies between a significant proportion of basic researchers and clinical researchers have therefore not been sufficiently explored. Consequently, the full potential for innovative investigator-initiated trials or trials with a translational research component has not been realized. These are major challenges that have to be addressed by the Theme for Innovation Cancer (hereafter: “Theme Cancer”) in the coming years in order to boost the impact of LUMC’s cancer research.

To achieve this, three fundamental goals have to be pursued in the short term:

- i) attract, foster and manage scientific talents, who are future world-leading researchers.
- ii) stimulate interaction between researchers and clinicians, thereby promoting the crossover of expertise.
- iii) increasingly couple cancer research to patient care and population health.

2. Description of:

Research

The Theme Cancer spans all aspects of the full “cancer cycle” from genetic risk and primary prevention over oncogenic mechanisms, diagnostics and therapy, to follow-up and cancer survivorship.

The LUMC performs high-quality basic and translational research pertaining to cancer in the fields of cancer immunology and immunotherapy, DNA repair and genomic instability, and cancer cell signaling and biology. Furthermore, highly-performing clinical research focuses on hereditary cancers, bone and soft tissue tumors, (uveal) melanoma, gynecological cancers, cutaneous lymphomas, among others. The LUMC has also provided, throughout the years, impactful contributions to the development of molecular and image-guided diagnostic tools, as well as trials exploring various therapeutic regimens including surgery, chemotherapy, radiotherapy, immunotherapy, and image-guided interventions.

Several cancer researchers at the LUMC are holders of prestigious grants from, for instance, the European Research Council (starting, consolidator, and advanced), the NWO talent program (Veni, Vidi, Vici) grants, and the Dutch Cancer Society (consortium, project, and fellowship grants). Furthermore, LUMC cancer researchers publish their research in top-tier journals such as *Nature*, *Cell*, or *NEJM*, and are actively engaged in the valorization of their findings.

Position in LUMC, UL, national and international

The Theme Cancer aggregates the largest proportion of research and clinical care that is performed at the LUMC. At least, 65% of departments at the LUMC and more than 75 Principal Investigators are actively involved in cancer research. On one hand, this is a major organizational challenge for the Theme Cancer. On the other hand, it is a tremendous opportunity to explore synergies between expertise and to foster

interdisciplinary research. Importantly, cancer researchers at the LUMC are active users of state-of-the-art technologies and drivers of technological innovation at the institute.

Several cancer research groups at the LUMC have worked in close collaboration with institutes of Leiden University, most notably, the Leiden Academic Centre for Drug Research but also the Institute of Biology Leiden, the Leiden Institute of Chemistry, and the Leiden Institute of Advanced Computer Science. Enormous opportunities can arise from closer interactions of the Theme Cancer with other institutes at Leiden University but also with industrial partners at the Bioscience Park.

At the national level, LUMC research has strong ties (including output) with all other UMC's, most notably with the Erasmus and Amsterdam Medical Centers. Of particular interest, the LUMC has in recent years developed productive and growing interactions with the Dutch Cancer Institute (NKI) and the Princess Maxima Center (PMC) that are important partners in the development of translational research coupled to clinical trials.

Privileged international partners in cancer research include KU Leuven (Belgium), Harvard University (United States), Karolinska Institutet (Sweden), Universities of London, Oxford, and Cambridge (UK), Institute of Cancer Research (UK), or University of Toronto (Canada), among others. Cancer researchers at the LUMC also take advantage of international collaborations provided by the LUMC within the context of League of European Research Universities (LERU) and Eurolife. Finally, Theme Cancer is strongly committed to support the LUMC Global initiative and support the establishment of purposeful and strategic international partnerships.

Coherence and synergy

Within the theme

The LUMC possesses an unique set of expertise that span knowledge on basic biology and cellular mechanisms, technological innovation, and clinical research. The development of platforms that support communication, mentorship, and project development between experts is a low-effort, high-impact initiative that will be undertaken by the Theme Cancer. On one hand, the Theme Cancer wants to foster creative and highly-original basic research that contributes to a knowledge-society and can eventually translate to ground-breaking clinical translations. On the other hand, the Theme Cancer also wants to accelerate the translation of basic research and improve the quality of clinical research by synergizing the expertise of our basic and clinical researchers. To this end, we have divided the Theme Cancer in 6 sub-themes (see Table 1), which have been established following consultation of our Cancer Research Advisory Council composed of a broad group of Principal Investigators and Clinicians at our institute (more than 75 members).

Sub-theme coordinators will be appointed to each sub-theme and will be required to organize symposia and other initiatives that promote the crossover of experiences and expertise between members. The Theme Cancer will also, in articulation with the Leiden Oncology Center, stimulate the participation of tumor working group members in the Theme's initiatives in order to foster the development of high-quality translational and clinical research. Of note, for the majority of defined sub-themes, communities have already been organized and are fully operational and can thus serve as a model for the development of initiatives elsewhere. The Theme Cancer will be a regular participant of the Top Research Seminars where high-quality scientific research will be shared with the rest of the LUMC's scientific community.

Cancer research Sub-themes	Link with LUMC Research Theme
1. Genome instability and cancer genetics DNA repair & replication, hereditary and somatic cancer alterations, genotype–phenotype associations: mechanisms, early detection, diagnosis & prognosis.	Medical Genomics Prevention & Lifestyle
2. Cancer immunology & immunotherapy Immunopathogenesis, tumor-host interactions, anti-cancer vaccine development, adoptive cellular immunotherapy, antibody-based cancer therapies.	Immunity
3. Pharmacogenomics and molecularly targeted therapy Molecular diagnostics, cell signaling pathways, pharmacogenetics & drug dosing	Academic pharma Medical Genomics
4. Image-guided cancer diagnostics & therapy Functional imaging, functional ex vivo imaging, proton therapy	Cell Tissue & Organ
5. Computational Oncology In silico modelling of individual tumors – LCCO, real life big data analysis	Population health
6. Leading initiatives in clinical research Geriatric oncology, cancer-associated thrombosis, prevention of complications, initiation of (inter)national IIT	Cardio-Vascular Prevention & Lifestyle Lifecourse Neuroscience Academic Pharma

Relation with other themes

The Theme Cancer has identified already ongoing relationships with the other innovation themes (Table 1). The majority of PIs that are participating in the Cancer Theme are also active members of other themes which promotes interdisciplinarity across the board. Importantly, other theme members will be regularly invited to our Theme’s initiatives and we will strongly support actions by the Research Board to promote inter-theme activities. One important aspect that deserves particular focus is the sharing of expertise and investments on state-of-the-art technologies (see section on relation with core facilities).

Relation to societal outreach themes

- **Oncology:** The Theme Cancer is intrinsically linked to and forms the core of innovation for the societal outreach theme Oncology. To promote Outreach initiatives we will pursue, through the different tumor workgroups of the LUMC Oncology Center (LOC), contacts with patient associations in order to communicate research initiatives and latest developments in the field. In cooperation with the Communication department of the LUMC, we will engage in the regular communication of important milestones achieved by our cancer researchers.
- **Population Health:** The research sub-themes that cover cancer prevention and early detection provide important input to the societal outreach theme Population Health. LUMC-specific aspects concern genetic risk profiles in cancers with a hereditary trait. Furthermore, researchers of the Theme Cancer are actively involved in implementing Lifestyle & Prevention content in LUMC education programs (e.g. bachelor Medicine).

- Regenerative Medicine: Some links exist to the societal outreach theme Regenerative Medicine, i.e. the hematopoietic stem cell transplantation program. However, Regenerative Medicine has a huge potential for cancer research with respect to reestablishing organs and/or their function after their destruction through radical locoregional cancer therapy (e.g. thyroid, other endocrine glands, reproductive organs etc.). Furthermore, a number of groups are dependent on models (e.g. iPSC) that are being developed together with Regenerative Medicine researchers.

Relation with Topreferral Care:

The Theme Cancer is intrinsically linked to the LUMC Oncology Center. The core mission of the LOC is to improve treatment outcome of cancer patients through innovation. Translation of the progress in knowledge and technology achieved within the Theme Cancer to the patient is organized through the Tumor Working Groups (TWG) of the LOC. The TWG define and address unmet clinical needs of patients with a particular type of cancer, often through their (inter)national leading role as defined through Nationally recognized Centers of Expertise and European Reference Networks. Through the Cancer Researchers participating in the TWG, these unmet clinical needs are communicated to the cancer research sub-themes to stimulate basic research addressing these specific needs and gaps of knowledge. Translatable research results are organized by the TWG into concrete and specific bed-to-bench and bench-to-bedside projects and ultimately into investigator-initiated interventional trials and noninterventional studies.

Relation with education/Graduate School:

Members of Theme Cancer are actively involved as coordinators or lecturers in bachelors and masters that fall under the responsibility of the Faculty of Medicine (LUMC), most notably Biomedicine and Medicine. Many LUMC cancer researchers are also coordinators/lecturers of courses organized as part of graduate schools, e.g. MGC and MolMed, and teach at Summer/Winter schools. Furthermore, cancer research groups are highly popular hosts for the development of student traineeships. The Theme Cancer will stimulate their members to expose students to the latest developments in cancer research. In particular, the ones pertaining to research developed “in-house” in order to motivate students and foster a sense of institutional identity and pride. In addition, our members can play an extremely important role as talent scouts through the identification of scientific talents with great potential to be enrolled in PhD programs. Finally, the Theme Cancer will work on the design of a PhD summer school aimed at forming a Cancer Theme community at the PhD level that can foster interdisciplinary research from a bottom-up perspective.

Relation with core facilities:

Theme Cancer members are avid users of the LUMC core facilities and are important drivers of technological innovation at our institute. The Theme Cancer will organize regular technological innovation symposia where the LUMC’s research facilities will have the opportunity to present the latest technological developments available for LUMC researchers. Furthermore, the Theme Cancer will regularly (yearly) make inventories of which technological innovations can benefit our cancer researchers and discuss with the research facilities opportunities for investment.

3. Participating researchers:

Name	Department	Name	Department
Akker, dr. ir. J.B. van den	MOLEPI	Asperen, Mw. Prof. dr. C.J. van	KG
Reinders, Prof. dr. M.J.T.	MOLEPI	Nielsen, Dr. M.	KG
Steyerberg, Prof. dr. E.W.	MOLEPI	Schmidt, Prof. dr. T.	LION
Putter, Prof.dr. H.	MOLEPI	Hiemstra, P.S.	LONG
Stiggelbout, Prof.dr. A.M.	MOLEPI	Postmus, Prof. dr. P.E.	LONG
Baker, D.A.	CCB	Slats, A.M.	LONG
Hoeben, R.C.	CCB	Smit, Prof. dr. E.F.	LONG
Szuhai, K.	CCB	Hardwick, prof. dr. J.C.H.	MDLZ
Wührer, Prof. dr. M.	CPM	Hawinkels, Dr. L.J.A.C.	MDLZ
Kroon, Dr. C.D. de	GYN	Pronk-van Montfoort, A.G.	MDLZ
van Poelgeest, Dr. M.I.E.	GYN	Burg, Prof. dr. S.H. van der	ONCO
Tollenaar, Prof. dr. R.A.E.M.	HLK	Gelderblom, Prof. A.J.	ONCO
Vahrmeijer, A.L.	HLK	Haanen, Prof. dr. J.B.A.G.	ONCO
Kuppen, Dr. P.J.K.	HLK	Hall, Dr. T. van	ONCO
Liefers, Dr. G.J.	HLK	Kapiteijn, H.W.	ONCO
Mesker, Dr. W.E.	HLK	Portielje, J.E.A.	ONCO
Mieog, Dr. J.S.D.	HLK	Dijke, Prof. dr. P. ten	CCB
Griffioen, M.	HEM	Neefjes, Prof. dr. J.J.C.	CCB
Heemskerk, mw. dr. M.H.M.	HEM	Vertegaal, Prof. dr. A.C.O.	CCB
Veelken, Prof. dr. H.J.	HEM	Broekman, M.L.D.	NECH
Vermaat, J.S.P.	HEM	Jager, M.J.	OOG
Doorn, R. van	HUID	Vu, T.H.K.	OOG
Tensen, C.P.	HUID	Bosse, T.	PATH
Attikum, Prof. Dr. H. van	HG	Bovee, Mw. Prof. dr. J.V.M.G.	PATH
Devilee, Prof. dr. P.	HG	Miranda, Dr. N.F. de	PATH
Maarel, prof. dr. ir. S.M. van der	HG	Morreau, J.	PATH
Mons, Prof. dr. B.	HG	Smit, Prof. dr. V.T.H.B.M.	PATH
Noordermeer, S.M.	HG	Bloem, Prof. dr. J.L.	RADI
Tijsterman, Prof. dr. M.	HG	Geus-Oei, L.F. De	RADI
Vreeswijk, Dr. M.P.G.	HG	Leeuwen, F.W.B. van	RADI
Arens, R.	IMMU	Lelieveldt, B.P.F.	RADI
Borst, Mw. Prof. dr. J.G.	IMMU	Vriens, Dr. D.	RADI
Dongen, J.J.M. van	IMMU	Alderliesten, Mw. dr. T.	RT
Ossendorp, F.A.	IMMU	Rasch, Prof. dr. C.R.N,	RT
Visser, mw. prof. dr. K.E. de	IMMU	Creutzberg, Prof.dr. C.L.	RT
Cobbaert, C.M.	KCL	Klok, F.A.	STOL
Guchelaar, Prof. dr. H.J.	KFT	Versteeg, H.H	STOL
Swen Dr. J.J.	KFT	Pluijm, G. van der	URO

4. Ambition for the next 5 years, including implementation plan and time lines

Output

The Theme Cancer will aim, through its initiatives, to see an increase, in the coming 5 years, in publications that involve basic and clinical researchers from different groups, departments, and innovation themes. The expectation is that the combination of expertise will translate into increased quality and impact of publications. A bibliometric analysis to evaluate changes in patterns of publication will be carried out in 2023 and 2025.

Grants national and international

One of the most urgent needs at our institute is the establishment of a KWF grant committee to support applicants and thereby increase success rates. The Theme Cancer has defined as one of its main aims to setup such a committee and maintain it throughout the years. At the European level, the Theme Cancer is committed to accompany the developments around Europe's Beating Cancer Plan. Where possible, and in coordination with the Directorate of Research, we will stimulate the coordination of consortia grants by LUMC cancer researchers. Also as part of talent management, the LUMC cancer researchers will continue to attract NWO talent scheme and ERC grants, and exploit other resources such as Worldwide Cancer Research

Talent

Scientific talent is at the basis of a successful research profile. As such, the Theme Cancer is strongly committed to attract, maintain, and develop scientific talent at our institute. To achieve this, scouting for highly talented prospective PhD students will be encouraged among Theme Cancer members so that a pool of highly-qualified candidates is available to integrate PhD programs. Further, and in coordination with the management teams of the remaining Themes we are highly supportive of the implementation of a tenure track to offer a career prospect to our most talented young scientists and to foresee the renovation of our senior academic staff. Finally, the Cancer Theme also aims at playing a role in the indication and evaluation of candidates for Full Professorship.

Infrastructures

In recent years, the LUMC has made important investments regarding infrastructure and technology (e.g. cytometry, mass spectrometry, iPSC hotel, NGS, etc.). Going forward, the Theme Cancer and its participants expect to play an important role in identifying and supporting strategic investments that 1) are likely to advance the quality of our scientific research, and 2) have the potential to benefit a large number of researchers, also across other Themes. The identification of strategic investments will be done in close collaboration with the core facilities and technological experts at the institute.

Societal impact

Through the tumor working groups, we will stimulate contact between researchers and patient organizations to promote education and transparency regarding scientific research. We will also accompany developments that are currently underway at the University to equip young researchers with tools to support outreach activities. Finally, in coordination with the Communication department of the LUMC and the Directorate Research the Theme Cancer will profile the works of our researchers and important milestones.