

Appendix I

Boards, teams, and groups

GENERAL SUPPORT TEAM

THE VALORIZATION SUPPORT TEAM

NETWORK OF CONSULTANTS

OPEN SCIENCE AND FAIR EXPERT GROUP

INTERNATIONAL ADVISORY BOARD

INTERNATIONAL REVIEW COMMITTEE

General Support Team

Elize Brolsma, *Project Communications Manager* (Lygature)
Dr. Alexander Duyndam, *Communications Manager* (Lygature)
Tracey Faase, *Financial Controller* (Lygature)
Dr. Ester Frische, *Head of Research and Community support*
Denis Groot, *Financial Controller* (Lygature)
Dr. Colete ten Hove, *Programme Manager*
Vesna de Jong, *Digital Communications Manager* (Lygature)
Soumela Kasperiouk, *Management assistant (since April 2021)*
Emanuela Lonardi, *Programme Coordinator*
Bianca-Olivia Nita, *Project Communications Manager* (Lygature)
Dr. Tale Sliedrecht, *Head of Strategy* (Lygature)
Marlinde Smit, *Programme Manager* (Lygature)
Dr. Jacqueline Staring, *Programme manager* (Lygature)
Dr. Inga Tharun, *Programme manager* (Lygature)

The Valorization Support Team

Dr. Saharla Ahmed, *Business Development*
Ian Bell, *Business Development*
Dr. Shobhit Dhawan, *Fund Manager*
Alina Boca- Eichner, *Data Entry Assistant (since January 2021)*
Dr. Veerle Fleskens, *Business Development*
Amber Liu, *Business Development*
Dr. Yuva Oz, *Business Development*
Emil Pot, *Business Development*
Dr. Alexander Turkin, *Business Development*
Mariëlle Veldhuizen, *Paralegal, Valorization Coordinator*
Dr. Koen Verhoef, *Business Development*

Network of Consultants

Dr. Danny Burg (D2team), *Drug Development Specialist*
Dr. Geert Frederix (UMC Utrecht), *Health Technology Assessment Specialist*
Dr. Ellen Hulskotte (Curare Consulting), *Clinical Trial Design Specialist*
Dr. Paul de Koning MD (de Koning coaching & consulting), *Drug Development Specialist (Retired April 2021)*

Drug Repurposing Advisory Board

Mario van der Stelt (Leiden University)
Roderick Beijersbergen (NKI)
Paul Geurink (LUMC)
Saman Honarnejad (Pivot Park Screening Centre)
Ellen Hulskotte (CURARE consulting)
Wilbert Zwart (NKI)

International Advisory Board

Teri Willey (Chair), VP for Business Development & Technology Transfer - Cold Spring Harbor Laboratory

Prof. Vishva Dixit, Genentech

Prof. Clare Isacke, ICR London

Prof. Richard Marais, Director of the CRUK Manchester Institute

Prof. Alberto Bardelli, Department of Oncology, University of Torino

Prof. Sabine Tejpar, UZ Leuven

Prof. Paul Workman, ICR London

Independent Review Committee

Prof. Susan Gasser PhD (Chair), Director emeritus Friedrich Miescher Institute

Prof. Josep Tabernero MD PhD, Medical Oncologist, Head of Medical Oncology at Vall d'Hebron University Hospital and Director at Vall d'Hebron Institute of Oncology (VHIO)

Prof. Liesbeth de Vries MD PhD, Medical Oncologist, Department of Medical Oncology UMCG

Prof. Richard Marais PhD, Director of the CRUK Manchester Institute & Onco International Advisory Board member

Derek Waddell, Founder & CEO of 81C Limited

Prof. Ivan Dikic, MD PhD, Director Institute of Biochemistry II, Goethe University Frankfurt

Dr. Tim Wells, CSO Medicines for Malaria Ventures & Non-Executive Director at Kymab Ltd.

Appendix II

Oncode in Numbers

ONCODE COMMUNITY

ONCODE OUTPUT

CLINICAL PROOF-OF-CONCEPT PROJECTS

TECHNOLOGY DEVELOPMENT PROJECTS

EQUIPMENT & INFRASTRUCTURE FUNDED PROJECTS

MEETINGS IN 2021

FOLLOW UP FUNDING ORIGINATING FROM BASE FUND RESEARCH

Oncode Community

Position	#	female/male
Oncode research community (31 Dec'20)	923	470/453
Oncode Investigators	43	9/34
Oncode Junior Investigators	18	8/10
Oncode Post docs & Senior Scientists	264	147/117
Oncode PhD students	369	208/161
Oncode technicians & supporting staff	230	128/102
PhD defences	40	20/20

Oncode Output

Publications	#	compared to baseline
Publication all OIs	443	311
Median impact factor all OIs	12.5	8.4
Co-publications with industry	70	36
Open Access (OA) publications all OI	345	203
Share of OA of total publications	78%	65%

Note: Reported bibliometric numbers are based on the sliding window principle (as further detailed in metric report). Briefly: The reported data covers publications from a three-year window, the reporting period year (2021) and the two-years preceding it (2019 and 2020). By using this 'sliding window', Oncode obtains a more robust estimation of the publication activity and citation impact of the publications by OIs.

Agreements	#	compared to 2018
Non-disclosure agreements	108	22
Research agreements	35	7
Material transfer agreements	75	13
License agreements	9	*
Other	20	25
*no baseline data available		

Invention Disclosures	#	compared to 2018
New invention disclosures	35	32
Legacy files	0	11
Non-Oncode	1	*
Portfolio Dec 31	98	43
*no baseline data available		

Patents	#	compared to 2018*
Priority filings	19	9
PCT filings	12	6
National filings	7	7
*no baseline data available		

New Ventures

Single Cell Discoveries B.V. (2018)
Cyclomics B.V. (2019)
Immagine (2020)
Lumento (2020)
Oncosence (taken up as an Oncode portfolio spin-off in 2021)
LiagoBio (2021)

Funding

	€	Compared to baseline
Total Funding attracted (incl. Oncode funding)	€61.2 million	€43.6 million
Total private funding attracted	€10.1 million	€5.12 million

Communication

Community Platform - Statistics 2021:

- 2,914 visitors generated 4,489 sessions and 9,807 pageviews
- 1,089 terms were edited within individual profiles
- 19 clicks for contact (email, LinkedIn, PubMed, phone)

Website statistics 2021:

- 28,652 visitors created 44,206 sessions, resulting in 106,416 page views

LinkedIn

- 4,477 followers on December 31st, 2021
- 889 new followers with a 4.57% engagement rate

Clinical Proof-of-Concept Projects update 2021

Newly-funded CPoC Projects

Mechanism of response and resistance to neoadjuvant PD-1 checkpoint blockade in vulvar squamous cell carcinoma.

Main applicant: Sjoerd van der Burg, LUMC

Funds awarded: € 663K

Year awarded: 2021

New epigenetic combination therapy testing for BAP1-deficient mEsoTheLioma, a double-arm prospective non-comparative phase I/II trial (BEETLE).

Main applicant: Maarten van Lohuizen, NKI

Funds awarded: € 799K

Year awarded: 2021

Tasquinimod as new treatment option in heavily pretreated patients with Myeloproliferative Neoplasms associated with bone marrow fibrosis

Main applicant: Rebekka Schneider, Erasmus MC

Funds awarded: € 511K

Year awarded: 2021

Maximizing treatment options for recurrent glioblastoma patients by whole genome sequencing-based diagnostics

Main applicant: Edwin Cuppen, UMC Utrecht

Funds awarded: € 745K

Year awarded: 2021

Completed CPoC Projects in 2021:

HDAC inhibitor vorinostat in resistant BRAF V600 mutated advanced melanoma

Main applicant: Rene Bernards, NKI

Technology Development Projects

PREDICATE - Towards precision medicine for colorectal cancer patients

Main applicant: Louis Vermeulen (Amsterdam UMC)

Funds awarded: € 150K

Validation of the FUNsice pipeline by target discovery and validation for metastatic colorectal cancer

Main applicant: Miao Ping Chien (EMC) & Louis Vermeulen (Amsterdam UMC)

Funds awarded: € 150K

Validation of the MISC-seq technology in paediatric rhabdoid tumours

Main applicant: Jarno Drost (PMC) & Jop Kind (Hubrecht Institute)

Funds awarded: € 90K

Gut restricted BMP inhibitors to treat metabolic diseases

Main applicant: Hans Clevers (Hubrecht Institute/PMC)

Funds awarded: € 148K

Live-cell screening for disruption of oncogenic condensates

Main applicant: Boudewijn Burgering

Funds awarded: € 150K

Development of DNA ligase III inhibitors to enhance response and overcome resistance to PARP inhibitors

Main applicant: Jos Jonkers (NKI)

Funds awarded: € 150K

Completed Projects in 2021

EZH2 + FGFR inhibitor Combination Therapy to Treat BAP1 Deficient Tumors

Main applicant: Maarten van Lohuizen (NKI)

Validation and optimization of Ultra-wide Field-of-View Optical Microscopy technology

Main applicant: Miao Ping Chien (Erasmus MC)

Turning Mutations into Patient Specific Biomarkers to Guide Personalized Treatment of Ovarian Cancer

Main applicant: Jos Jonkers (NKI)

Preclinical proof-of-concept studies of advanced lipid metabolism inhibitors

Main applicant: Mario vd Stelt (Leiden University)

Establishing AGN192403 as a first-in-class, orally-available PD-1 inhibitor

Main applicant: Daniel Peeper (NKI)

Repurposing BACE1 Alzheimer's inhibitors for immunotherapy

Main applicant: Daniel Peeper (NKI)

Infrastructure & Technologies Funded Projects

No Major investments were made within the I & T programme in 2021

Follow up funding originating from base fund research

Oncode base funds provide OIs with the ability to quickly adapt their approach and allocate funds towards promising new findings. The preliminary data created by these base fund projects have already led to many successful national and international grant applications. All grants that have been obtained on the basis of Oncode base fund research are listed below.

KWF research grant, €818K

Oncode Investigator: Reuven Agami (NKI)

Motivation: All the projects related to aberrant protein production, sloppiness in mRNA translation, and substituents were mostly financed by Oncode. Because of the availability of Oncode funding, we could push forward investigating this novel phenomenon. Starting from June 2021, we received dedicated support from KWF for Sloppiness and pursued this line of research through this route.

NWO, ENW-Klein grant, €720K (awarded in 2020)

Oncode Investigator: Michiel Vermeulen (Radboud University)

Motivation: The initial interaction proteomics datasets we generated, supported by Oncode base funds, served as a basis for an EMBO long-term post-doc fellowship (awarded to K. Kliza) and an ENW-KLEIN2 project in collaboration with Dima Filippov.

ODAS foundation: €355K

Oncode Investigator: Den Boer (PMC)

Motivation: We used the Oncode base fund to pioneer these types of immunotherapeutics/niche studies, generating (pilot) data to gain expertise and show proof-of-concept for this innovative field of research. In 2021, additional funding was secured (ODAS grant) for this research, which is performed in collaboration with the tumor immunologists and CAR-T/immune-therapists in our center.

ZonMw open competition: €750K

Oncode Investigator: Peter ten Dijke (LUMC)

Motivation: Our expertise/insights and broad array of innovative cellular assays have provided the basis for ZonMW open competition (funded) and other grant applications (pending).

KWF research grant: €714K

Oncode Investigator: Jurian Schuijers (group Boudewijn Burgering (UMC Utrecht))

Motivation: The work performed within the frame of Oncode provided the preliminary data that enabled a successful application for a KWF grant by Dr Jurian Schuijers.

KNAW research grant: €250K

Oncode Investigator: Jop Kind (Hubrecht institute)

Motivation: Our Oncode base fund allowed us to further develop a method to generate proof-of-concept. Based on these pilot experiments, we have now secured funding from a KNAW research fund (250k) to further develop the project in collaboration with Jan Paul Medema.

NWO Vidi grant: €800K

Oncode Investigator: Jarno Drost (PMC)

Motivation: In collaboration with the De Wit group, we found that derailed enhancer landscapes drive oncogene expression in MRT. A manuscript describing our findings is currently in preparation. This base fund project provided preliminary data that was included in my NWO Vidi proposal.

KWF research grant: €420K

Oncode Researcher: Susanne Lens (UMC Utrecht)

Motivation: Research conducted using Oncode base funds has allowed me to gather preliminary data for a new idea and method that supported the successful application for a KWF research grant.

NWO consortium grant: €3.5M

Oncode Investigator: Jop Kind (Hubrecht Institute) and Michiel Vermeulen (Radboud University)

Motivation: We obtained our first big NWO consortium grant (NWO/PSIDER), a project I had initiated together with Michiel Vemeulen. We will develop human embryo models to study the mechanisms of implantation into the uterus and the role of chromosome copy number variations as the cause for miscarriages. For this project we will use EpiDamID (developed as described under Oncode base fund project A) to obtain single-cell epigenetic and transcriptomic measurements.

KWF research grant: €660K (awarded in 2020)

Oncode Investigator: Madelon Maurice (UMC Utrecht)

Motivation: Without Oncode support, it would have been difficult to initiate this research line as the work is entirely new to my lab and a proven track record is commonly required to acquire funding. With our preliminary findings we obtained KWF funding to continue our efforts.

Boehringer Ingelheim: €175K

Oncode Investigator: Linde Meyaard (UMC Utrecht)

Motivation: Our studies on a non-disclosed target, for which novel initiatives were previously funded by Oncode base funding, have progressed to be mainly funded by collaborative research agreements with non-private partners, including animal studies in disease models.

KWF YIG: €560K

Oncode Investigator: David Huels, (Jan Paul Medema group (Amsterdam UMC))

Motivation: The project only recently started in the lab but has already yielded important insights. Using organoid technology in different ECM matrices we reveal that regenerative populations are observed when cells are placed in collagen. The underlying mechanism is now part of the YIG project of David Huels who developed the project in my lab.

KWF research grant : €750K

Oncode Investigator: Sylvie Noordermeer (LUMC)

Motivation: This project has been funded by my Oncode base funds. The preliminary data obtained enabled us to get funding from KWF (750K) to proceed with the project for the next 4 years.

NWO Vidi: €800K

Oncode Investigator: Hugo Snippert (UMC Utrecht)

Motivation: Initiated with an Oncode base fund. I will expand its scope using a newly acquired NWO VID I grant.

Non disclosed industry grant: €400K

Oncode Investigator: Anne Rios (PMC)

Motivation: The model has sparked the interest of a major industrial player for understanding human milk production and downstream effects on gut homeostasis, resulting in a sponsored contract for a PhD position.

KWF consortium grant: €1M (awarded in 2020)

Oncode Investigator: Anne Rios (PMC)

Motivation: Our BEHAV3D platform for accessing cellular immunotherapy efficacy and mode of action has now been rolled out over several research projects, including two funded consortia grants and a project

sponsored by a main player in the pharmaceutical industry. This will further validate the platform and especially its potential to guide and improve clinical trial design for immune-oncology drugs.

NKI foundation €3.5M

Oncode Investigator: Bas van Steensel (NKI)

Motivation: The Oncode Synergy scheme has catalysed the formation of a strong consortium of seven labs that have now started a large project (supported by external funding) to study noncoding mutations in cancer genomes

KWF research grant: €422K

Oncode Investigator: Louis Vermeulen (Amsterdam UMC)

Motivation: We found that the compound lithium has a chemopreventive effect on adenoma development in mice. We patented this finding and we recently obtained funding from the Dutch Cancer Society (KWF) to perform a clinical trial in humans with familial adenomatous polyposis.

KWF grant: €710K, **Health-Holland PPP match call:** €348K

Oncode Investigator: Louis Vermeulen (Amsterdam UMC)

Motivation: In 2021, we obtained 2 grants to be able to further study effective treatment of PMD: One KWF grant (together with Dr. Maarten Bijlsma, and Prof. Dr. Onno Kranenburg) and a TKI grant (with Dr. Maarten Bijlsma and the drug formulation company Avivia BV).

NWO research grants: €247K and €295K

Oncode Investigator: Wim Vermeulen (Erasmus MC)

Motivation: Funding *C. elegans* research is intrinsically challenging within the Dutch funding-landscape, but through base-fund enabled results we acquired two *C. elegans*-associated research grants (NWO-ENW: ALWOP.494; and 711.018.007).

Appendix III

Advice letter IAB

Appendix IV

Oncode Investigator Research Summaries

Will be provided separately.