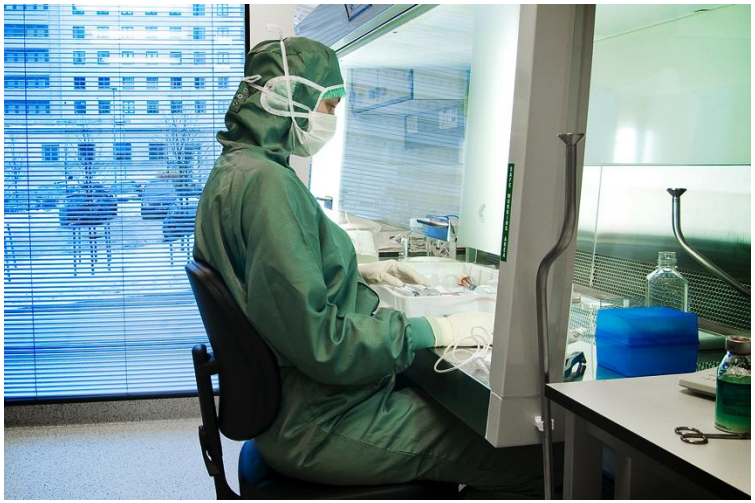
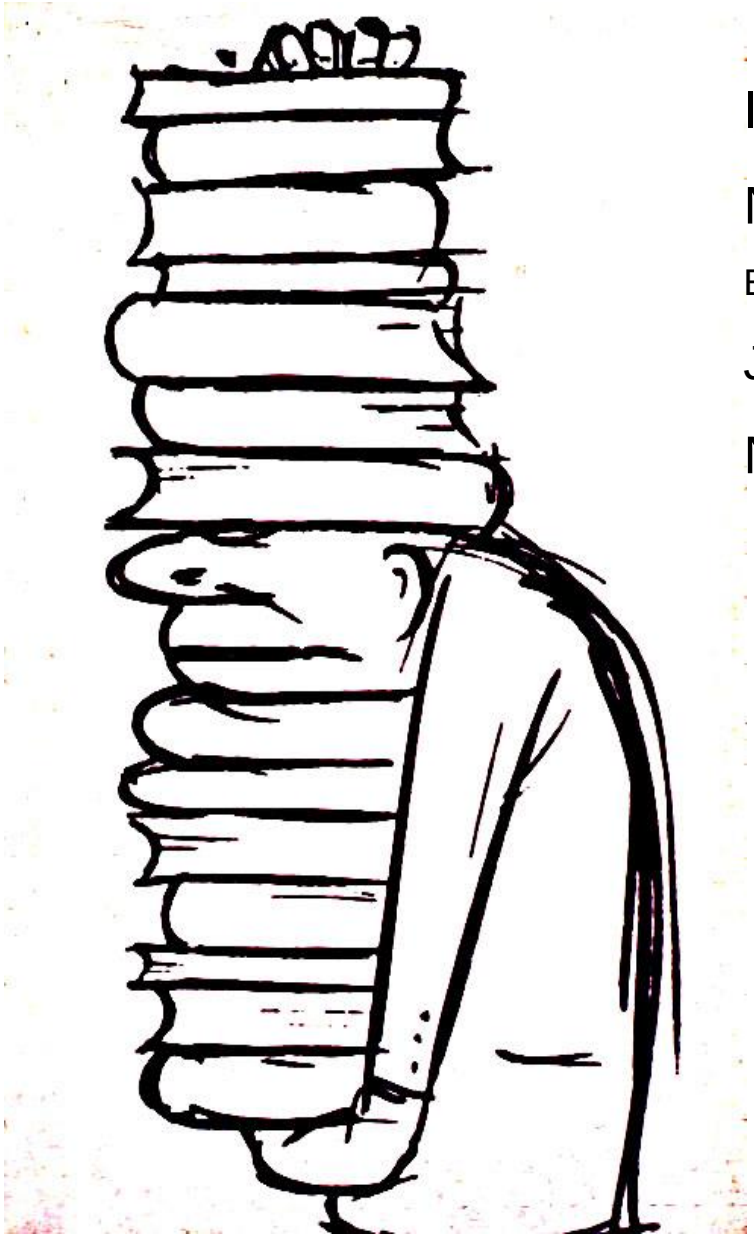
Why should we make a Nordic Center of Cell & Gene Therapy in Oslo?

Department of Cellular Therapy - for GMP production of cell products - in size one of the largest in Europe -------- a 50 mill NOK investment!!!





INSPECTED AND ACCREDITATED BY:

Norwegian Health and Social Department

EU cell directive (2004/23/EC)

JACIE(FAHCT)

National Marrow Donor Program(NMDP)

Statens Legemiddelverk

GMP production of cell products

(EU directive 2003/94EC/91/412/EC)

Paul Ehrlich Institute, Germany

GMP production of DCs for German AML patients

Cancer treatments

Classical mainstays

Surgery

Radiation

Chemotherapy

Other treatments

Hormone therapy

Small molecule targeted therapy

Immunotherapy

Bone marrow transplantation

Immune response Modifiers

Antibody therapy

Cancer vaccines
Peptides
Dendritic Cells

Adotive T-cell Therapy

Immunotherapy programs at Department of Cellular Therapy

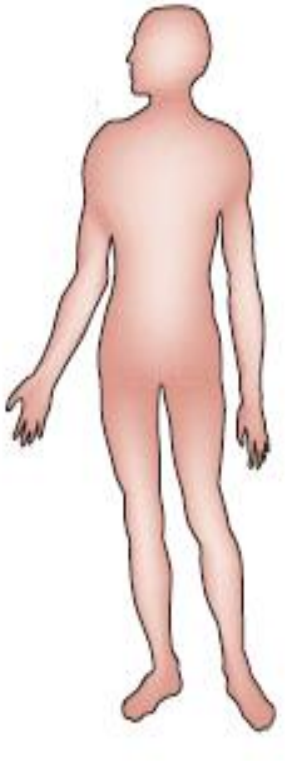
Academic protocols:

- Adjuvant DC vaccines in operable high risk prostate cancer – closed. Pi: Svein Dueland
- Randomized DC vaccines in operable Glioblastoma under development PI: Einar Vik-Mo
- DCs in NHL. PI: A. Kolstad
- NK cell therapy under development PI: Kalle Malmberg
- LMU DC AML (DCs produced in Oslo for patients treated in Munich) PI: Marion Subklwe
- TCR-CRC-001: MSI+ colon ca (REC approved) PI Svein Dueland

Comercial protocols:

- Medigene DC AML – phase I/II only Norwegian patients. Pi Yngvar Fløisand
- Alden DCs in metastatic prostate cancer (DCs produced in Oslo for patients in Bergen)
- Norvartis CAR CD 19: Relapsed and refractory peadiatric ALL and adult NHL. PI ALL Jochen Buchner, PI NHL Harald Holte

Principle of adoptive T cell immunotherapy



PBMC

isolate
immune cells

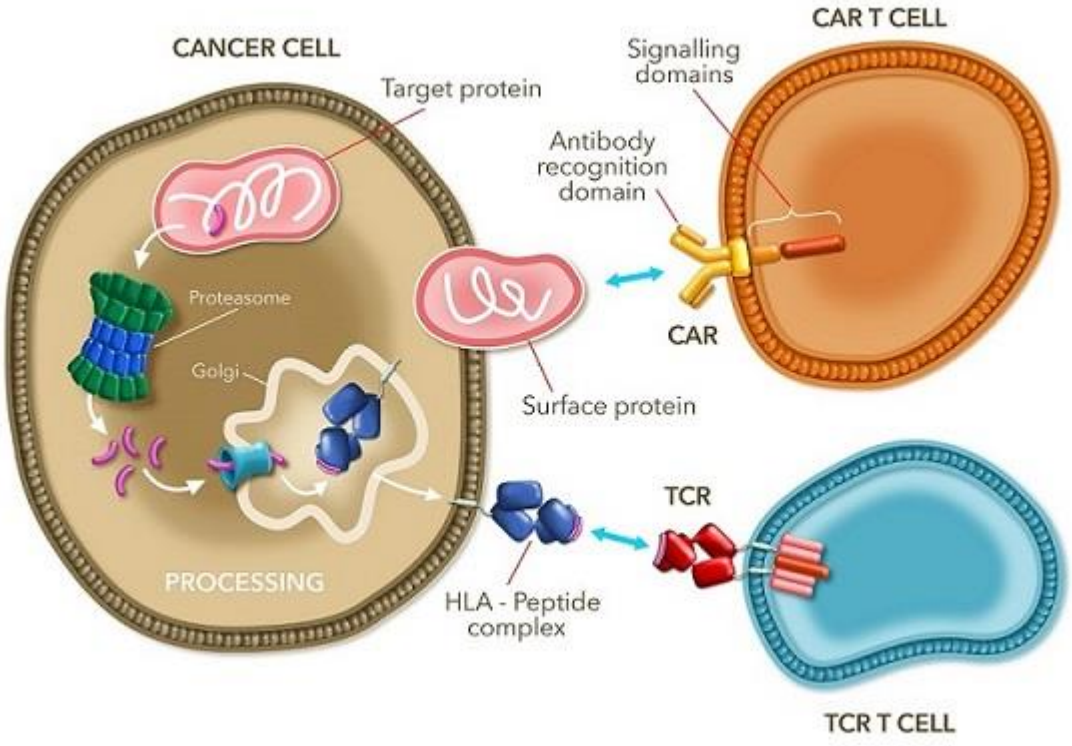
reactivate

expand

gene modify

reinfuse T cells that recognize tumor

CAR and TCR therapy



From http://www.adaptimmune.com/technology/

CAR:
- Clinical responses
- Not dependent on HLA
- Limited target antigens
- On-target toxicity

TCR:
-Clinical responses
-Many targets
- Toxicity
- HLA downregulation (tumour escape)

An Immune System Trained to Kill Cancer

rkounis for The New York Times

Dr Carl June, University of Pennsylvania

All patients eligible

No need for HLA matching

Offered to young as well as elderly patients

>90% of ALL patients treated with CD19 CARS T-cells in CR

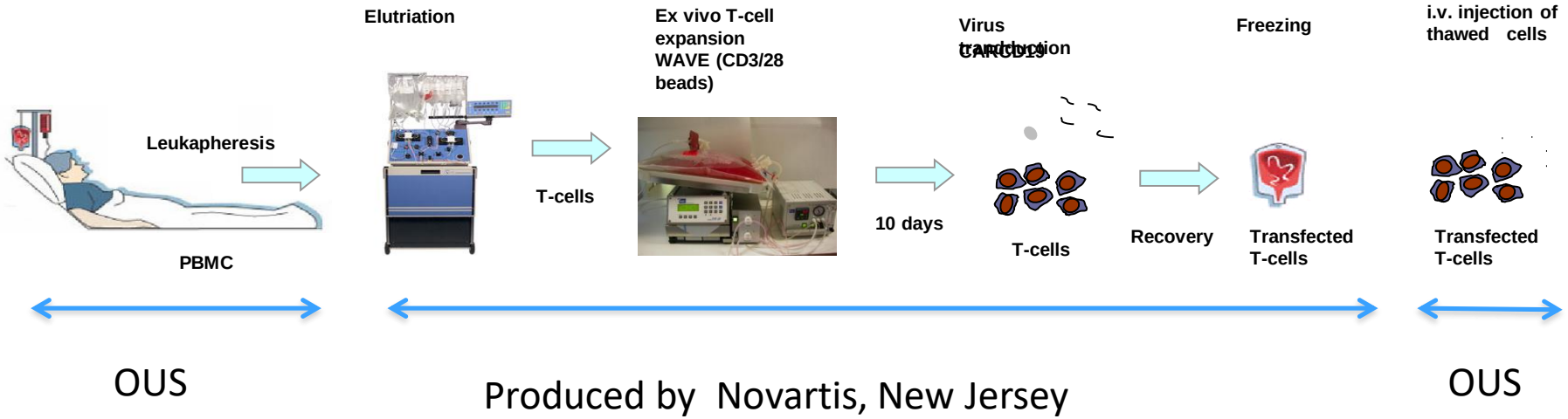
”Engineered T cell therapies likely to replace allogeneic transplantation”

Novartis study

- Evaluate efficacy and safety of CTL019 CAR-cells
- Pediatric protocol: CCTL019B2202

Pediatric ALL	
Country	Site
US	14 sites (running in 13 sites per Oct 2015)
Spain	**Barcelona**
France	**Paris**
Germany	**Frankfurt**
Italy	**Monza**
Austria	**Vienna**
Norway	**Oslo**
Belgium	**Ghent**
Canada	2 sites
Australia	1 site
Japan	2 sites

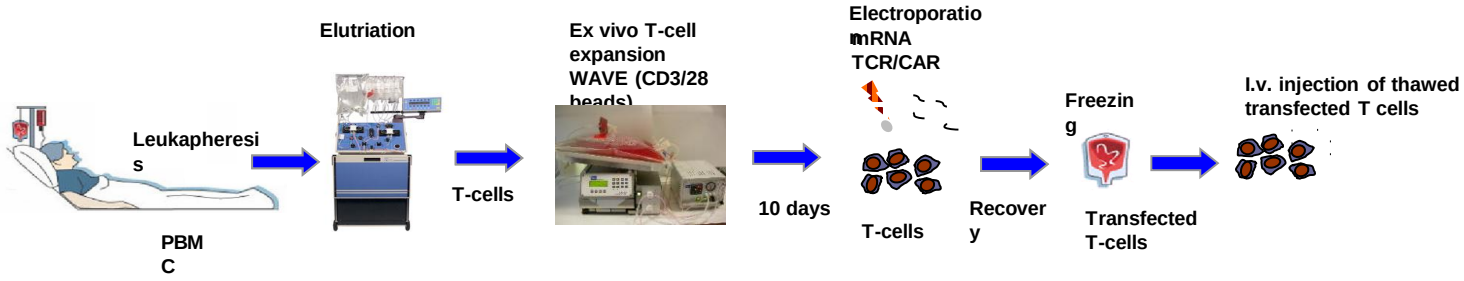
A Phase II, single arm, multicenter trial to determine the efficacy and safety of CTL019



- In pediatric patients with relapsed and refractory B-cell acute lymphoblastic leukemia (04/2015)
- In adult patients with relapsed and refractory high grade B-cell lymphoma(04/2015)
- **WHY SHOULD WE NOT OFFER PHARMA TO PRODUCE FOR NORDIC PATIENTS IN OSLO – DO WE HAVE THE KNOWHOW????**

Clinical T-cell platform for CAR/TCR adoptive T-cell therapy

WE HAVE !!!!!!!



Documentation required on cellular therapy products

Investigational Medicinal Product Dossier (IMPD)
(e.g. Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials, EMA/CHMP/BWP/534898/2008)

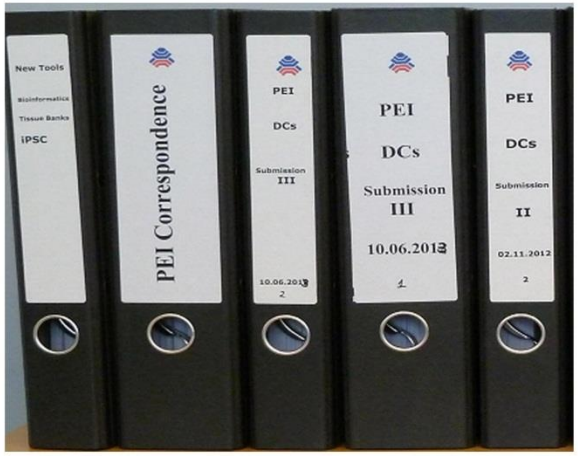
Quality Data *
Non-Clinical Data *

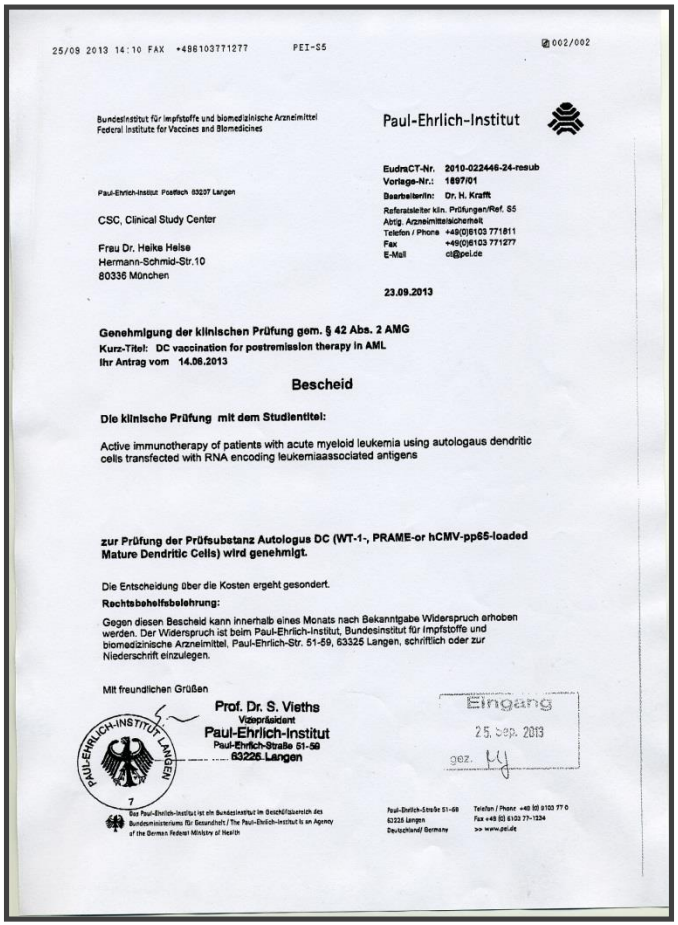
Clinical Data

Study Protocol

Investigator's Brochure

GMP documentation to the Medical Agency—how to become professional through a Nordic Center for Cell & Gene therapy?





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Federal Institute for Vaccines and Biomedicines

Paul-Ehrlich-Institut

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CSC, Clinical Study Center

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23.09.2013

Genehmigung der klinischen Prüfung gem. § 42 Abs. 2 AMG
Kurz-Titel: DC vaccination for postremission therapy in AML
Ihr Antrag vom 14.06.2013

Bescheid

Die klinische Prüfung mit dem Studientitel:

Active immunotherapy of patients with acute myeloid leukemia using autologaus dendritic cells transfected with RNA encoding leukemiaassociated antigens

zur Prüfung der Prüfsubstanz Autologus DC (WT-1-, PRAME-or hCMV-pp65-loaded Mature Dendritic Cells) wird genehmigt.

Die Entscheidung über die Kosten ergeht gesondert.

Rechtsbehelfsbelehrung:

Gegen diesen Bescheid kann innerhalb eines Monats nach Bekanntgabe Widerspruch erhoben werden. Der Widerspruch ist beim Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel, Paul-Ehrlich-Str. 51-59, 63325 Langen, schriftlich oder zur Niederschrift einzulegen.

Mit freundlichen Grüßen

Prof. Dr. S. Vieths
Vizepräsident
Paul-Ehrlich-Institut
Paul-Ehrlich-Straße 51-59
63225 Langen

PAUL-EHRLICH-INSTITUT LANGEN

Eingang
25. Sep. 2013
gez.

Das Paul-Ehrlich-Institut ist ein Bundesinstitut im Geschäftsbereich des Bundesministeriums für Gesundheit / The Paul-Ehrlich-Institut is an Agency of the German Federal Ministry of Health

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63225 Langen
Deutschland/ Germany

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Fax +49 (0) 6103 77-1234
>> www.pei.de

In-Box

22,3 kg

Out-Box

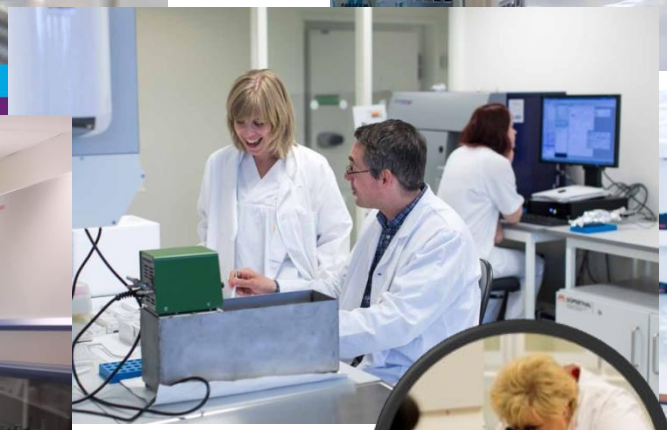
5g

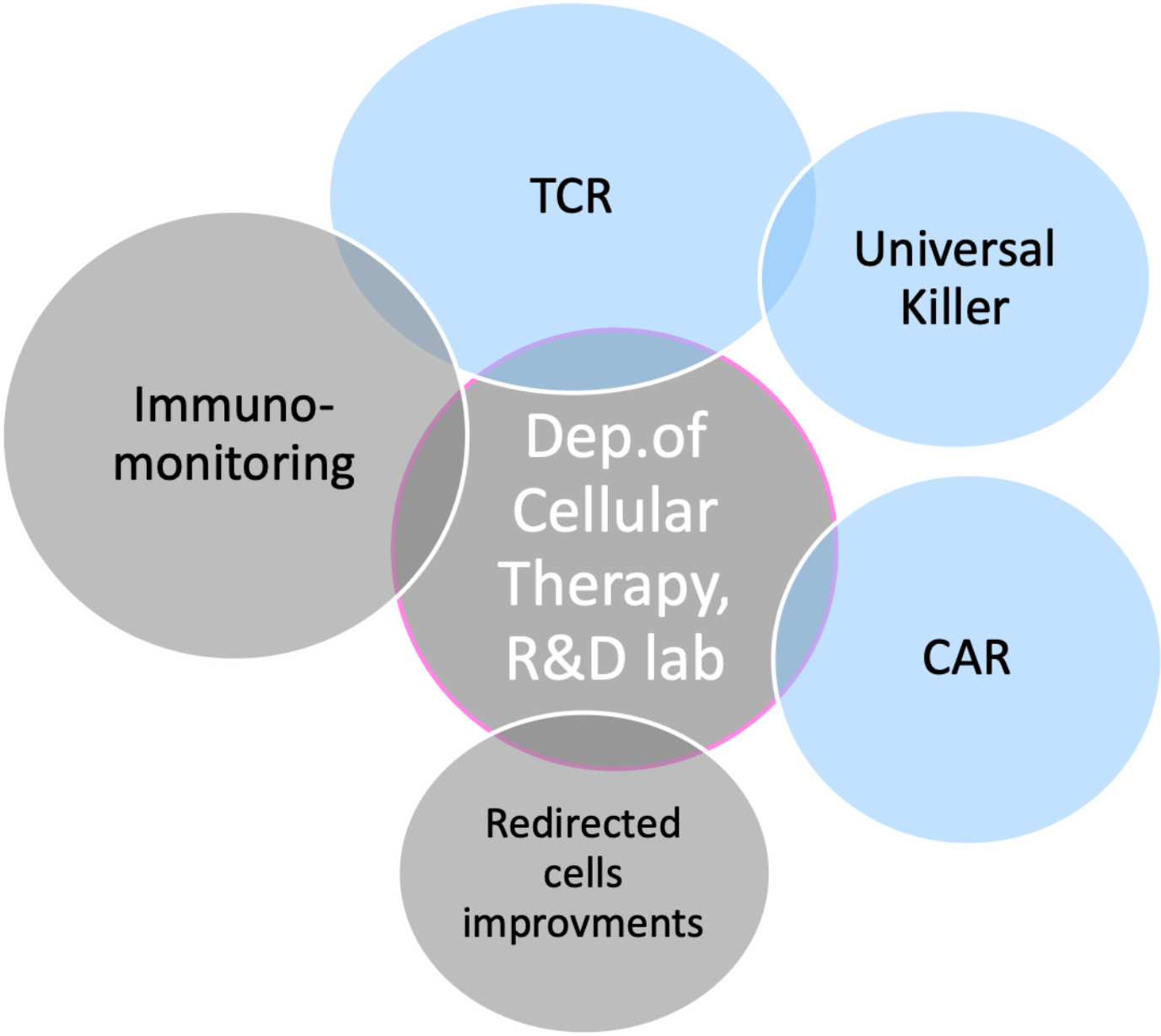
BASIC KNOWHOW AND DEVELOPMENT OF ADOPTIVE T-CELL THERAPY

OSLO CANCER CLUSTER

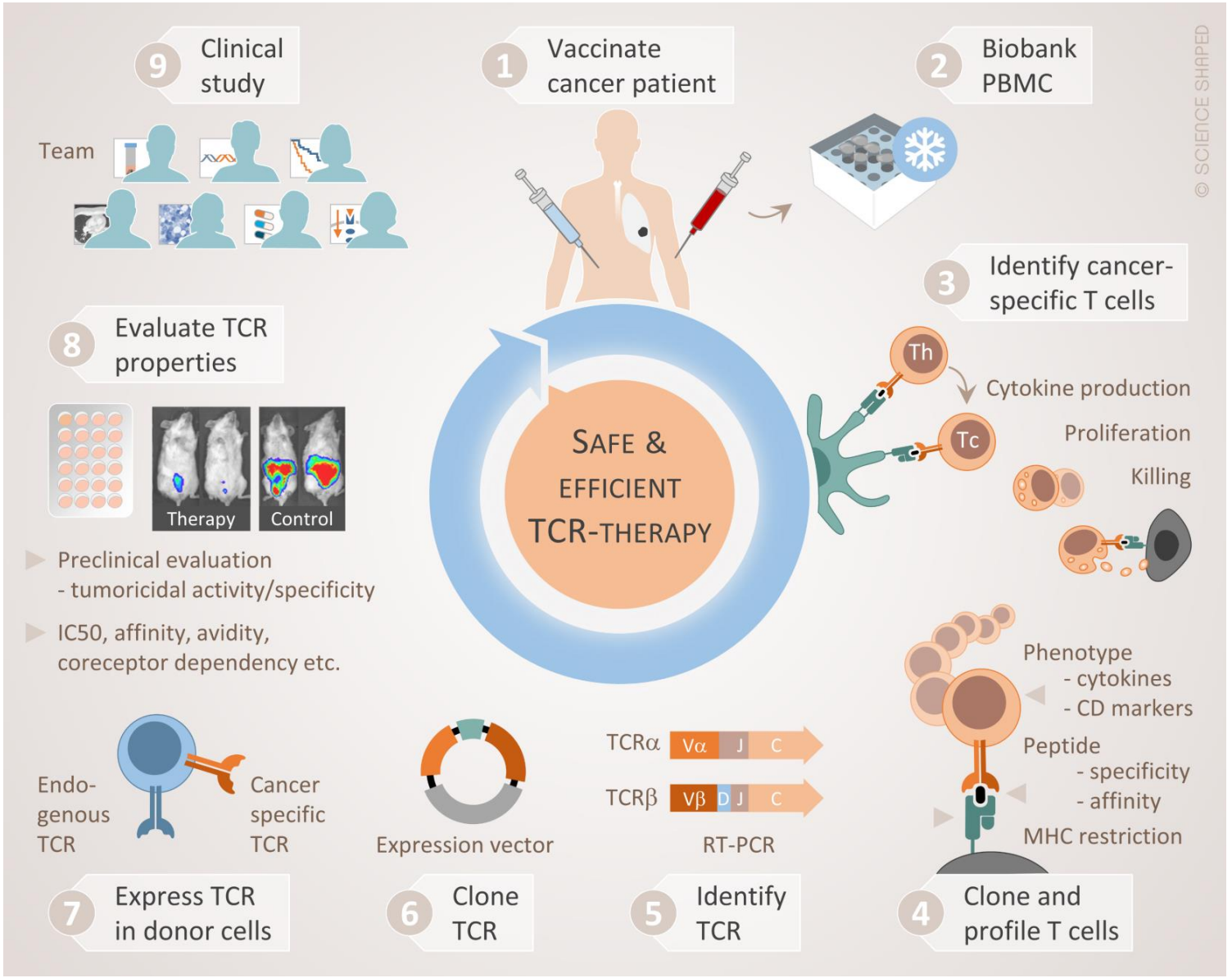
Immunomonitoring and R&D Laboratory
Department of Cellular Therapy

FROM CANCER RESEARCH TO CURE




TCR
Universal Killer
Immuno-monitoring
Dep.of Cellular Therapy, R&D lab
CAR
Redirected cells improvments

TCR platform



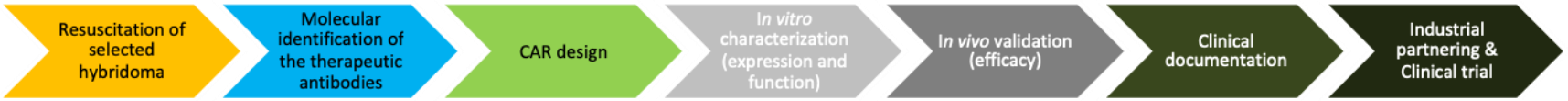
Technology base - TCRs

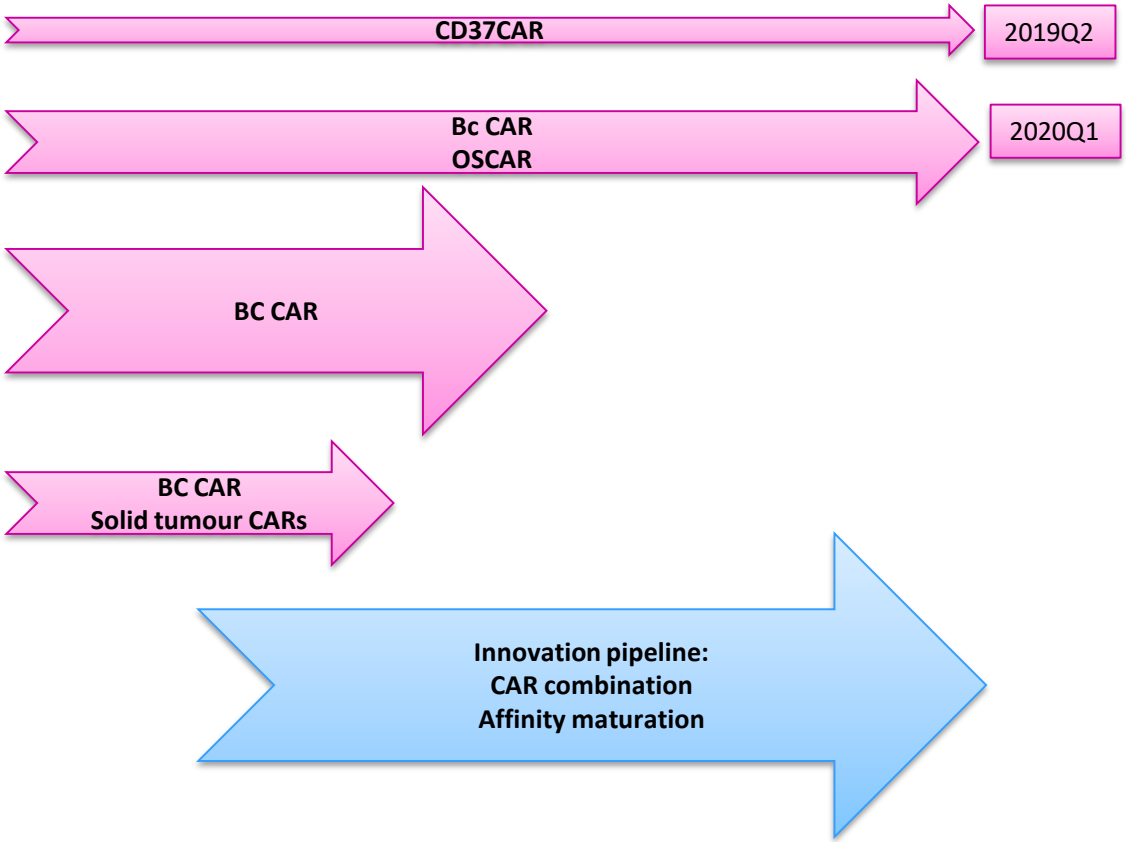
TGFβRII	hTERT	KRAS
• MSI+ cancers • Colorectal cancer (15%) • Endometrial cancer • Gastric cancer	• >90% of all cancers • Lung cancer • Melanoma • Prostate cancer	• Pancreatic cancer (98%) • Colorectal cancer (45%) • Lung cancer (31%) • Multiple Myeloma (23%)

- Potential to treat several high unmet need cancers…

LICENCED TO ZELLUNA IMMUNOTHERAPY AS

CAR pipeline



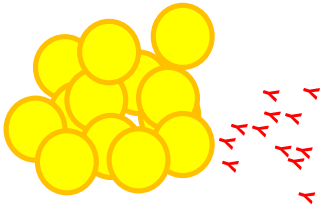


>10 CAR and > 20 hybridoma in the freezers

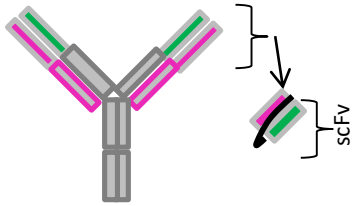
Chimeric Antigen Receptor: pre-clinical platform/necessary steps

Sequence identification

scFv design and CAR building

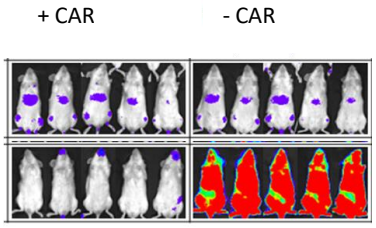


hybridoma



antibody

CAR assessment

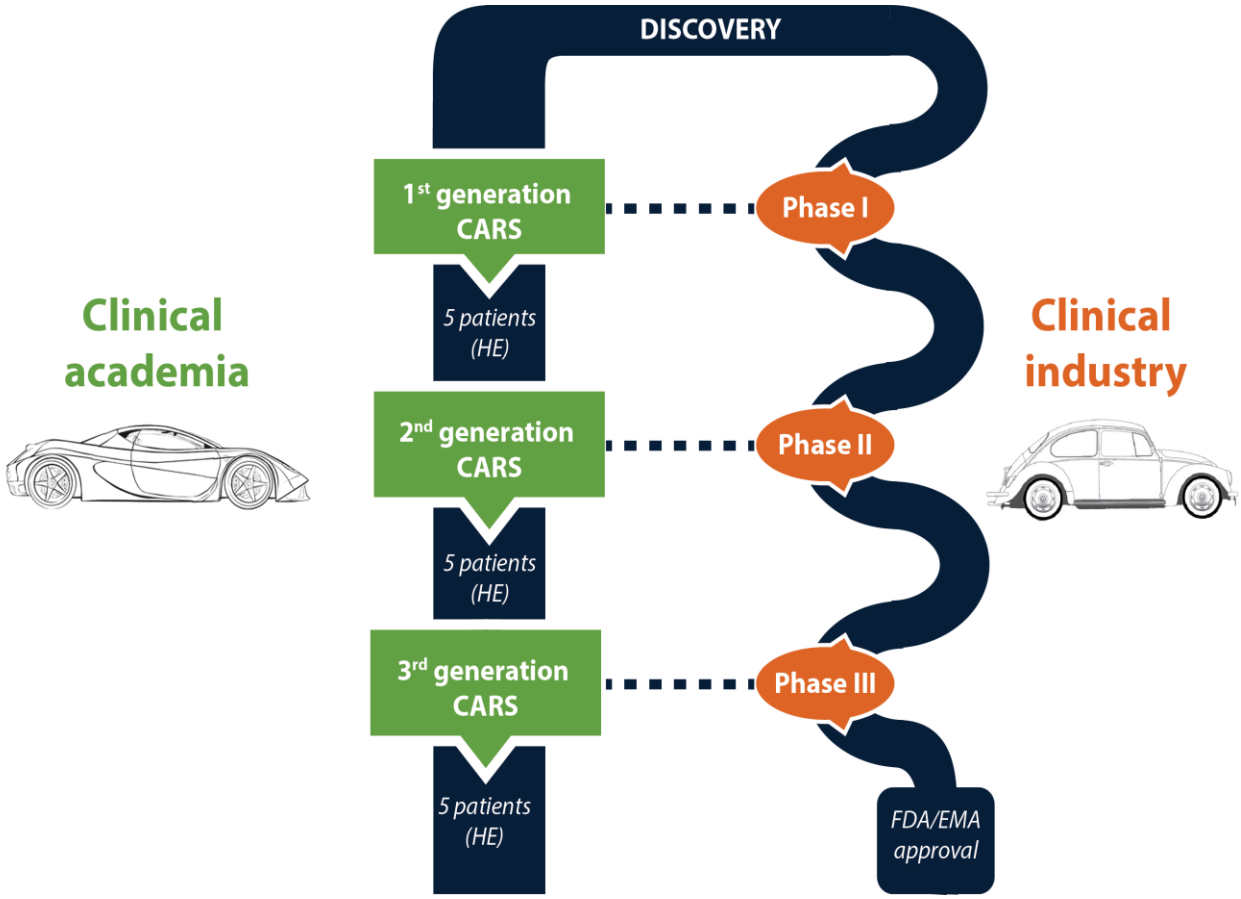


Tumor

Tc expression:

- In vitro validation
- In vivo validation
- Specificity assessment

Adoptive T-cell therapy- Industry/ Academia collaborations and how to bring it fast to patients through a Nordic Center for cell & Gene therapy?



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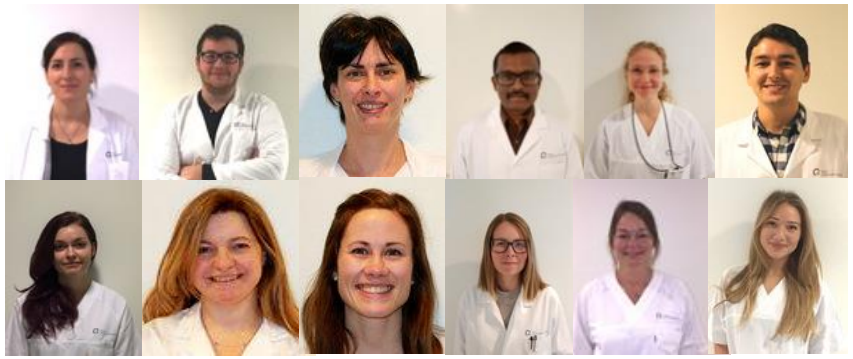
THE RADIUM HOSPITAL INNOVATION CAMPUS

Acknowledgements



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HELSE SØR-ØST

NORWEGIAN CANCER SOCIETY

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The Research Council of Norway

Radiumhospitalets Forskningsstiftelse
THE NORWEGIAN RADIUM HOSPITAL RESEARCH FOUNDATION

zelluna IMMUNOTHERAPY

Visit: celltherapy.no