

**EYE
AM NOT
ALONE**

EDUCATING, SUPPORTING & BUILDING HOPE
FOR THE OCULAR MELANOMA COMMUNITY



Eye Am Not Alone (EANA) Patient Retreat
Saturday Session - March 3, 2012

Immunotherapy of Uveal Melanoma

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Department of Dermatology
University Hospital Erlangen

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Caroline Bosch-Voskens, MD

Caroline Bosch-Voskens is an Assistant Physician in the Department of Dermatology at the University of Erlangen in Germany. Caroline graduated from Medical School at Leiden University in her home country The Netherlands. During medical school, she conducted her scientific graduation project at the Wellcome Trust Research Laboratories, Blantyre, Malawi, Africa, in 2002. This project evaluated different techniques to diagnose hookworm as part of a large research project on aetiology, pathogenesis and long-term outcome on severe anemia in Malawian children.

After graduating from medical school in 2004, she started to work as a research fellow at the University of Maryland, Baltimore, USA. Here, immuno-monitoring studies of a phase I clinical trial on peptide-based cancer vaccines were combined with basic laboratory studies on cellular immunotherapy. In 2009, Caroline returned to Europe and was awarded a training position in the department of Dermatology, University of Erlangen, Germany under supervision of Prof. G. Schuler. She is currently working as a resident and is involved in clinical studies on RNA transfected dendritic cells in melanoma patients. A large Phase III clinical trial using these dendritic cells as prophylactic treatment in uveal melanoma patients upon primary diagnosis is expected to start recruiting in the coming months.

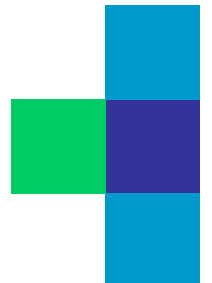
Immunotherapy of uveal melanoma

“Learning to distinguish between friends and foes”

Eye Am Not Alone Patient Retreat, 03.03.2012, Washington DC

Caroline Bosch-Voskens, MD

Department of Dermatology
University Hospital Erlangen



Diagnosis

- Treatment of the tumor in the eye
 - Radiotherapy
 - Surgery
- Wait and hope



What can I do once my cancer has spread?

Local treatment

Radiotherapy

Surgery

Systemic treatment

Chemotherapy

Kinase-Inhibitors (e.g. MEK-Inhibitors)

Immunotherapy (e.g. Ipilimumab)



Immunotherapy - principle

Teaching our own immune system to recognize and destroy existing tumor formations

Teaching our own immune system to recognize and destroy solitary tumor cells in order to maintain a tumor-free situation

Potential long-lasting therapy effect



Main characters of our immune system

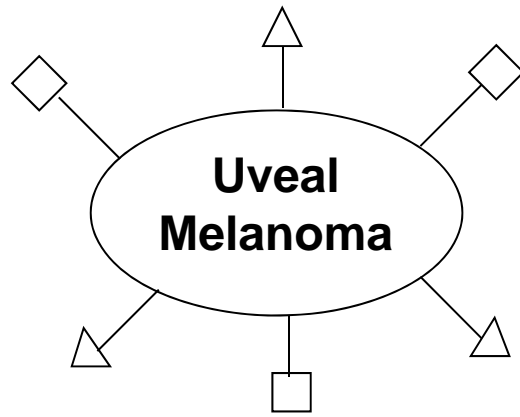
Killer cells – release toxic particles, which „kill“ unwanted cells (eg. bacteria, tumor cells)

Dendritic cells – provide killer cells with the necessary signals, which induce killer cell division and multiplication

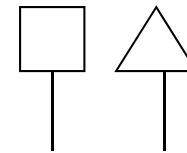
B cells – produce so called „antibodies“, which directly destroy unwanted cells or indirectly activate killer cells



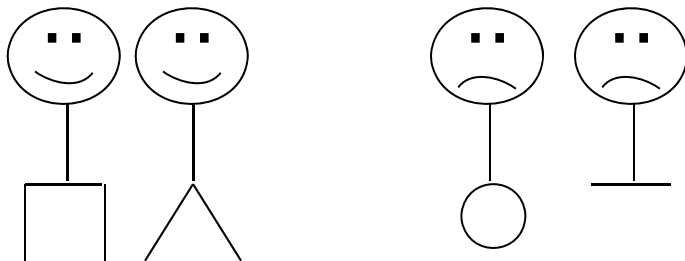
Immunotherapy of uveal melanoma



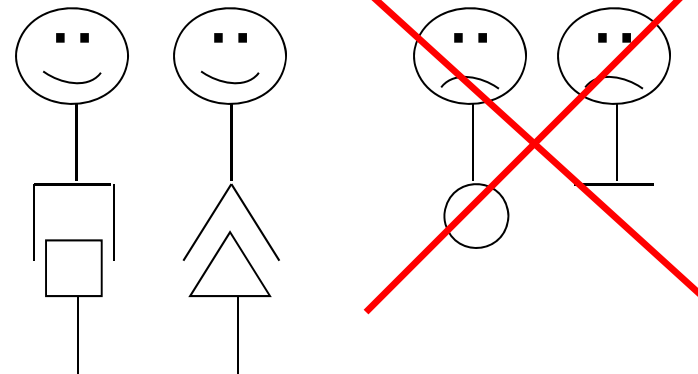
Uveal melanoma-specific „Targets“



KILLERCELLS



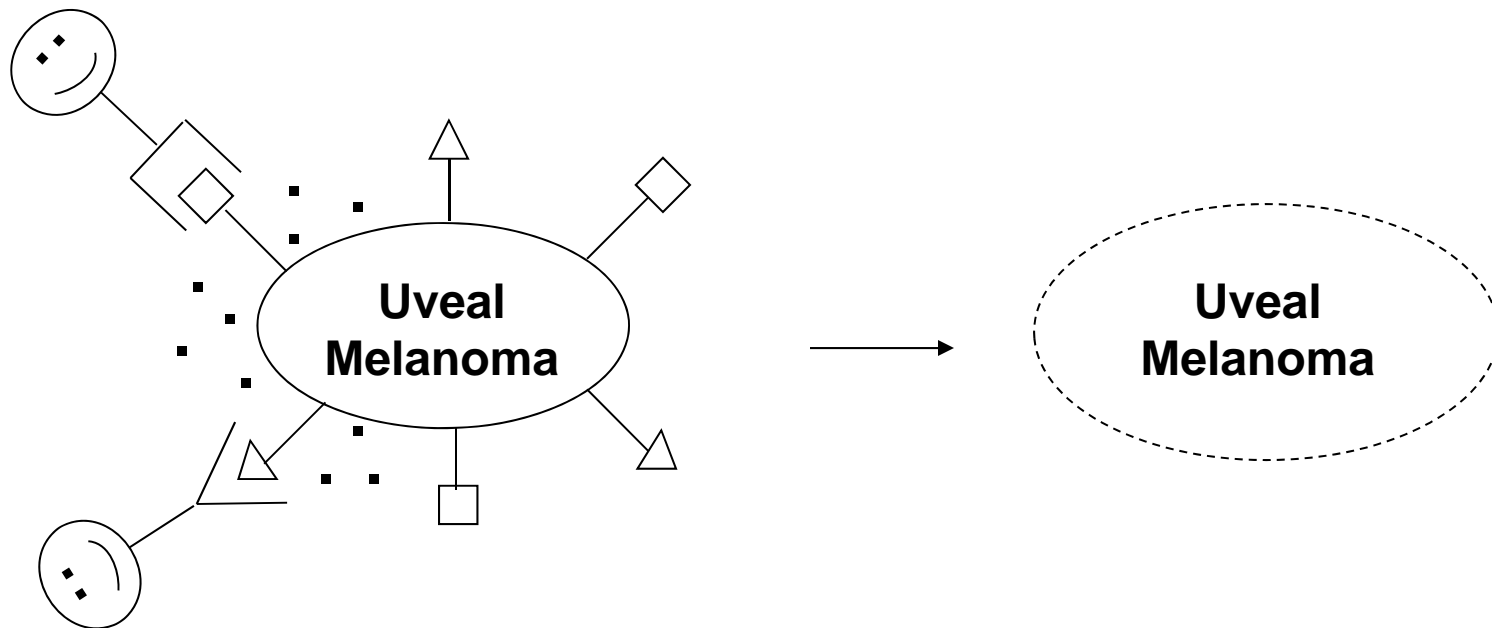
KILLERCELLS are always specific



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Immunotherapy of uveal melanoma



Natural immunity

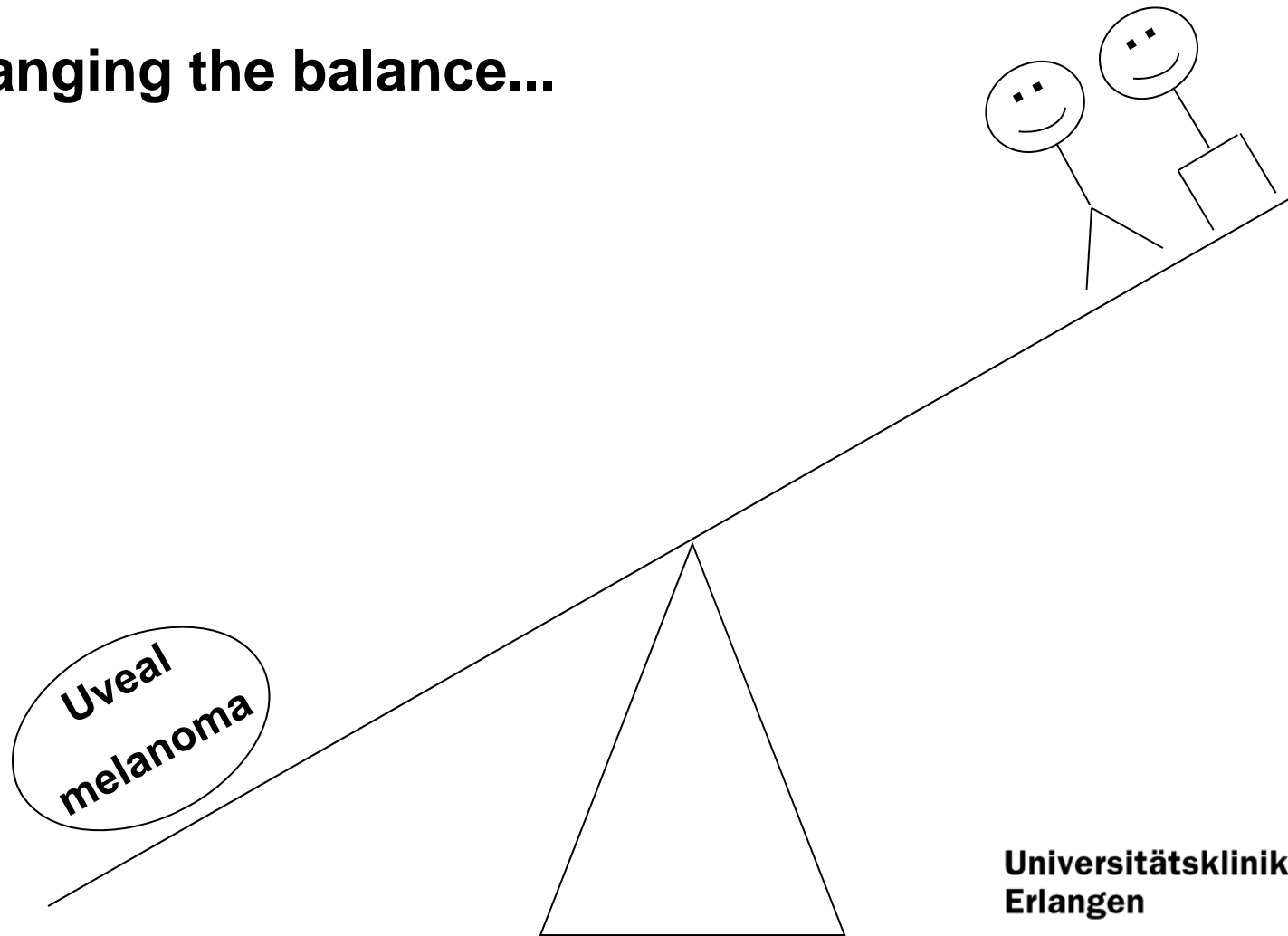
Every cancer patient already has some killer cells which actively recognize and kill unwanted cancer cells

...nevertheless...they are hard to find...
(1:1 million)



Immunotherapy - principle

Changing the balance...



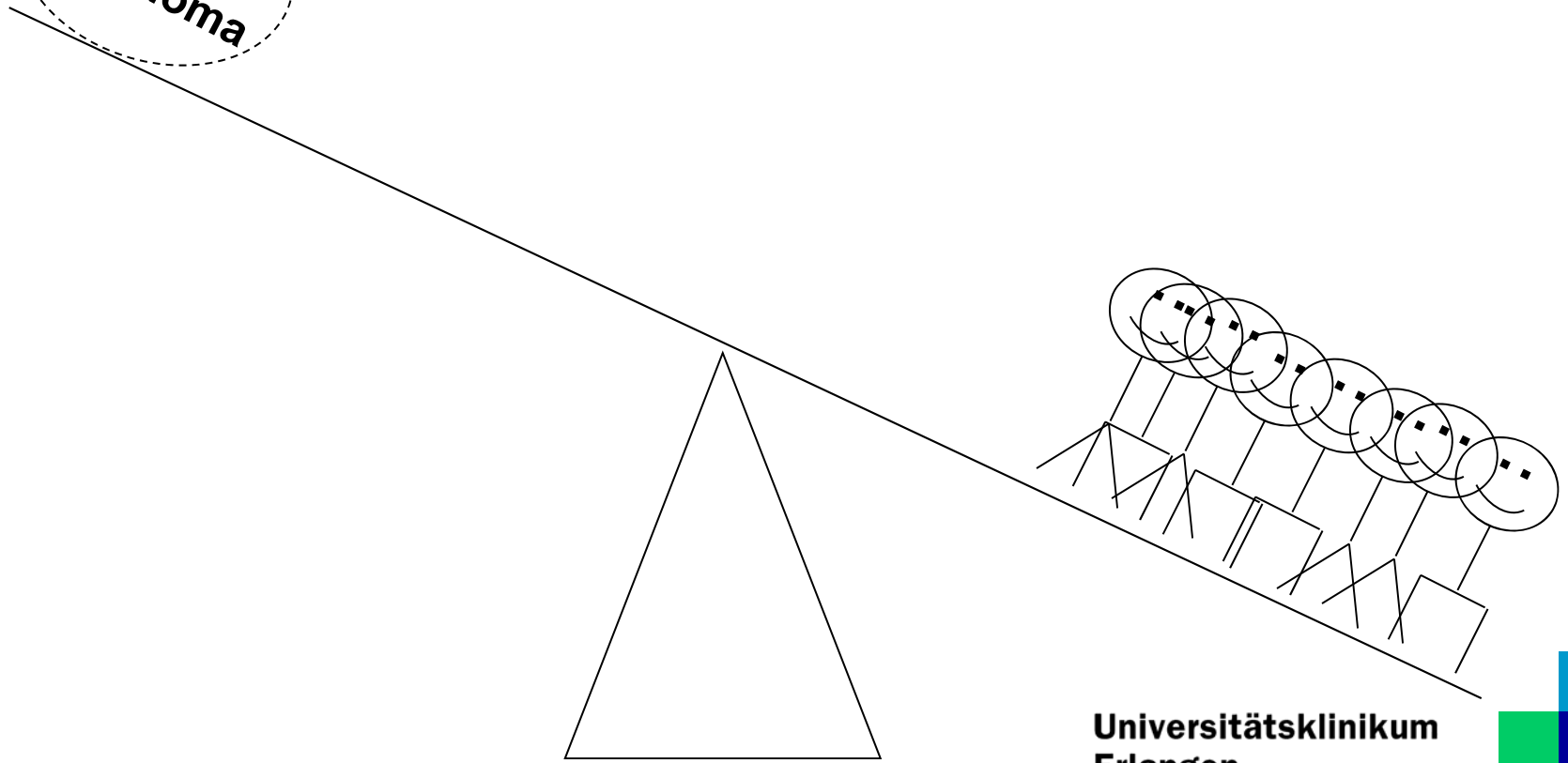
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Immunotherapy - principle

...into our favour!

Uveal
melanoma



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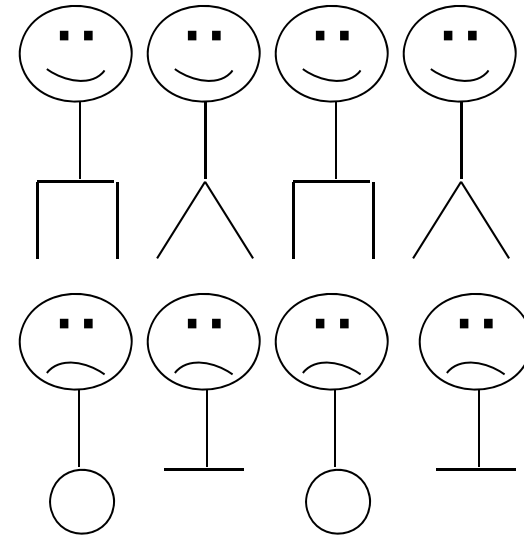
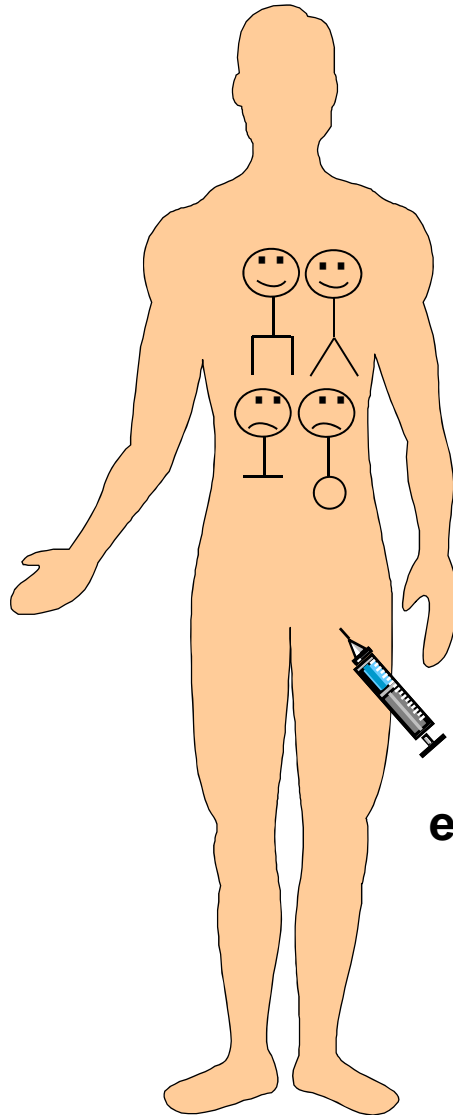


Generation of killer cells

- Expansion of killer cells inside the body by cytokine-treatment
- Specific expansion of killer cells outside the body
- Specific expansion of killer cells inside the body through the use of your own helper cells (e.g. dendritic cells)



Therapy with cytokines

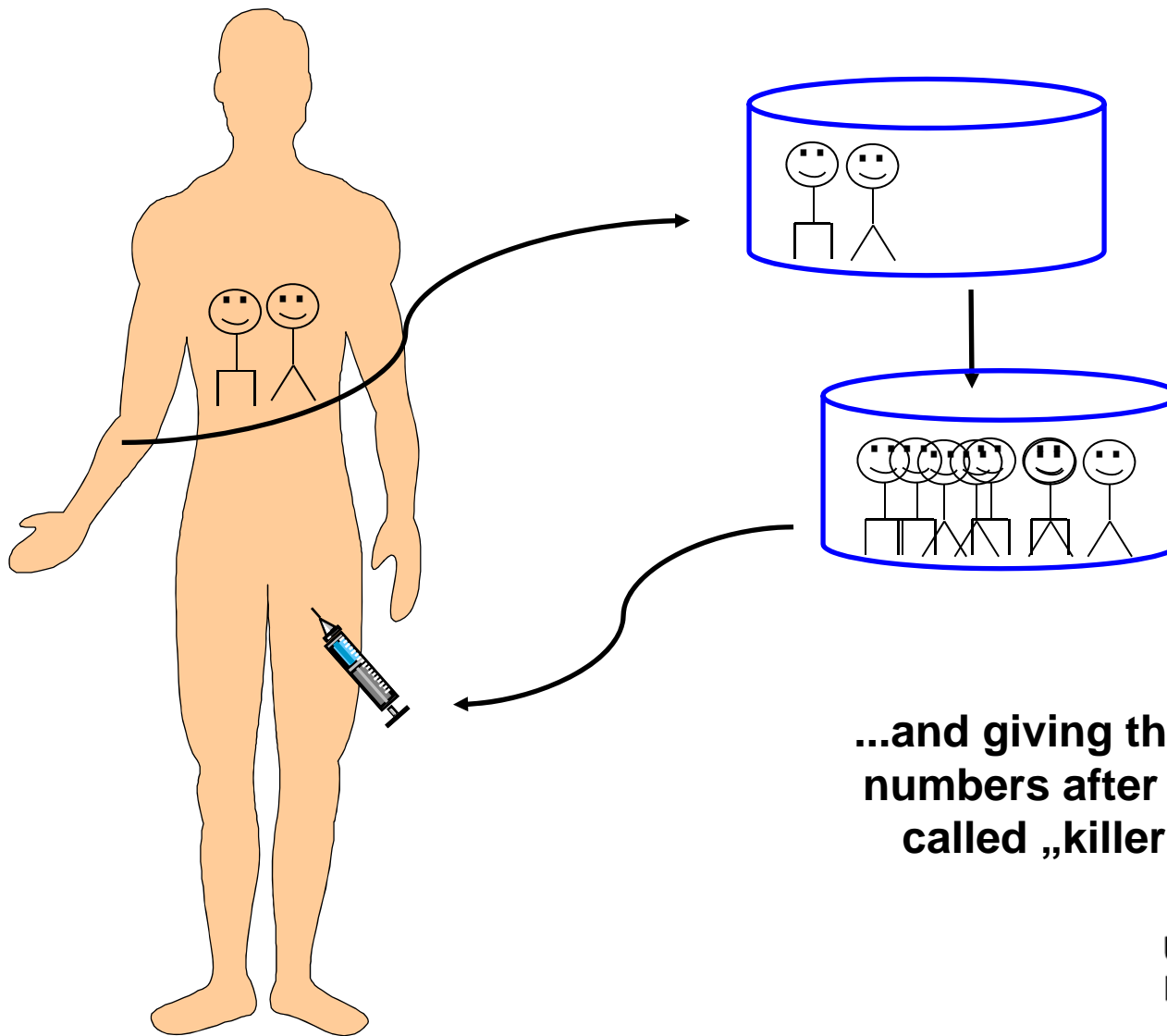


Cytokines
e.g. Interleukin-2;
Interferon

**Treatment with cytokines induces
non-specific expansion of killercells**



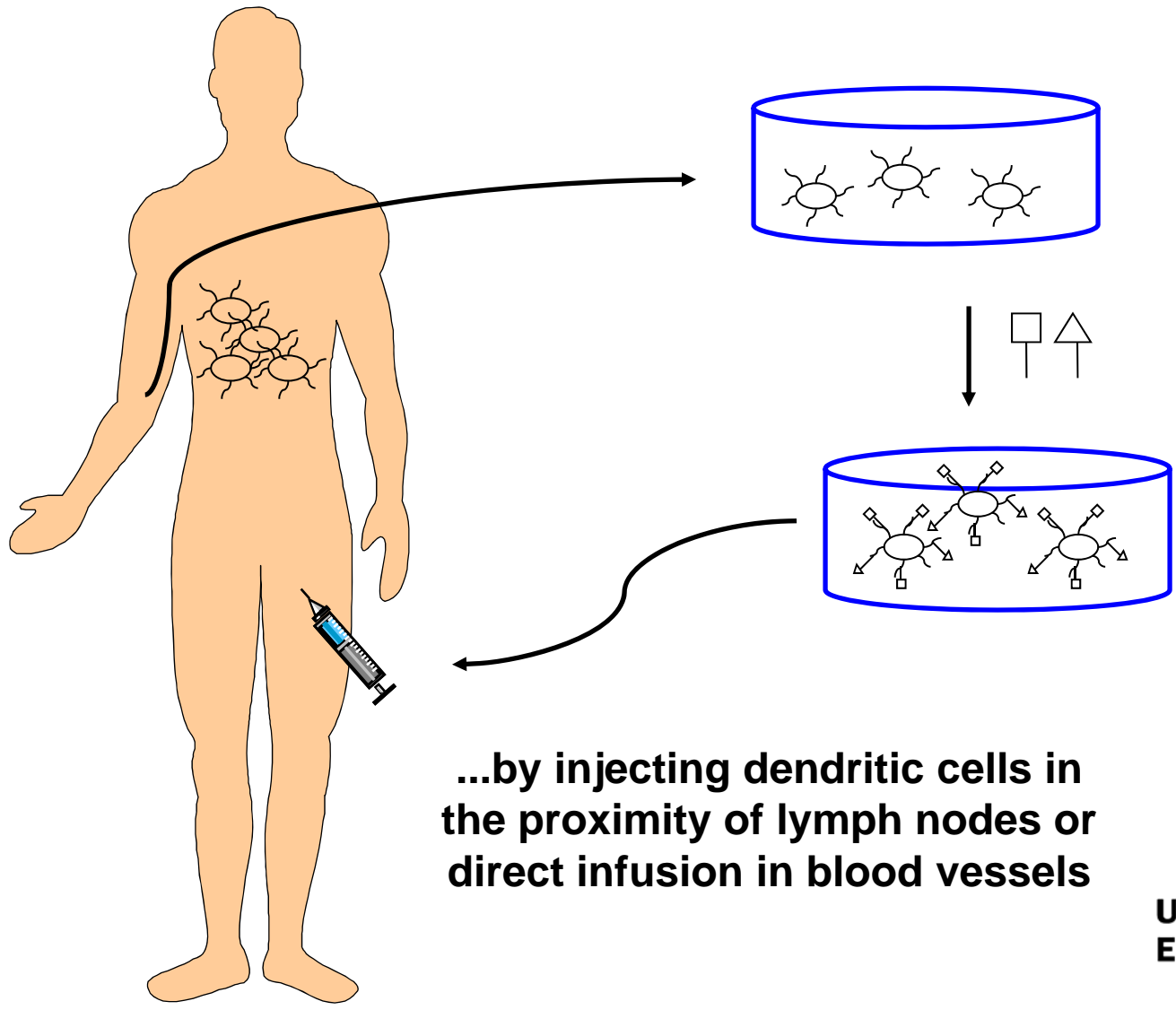
Expansion of specific killer cells outside the body



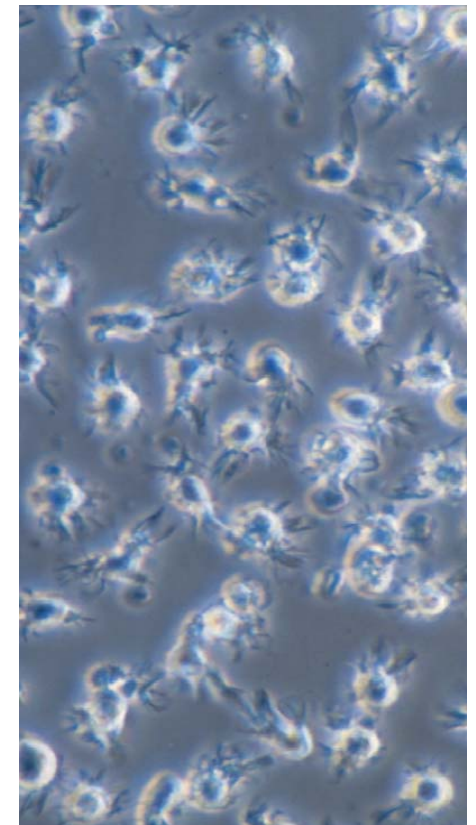
...and giving them back in large numbers after expansion (also called „killer cell transfer“)



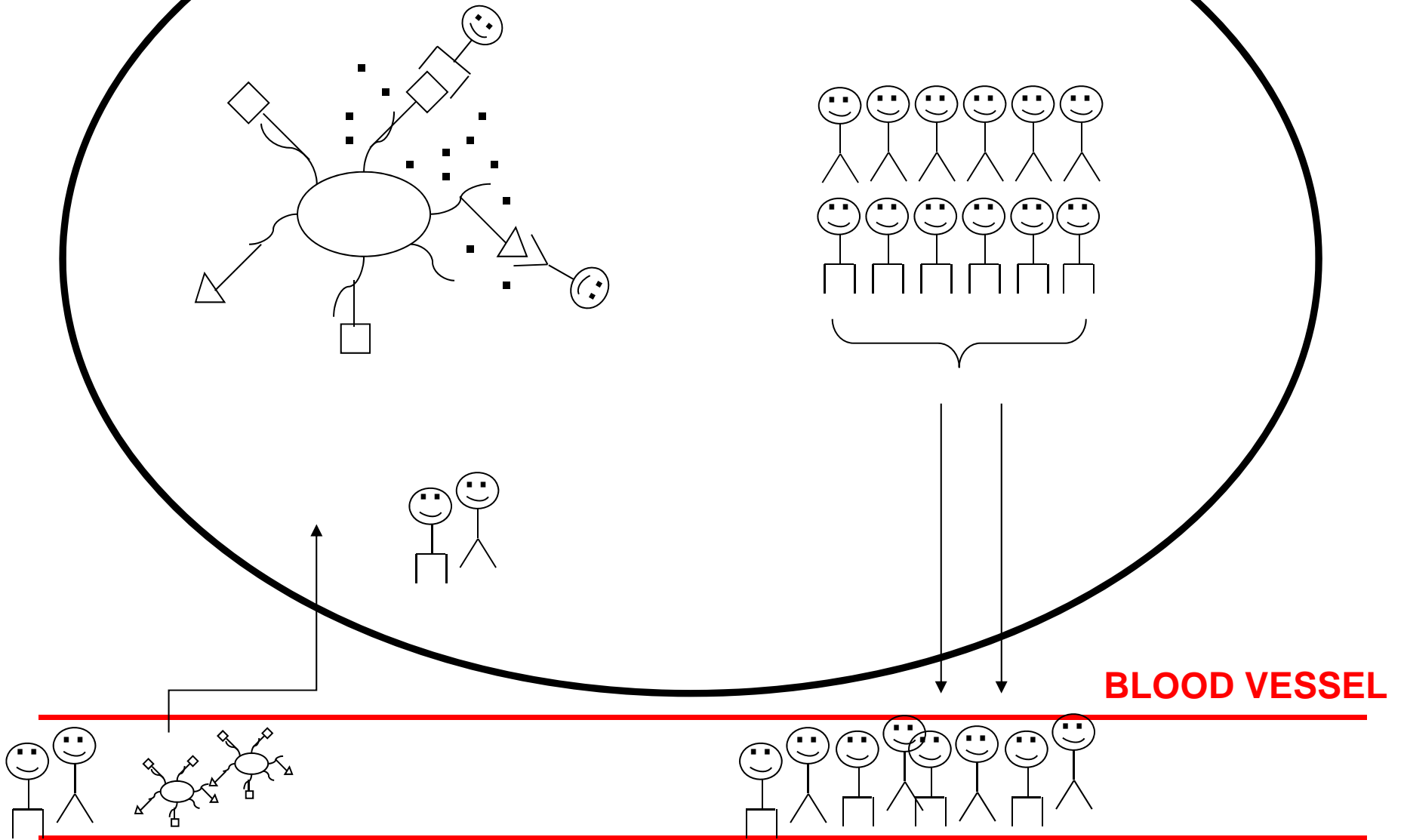
Expansion of specific killer cells through the use of dendritic cells



...by injecting dendritic cells in the proximity of lymph nodes or direct infusion in blood vessels



LYMPH NODE



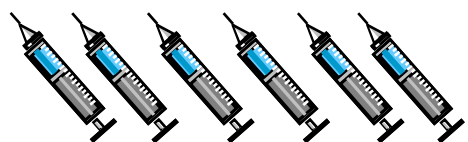
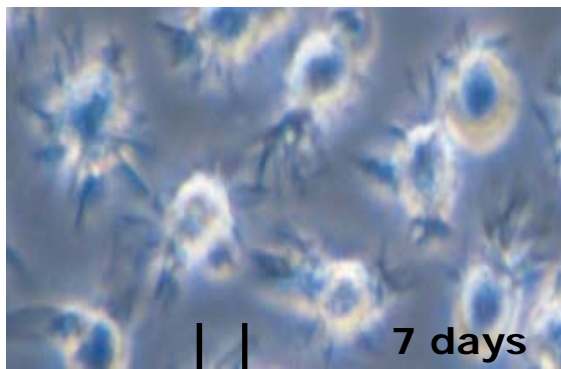
Phase III Clinical Trial in monosomy 3⁺ uveal melanoma patients

Goal: To prolong disease-free survival in monosomy 3⁺ uveal melanoma patients by adjuvant treatment with autologous tumor-loaded dendritic cells

- Treatment starts right after first diagnosis
- Dendritic cells are loaded with your own specific uveal melanoma targets
- Study is IRB approved; funding is pending



Phase III Clinical Trial in monosomy 3+ uveal melanoma patients



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Antibodies

Directly destroy unwanted cancer cells or indirectly activate killer cells by releasing the brakes of our immune system

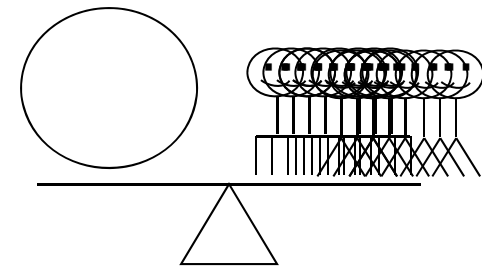
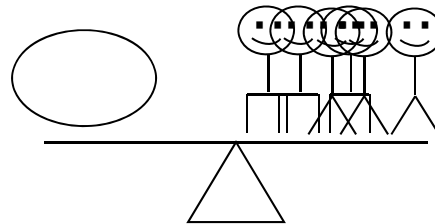
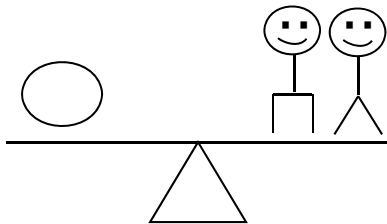
Ipilimumab (Yervoy®):

First FDA approved antibody for the treatment of metastatic melanoma; releases the brakes of our immune system



When do I start Immunotherapy?

- The immune system needs time to get started
- Tumor growth may continue during the first weeks of treatment
- Minimal disease or a tumor-free situation are in general the ideal starting point
- **Potential long-lasting therapy effect**



What can I expect from Immunotherapy?

- Potential clearance of single tumor cells and/or destruction of small tumor formations
- In single cases destruction of large tumor formations
- Combined strategy of surgery/radiation and immunotherapy

- Prolonged tumor-free and/or overall survival



Currently approved Immunotherapies

Cytokines – for the treatment of skin melanoma
(Interleukin-2; Interferon-alpha)

Dendritic cells – for the treatment of prostate cancer
(Provenge®)

Antibodies – for the treatment of metastatic
melanoma including uveal melanoma (Yervoy®)



Common side-effects

- Fever
- Shivering
- Joint pains
- Skin reactions
- Itchiness
- Headache
- Tiredness
- Vitiligo
- Uveitis



Ipilimumab

- Associated with severe autoimmune reactions (60% of treated patients)
- Rapid and unexpected onset
- Side-effects are in general reversible by early recognition and prompt medical treatment
- Demands a high degree of awareness among patients and physicians



Clinical trials

- Studies recruiting uveal melanoma patients are increasing
- Studies specifically designed for uveal melanoma patients are increasing

www.clinicaltrials.gov



Acknowledgements

Department of Dermatology
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Prof. G. Schuler

Dr. B. Schuler-Thurner

Prof. E. Kämpgen

Dr. M. Erdmann

Ms. S. Rosenheinrich

Ms. D. Schuster



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