

Targeted Immunotherapy in Childhood Leukemia

COST Action Cancer Nanomedicine
– From the Bench to the Bedside

16.06.2022

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www.med.uni-magdeburg.de



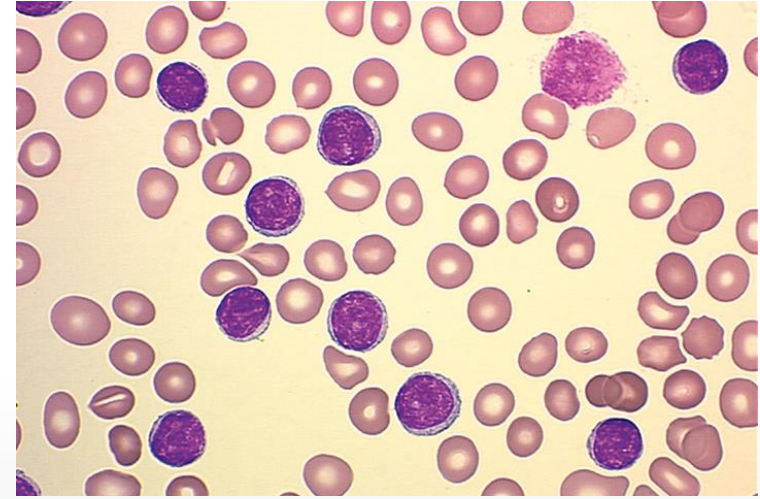
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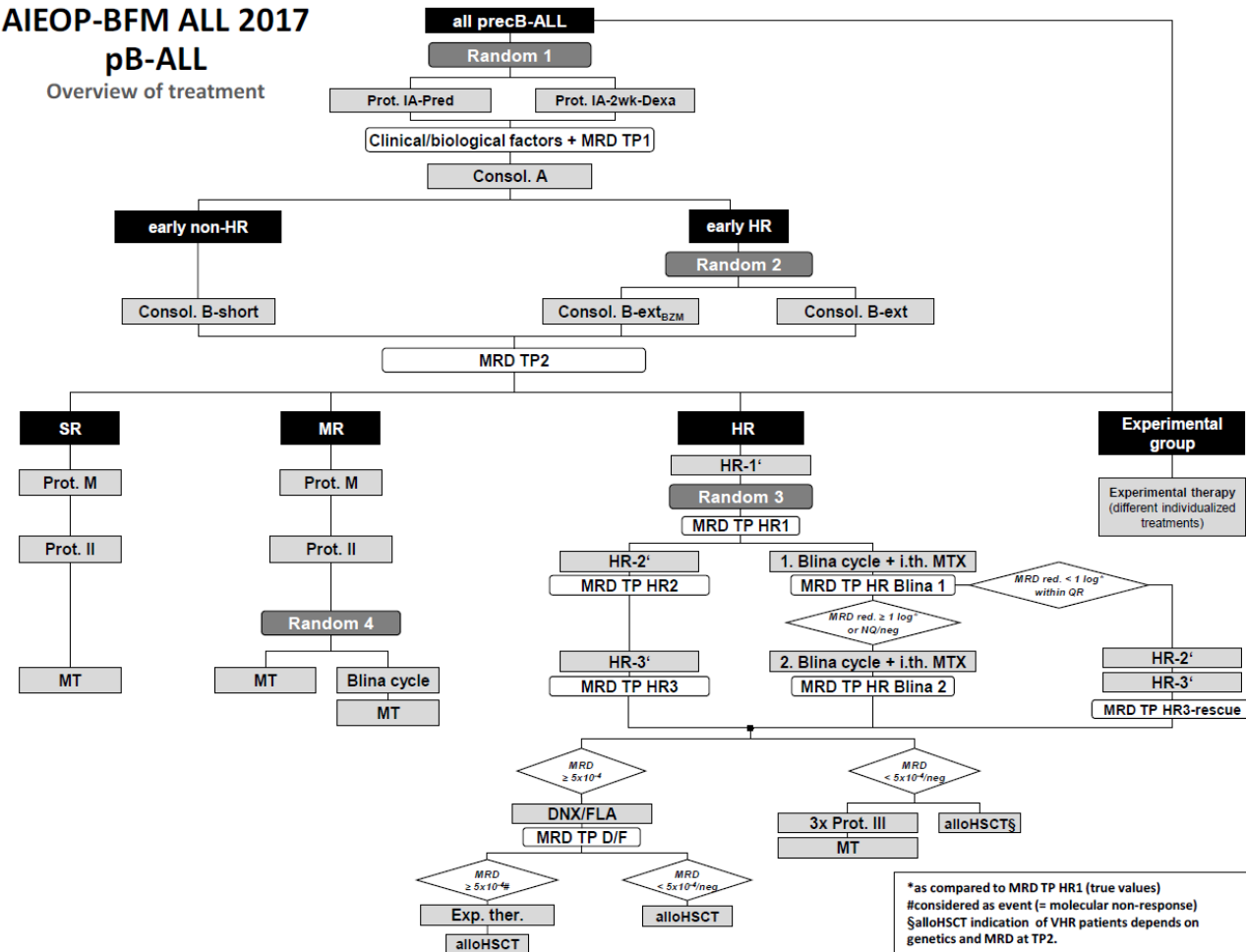
Childhood Leukemia

- Most common malignancies in childhood
- Acute lymphoblastic leukemia (ALL) > acute myeloid leukemia (AML)
- ALL has a favorable prognosis
- ALL relapse has a less favorable prognosis
- ALL is a model entity for cancer immunotherapy

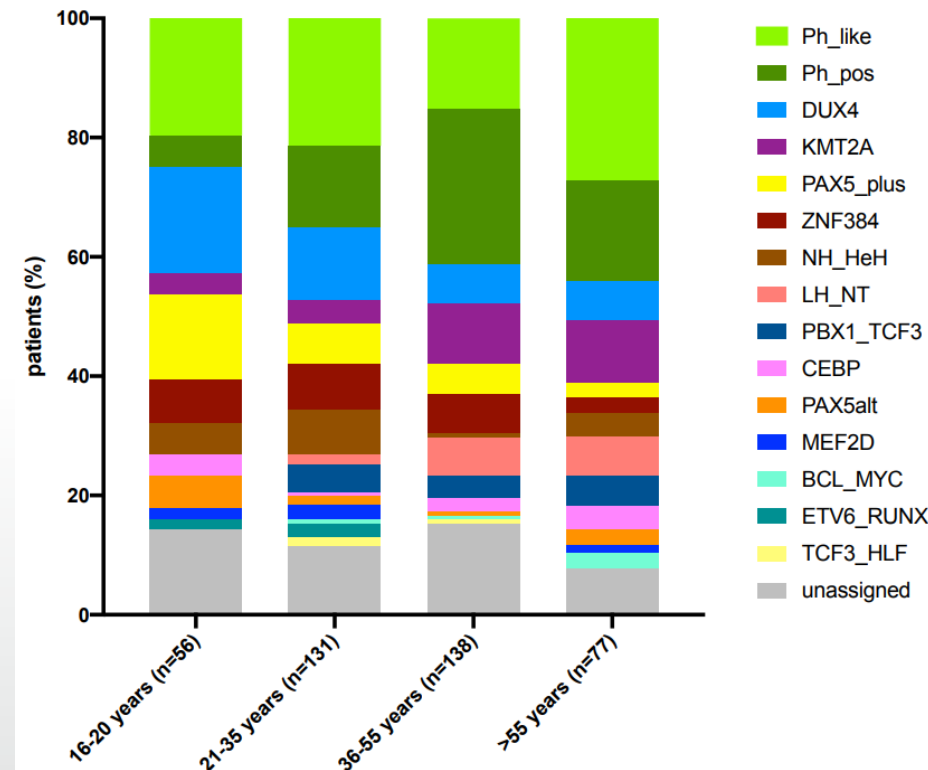


AIEOP-BFM ALL 2017

AIEOP-BFM ALL 2017 pB-ALL Overview of treatment

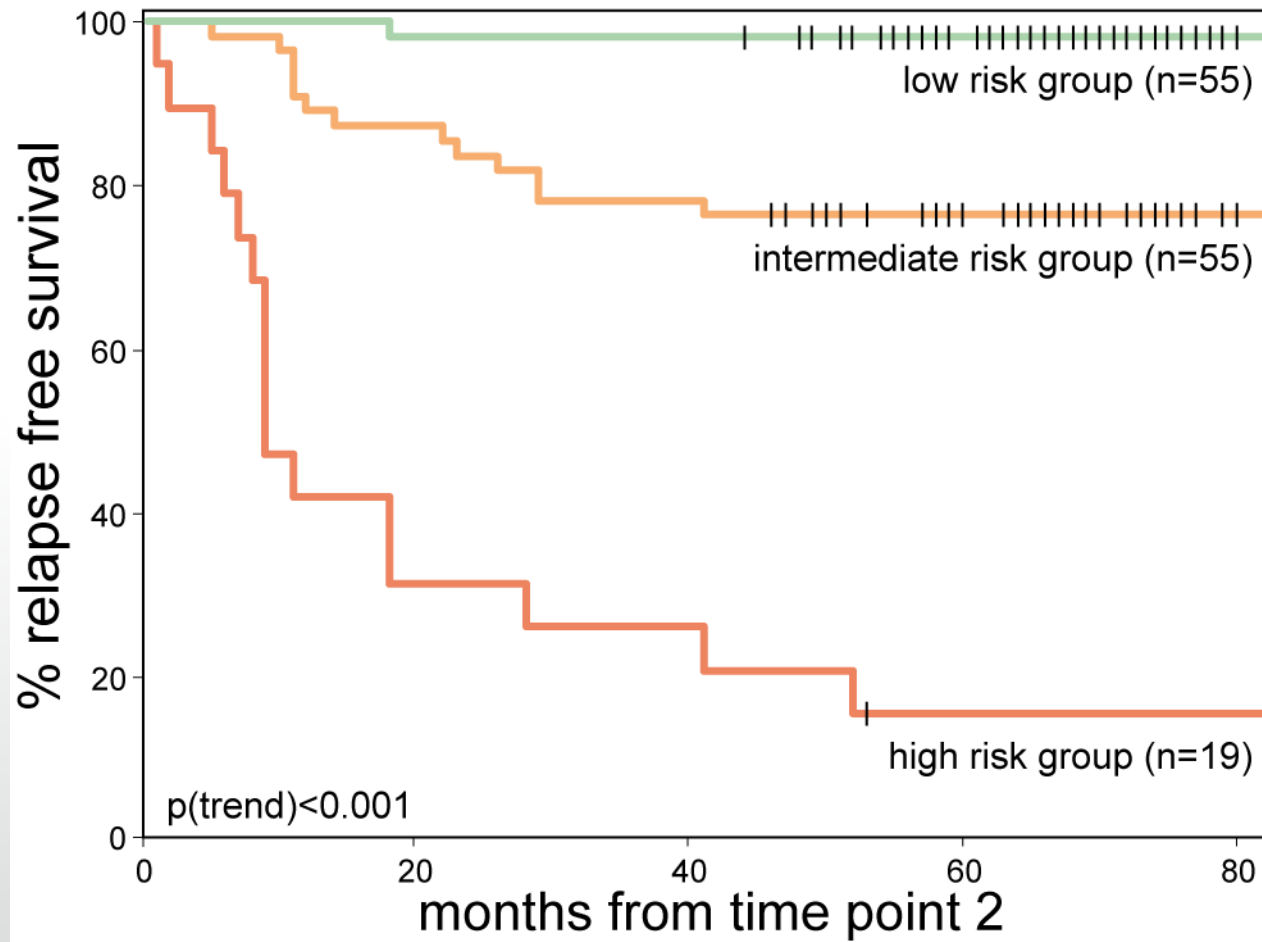


ALL - genetics



Molecular diversity and age distribution in BCP-ALL
(Bastian, Leukemia 2019, ASH 2020)

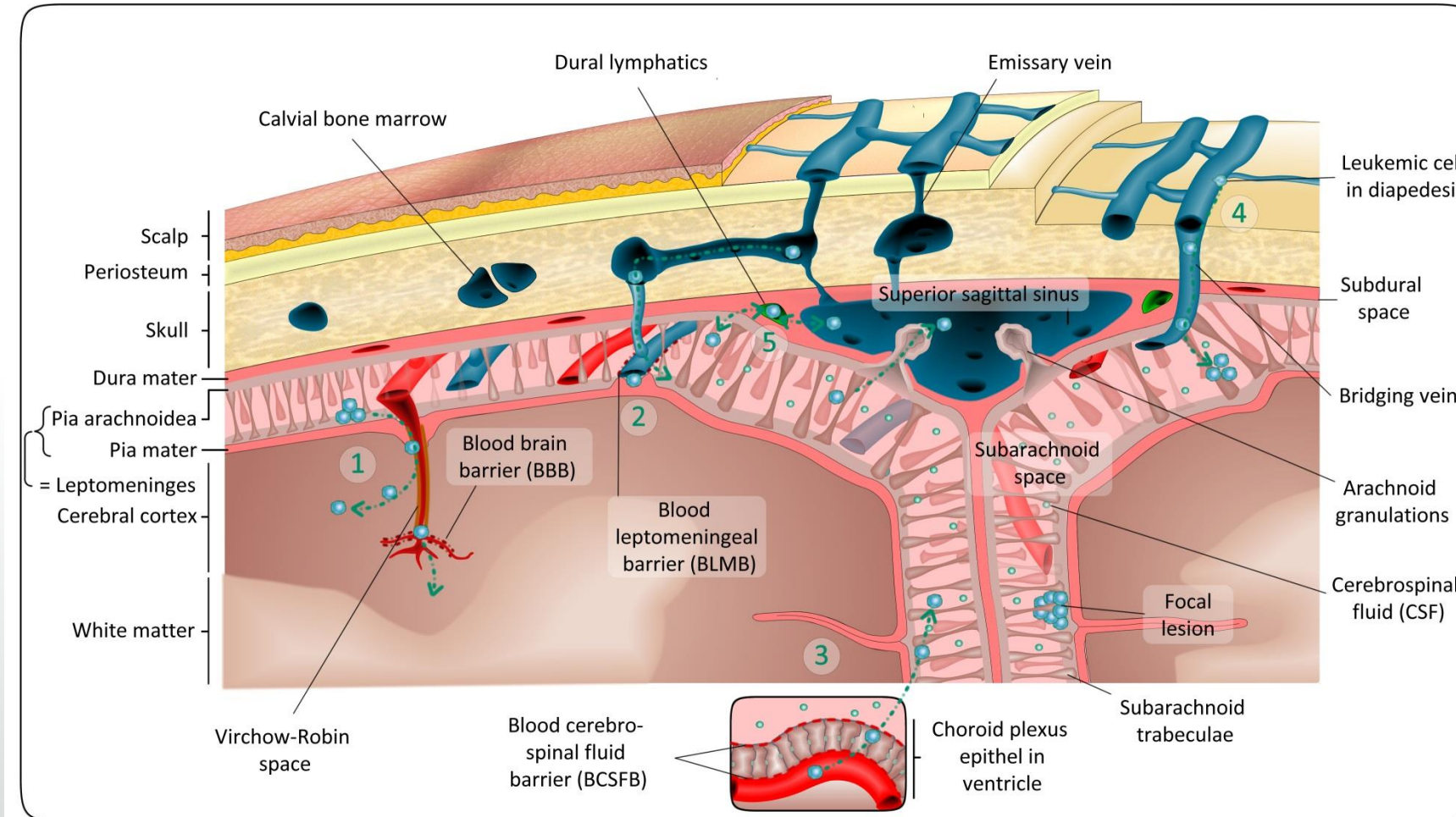
ALL – prognosis according to MRD



Van Dongen et al., Blood, 2015

What makes an immunotherapy successful ?

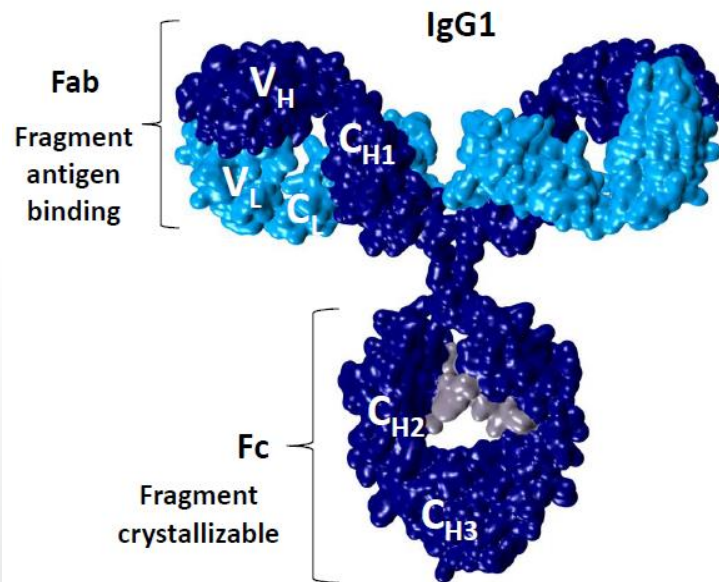
Compartments of leukemic disease – the CNS



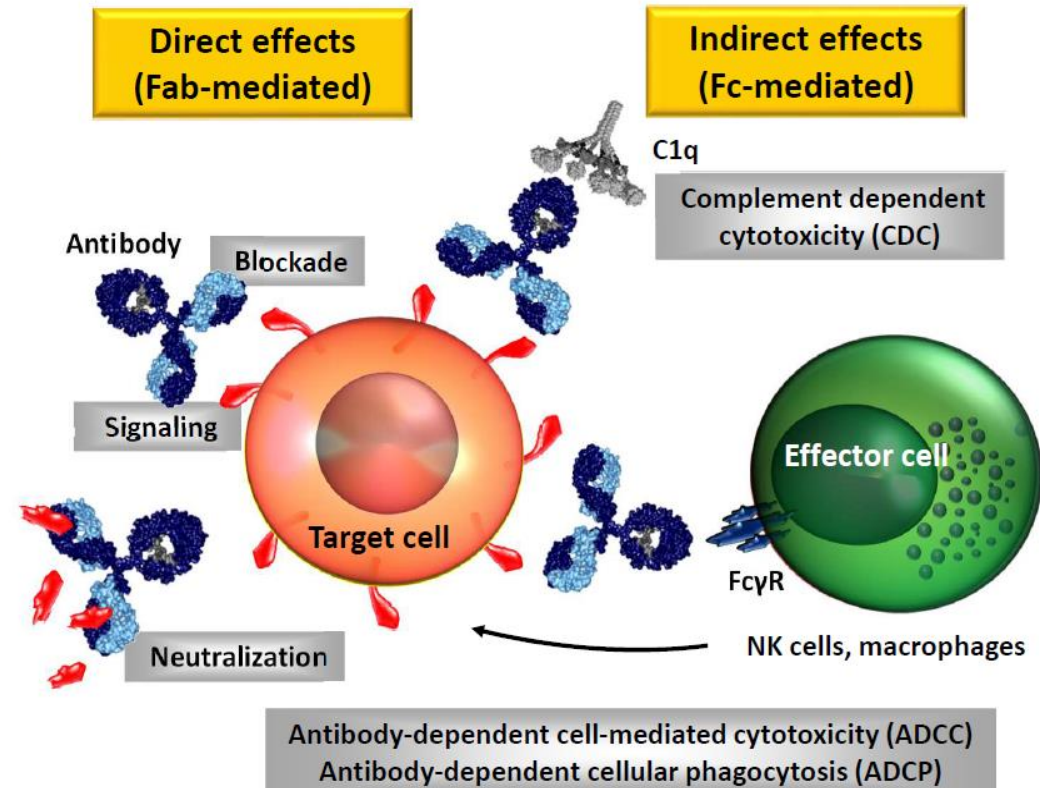
Lenk et al., Cancer and Metastasis Reviews, 2020

Types of immunotherapies

Specific antibodies



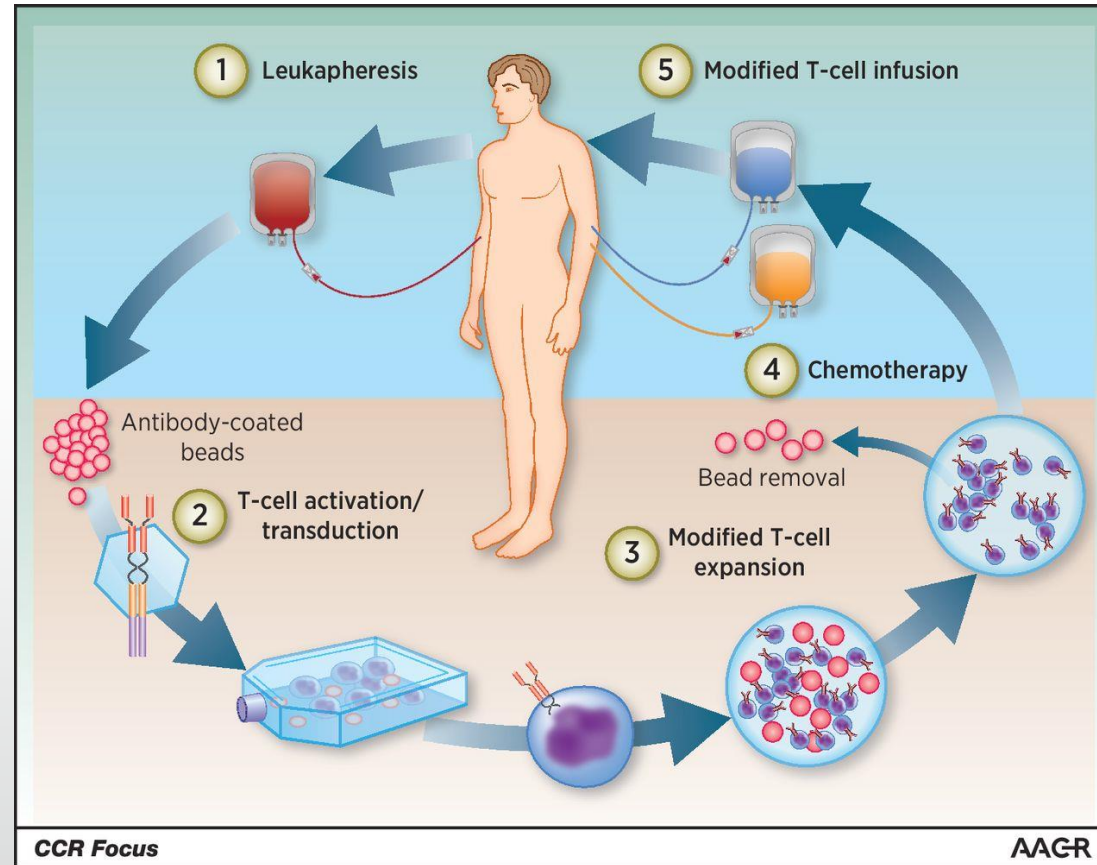
(pdb-file kindly provided by M. Clark)



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Types of immunotherapies

CAR-T-cells



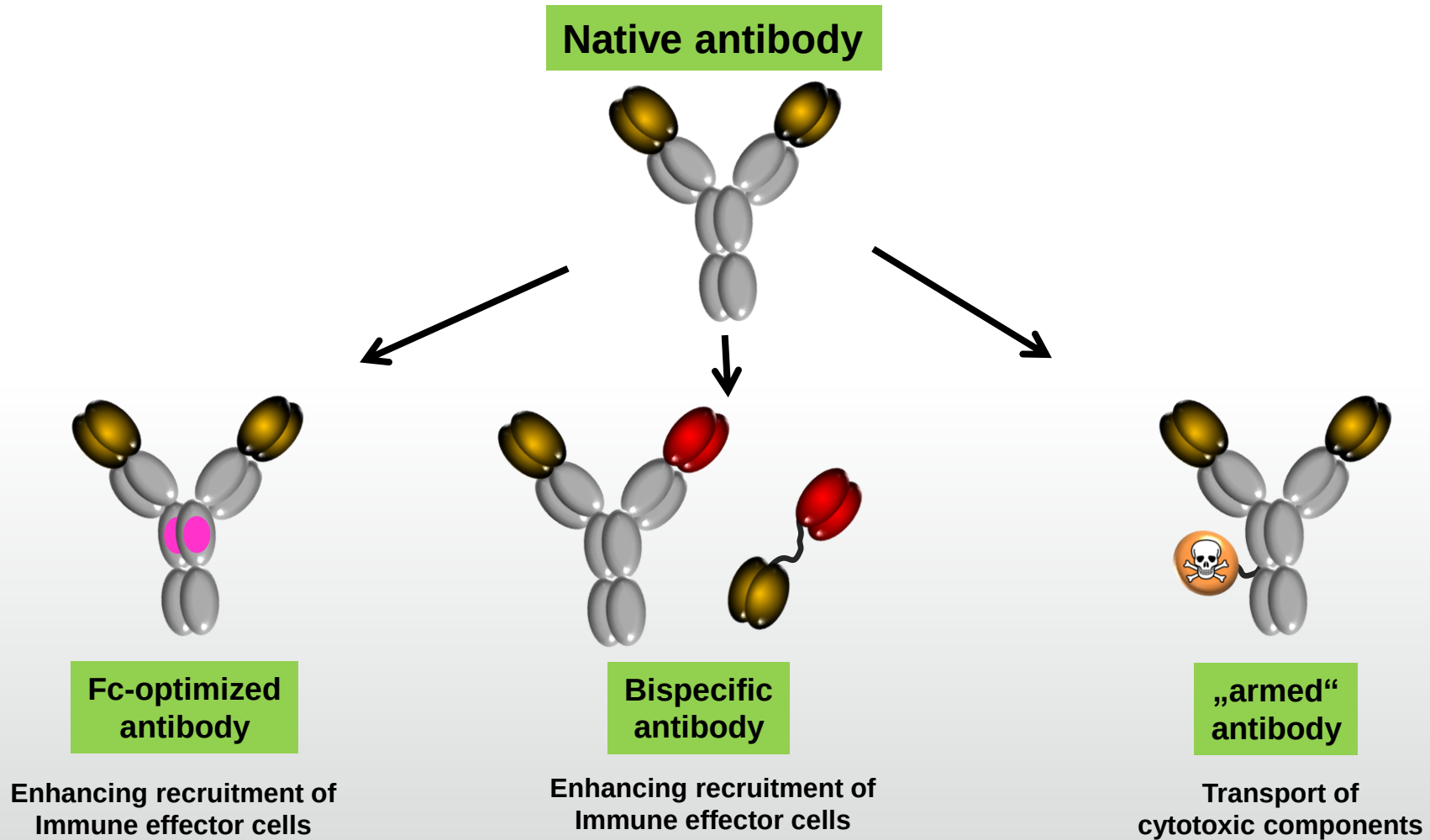
Focus of my working group

Developing novel immunotherapy strategies for ALL and other B-cell malignancies

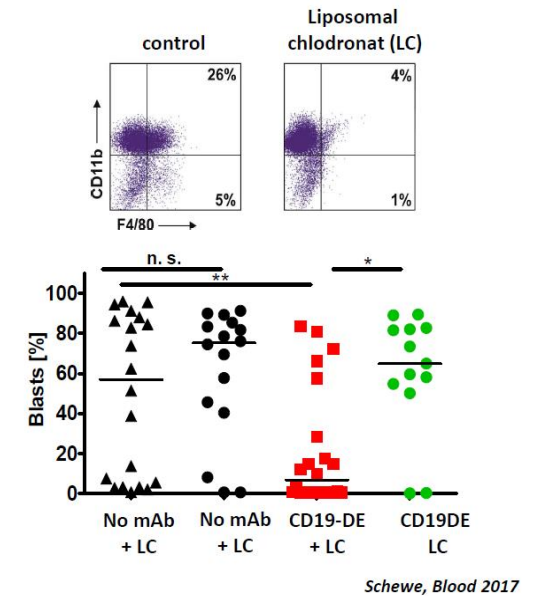
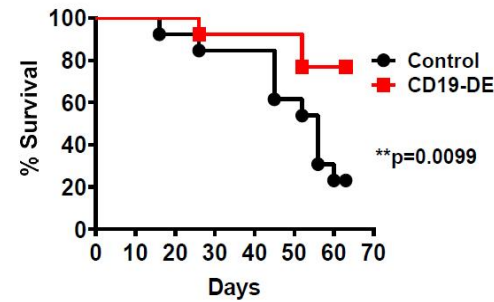
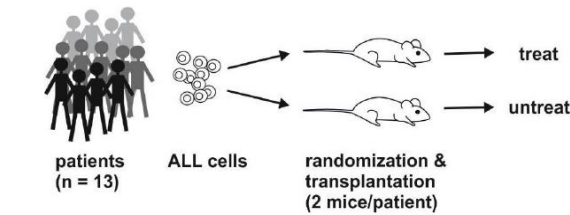
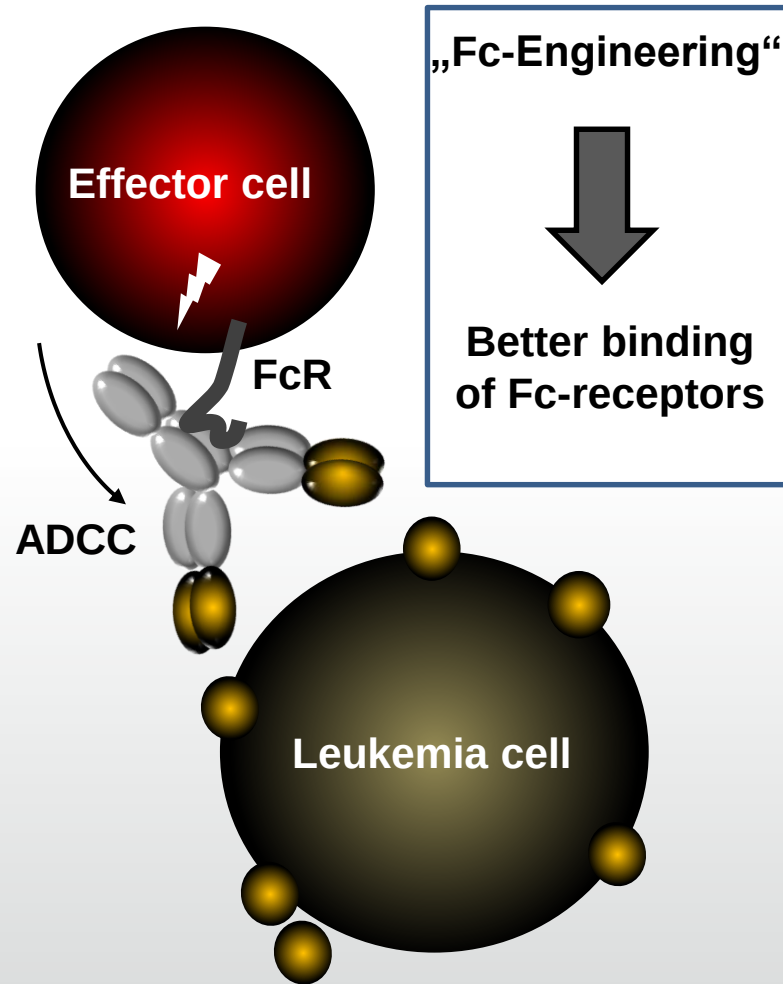
- Optimizing antibody constructs
 - Better effector cell recruitment
 - Extramedullary efficacy
- Combination therapies to enhance efficacy



Optimizing antibody constructs

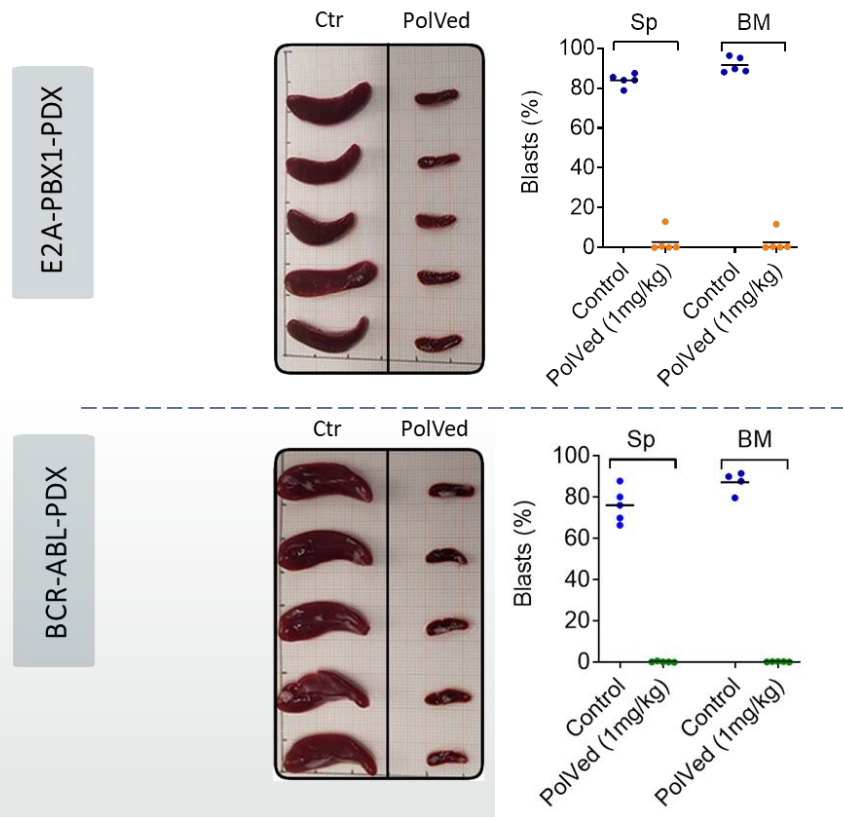
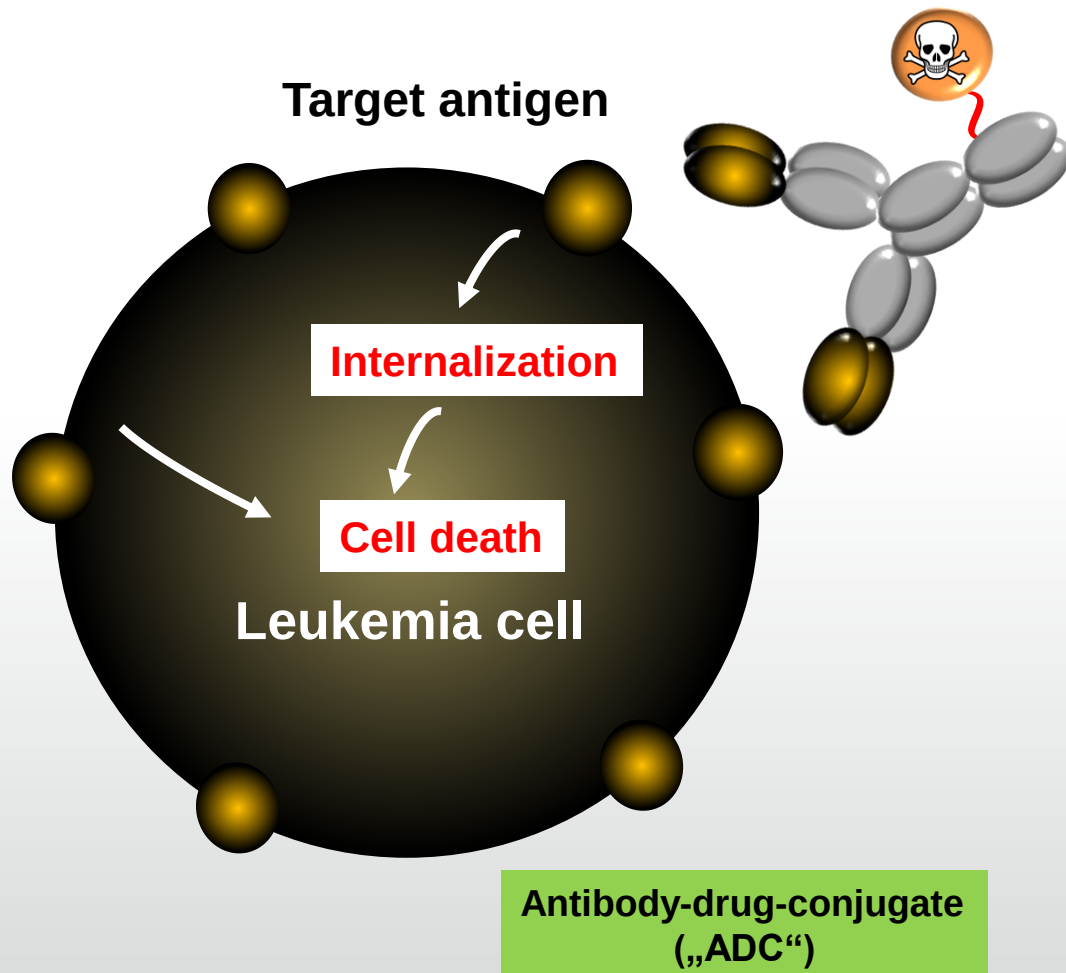


Optimizing antibody constructs



Schewe et al., Blood, 2017

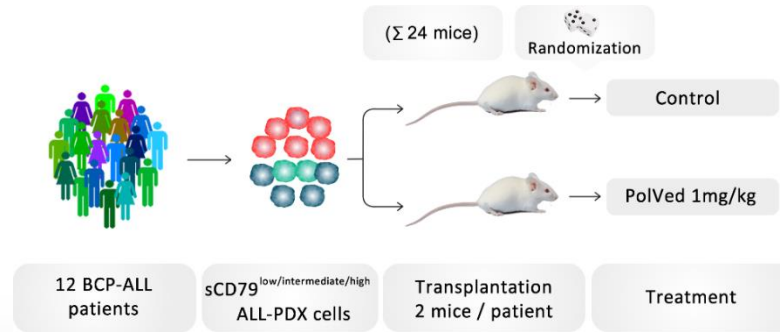
Optimizing antibody constructs, armed antibodies



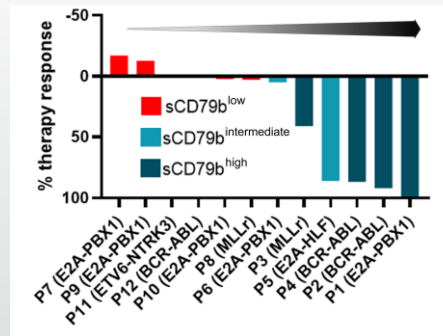
Lenk et al., Blood, ASH-Abstracts, 2021

Optimizing antibody constructs, armed antibodies

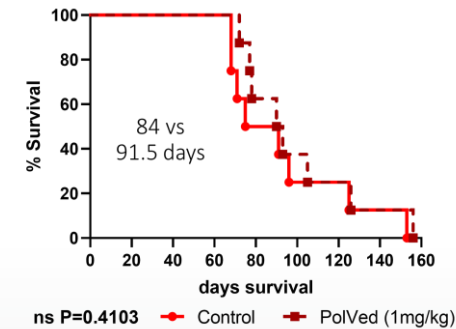
Polivy is effective in a variety of CD79b⁺ PDX-ALL samples



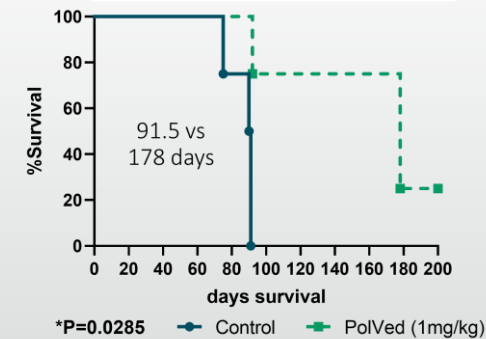
In vivo response to PolVed therapy



Mouse survival CD79b^{low/intermediate} PDX

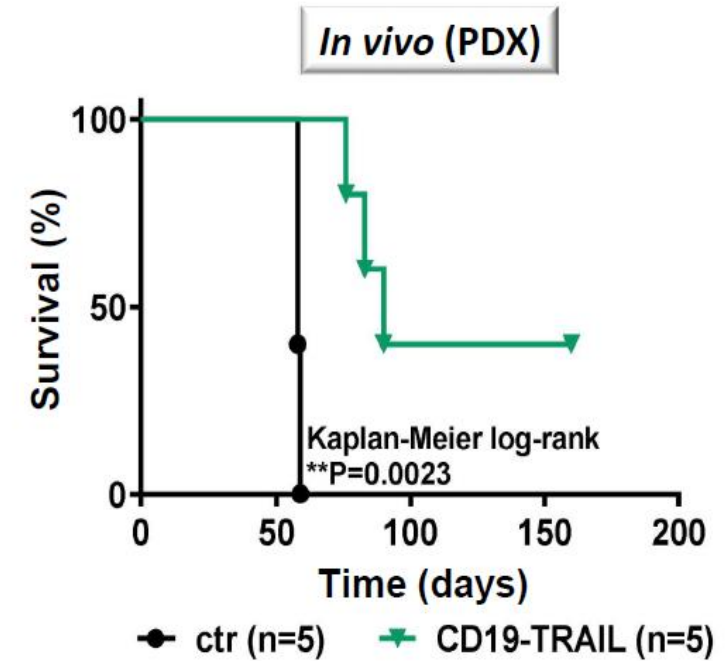
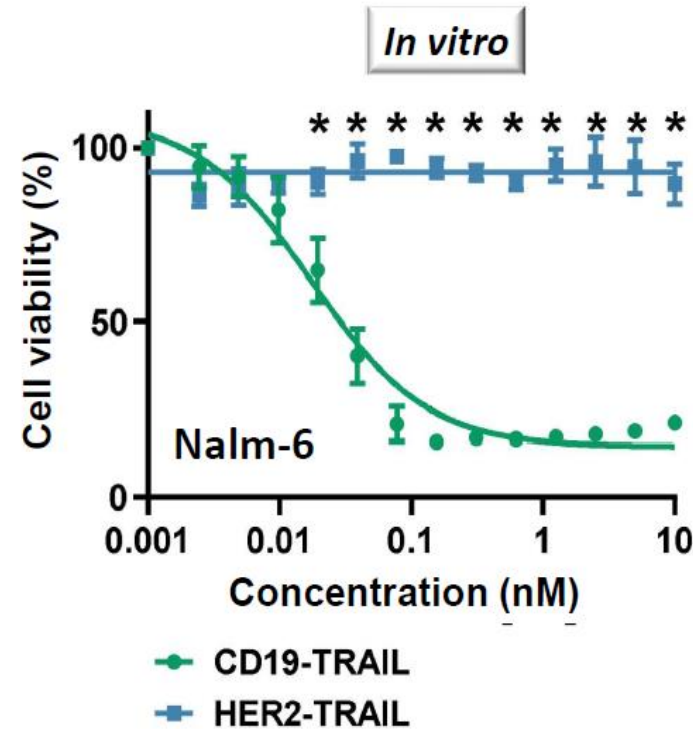
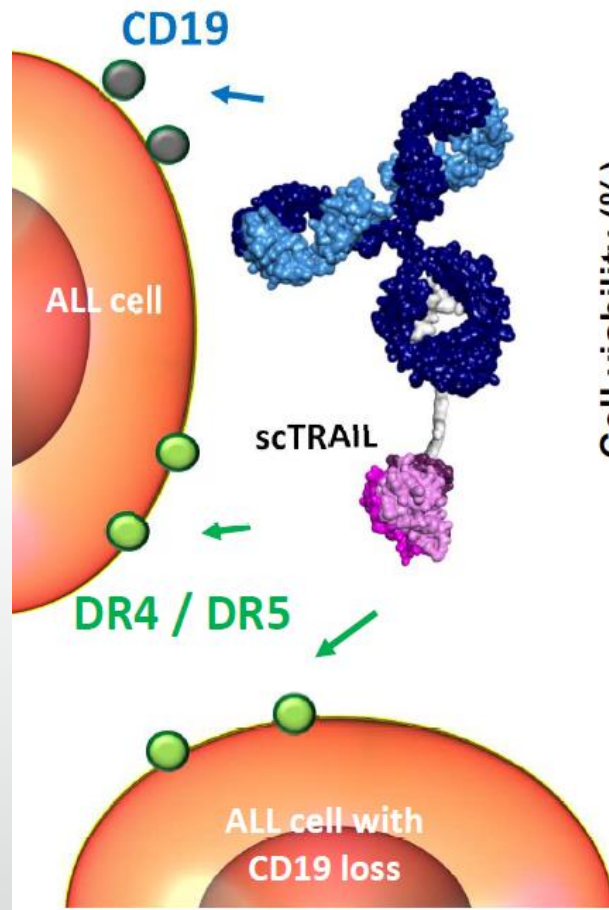


Mouse survival CD79b high PDX



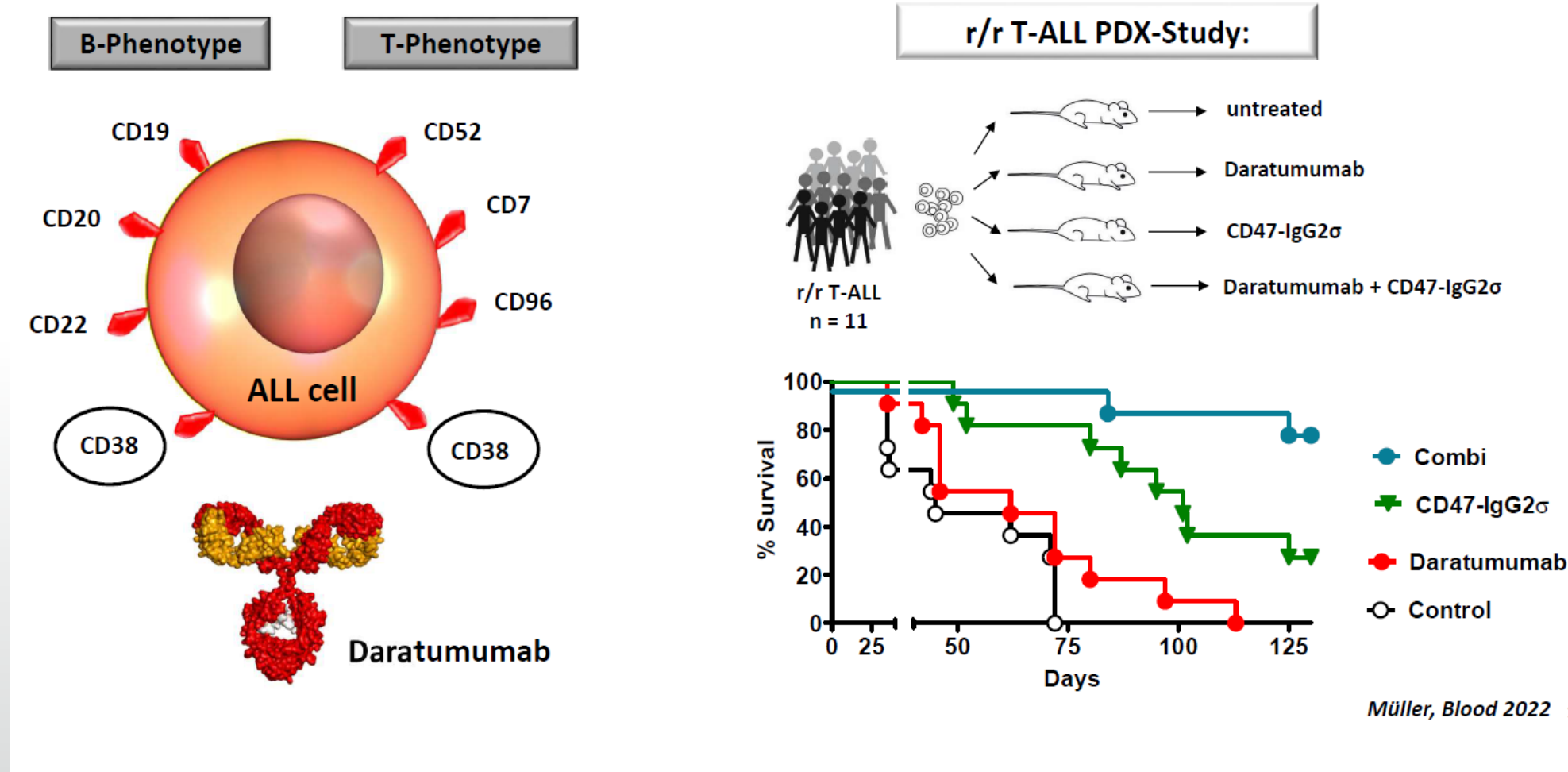
Lenk et al., Hemasphere, *in revision*

Optimizing antibody constructs, armed antibodies

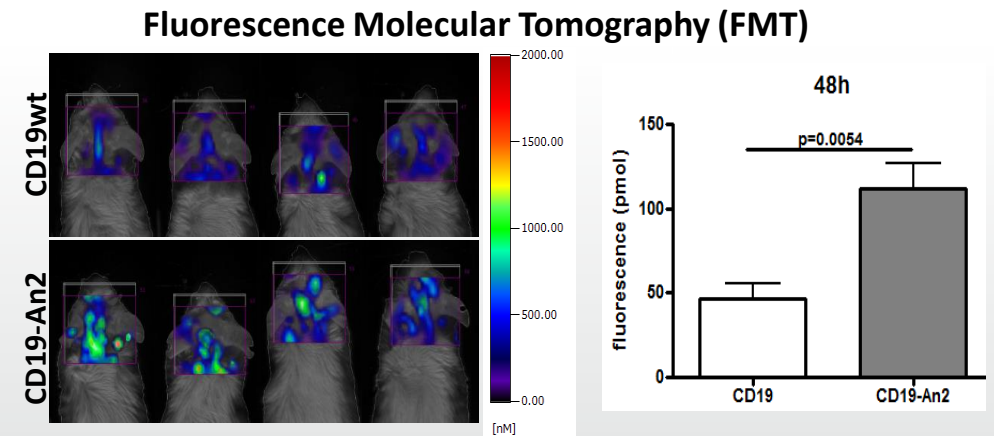
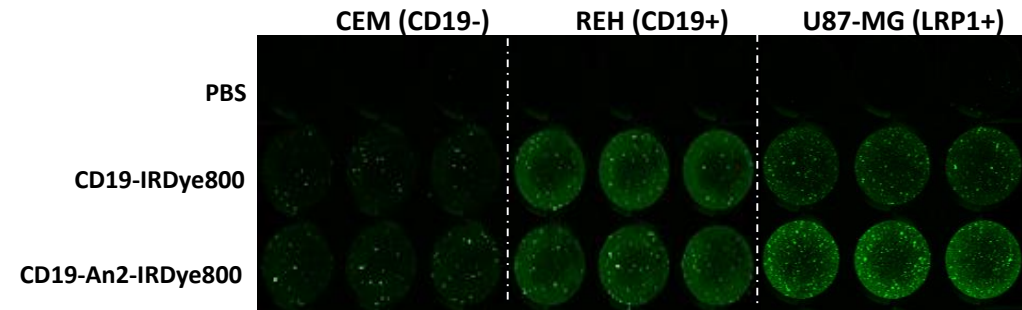
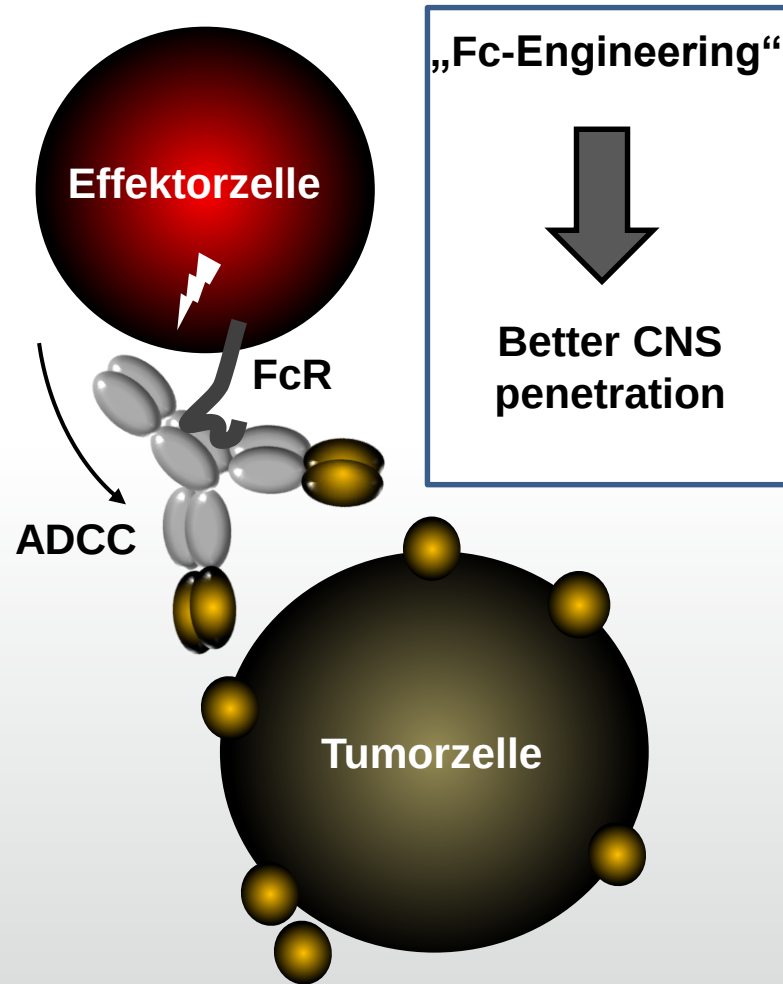


Winterberg, J Clin Med 2021 19

Optimizing antibody constructs, combinations



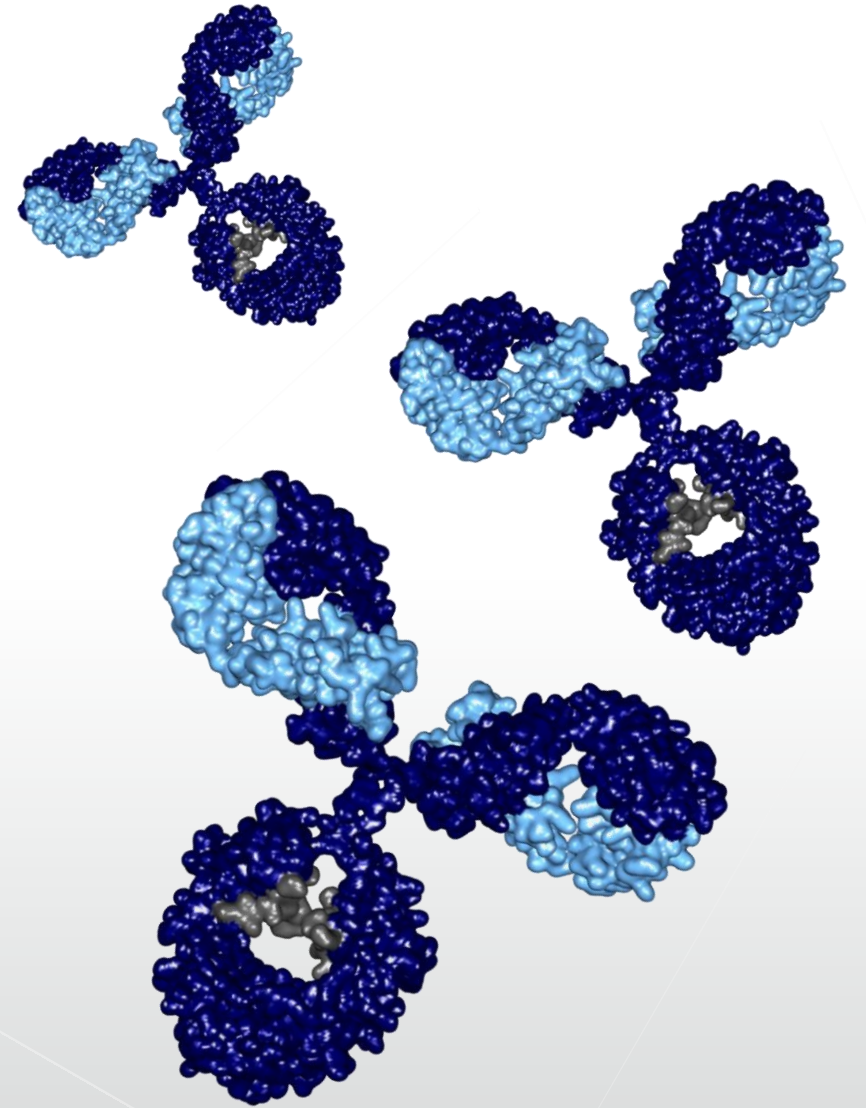
Optimizing antibodies, crossing barriers



Winterberg et al., *unpublished*

Future perspective

- Antibodies as designer molecules to bring precision medicine to cancer patients
- Antibody design confers a large and flexible armamentarium in order to tackle challenges in tumor therapy
- Antibody engineering may profit from developments in nanotechnology
- Future cooperations are welcome



Thank you for listening