Cancer killer profile: T cell fitness, autologous or allo T cell, T cell or NK?

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CDDF
Cancer Drug Development Forum

HYBRID WORKSHOP
29-30 NOVEMBER 2021

Overview of current clinical trials using cellular immunotherapies to treat haematological malignancies

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- Overview of current clinical trials using different cell types.
- Overview of current targets tested in acute myeloid leukaemia cellular immunotherapy.
- Searching of phenotypic signature of NK cells suitable for adoptive transfer immunotherapies.
- Immuno-monitoring of adoptively transferred immunotherapeutic cells.

Overview of current clinical trials using cellular immunotherapies to haematological malignancies

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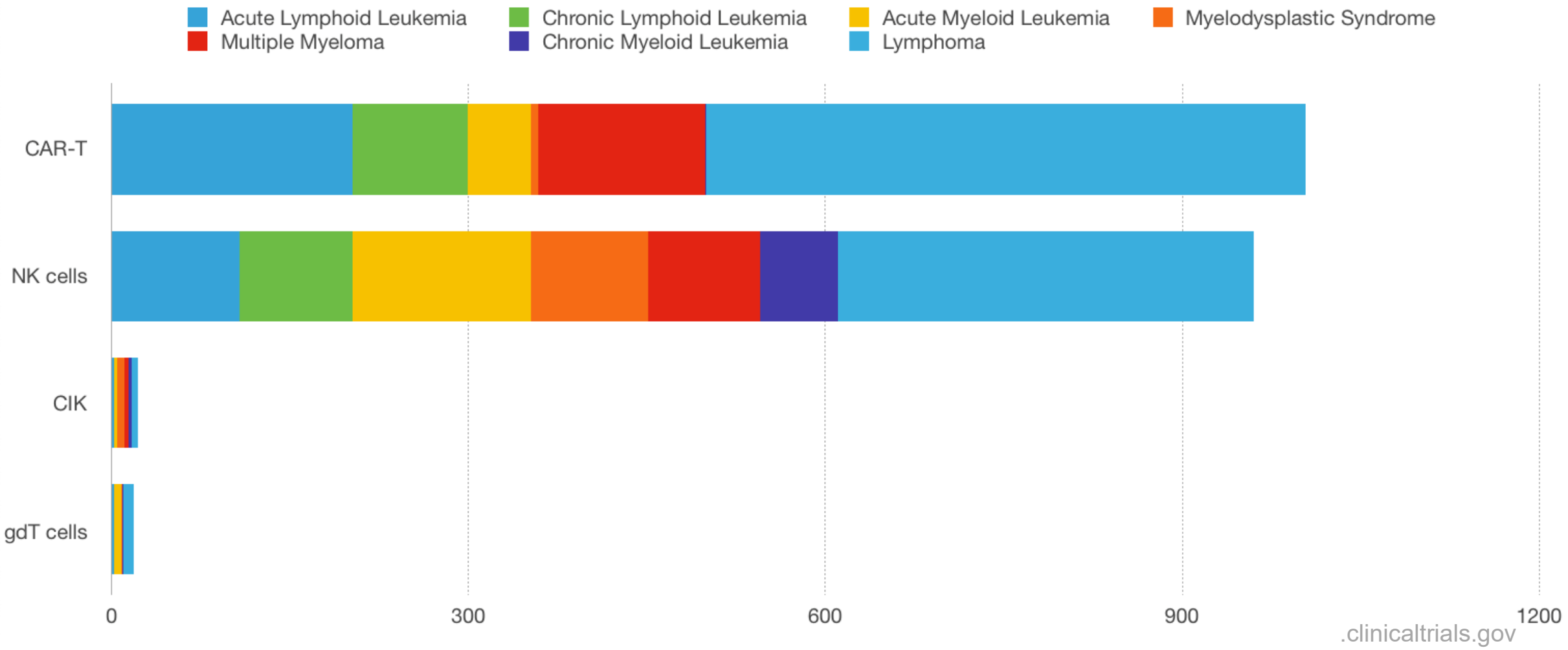

Haematological malignancies are 7% of newly diagnosed cancers

Cellular immunotherapy in haematological malignancies

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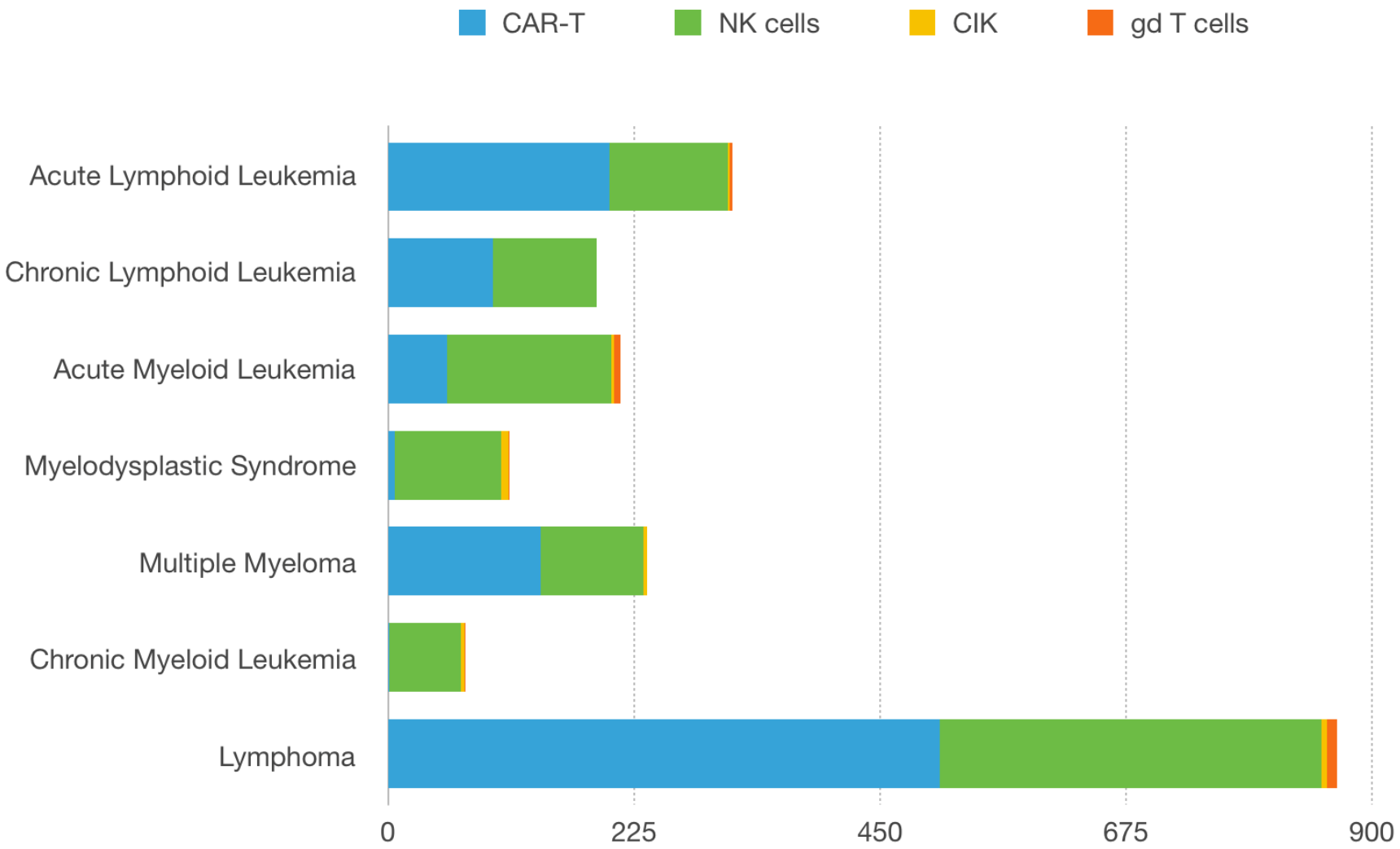

.clinicaltrials.gov

Cytotoxic cells in hematologic malignancies

Overview of clinical trials using adoptive transfer of cytotoxic cells

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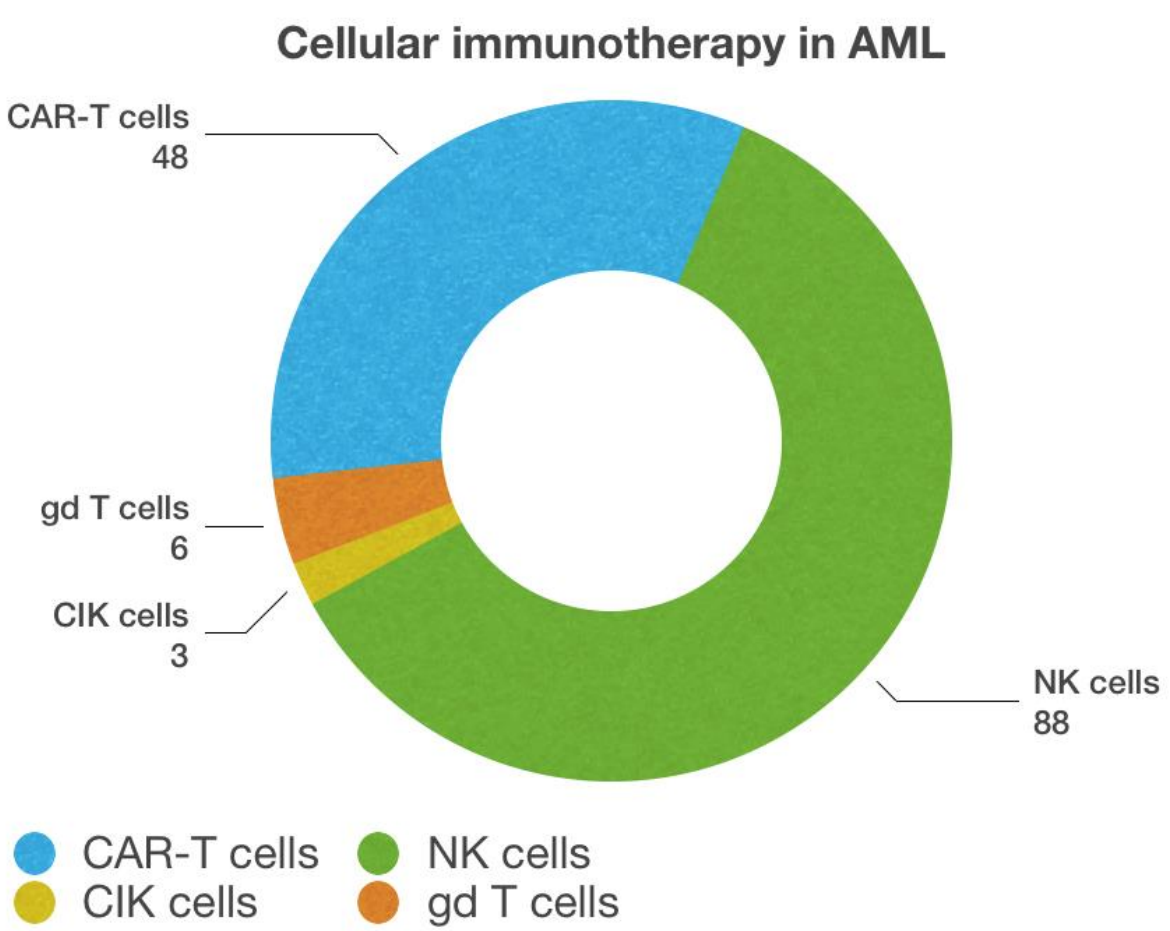

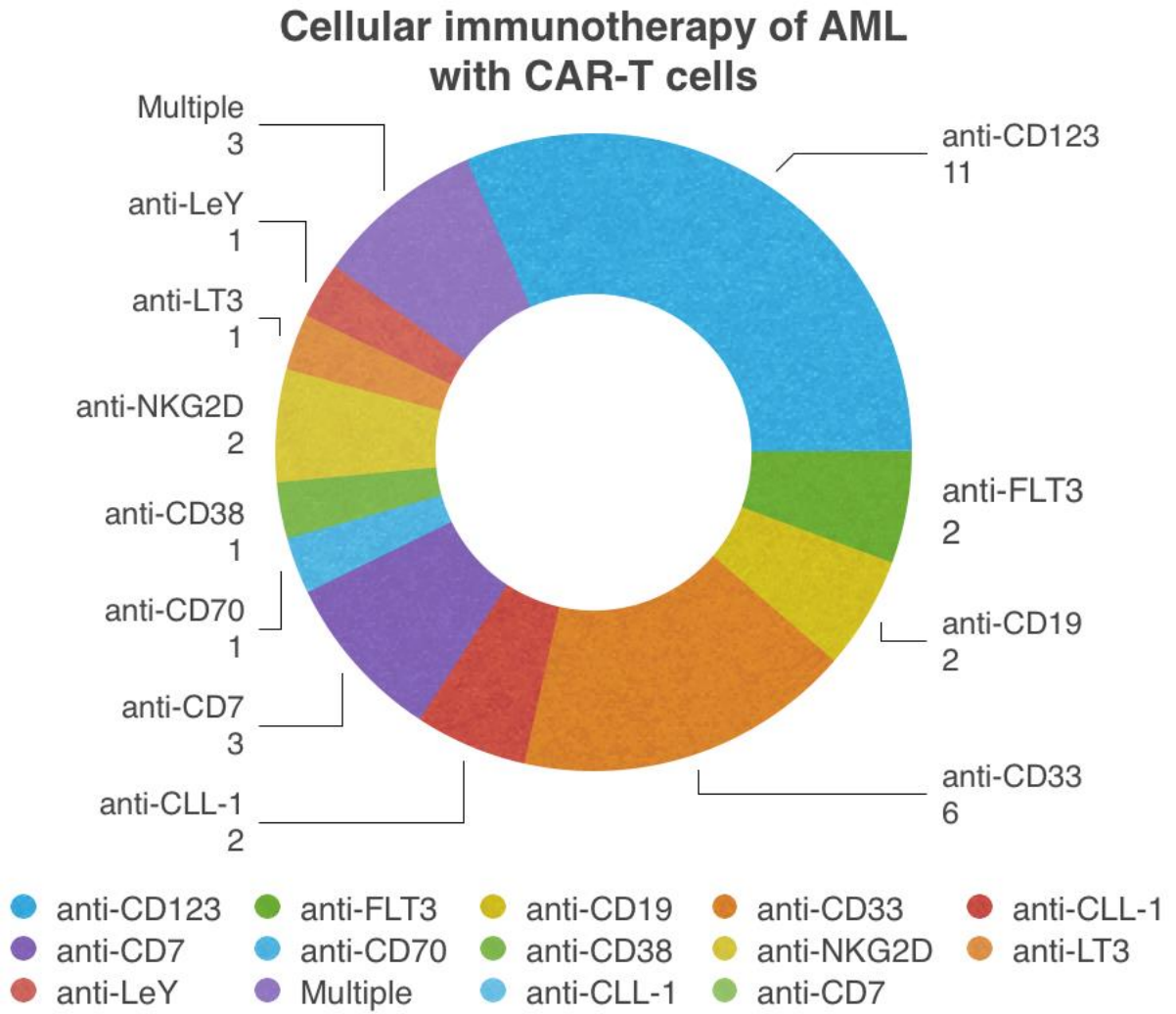

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Major candidate cell types for cellular immunotherapies in haemato-oncology

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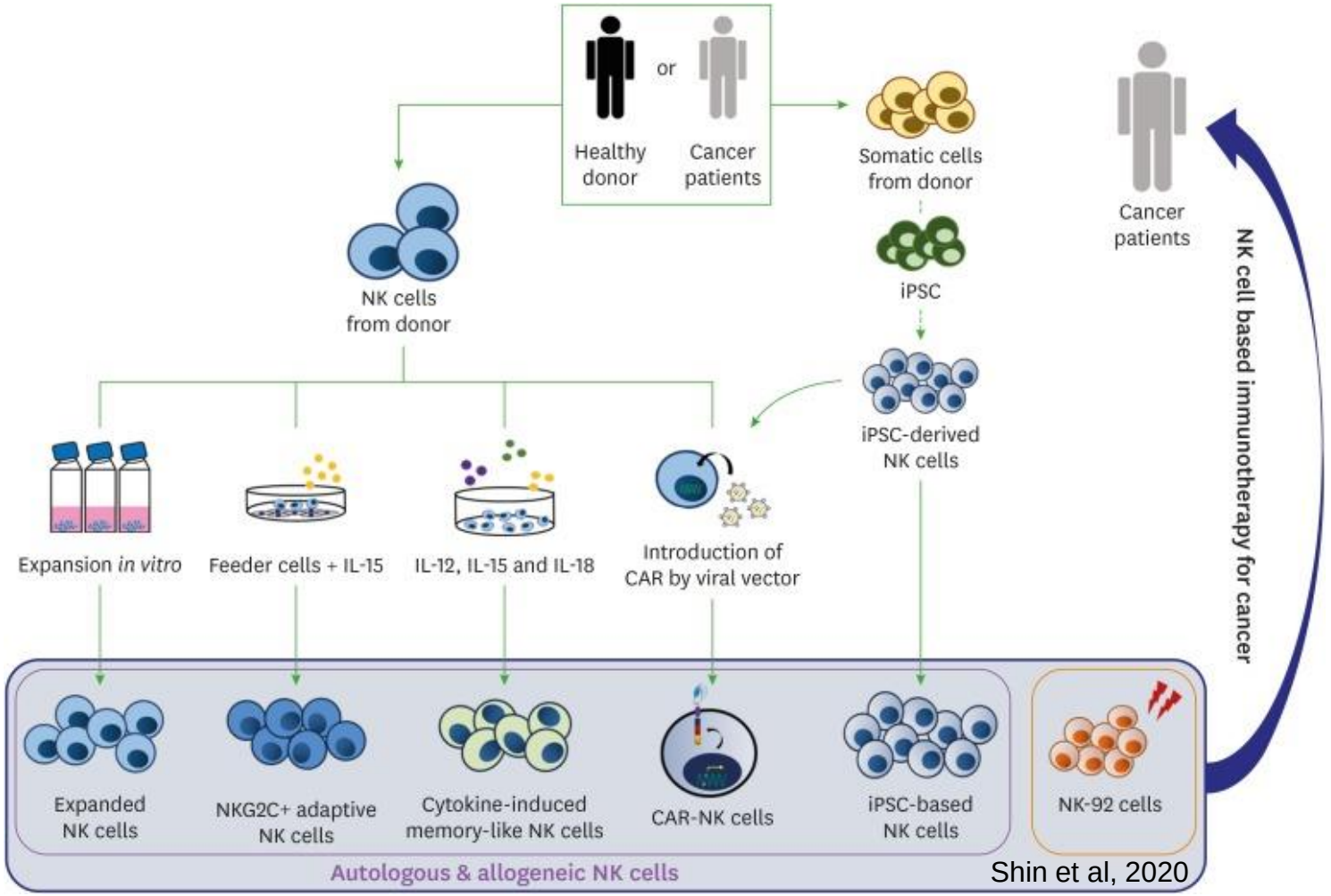
Comparison NK cells and CAR-T cells

	CAR-T cells	NK or CAR-NK cells
Source	autologous T cells	allogeneic or haplo-identical (PBMCs, UCB, iPSCs, hESCs, HPCs, NK cells, NK cell lines)
Transduction efficiancy	high	low
***In vivo* persistence**	↑↑	↓↓
Safety	↑	↑↑↑
Efficacy	↑ (CAR)	↑↑↑ (CAR and innate mechanisms)
Status	several comercial products	numerous clinical trials

Fitness and persistence of immunotherapeutic cells upon adoptive transfer

Experimental protocols of *ex vivo* expansion of NK cells.



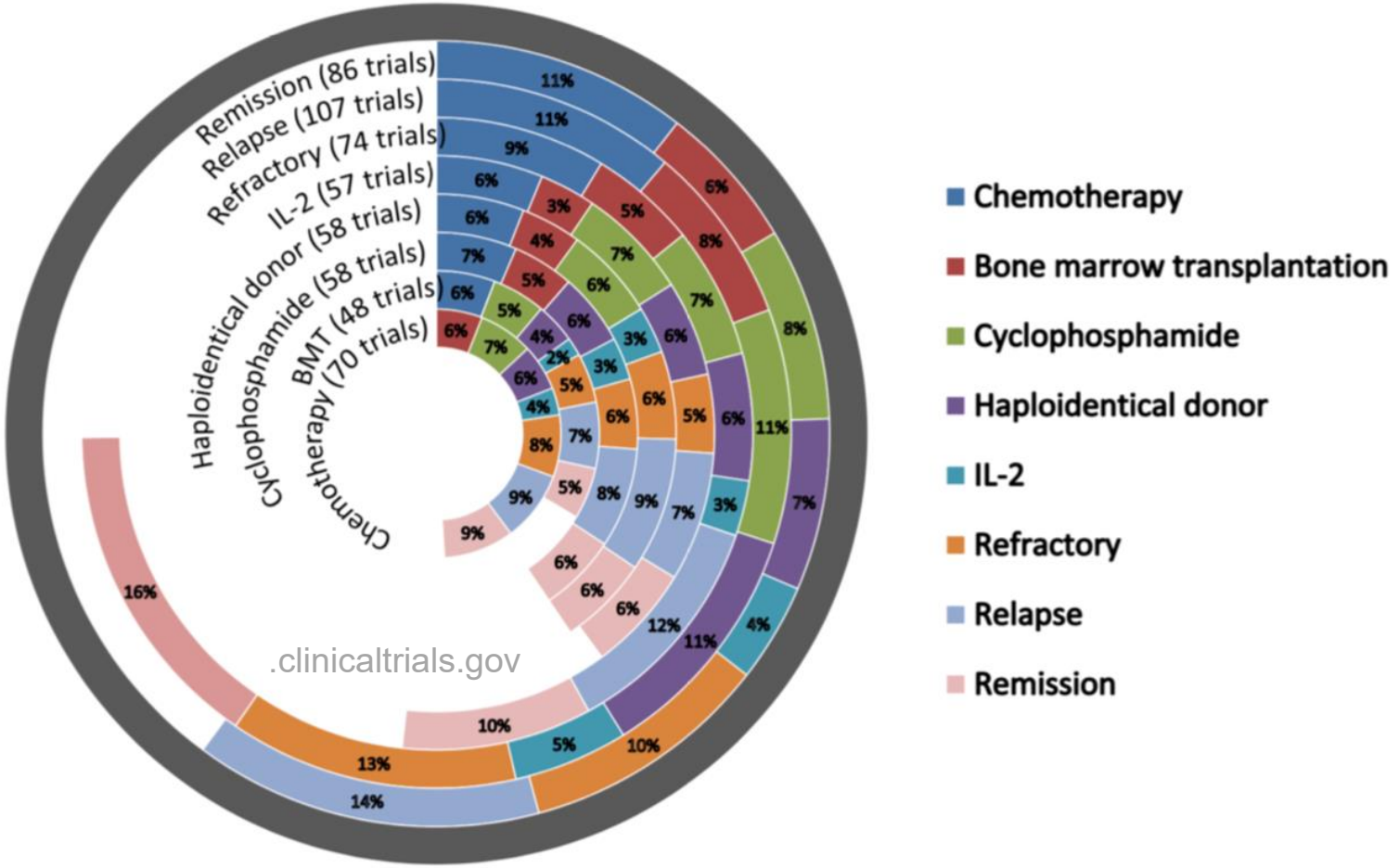
Shin et al, 2020

Source of allogeneic NK cells:

- PBMCs
- UCB
- iPSCs
- hESCs
- HPCs
- NK cell lines

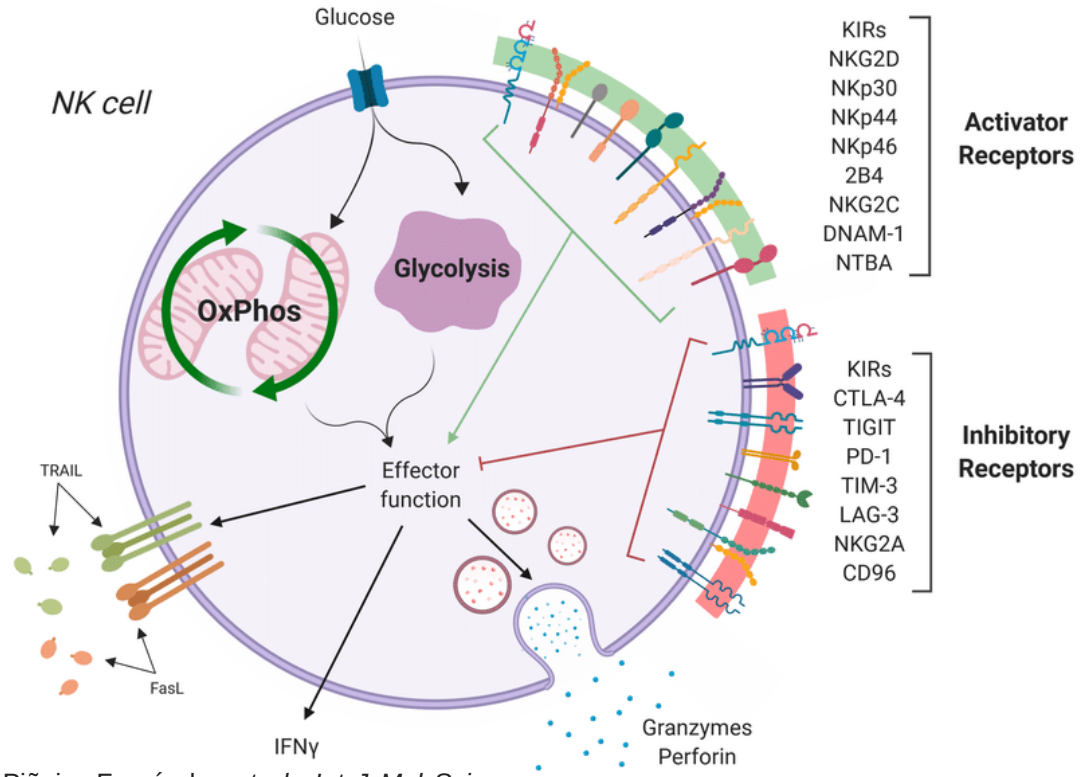
Landscape of NK cell ex vivo expansion protocols and cell sources

Different approaches to adoptive transfer of therapeutic NK cells in treatment of AML

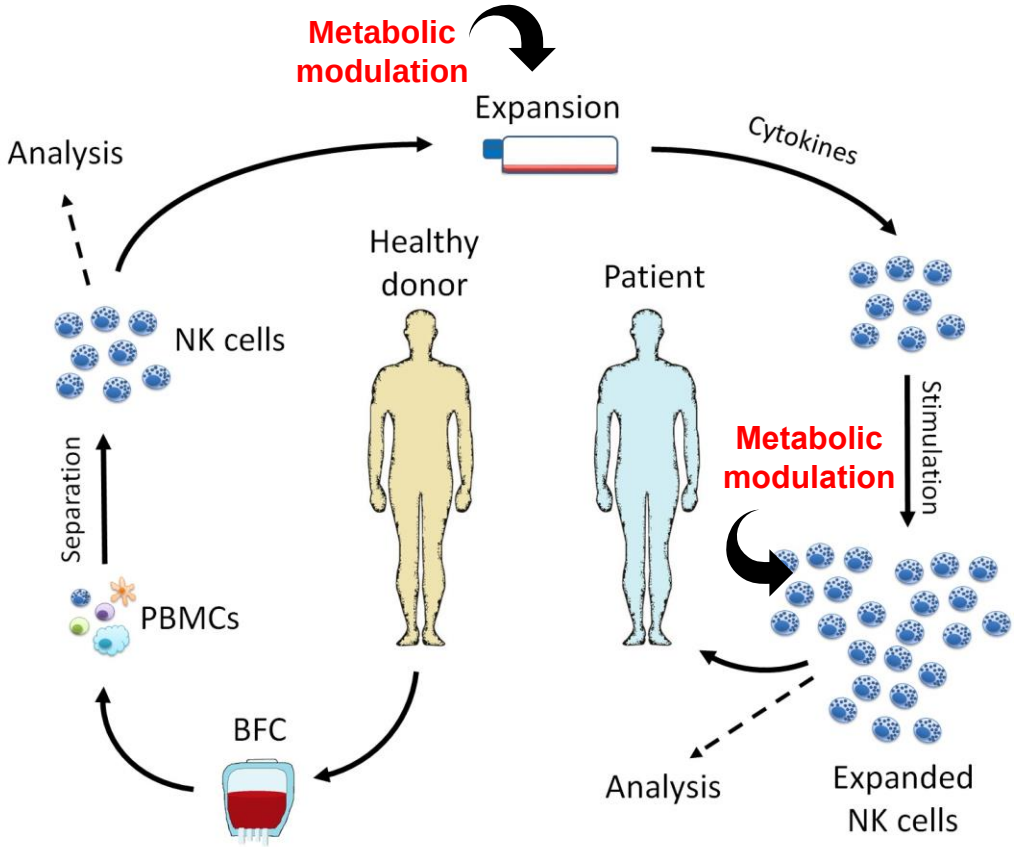


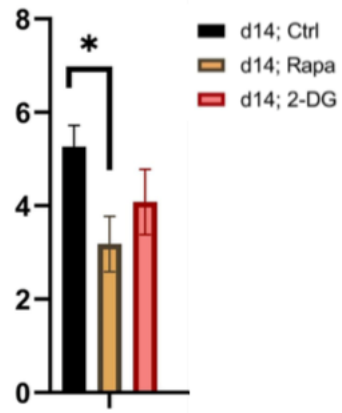
Complex situation in search for AML cellular therapy

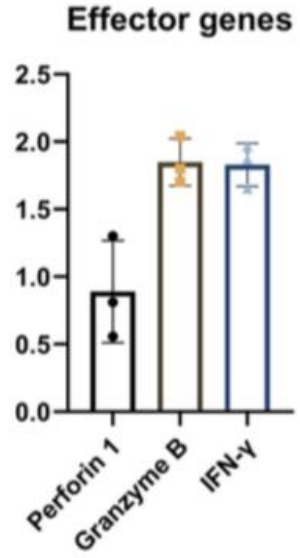
Metabolic status as part of NK cell fitness



Piñeiro Fernández *et al.*; *Int J Mol Sci.* 2019







Fitness of cells for adoptive transfer therapy

Summary:

- Different outcomes of CAR-T cells and NK cells therapy are due to different biological roles of the cells
- Both NK and CAR-T cell research needed specifically for AML and MS cellular therapies
- Immunometabolism is an important part of cytotoxic cells fitness

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