SCANCELL

DEVELOPING ANTIBODIES AND VACCINES FOR CANCER

GlyMabs® for T cell redirection

LSE: SCLP.L

Targeting post-translationally modified ‘neo-antigens’

Deliver differentiated products for unmet markets

ANTIBODIES

targeting glycans preferentially expressed on tumours

GlyMab®

anti-glycan mAb x 4

targeting GI, SCLC and ovarian cancers

anti-glycan mAb x 1

targeting tumour cells and tumour infiltrating T cells

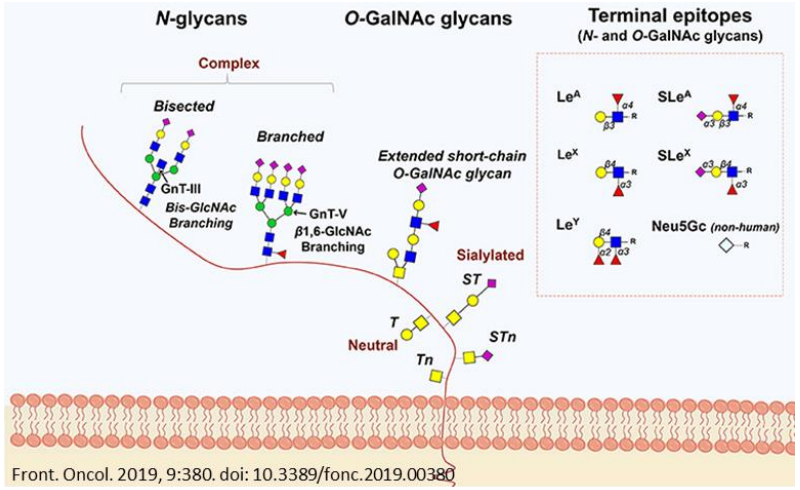
anti-protein mAb x 1

targeting gastric cancer

AvidiMab®

AvidiMab®

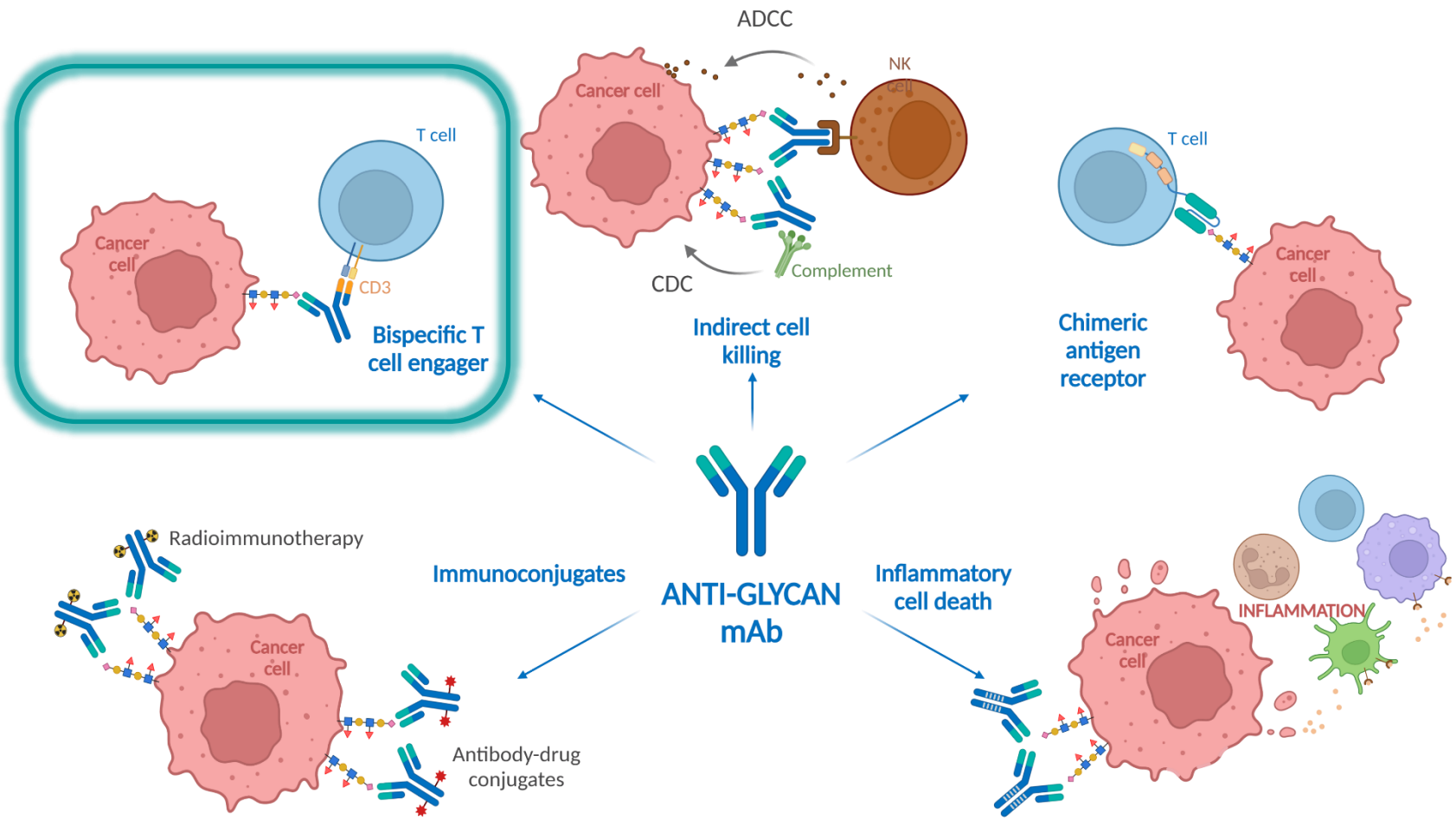
Avidity enhancing platform for therapeutic antibodies



Portfolio of patent-protected anti-glycan antibodies with excellent specificity, binding strongly to tumours and showing restricted normal tissue expression

Each antibody can be developed into multiple products

Expression of same glycan on multiple proteins and lipids



NK cell = natural killer cell; ADCC = antibody-dependent cellular cytotoxicity; CDC = complement-dependent cytotoxicity

SCANCELL

DEVELOPING ANTIBODIES AND VACCINES FOR CANCER

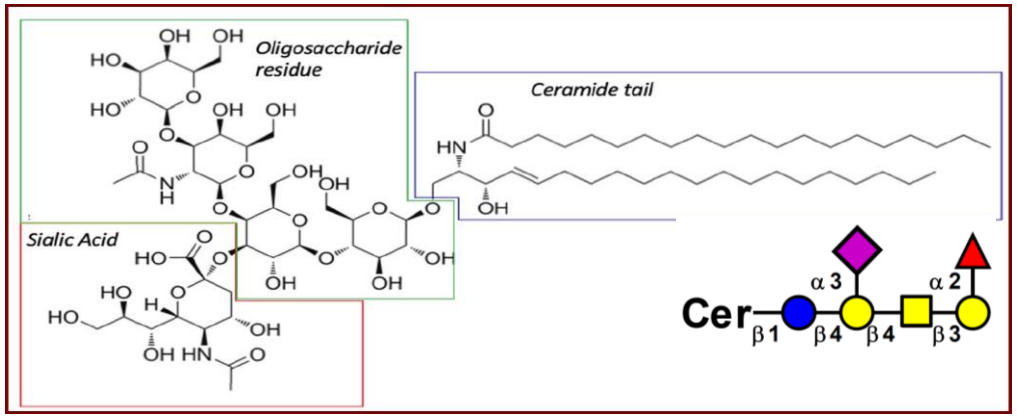
SC134 a fucosylGM1 targeting antibody for Small-Cell Lung Cancer (SCLC) treatment

LSE: SCLP.L

SC134 GlyMab® - binds fucosylGM1 specifically and with nanomolar avidity

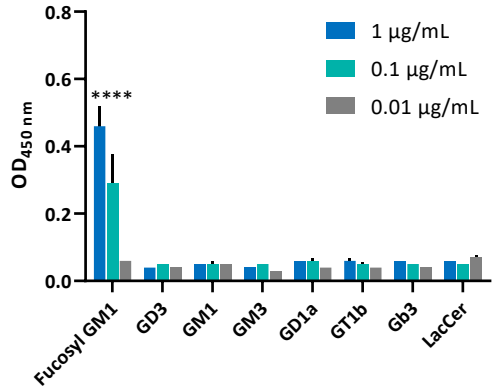
What is the target?

FucosylGM1 (fucGM1) is a cell surface glycosphingolipid



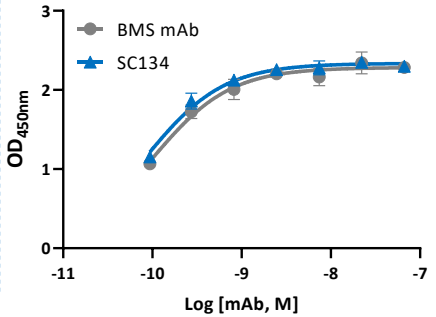
- plays pivotal role in cancer cell proliferation, invasion, metastasis, and immune escape
- overexpressed in large percentage of SCLC tissues
- virtually absent from normal healthy tissues

SC134 is specific for fucGM1

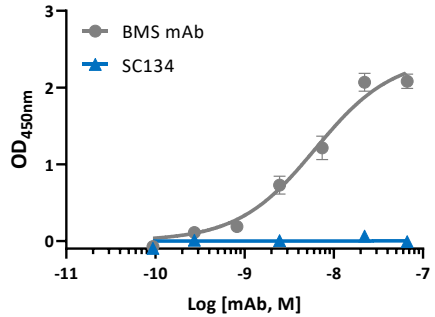


No cross-reactivity with GM1
SC134 compares favourably to BMS mAb

fucGM1 binding

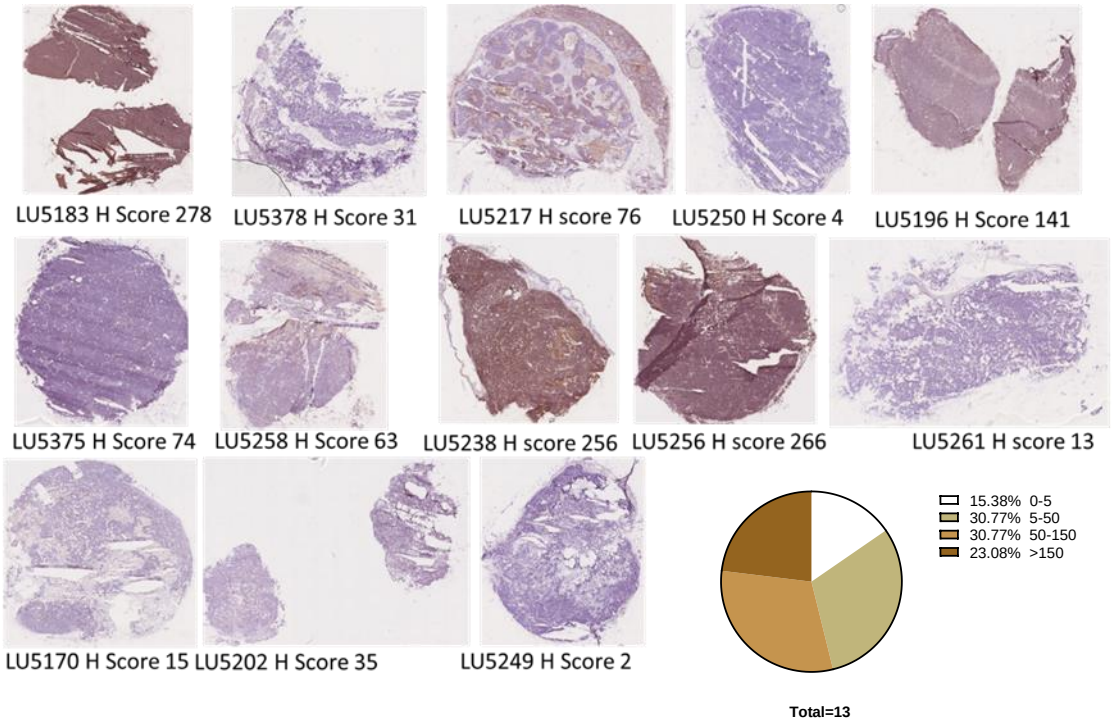


GM1 binding



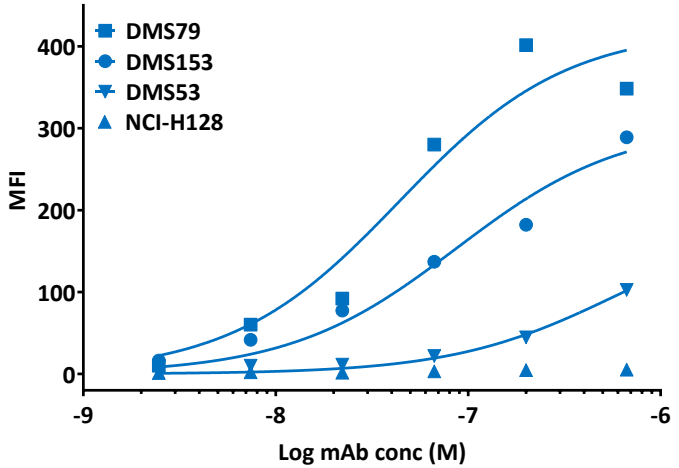
FucosylGM1 expression is widely expressed in SCLC tissues

Over 70% of SCLC tissues express fucGM1

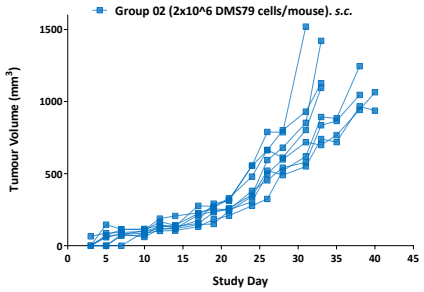


- fucGM1 distribution in SCLC tissues matches literature reports

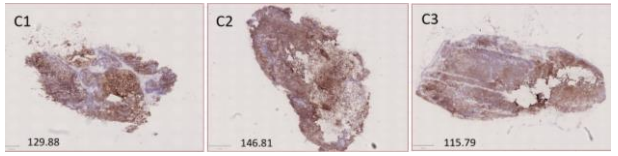
FucGM1 expression in a range of SCLC cell lines



DMS79 CDX model

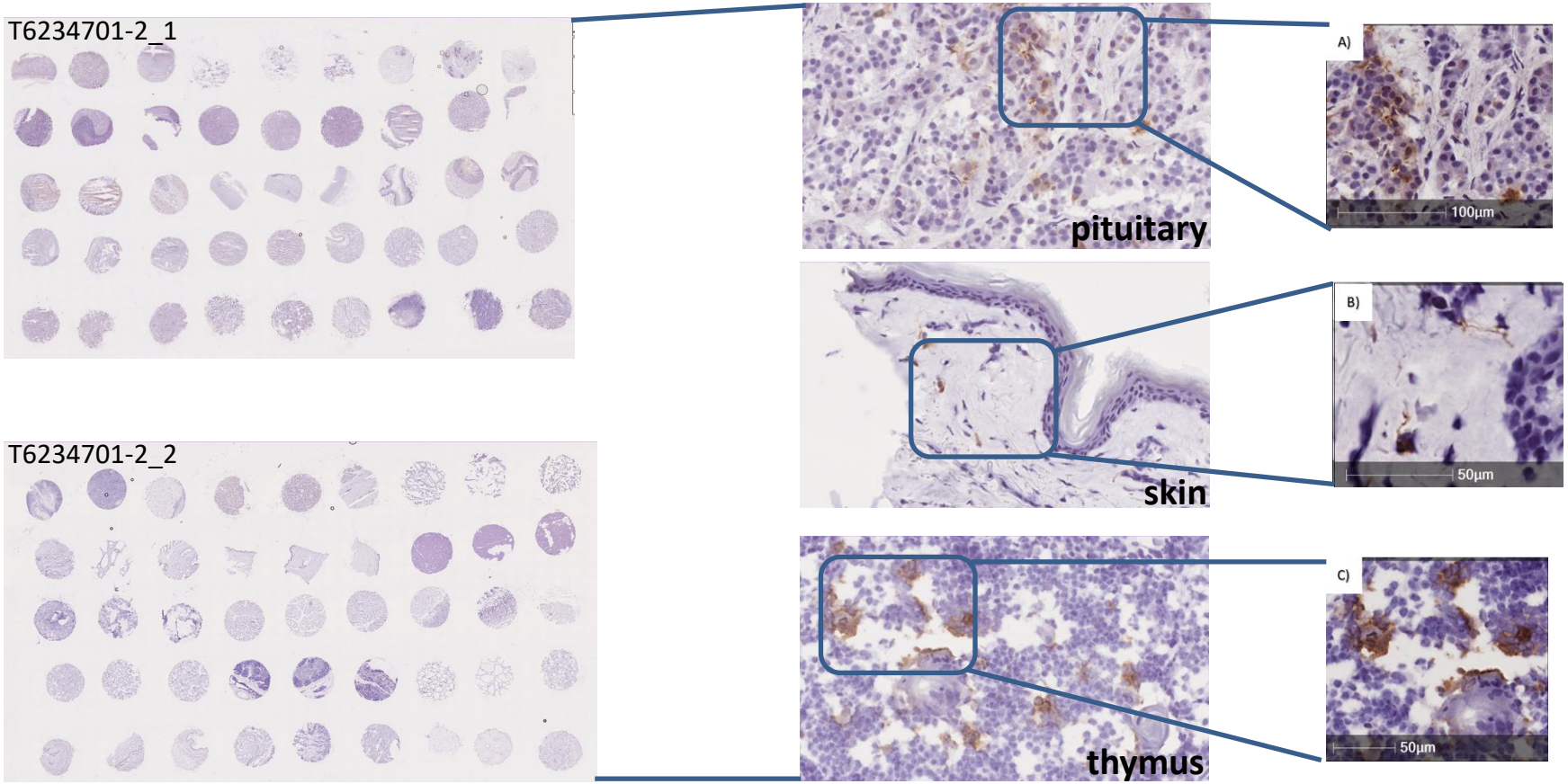


DMS79 is a relevant *in vivo* SCLC model



Restricted fucosylGM1 expression in healthy human tissues

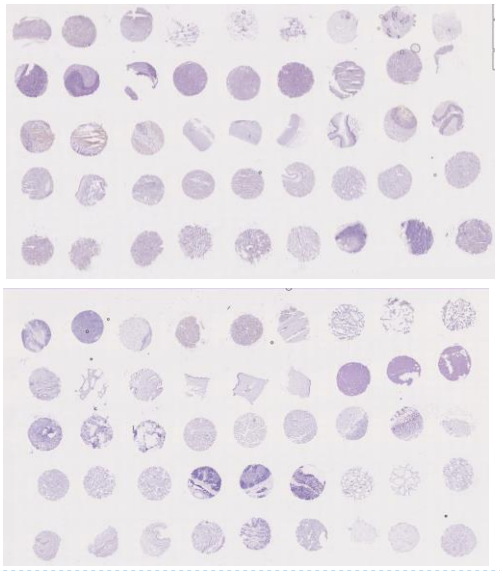
Frozen human tissue arrays show absence of fucGM1 expression in majority of human healthy tissues



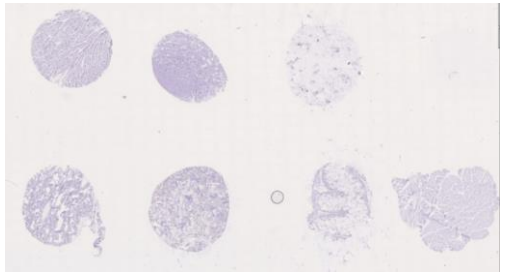
➢ **only three tissues with weak fucGM1 expression: human pituitary (1/3), skin (2/3) and thymus (3/3)**

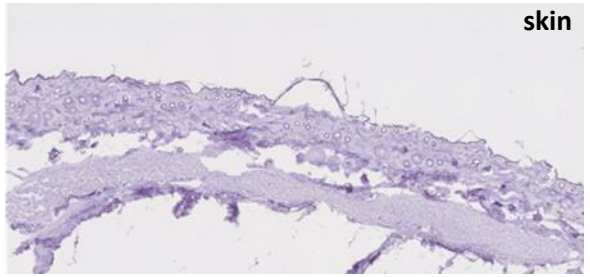
FucosylGM1 is expressed in animal tissues, species-dependent distribution

Rat and Cynomolgus monkey models match the limited normal human target distribution

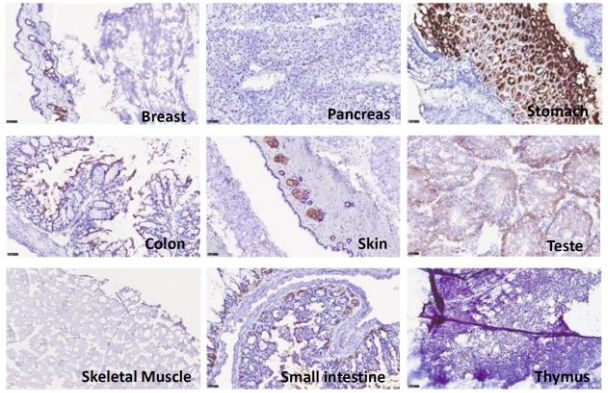


- only two genuinely positive tissues out of twenty-six
- mesothelium and stomach





- absence of positive SC134 staining of Cynomolgus Monkey tissues
- limited frozen Cynomolgus tissue availability



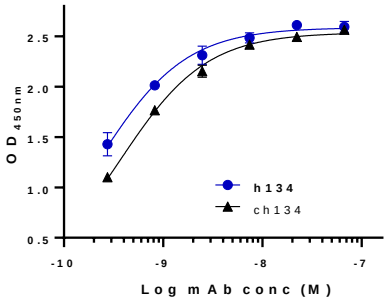
- nine mouse tissues show positive SC134 staining

- tumour selective target => ideal for T cell redirecting bispecific (TCB) development for SCLC therapy

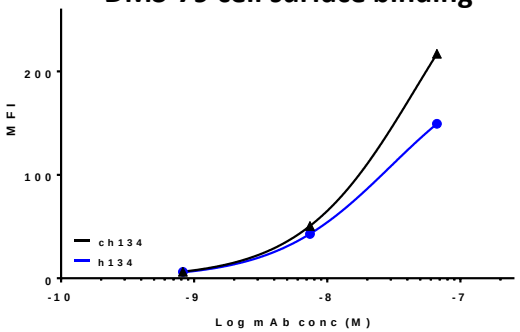
SC134, a humanised lead candidate

Humanised SC134 (h134) matches fucGM1 glycolipid and cell surface binding of the parental ch134

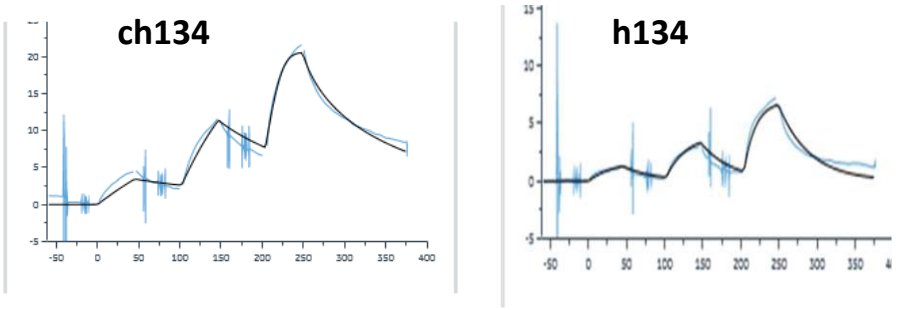
fucGM1 lipid ELISA



DMS-79 cell surface binding



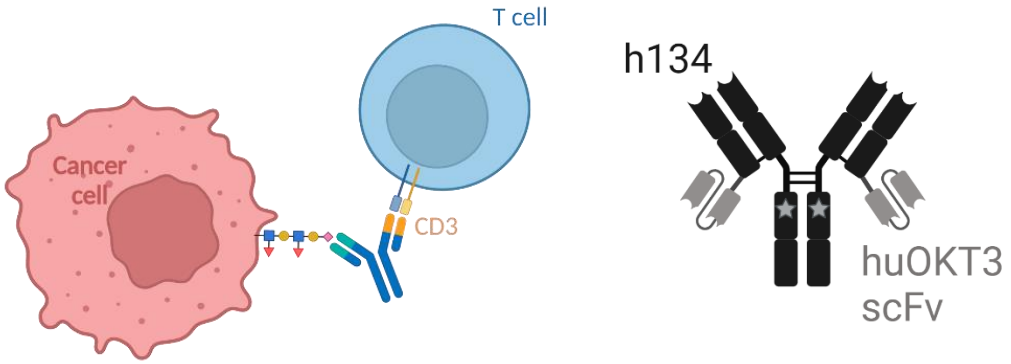
*SPR using the glycan headgroup grafted onto BSA does not mimic the natural lipid target binding



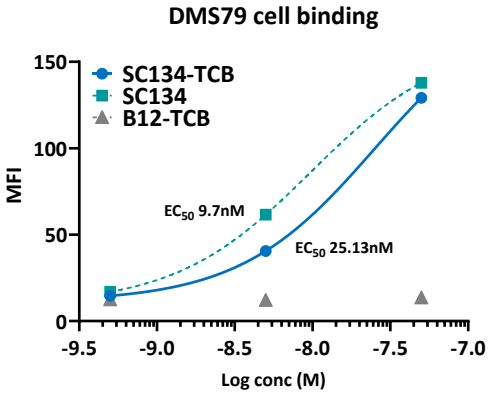
h134 – functional characteristics			
	ELISA (EC50, M)	cell binding (EC50, M)	SPR* (KD, M)
ch134	3.7E-10	4.7E-08	2.8E-08
h134	**2.3E-10**	**3.0E-08**	**1.2E-07**

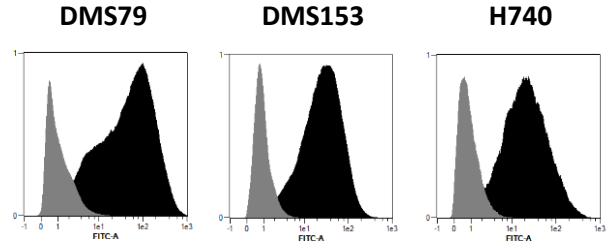
SC134-TCB targets SCLC cell lines and engages pan T cells

SC134-TCB, 2+2 format based on h134 and huOKT3 scFv

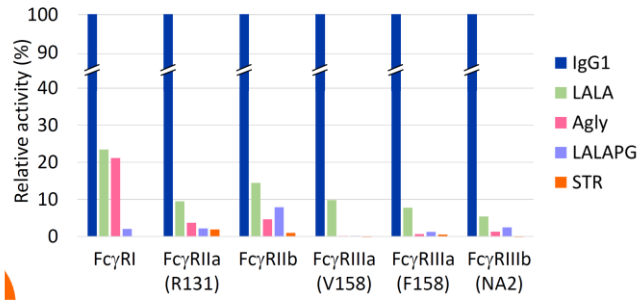


SC134-TCB maintains avid cell surface binding across a range of SCLC cell lines

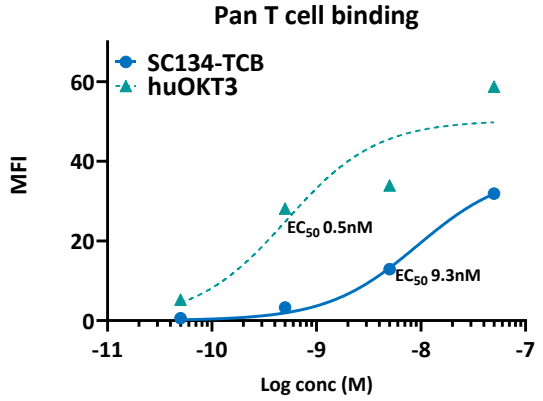




Fc silencing incorporated into h134 via three point mutations 'STR'

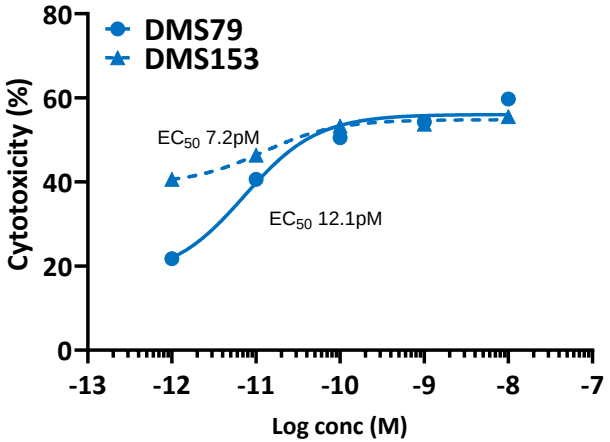


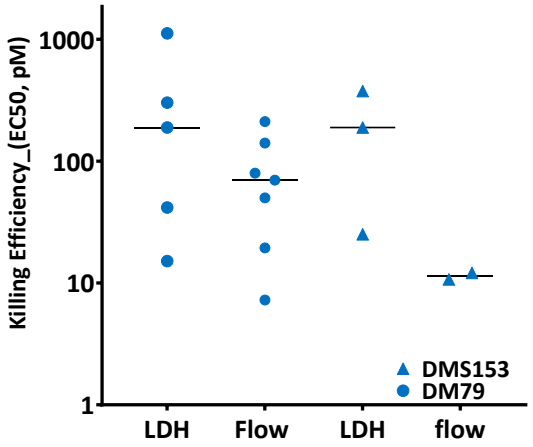
SC134-TCB exhibits nanomolar T cell binding

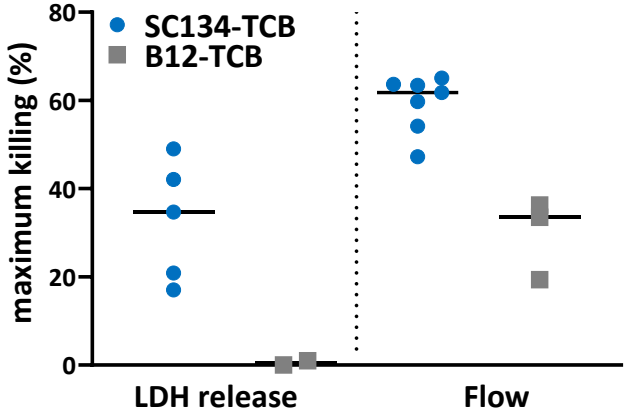


SC134-TCB shows potent T cell mediated cancer cell killing

Picomolar to subnanomolar SCLC cell killing, across a range of donors

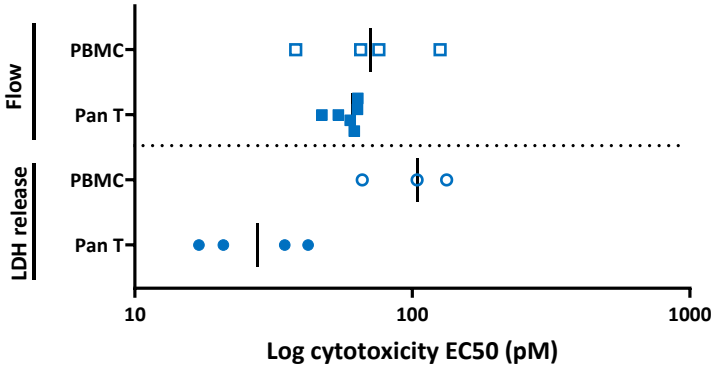






- picomolar cell lysis efficiency of DMS79 and DMS153
- donor-dependent cell killing, across two complementary assays

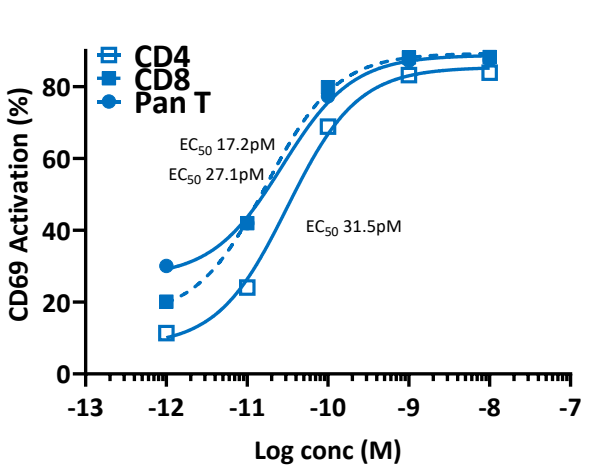
DMS79 killing pan T vs huPMBC

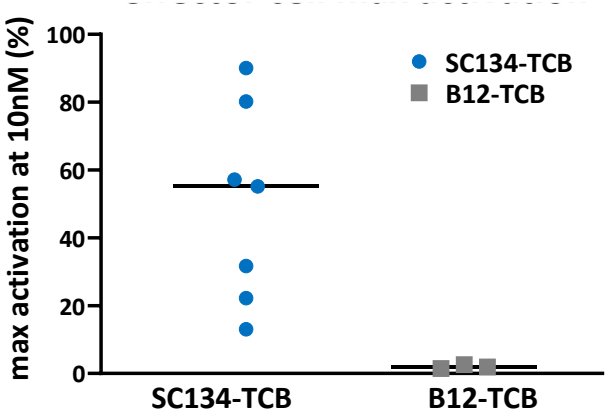


SC134-TCB engages pan T as well as human PBMC

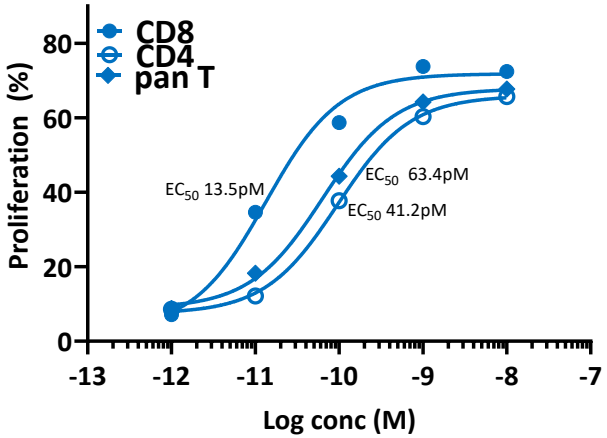
SC134-TCB mediates target-dependent effector cell activation and proliferation

Picomolar T cell activation





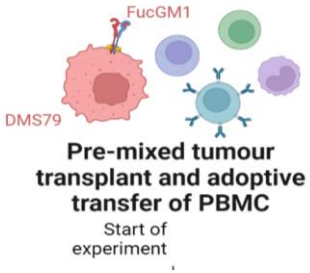
Effective T cell proliferation

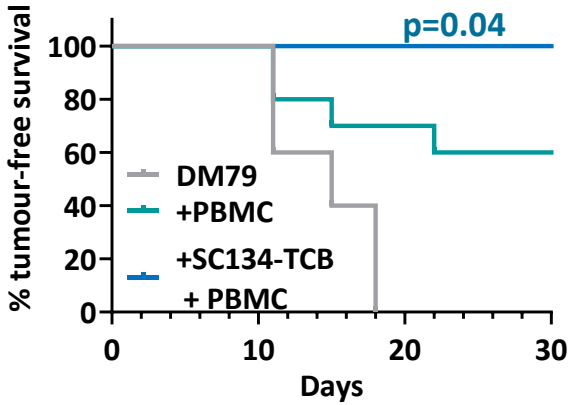


- **efficient activation of CD4 and CD8 T cells through co-engagement of SC134-TCB with target cells**
- **no activation in the absence of target engagement (B12-TCB)**
- **proliferation of CD4 and CD8 T cells upon target engagement by SC134-TCB**

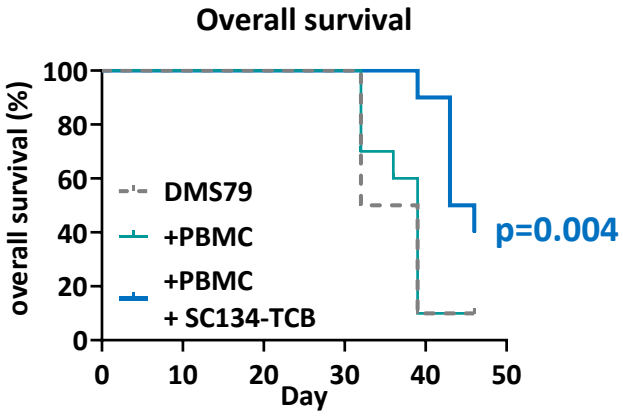
SC134-TCB shows potent *in vivo* (NSG) effector cell - mediated DMS79 killing

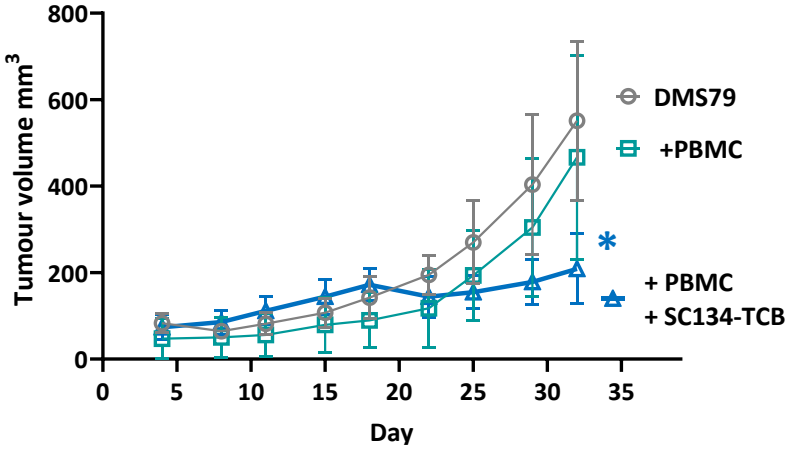
Significant *in vivo* anti-tumour effect of SC134-TCB against DMS79





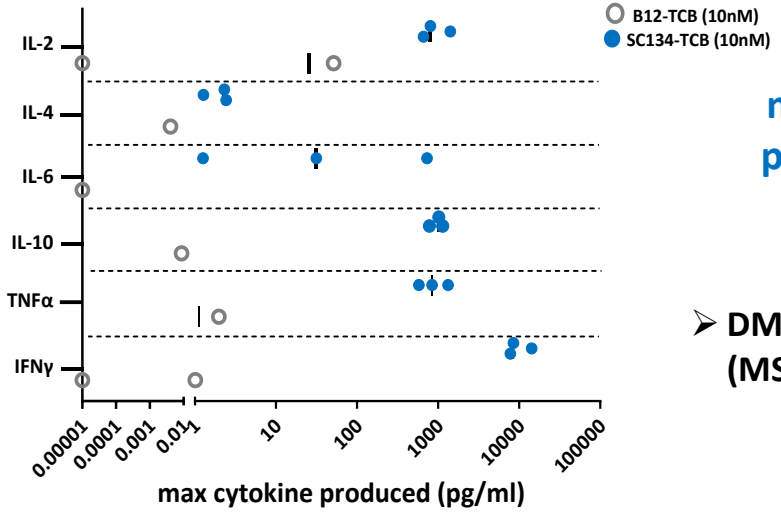
- admixed huPBMC:DMS79 at 1:1
- SC134-TCB mediated significant tumour-free survival advantage





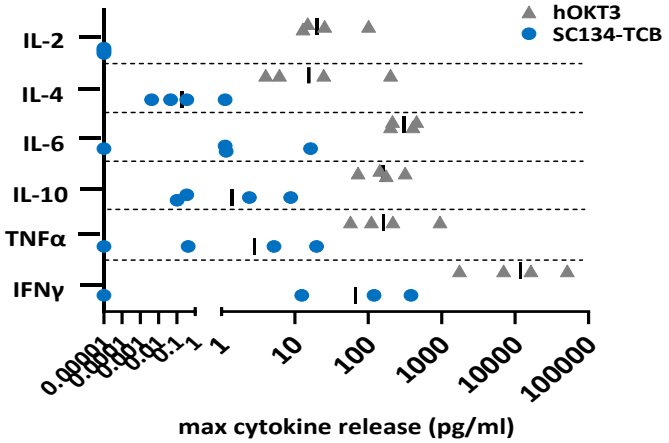
- separate dosing huPBMC:DMS79 (5:1)
- significant tumour control by SC134-TCB
- 40% overall survival in SC134-TCB treated group

SC134-TCB induces multifunctional cytokine release, only on target engagement



Target-mediated multifunctional cytokine production by SC134-TCB

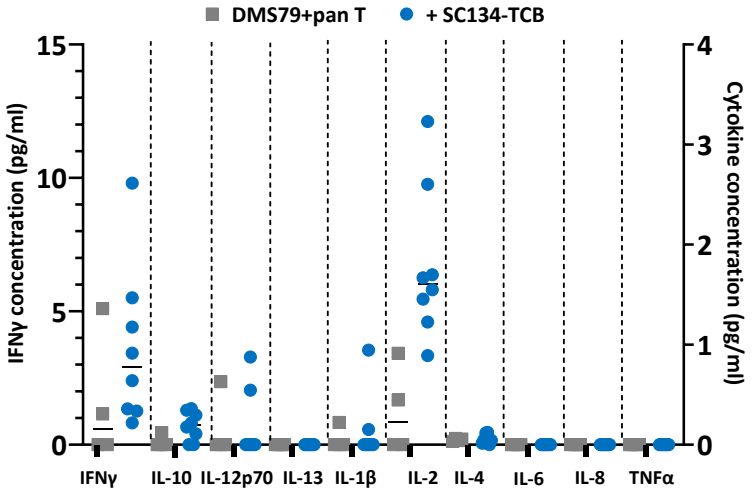
- DMS79-panT coculture supernatant (MSD, pro-inflammatory panel)



Limited cytokine production in absence of target engagement

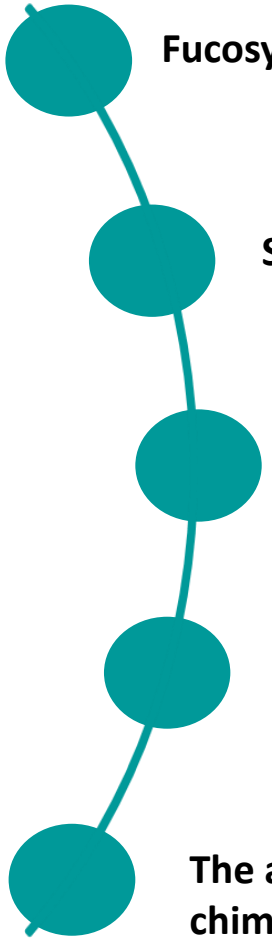
- Whole blood analyses (n=4 donors) (MSD, pro-inflammatory panel)

Limited cytokine presence in mouse sera



- 24hrs post-SC134 TCB dosing (NSG, DMS79 + pan T cells), (MSD, pro-inflammatory panel)

Conclusions



FucosylGM1 glycolipid is a SCLC-selective target

SC134 has therapeutic potential to target the majority (>70%) of SCLC as a T cell redirecting antibody

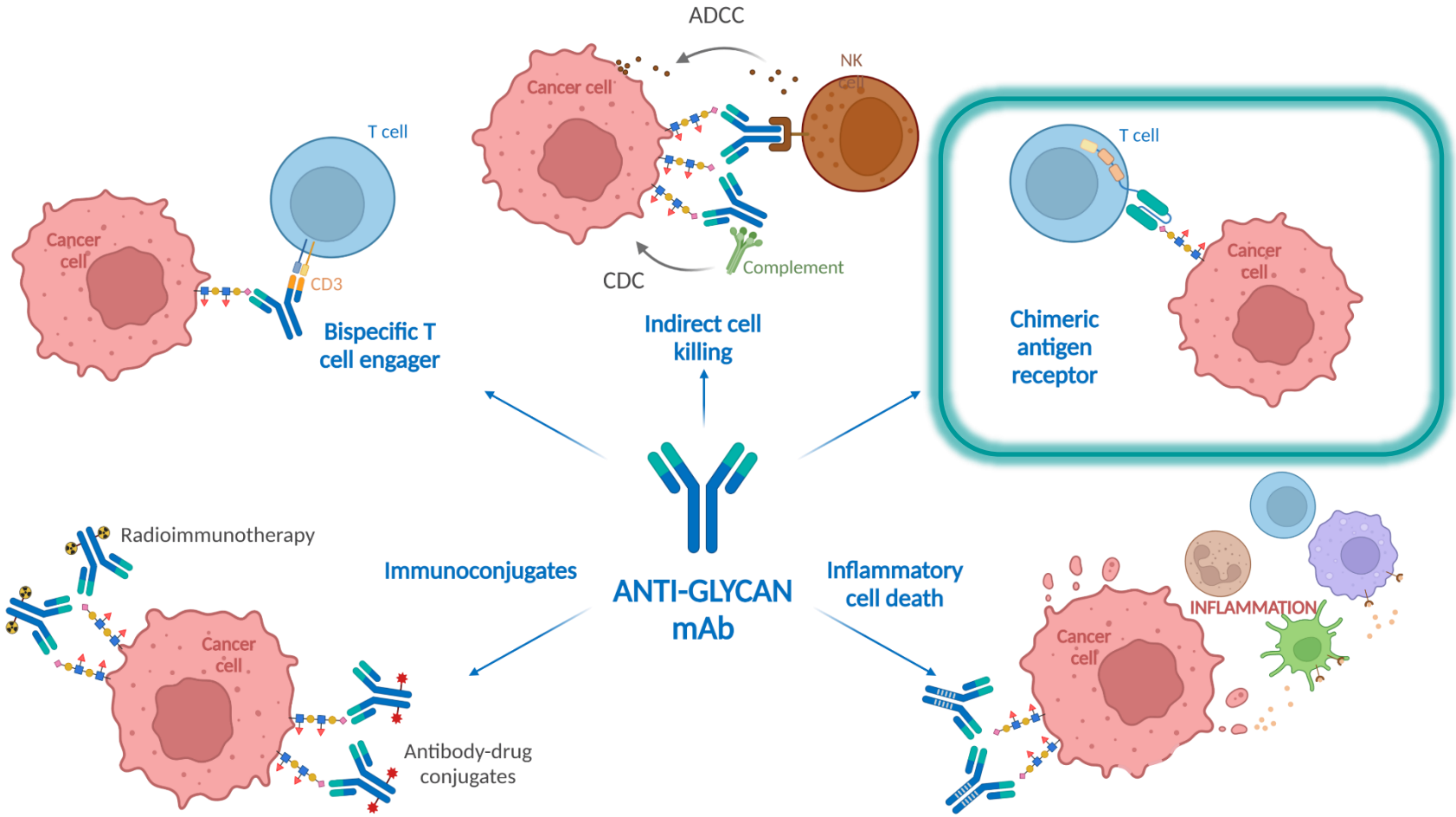
There are currently no long-term treatment options for SCLC patients

Scancell filed a patent application on anti-fucosylGM1 antibodies - publication number WO2021/043810A1

The antibody could be utilized as an antibody drug conjugate (ADC), T cell-redirecting bispecific (TCB) or chimeric antigen receptor (CAR) and is available for in-licencing

Each antibody can be developed into multiple products

Expression of same glycan on multiple proteins and lipids



NK cell = natural killer cell; ADCC = antibody-dependent cellular cytotoxicity; CDC = complement-dependent cytotoxicity

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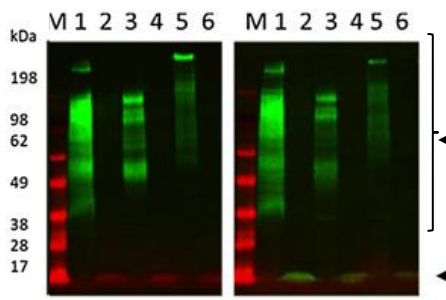
SC129 targeting sialyl-di-Lewis a for GI cancer treatment through CAR-T therapy

LSE: SCLP.L

SC129 GlyMab® targets sialyl-di-Lewis a on glycoproteins only

Sialyl-di-Lewis a is associated with multiple cell surface glycoproteins

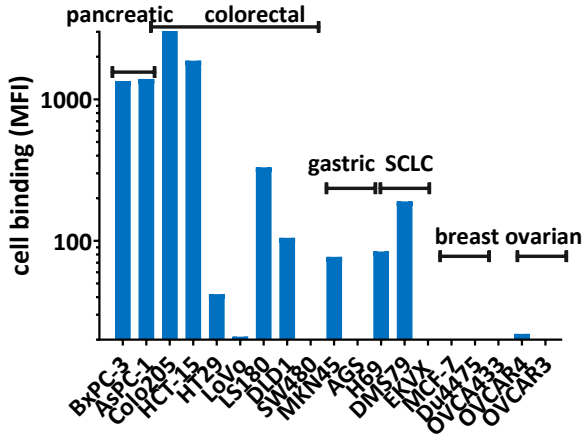


Cell lysates and lipid extracts of COLO205, HCT15 and BxPC3 (L->R)

glycoproteins

glycolipid

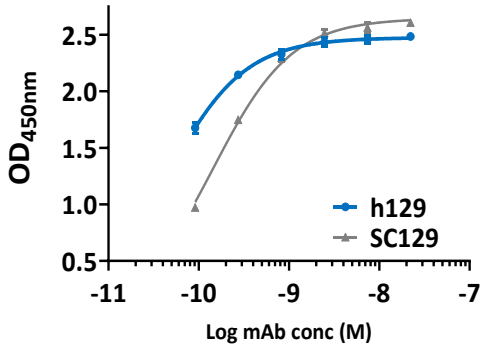
- CA19.9 (sialyl-Lewis a) is also associated with glycolipid

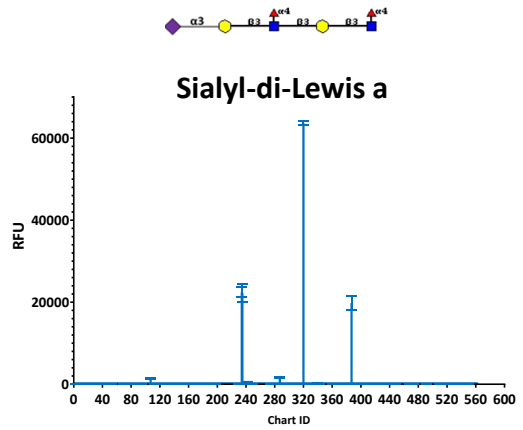


- sialyl-di-Lewis a is widely expressed on cancer cell lines

Mol Cancer Ther. 2020 Mar;19(3):790-801

Humanised SC129 lead maintains sialyl-di-Lewis a specificity

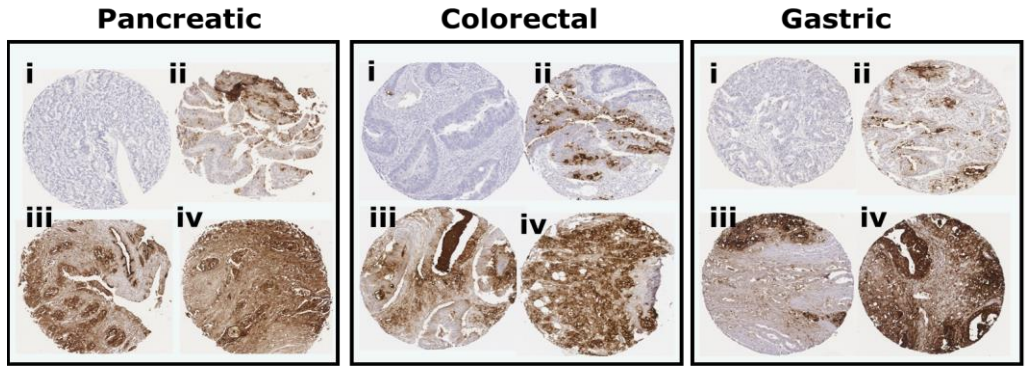




- elisa binding and high density glycan array

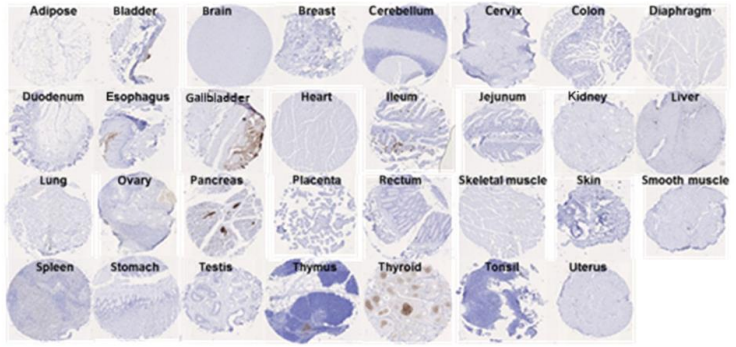
Sialyl-di-Lewis a is a GI tumour selective target with limited normal tissue distribution

SC129 targets a large percentage of pancreatic, gastric and colorectal cancer tissues



cancer	% positive tissues (n/total)
pancreatic	74 (135/182)
gastric	50 (46/92)
colorectal	36 (100/281)

Sialyl-di-Lewis a exhibits a very restricted normal tissue binding

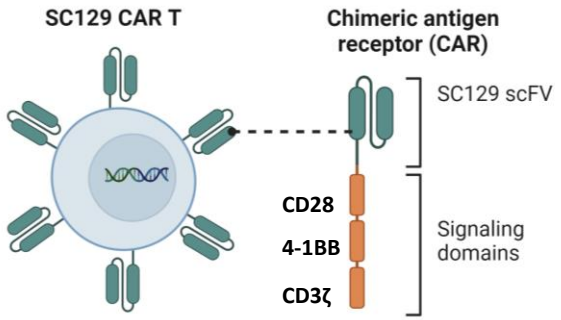


- most normal healthy tissue do not express sialyl-di-Lewis a
- a few positive tissues, in a subset of donors, with weak staining intensity

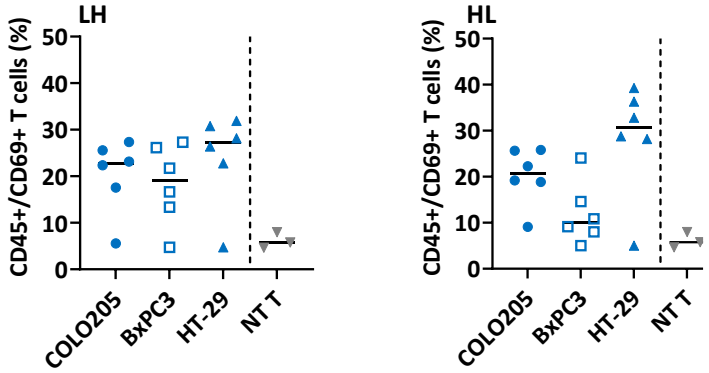
- tumour selective target => ideal for CAR development for GI solid tumour therapy

SC129-CAR targets sialyl-di-Lewis a on CRC and pancreatic cell lines

SC129-CAR, incorporates 129scFv and CD28 + 4-1BB signalling domains

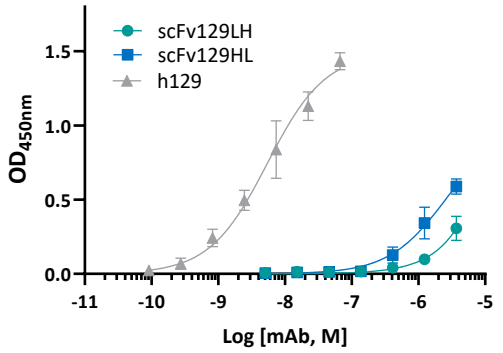


Activation of SC129-CAR T cells in target positive colorectal and pancreatic co-cultures



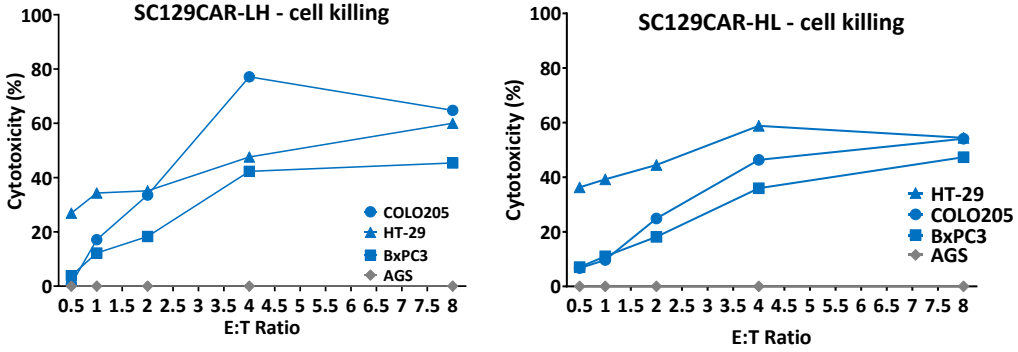
➢ T cell activation measured via CD69 expression, LH and HL scFv orientation

scFv129 retains target binding



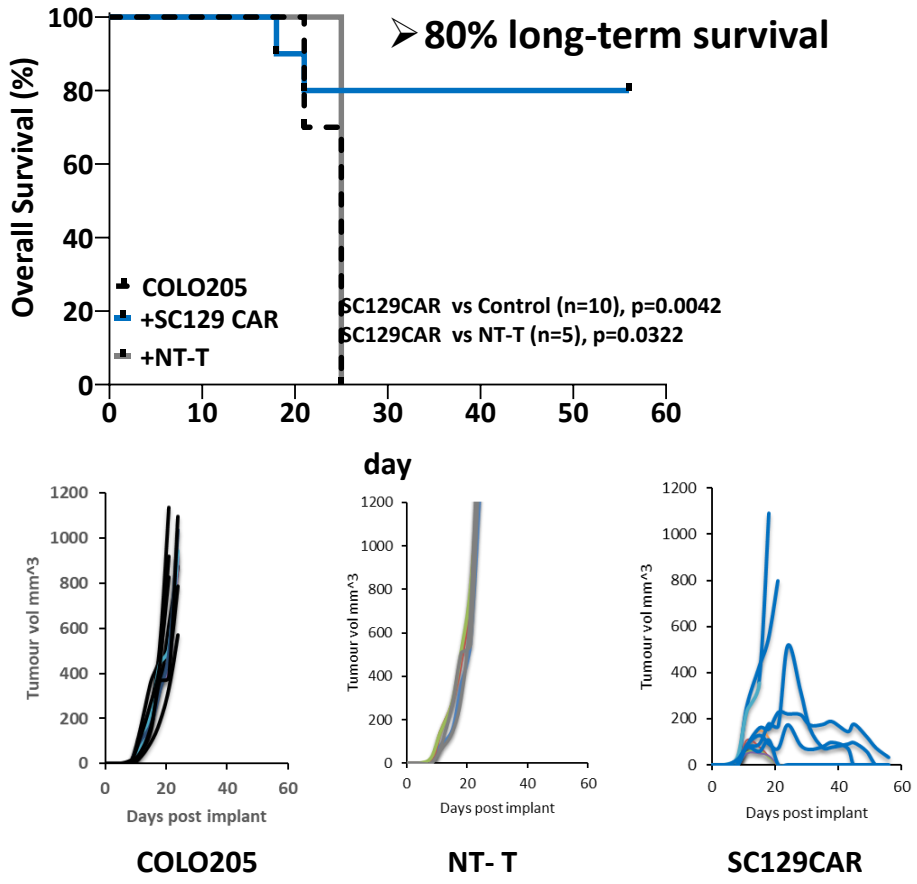
➢ ELISA target binding by scFv129

SC129 CAR displays effective *ex vivo* killing of target positive cell lines

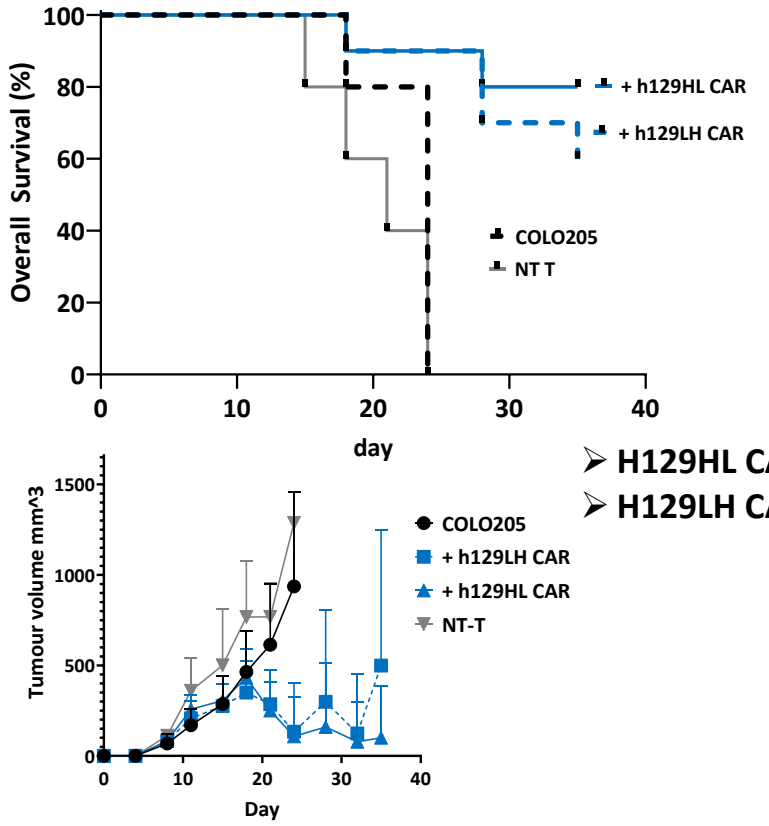


SC129-CAR T cells deliver very effective tumour control *in vivo* (NSG)

Significant anti-tumour impact by SC129-CAR T (COLO205, NSG)



Significant anti-tumour impact by h129-CAR T (COLO205, NSG)



- **H129HL CAR : 80% survival**
- **H129LH CAR: 60% survival**

SC129 GlyMab® - a sialyl-di-Lewis a targeting antibody

- **SC129CAR targets sialyl-di-Lewis a on glycoproteins only**
- **Therapeutic potential in GI cancers**
- **Extensive tumour but low normal tissue binding compared to sialyl-Lewis a binding antibodies**
- **Licensed to Genmab for antibody drug conjugates (ADC), T cell bispecifics (TCB) and radioimmunotherapy, rights to chimeric antigen receptor (CAR) therapy available**
- **Patent filed on sialyl-di-Lewis a antibodies - publication number WO2017/033020A1**

Thank you

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