

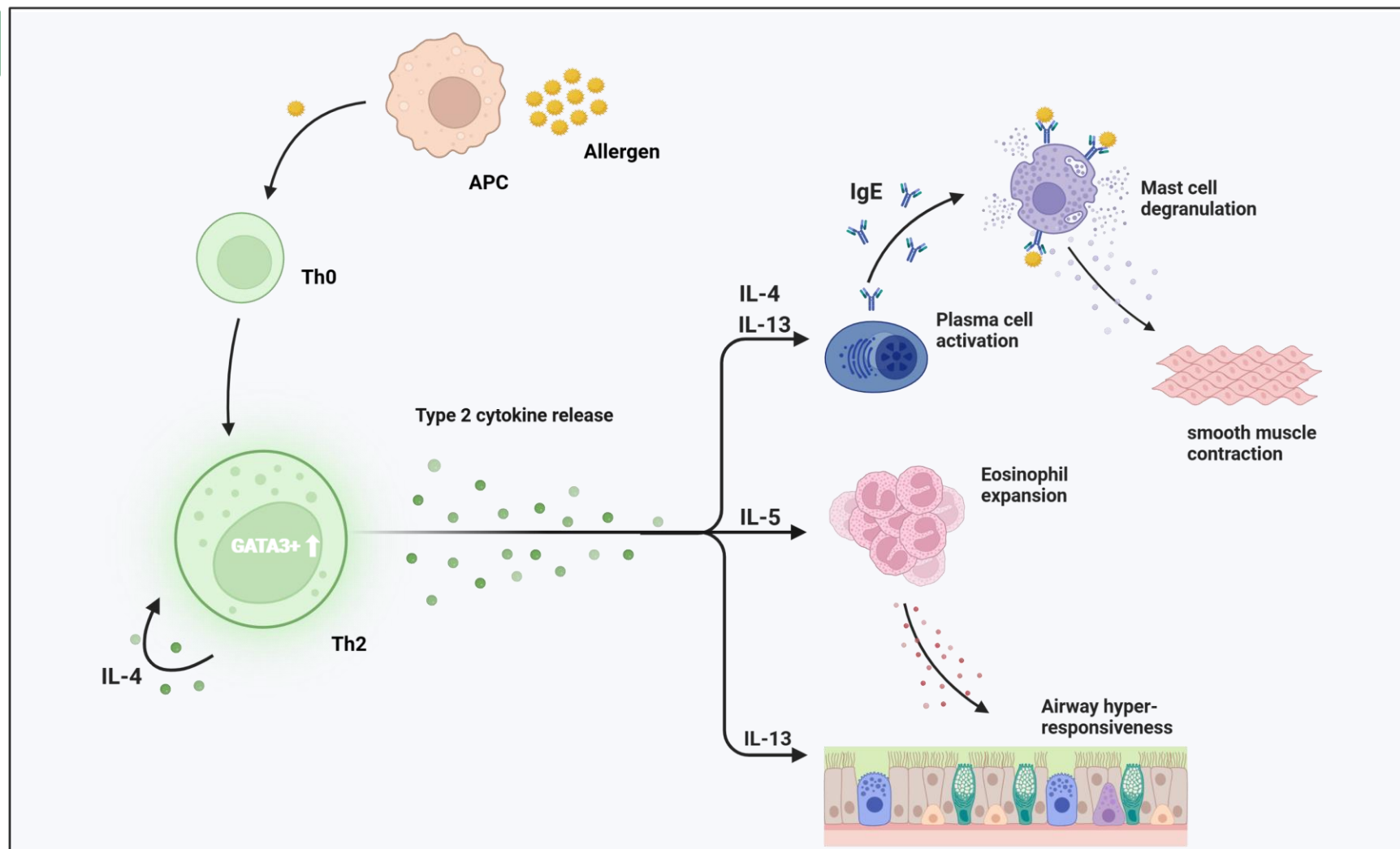
PBAE-Based Pulmonary siRNA Delivery to T-Cells

A Potential Approach for Asthma Therapy

Anny Nguyen
17th July 2025

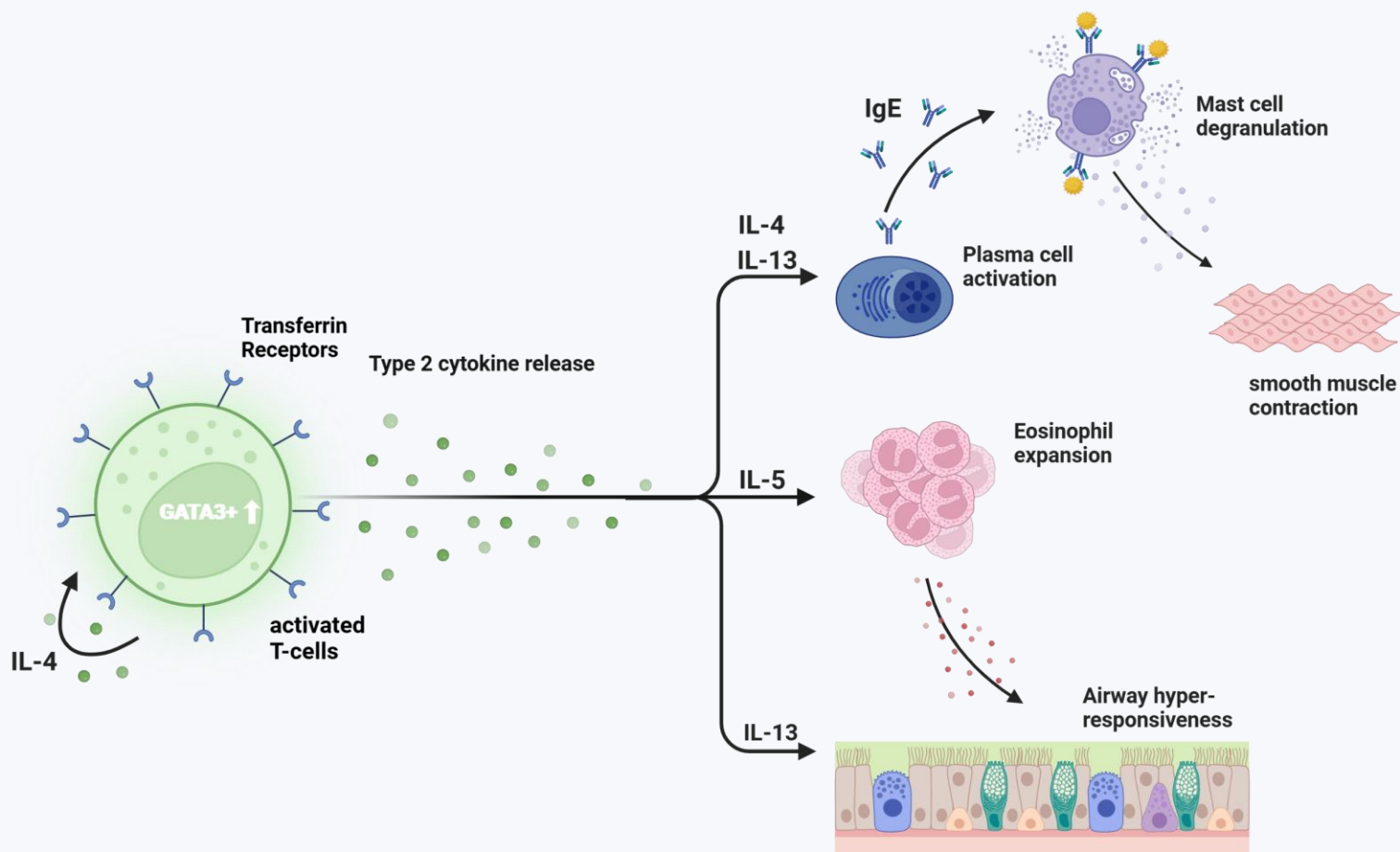
Merkel Group

→ GATA3 expression ↑



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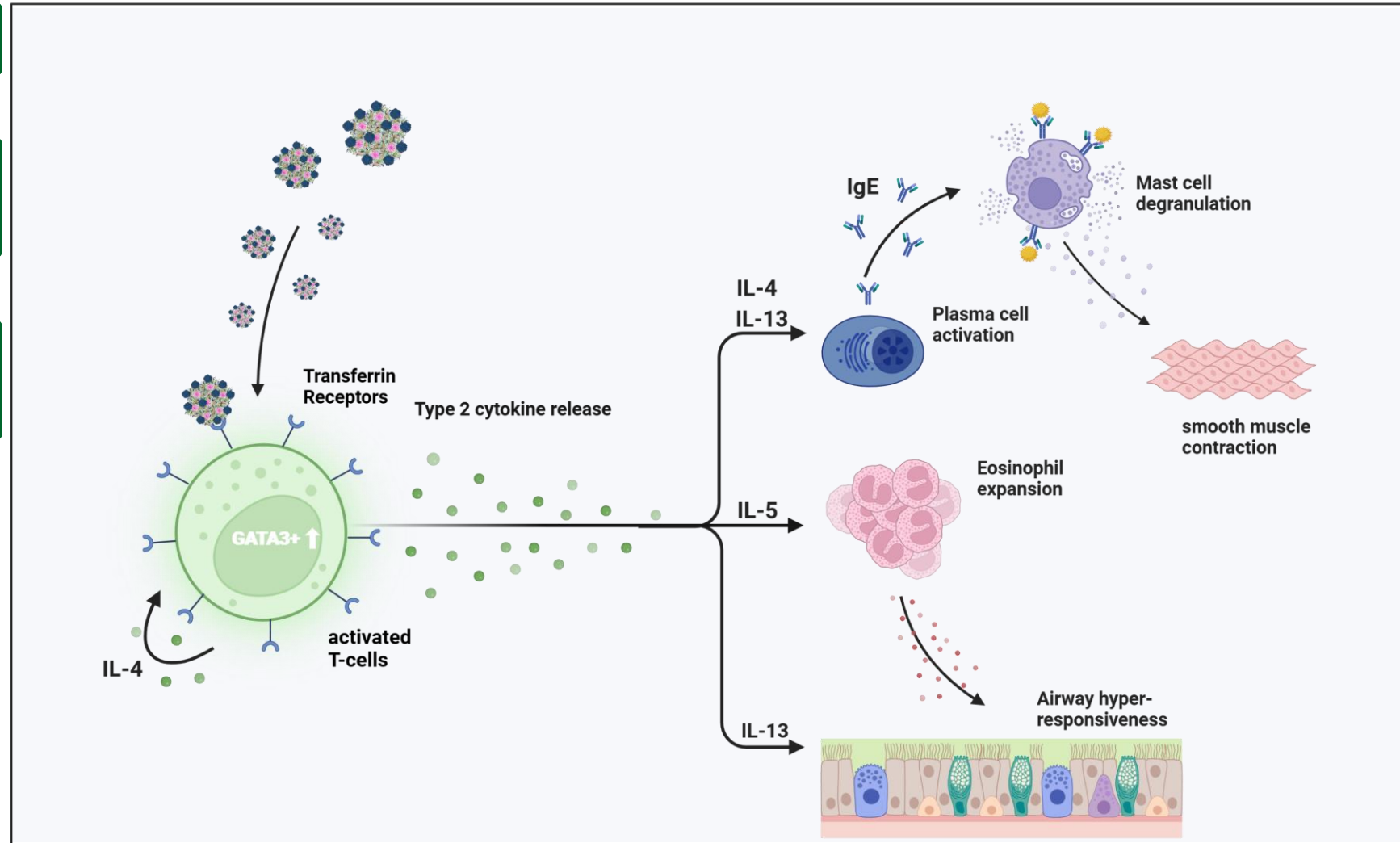
→ Transferrin Receptors in
activated T-cells ↑



→ GATA3 expression ↑

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activated T-cells ↑

→ Transferrin decorated siRNA
nanocarriers against GATA3

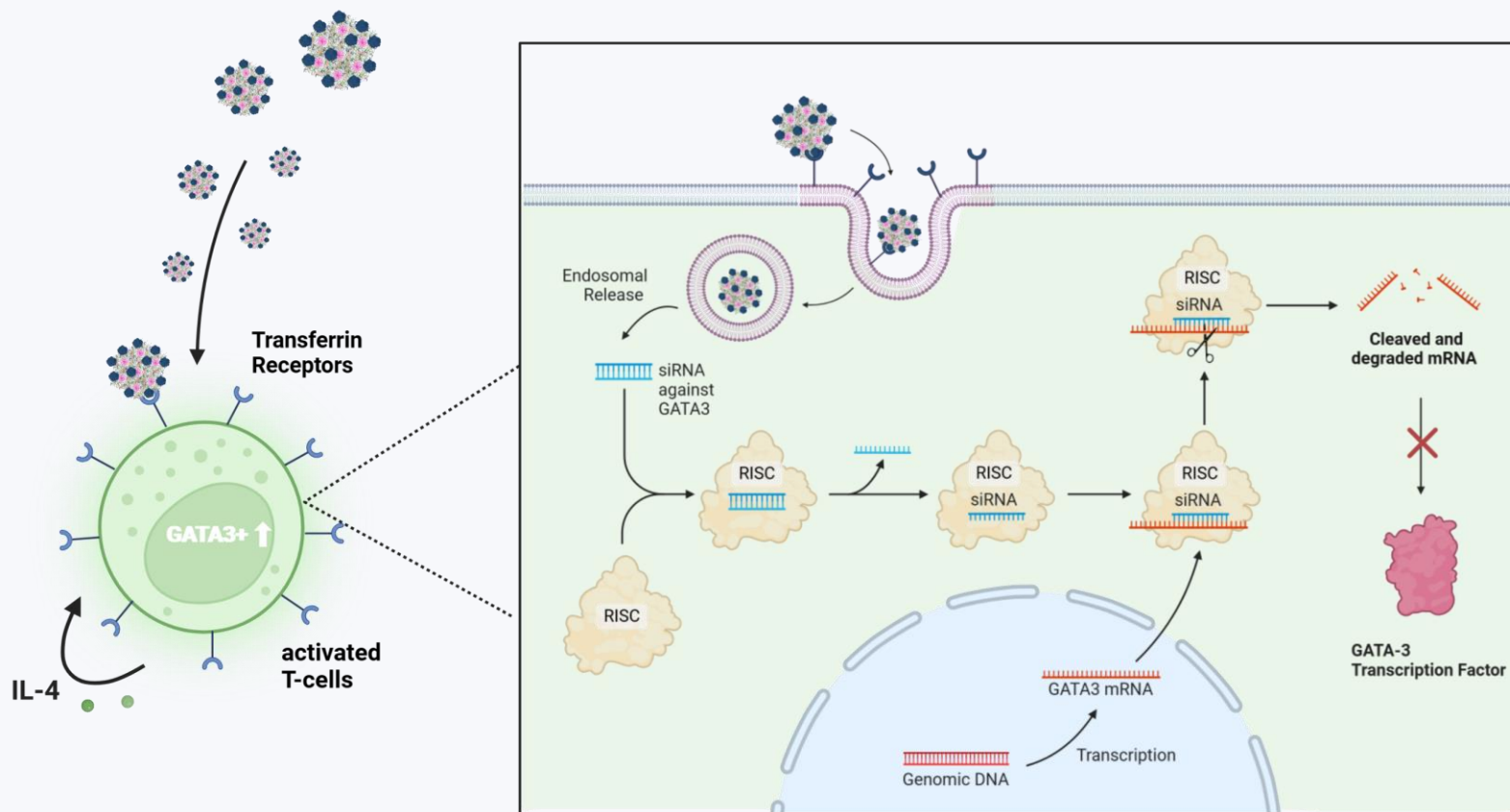


→ GATA3 expression ↑

→ Transferrin Receptors in
activated T-cells ↑

→ Transferrin decorated siRNA
nanocarriers against GATA3

→ siRNA degrades GATA3
mRNA



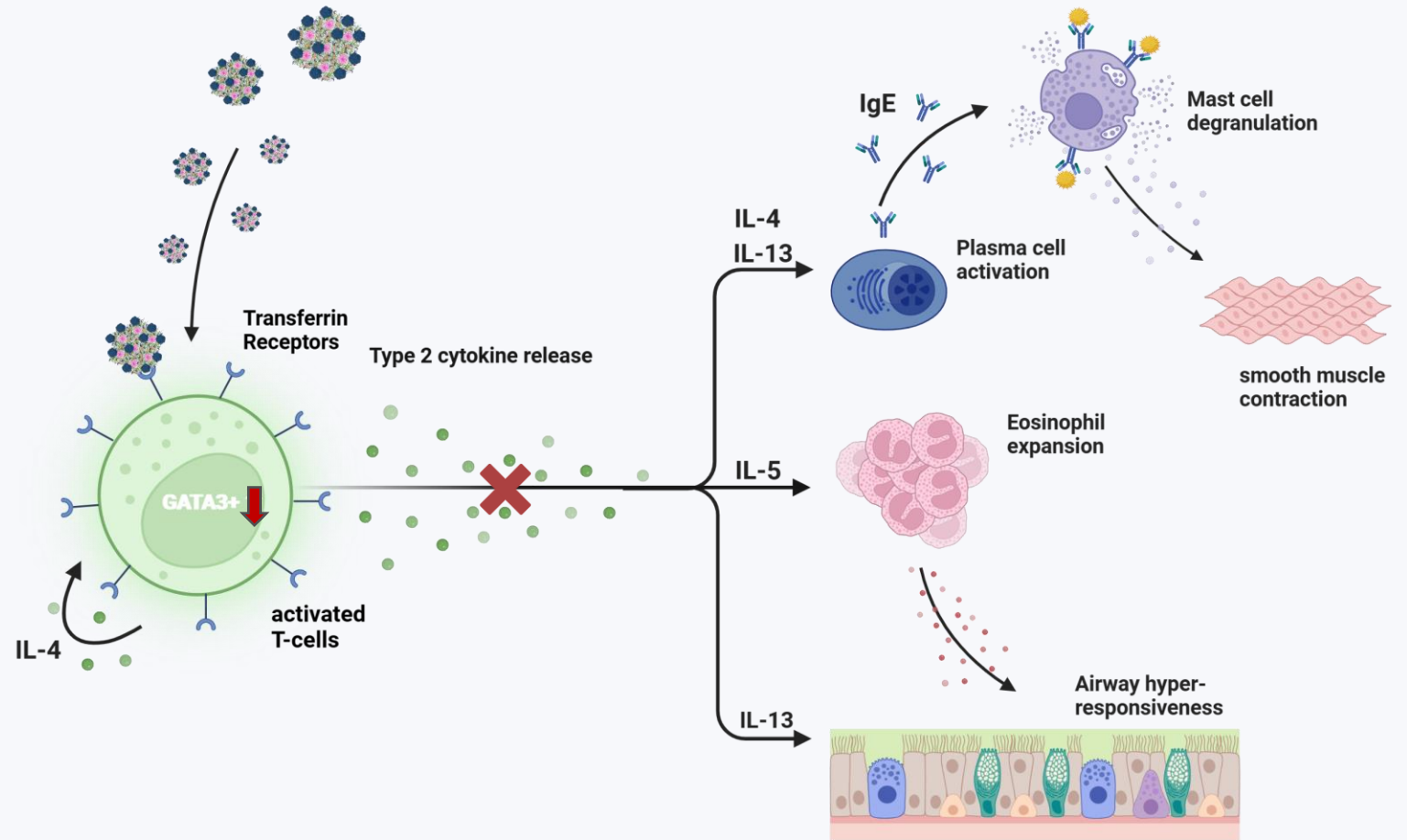
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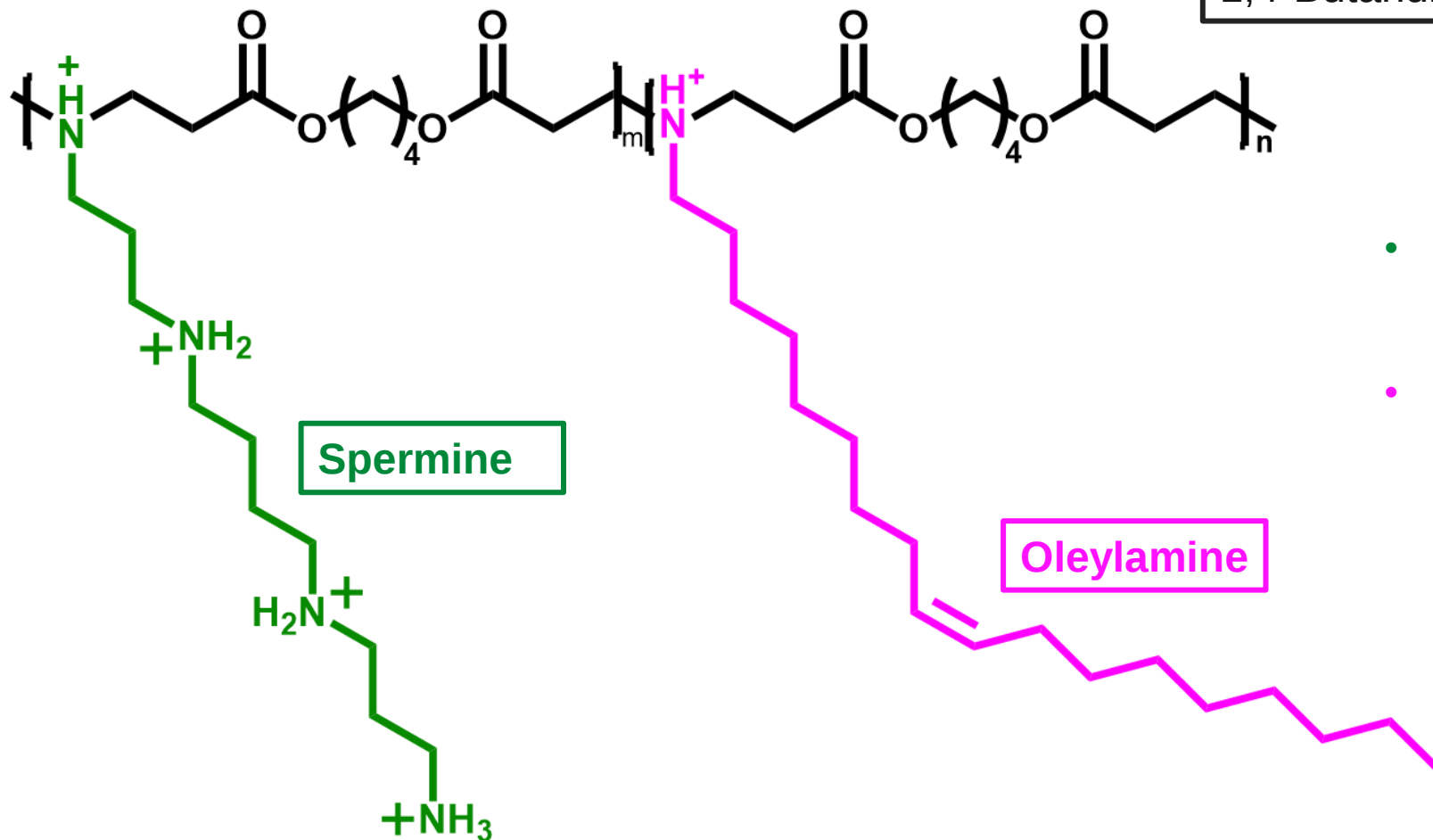
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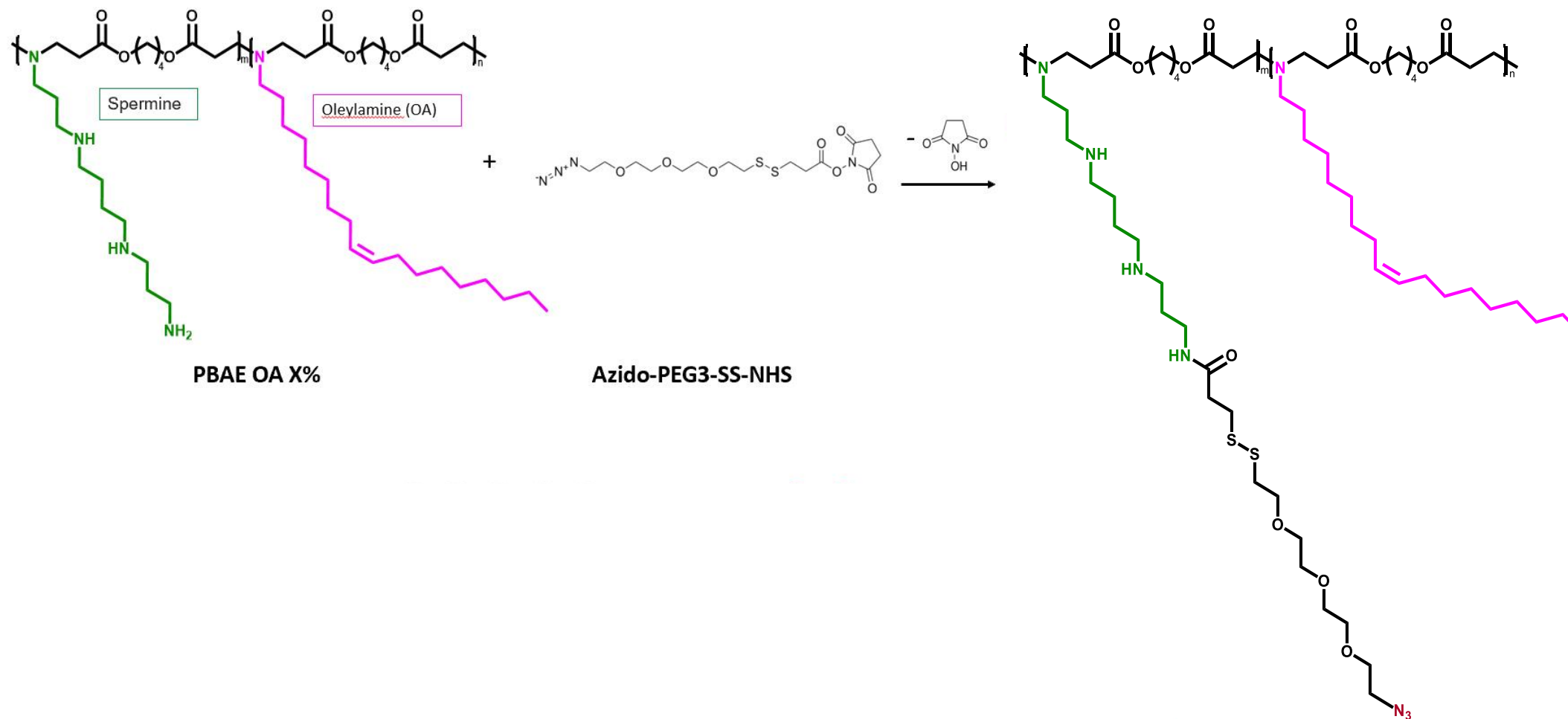
→ Inflammatory cytokines ↓



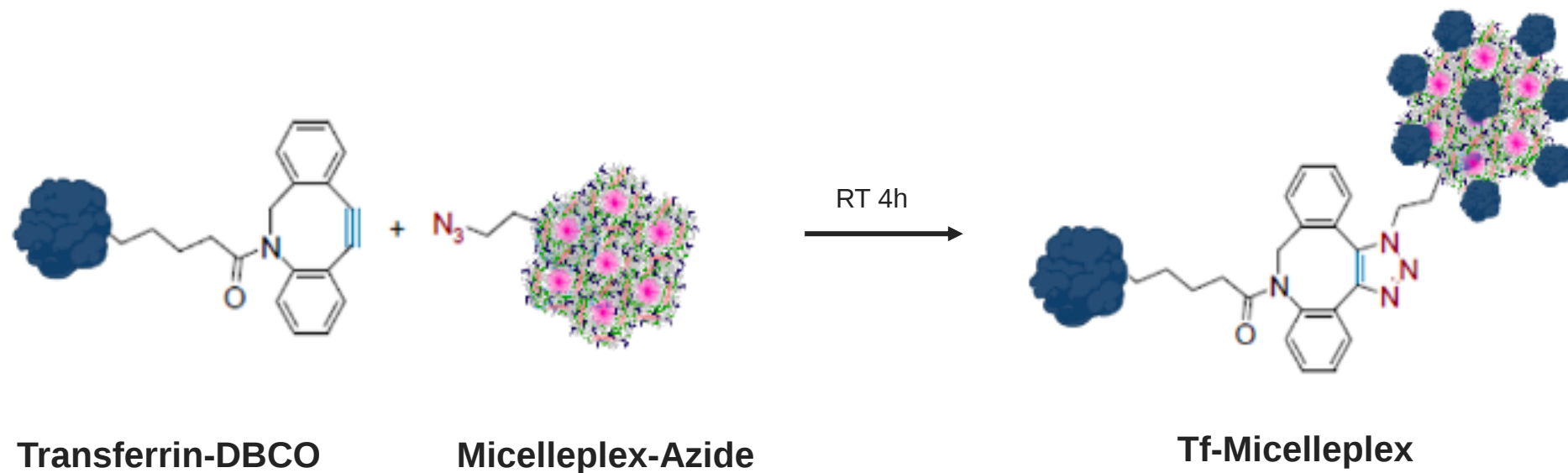
1,4-Butandiol Diacrylate Backbone

• Encapsulation Efficiency • Endosomal Escape 

Particle Functionalization and Formation



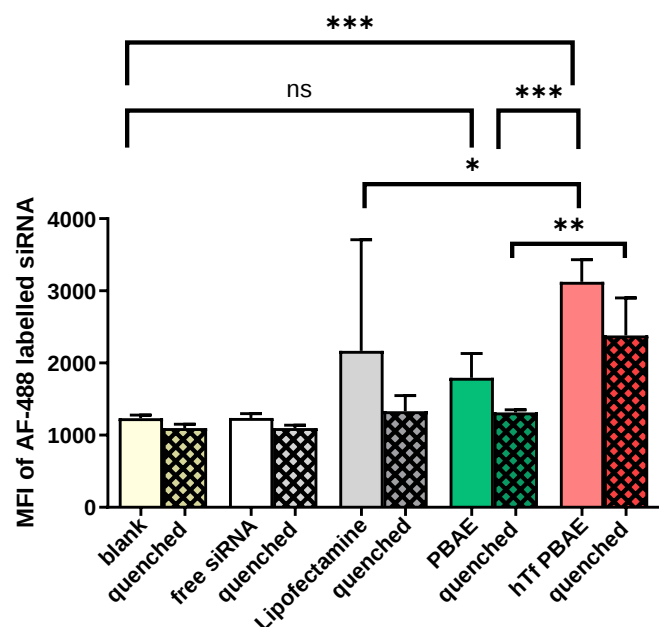
Postmodification: Transferrin Conjugation



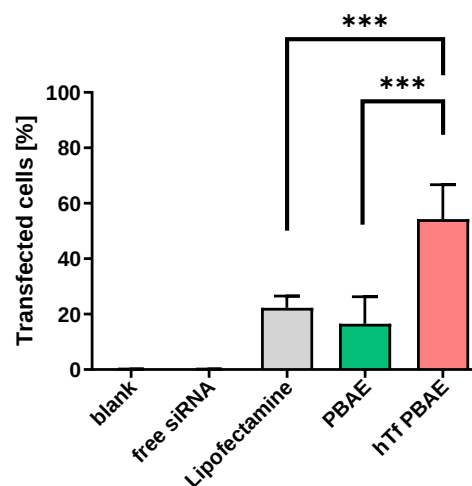
Evaluation of cellular uptake

- Cellular uptake experiments were performed in 500 000 T-cells/well utilizing 25 pmol AF488-labeled siRNA and Micelleplexes with and without conjugated Transferrin
- Evaluation was performed by flow cytometry after 4h incubation time

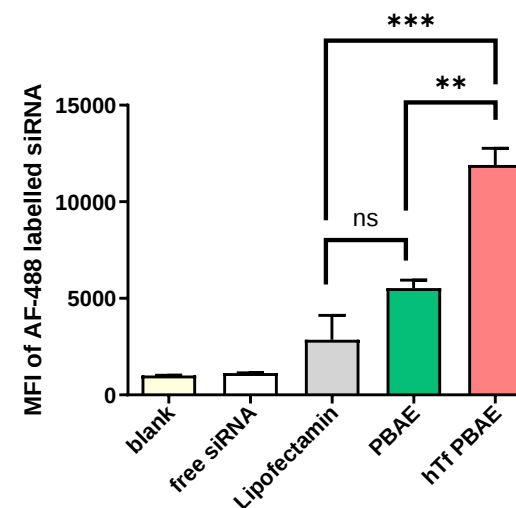
Jurkat cells



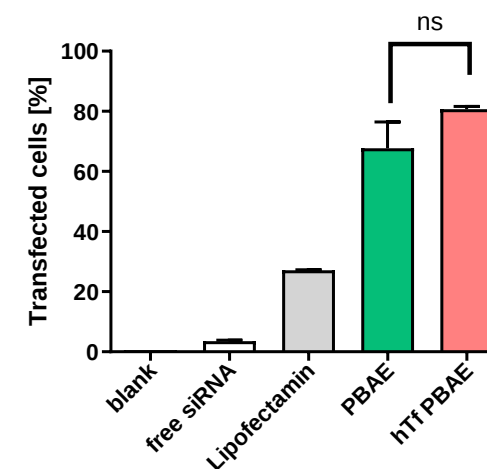
Transfected cells [%]



Primary human Th₂-cells

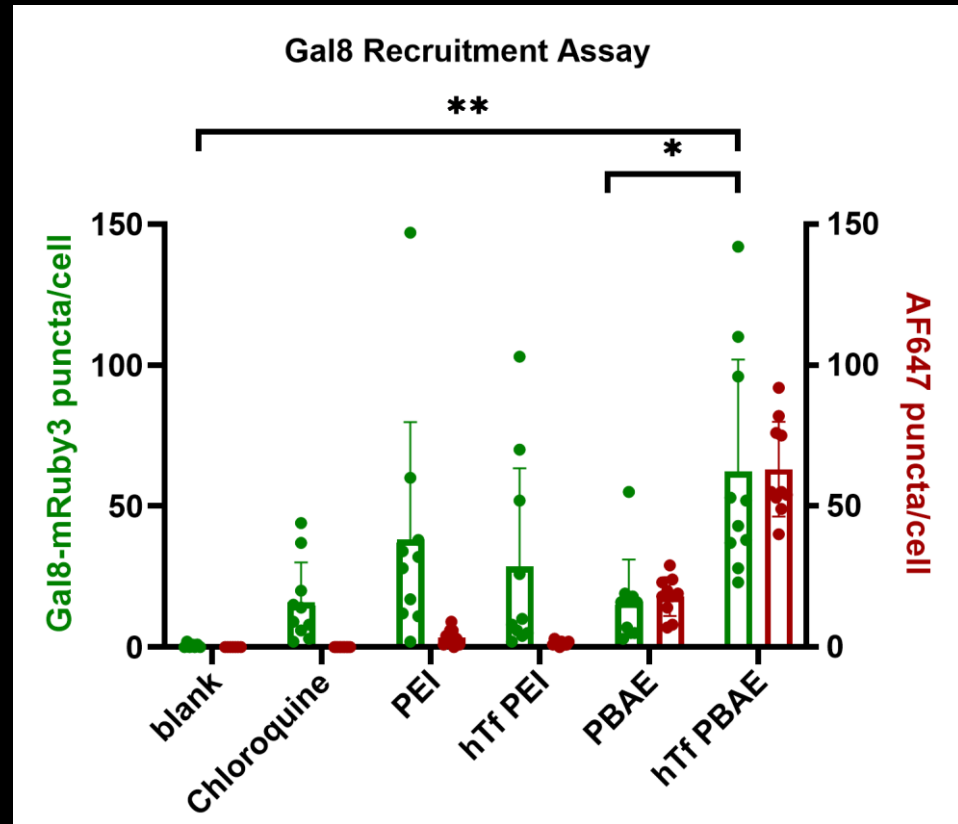


Transfected cells [%]



Gal-8 Recruitment Assay: Evaluation of the Endosomal Escape Potential

- Incubation of **50 pmol** labelled siRNA particles in **10 000 Hela-Gal8-mRuby3 cells/well**
- Evaluation was performed by confocal microscopy after **24h** incubation time



blank

Tf-PEI

PBAE

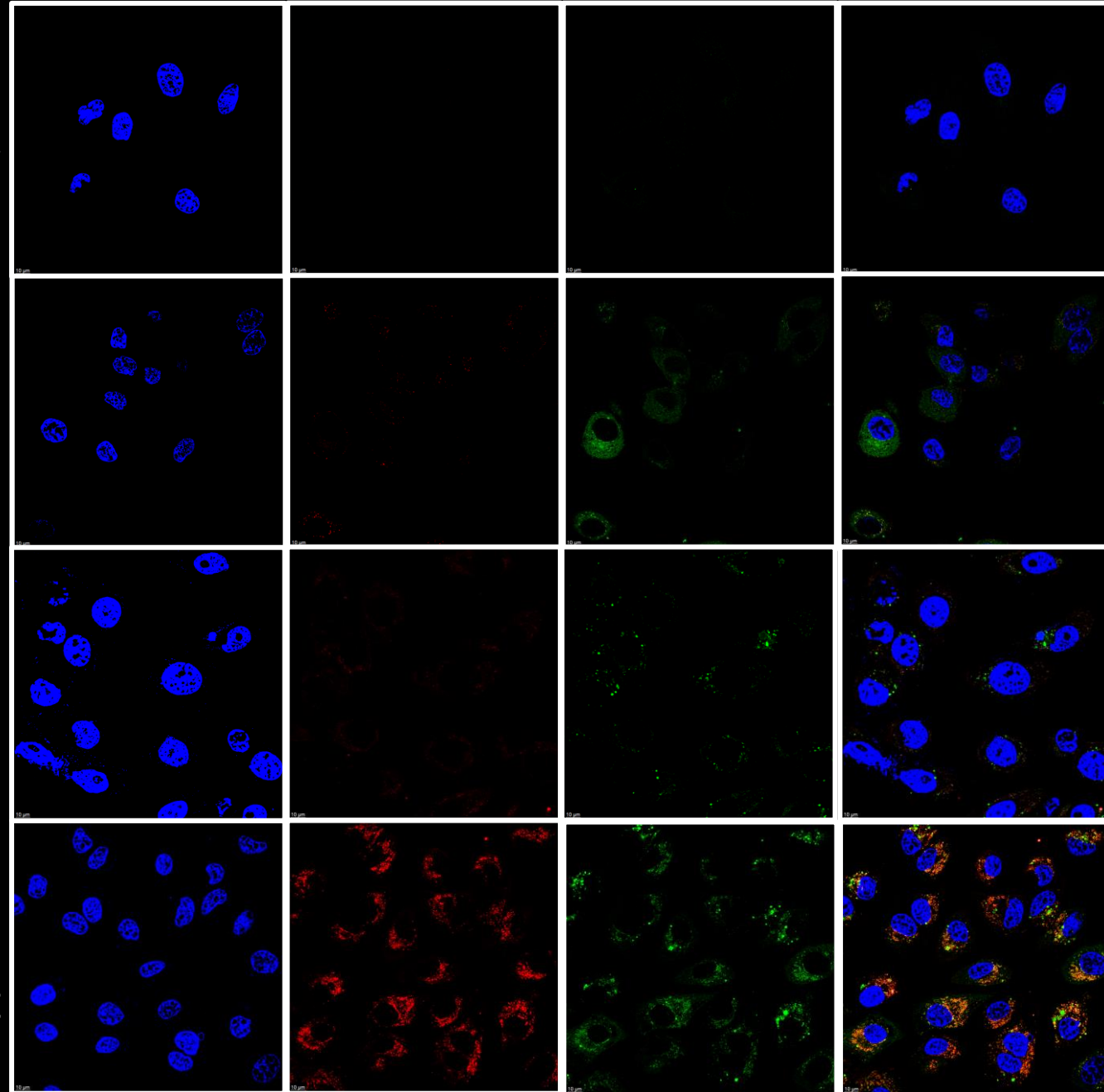
Tf-PBAE

DAPI

siAF647

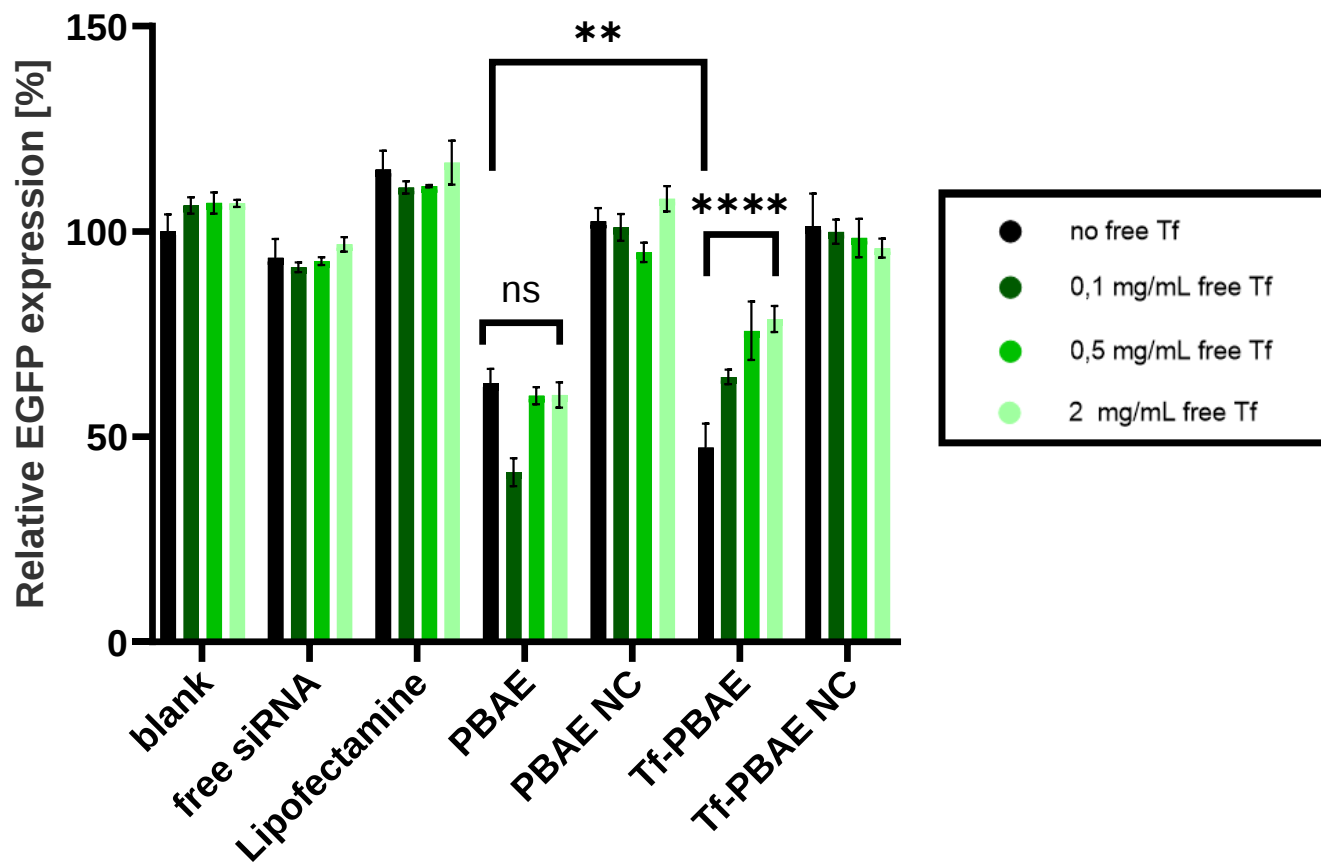
mRuby

merged



Evaluation of Gene Knockdown Potential

- **100 000 Jurkat Cells/well** were activated with **100 nM PMA** and **0,25 µM Ionomycin**
- Knockdown experiments were performed utilizing **50 pmol siEGFP** and **Micelleplexes with and without conjugated Transferrin**
- Evaluation was performed by **flow cytometry after 48h incubation time**



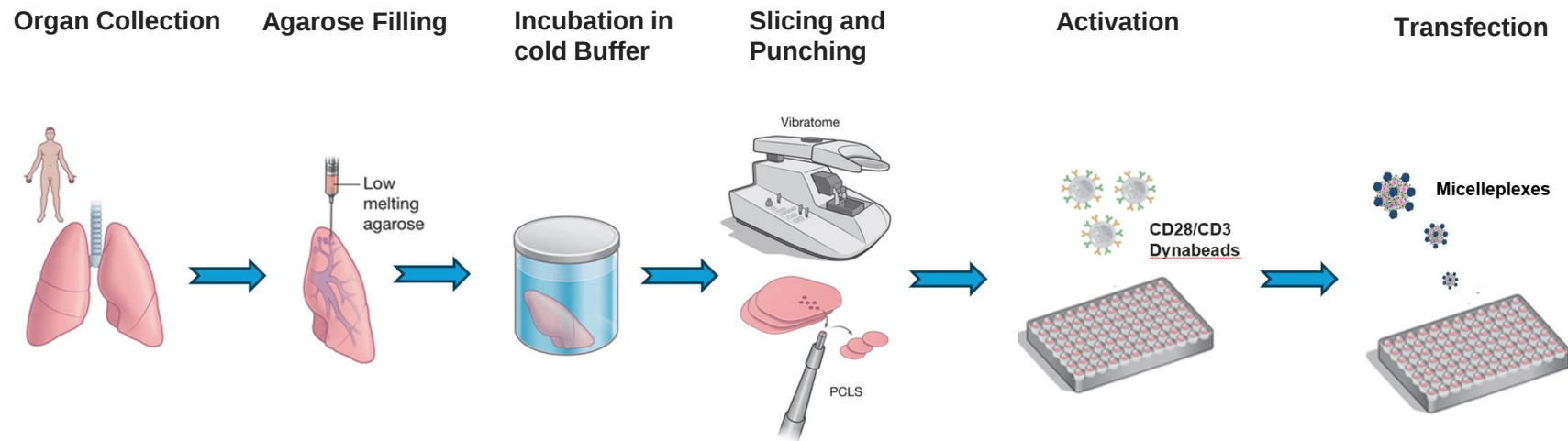
→ Knockdown efficiency of targeted particles enhanced compared to non-targeted *in vitro*

→ Receptor competition reduces knockdown efficiency for targeted particles

Tf-PBAE Micelleplexes: GATA-3 Knockdown in Human Lung Tissue

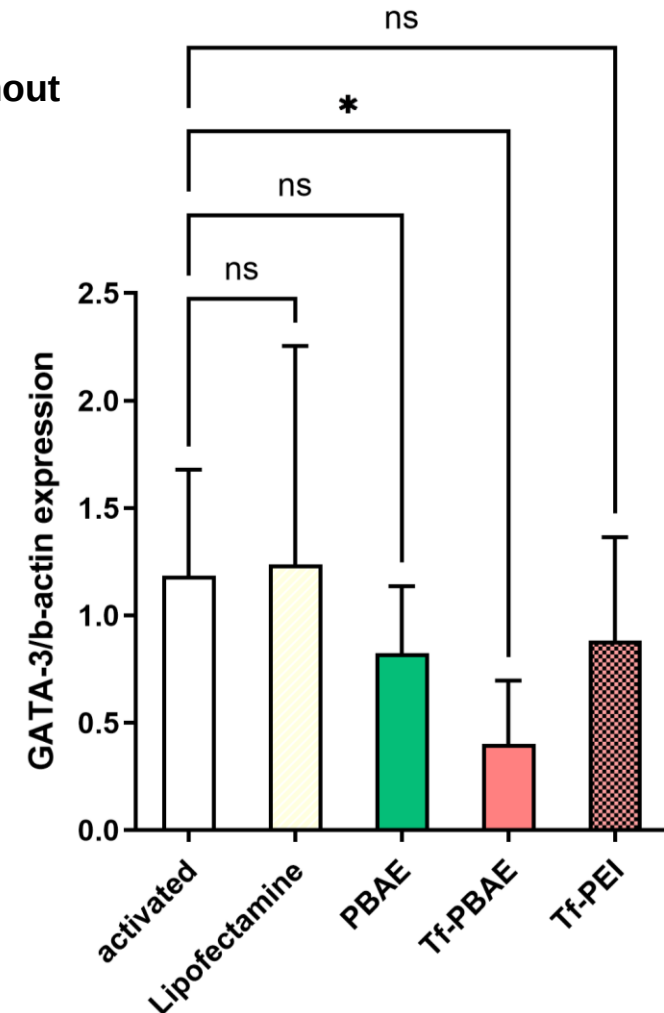
Evaluation of Therapeutical Knockdown

- **Three lung slices/well** were activated with **CD3/CD28 Dynabeads** for **72 h**
- Knockdown experiments were performed utilizing **100 pmol siGATA3** and **Micelleplexes with and without conjugated Transferrin** for **48 h**
- Evaluation was performed by **Real Time qPCR**

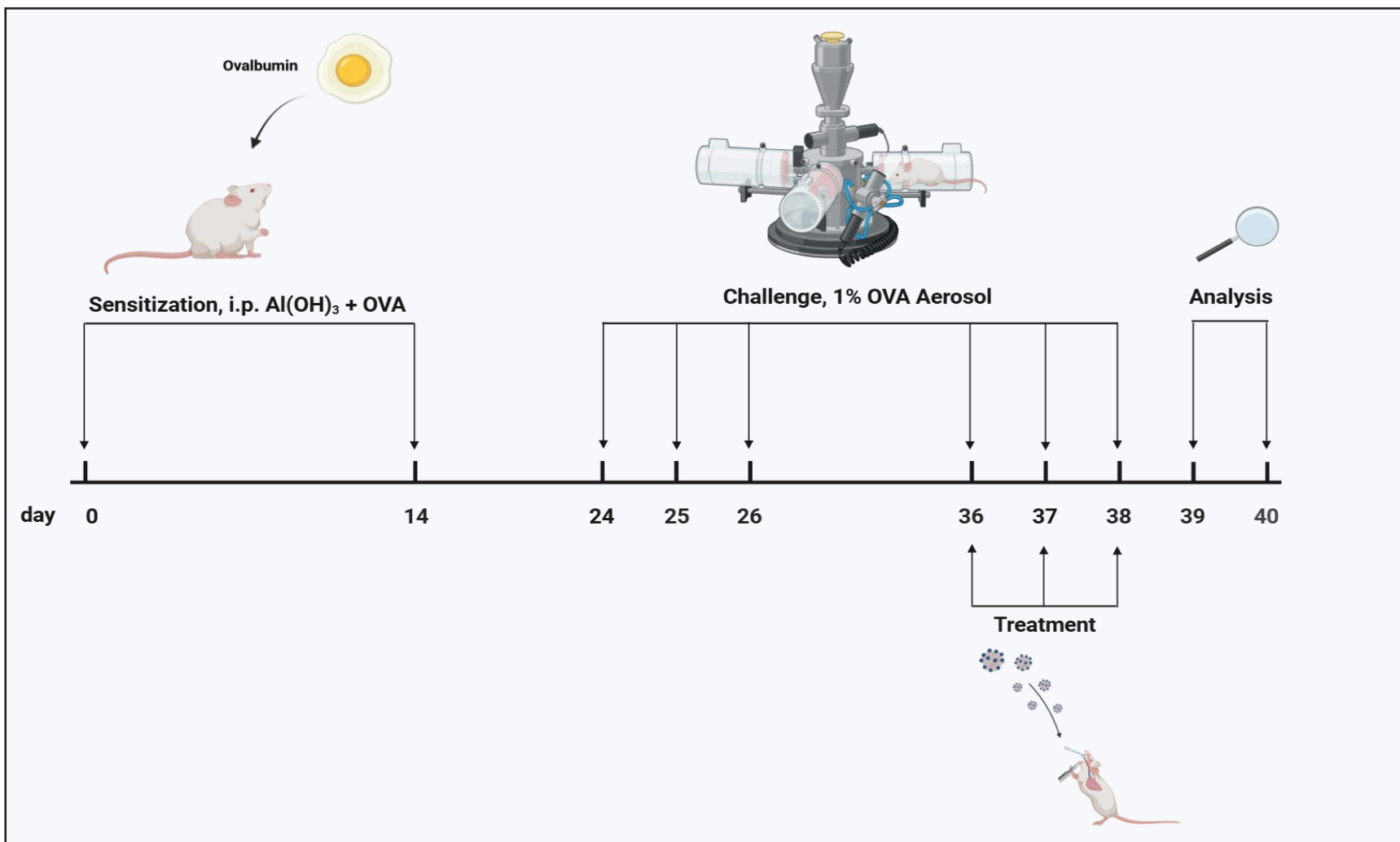
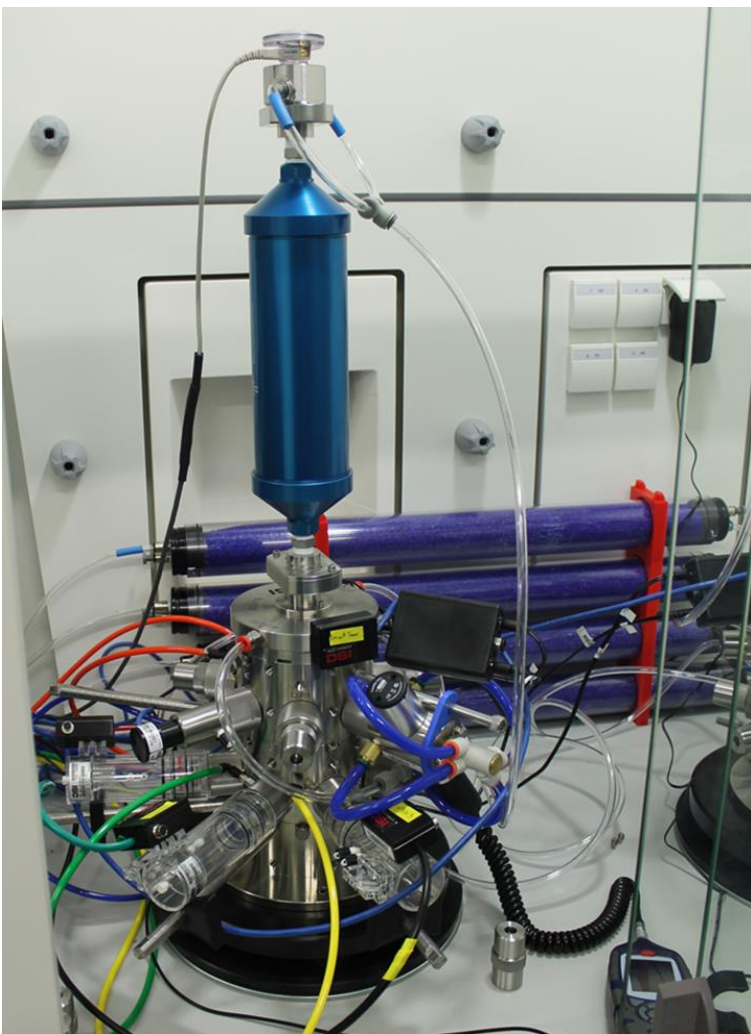


→ Significant enhancement of knockdown efficiency observed in *ex vivo* human lung tissue

GATA-3 Knockdown in PCLS

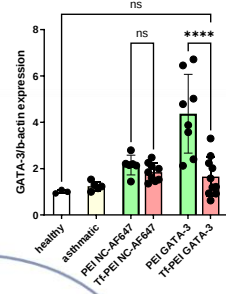


Sneak Preview: *In vivo* studies

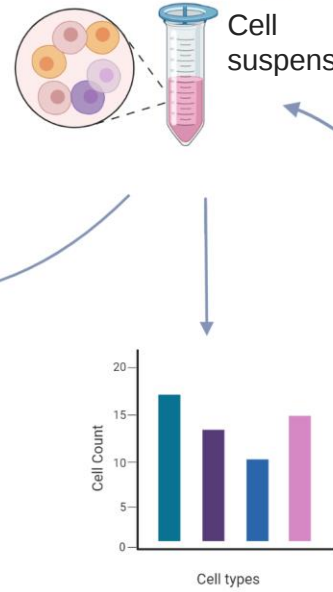


Sneak Preview: *In Vivo* studies

GATA-3 expression

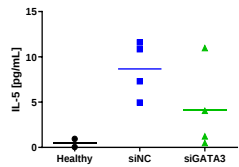


Cell suspension

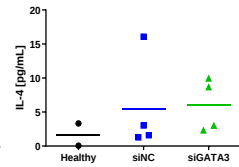
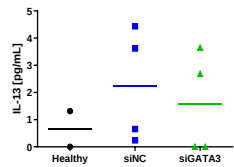


Cell Count

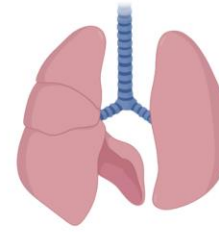
Single Cell Suspension



Cytokine Concentration in BALF



Cytokine concentration

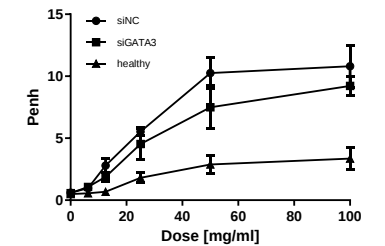
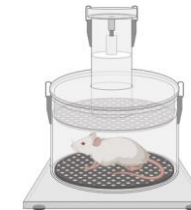


Histological analysis



BAL

BALF



Methacholine Challenge

LMU

LUDWIG-
MAXIMILIANS-
UNIVERSITÄT
MÜNCHEN

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Merkel Group



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