

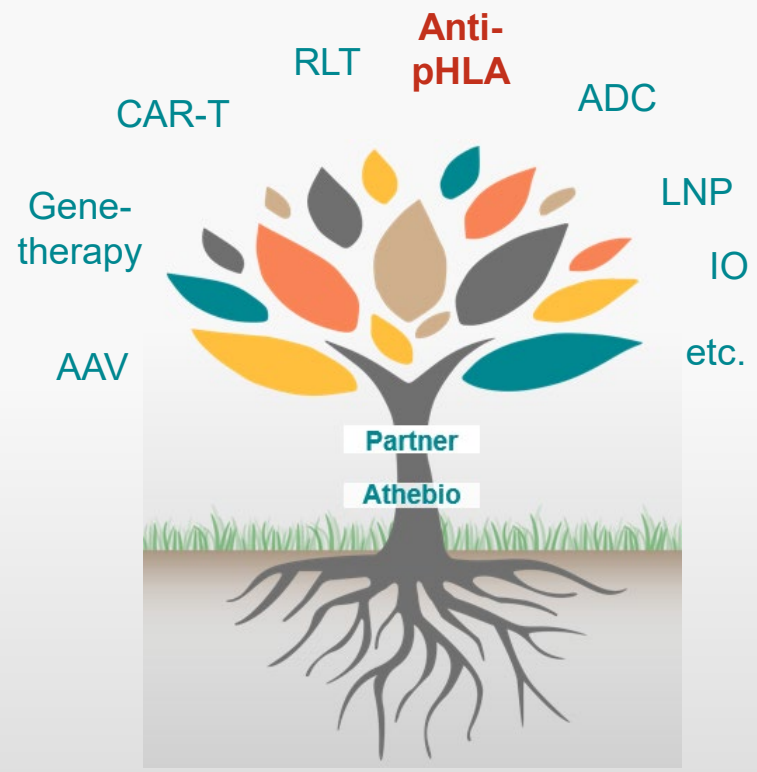
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Athebody[®] Technology

**Enabling
Next-generation
pHLA Therapeutics**

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Our roots: Designed Ankyrin Repeat Proteins (DARPin^s)



Knowhow, Patents
Athebody[®] DARPin^s &
libraries

Purpose

- We are here to enable drug developers to create superior targeted therapeutics of **advanced efficacy and safety** and thereby increased probability of **clinical success**.

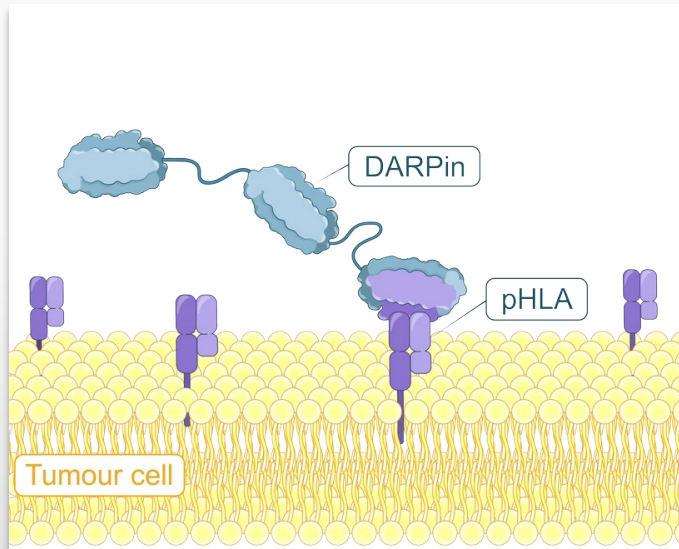
Vision

- We revolutionize drug development by bringing the design and selection of DARPin^s to perfection and establish them as **state-of-the-art** building blocks of targeted therapeutics. We aim for **high return on investment** for our partners and us through **collaborative breakthrough innovation**.

Mission

- We **enable** innovative drug developers to create superior targeted therapeutics by providing them with **tailor-made** “plug and play” DARPin^s, working together in a co-creative space, and supporting them with **in-depth expertise** and superb service.

Next-generation of pHLA Therapeutics



pHLA Therapeutics

- Complexes formed by the human leukocyte antigen (HLA) and peptides derived from intracellular proteins (pHLA complexes) **extend the druggable target space**.
- The development of pHLA therapeutics is extremely challenging because of possible toxic on- or off-target effects. Thus, **increasing the therapeutic window** of such drugs is key.
- T- cell receptor (TCR) mimetics (TCRms) are pHLA therapeutics engineered to overcome the limitations of natural TCRs (e.g., low affinity, low specificity and low stability).

Athebio

- We provide tailor-made **DARPin building blocks** to create superior TCRms of advanced efficacy and safety and thereby **increase the probability of clinical success** for our partners.




Limitations and Needs of pHLA Therapeutics



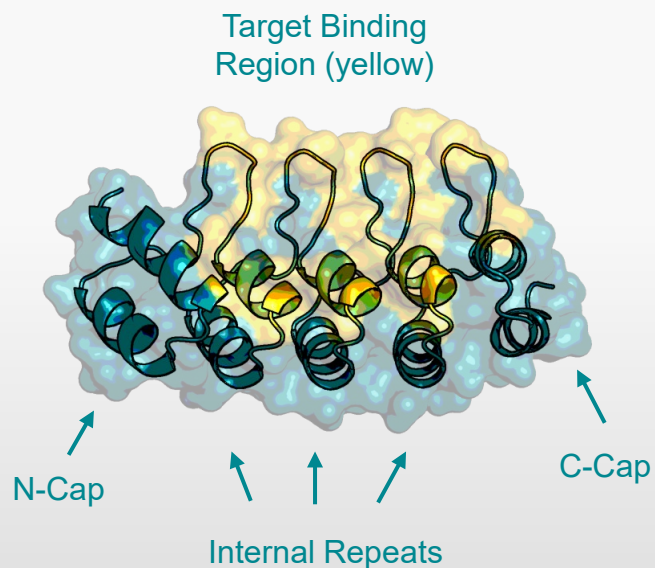
Our solution: Athebody[®] DARPin Building Blocks

Needs

-  Safety: manageable toxicity
-  Efficacy: long-lasting response
-  Good Manufacturability
-  Strong protection and FTO

-  Unparalleled binding specificity and simple to generate multi-specificity; Straightforward “plug and play” format tuning, e.g., to prevent T cell exhaustion
-  Best-in-class DARPins with superb and reliable developability properties
-  Athebody[®] DARPins are covered by a strong IP portfolio and with good FTO prospects

Athebody[®] building blocks are based on **clinically validated, hyper-versatile** DARPs



Hyper-versatility

- DARPs are based on natural ankyrin repeat proteins and exceed the versatility of immunoglobulins by far (Stumpff M.T. et al. 2020).

Clinical validation

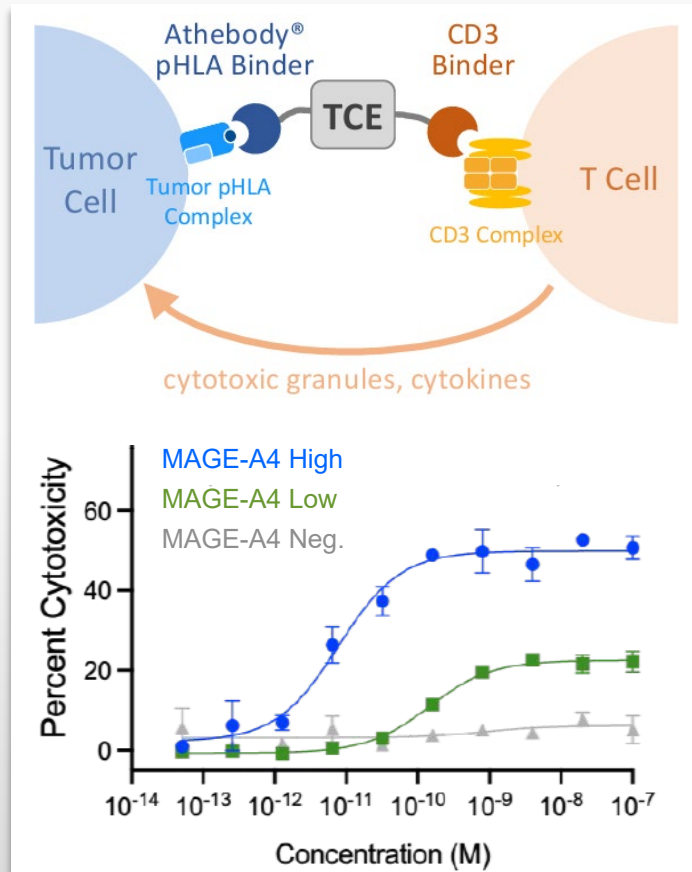
- DARPs are clinically fully validated by Molecular Partners and their collaborators.

Athebody[®] DARPs

- Rigid-body binding provides **exceptionally high (pHLA) target specificity** and affinity (down to single digit pM).
- **Ease to generate multi-specificity** far beyond bi-specifics.
- **Plug & play**: Easily plug into immunoglobulin formats.
- **Superb developability** with no aggregation tendency based on exceptionally high thermal stability (Schilling J. et al. 2021)

Case Study: Athebody[®] DARPin T-cell engagers (TCEs)

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DARPin-TCE and LDH release assay figures adapted from Ramirez A. et al. 2022

Generation of Athebody[®] DARPin TCEs

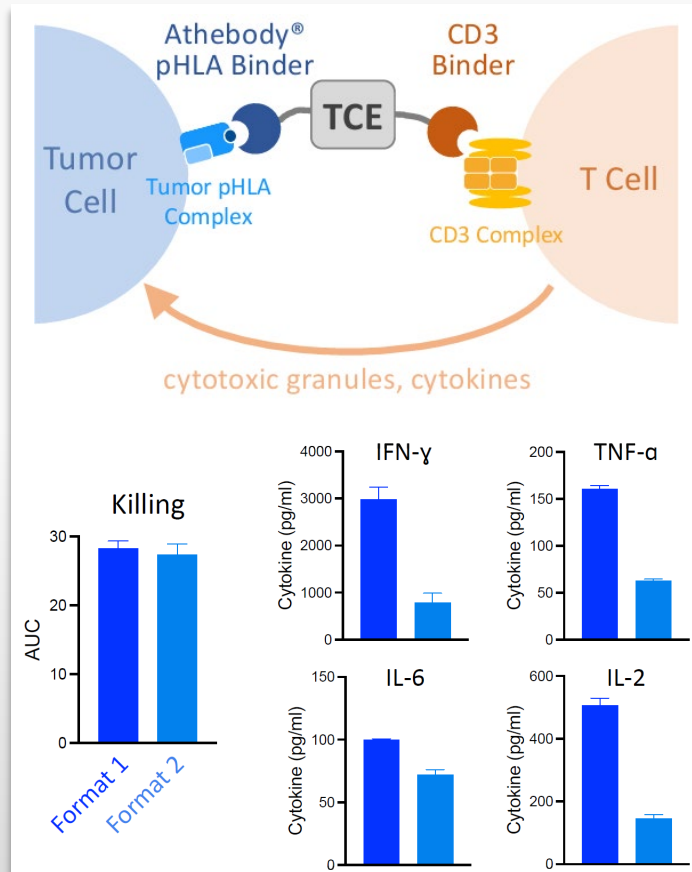
- 3T-Biosciences teamed up with us to generate next-generation of pHLA Therapeutics using our Athebody[®] DARPin building blocks.
- We selected highly specific Athebody[®] binders against a peptide from the cancer-germline antigen MAGE-A4 bound to HLA-A2.
- 3T-Biosciences easily plugged these Athebody[®] building blocks into their TCE formats comprising CD3 binding functionality.

Exceptional Therapeutic Window

- LDH release assay (E:T = 10:1, 48 hrs).
- The resulting DARPin-TCEs induce high potency killing of MAGE-A4-expressing cancer cell lines (MAGE-A4 Low: ~30 pHLA molecules/cell) with no detectable killing of corresponding antigen-negative cells (CRISPR/Cas9 k-o).

Case Study: Athebody[®] DARPin T-cell engagers (TCEs)

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DARPin-TCE and cytokine release assay figures adapted from Ramirez A. et al. 2022

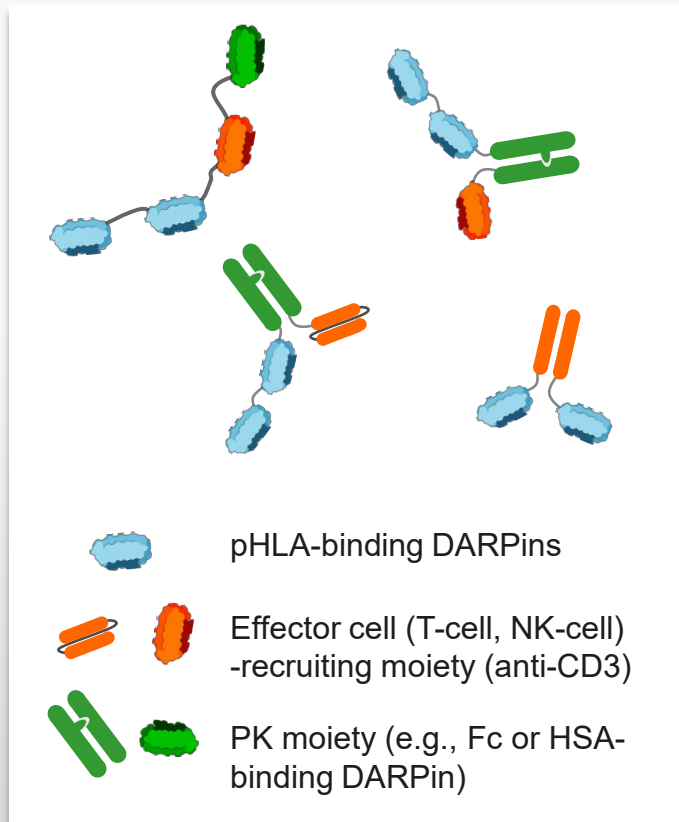
Killing Activity is Decoupled from Cytokine Release

- Whereas two Athebody[®] DARPin-TCE designs (Format 1 & 2) show equivalent killing activity, Format 2 induces significantly lower levels of cytokine release, which may reduce the risk of cytokine release syndrome in the clinic.

TCE Case Study: Conclusions

- Tailored Athebody[®] binder selection followed by simply plugging them into various TCE formats allowed 3T-Biosciences to identify DARPin-TCE leads of unparalleled efficacy and safety profiles.
- These DARPin-TCEs also exhibit favorable developability profiles (Ramirez A. et al. 2022).
- Low cytokine release likely translates into less severe T-cell exhaustion and thus long-lasting responses (Yi J.S. et al. 2010).

Next-generation of pHLA Therapeutics



Benefits of Athebody® DARPin Building blocks

- Potential to significantly **increase clinical success rates** by improving efficacy while reducing toxic side effects, by
 - Off-tumor off-target tox reduction (e.g., by increased on-target specificity based on their unparalleled binding specificity)
 - Off-tumor on-target tox reduction (e.g., by conditional activation)
 - Optimal exposure (e.g., by PK-engineering)
 - Addressing tumor heterogeneity (e.g., by multi-specific formats)
- **Plug and play:** Athebody® building blocks can be plugged into existing modalities (e.g., CAR-T cells, Fc-fusions, ...) and allow accessing new design spaces.
- Excellent developability properties based on their superb folding and high thermostability.
- Beside oncology, Athebody® pHLA therapeutics could be applied in other fields such as virology.

Let's co-create the next generation of pHLA Therapeutics!



- Our proprietary Athebody® platform & expertise
- Our innovation power and out-of-the-box thinking



**DARPin-pHLA therapeutics
with improved
Safety and Efficacy**

You

- Your product ideas and expertise to develop pHLA therapeutics
- Your commitment to innovation in drug development

Leadership team: **Joining complementary forces** around DARPin pioneers

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Patrik Forrer 

CEO, Board President

Initiator of the repeat protein technology; visionary and strategic thinker; co-founder of Molecular Partners AG (SIX: MOLN); strong background in protein sciences, preclinical drug development and IP/Legal.



Lorenz Kallenbach 

Board Member, IP & Legal

Background in biochemistry; German and European patent attorney and senior patent counsel in Merck KGaA's healthcare division.




Johannes Schilling 

VP Science Operations

Repeat protein and protein structure expert; former project leader for the Designed Ankyrin Repeat Protein platform at Molecular Partners AG.




Christian Jost 

VP Early Partnering

Repeat protein, antibody & immuno-oncology expert. Former Senior Scientist at the Roche Innovation Center Zurich.




Joachim Schnabl 

VP Information Technology

Bioinorganic chemist, structure expert; worked in Science Communication and as an Information Consultant for Chemistry and Pharmacy at ETH Zurich.



Lukas Wallacher 

VP People, Team & Culture, VP Finance, Director BD

Background in medicine, business economics, and philosophy; former founder of a digital start-up and business model innovation consultant at BMI Lab AG, Zurich.

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Team Athebio: We empower drug developers



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