

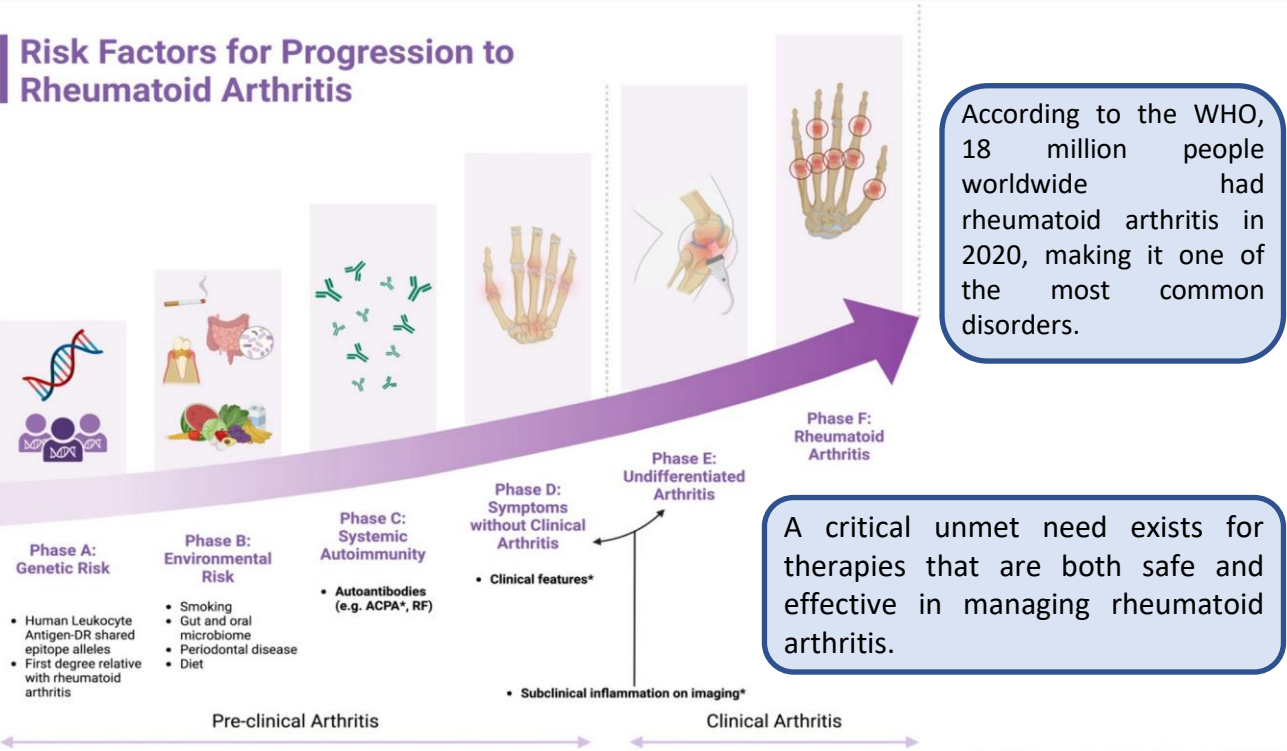
Dendrimer-Antibody Conjugates: An Innovative Approach for Targeted Intracellular Antibody Delivery

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Adalimumab in Rheumatoid Arthritis: An Unmet Need in Controlling CNS Inflammation and Microglial Activation

Risk Factors for Progression to Rheumatoid Arthritis



According to the WHO, 18 million people worldwide had rheumatoid arthritis in 2020, making it one of the most common disorders.

A critical unmet need exists for therapies that are both safe and effective in managing rheumatoid arthritis.

Adalimumab shows proven efficacy in controlling inflammation in rheumatoid arthritis.



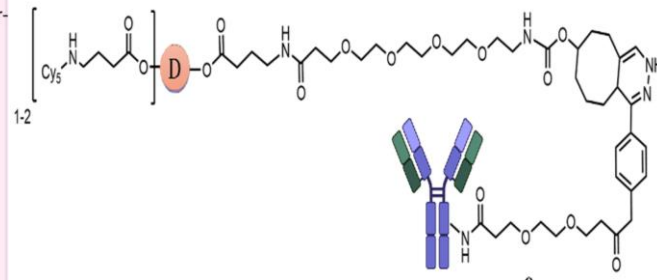
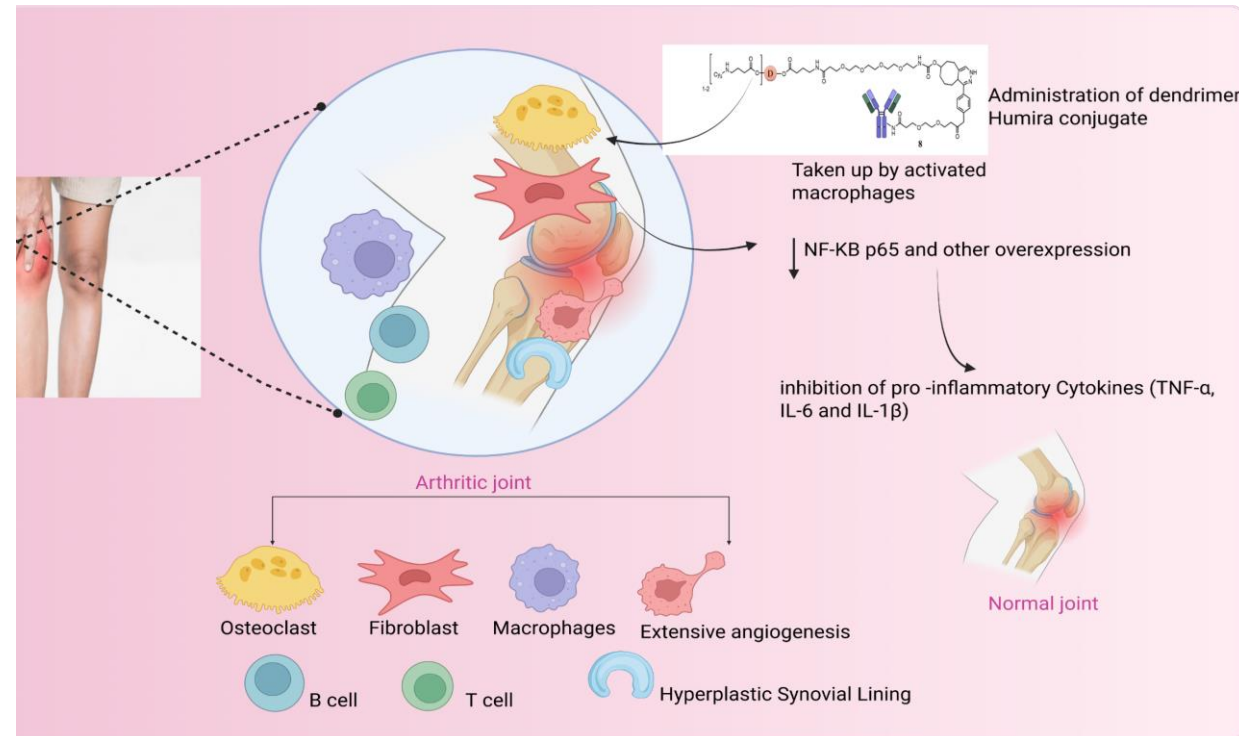
Prolonged use may have increased susceptibility to infection and Immune-related complications.



Major Challenge

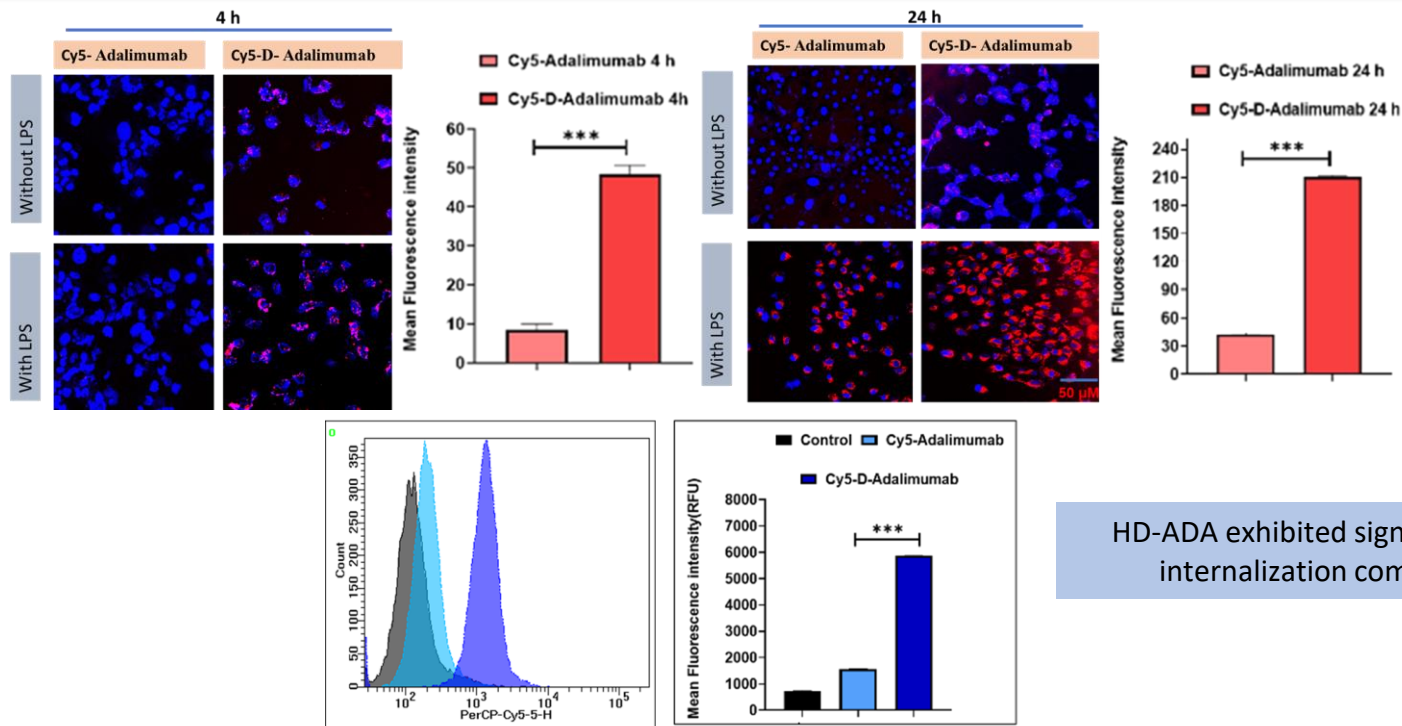
Delivering antibodies to **intracellular and inflamed tissue targets.**

Synthesis and Mechanism of HD-Adalimumab



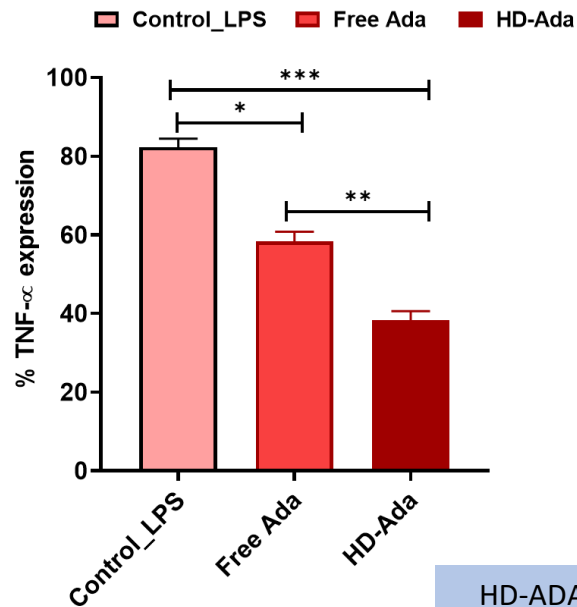
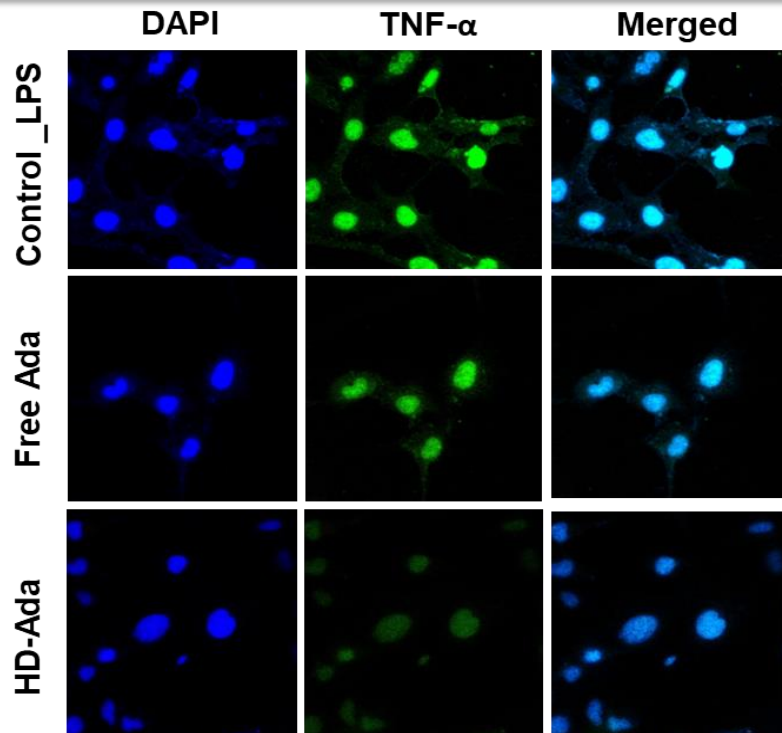
HD-ADA was synthesized via a click chemistry approach.

Cy5-Labeled HD-Adalimumab Demonstrated Enhanced Cellular Uptake in HMC3 Cells Compared to Free Adalimumab



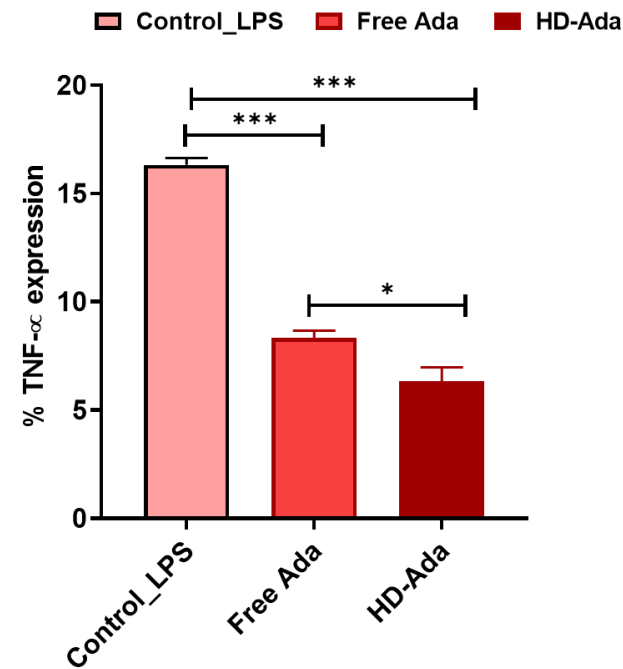
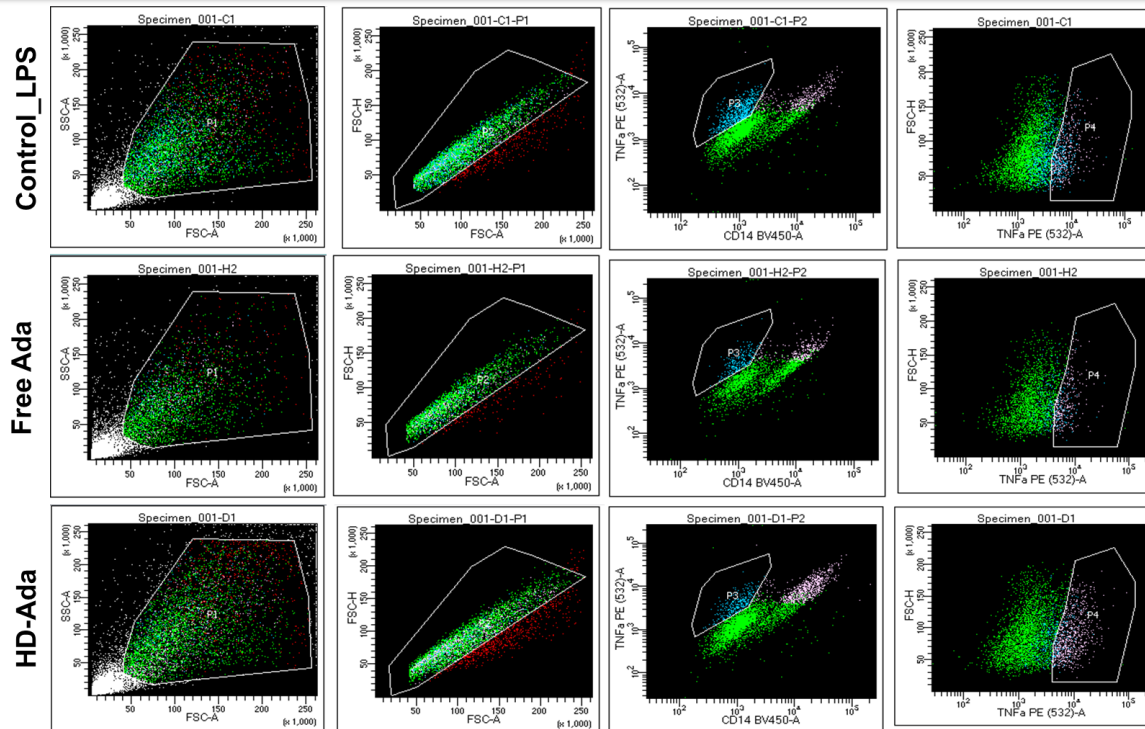
HD-ADA exhibited significantly higher cellular internalization compared to free ADA.

Enhanced TNF- α Suppression by HD-Adalimumab Over Free Adalimumab in HMC3 Cell Lines

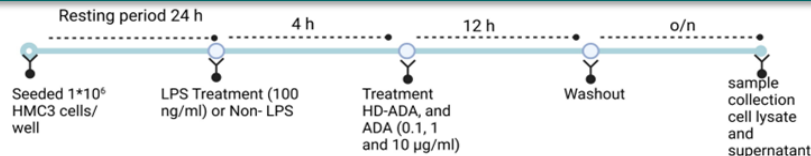


HD-ADA exhibited superior efficacy in reducing intracellular TNF- α levels in LPS-stimulated cells.

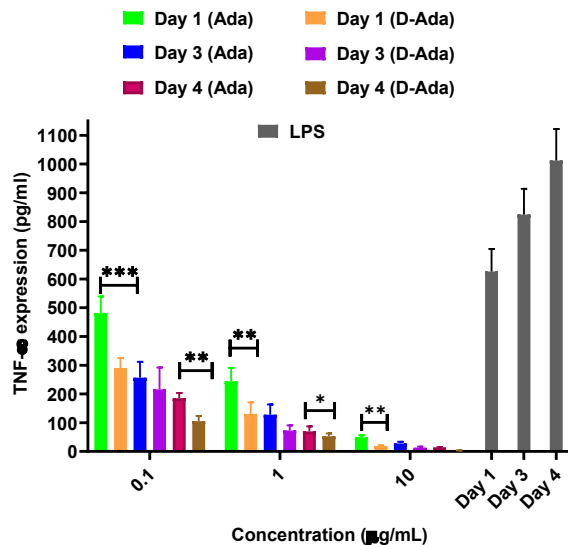
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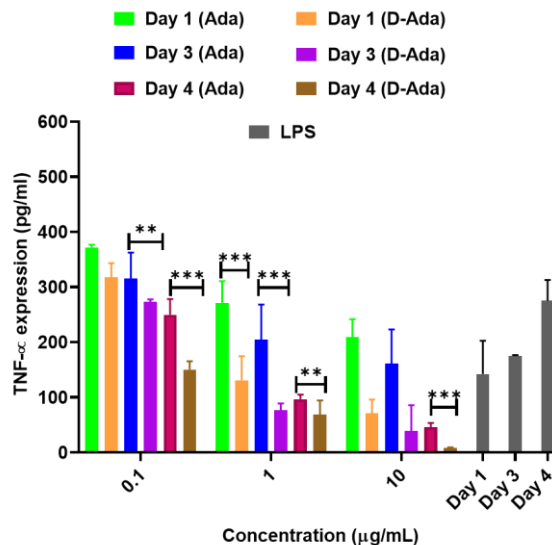
HD-Ada Significantly Enhances TNF- α Suppression Compared to Free Adalimumab in HMC3 Cells



Supernatant

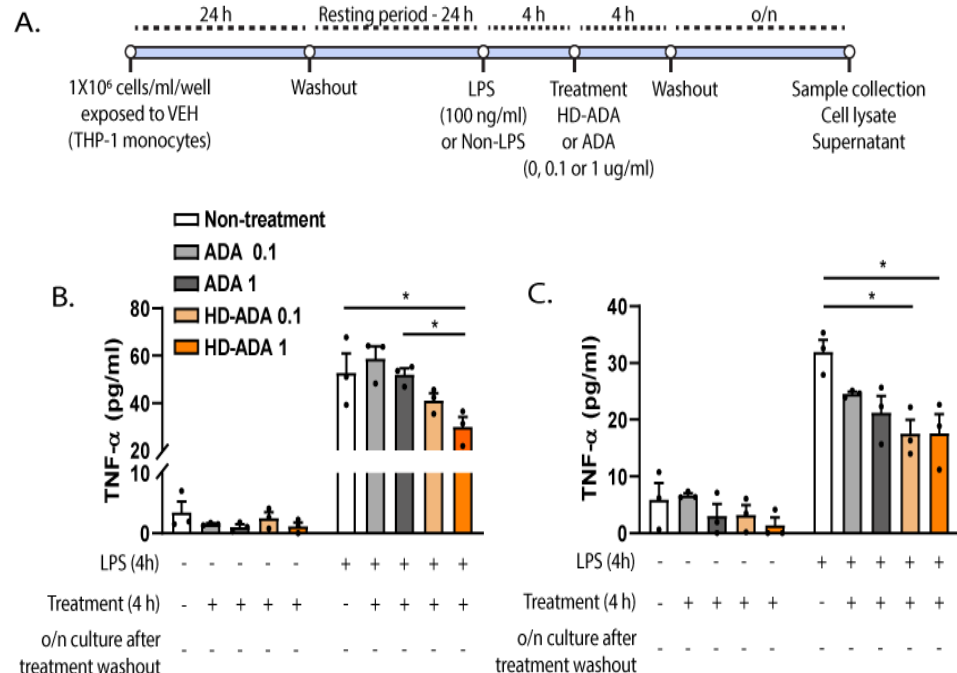
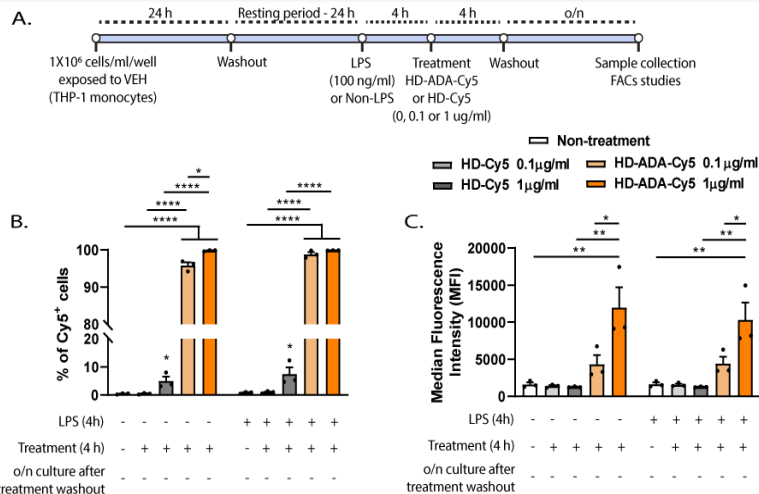


Lysate

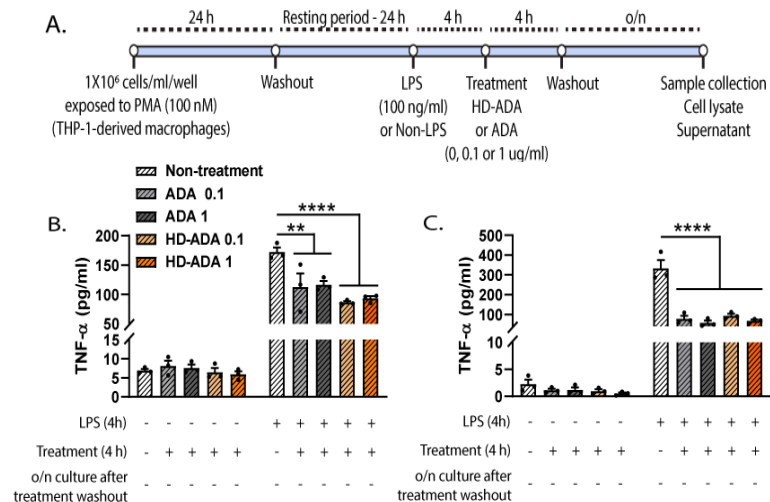
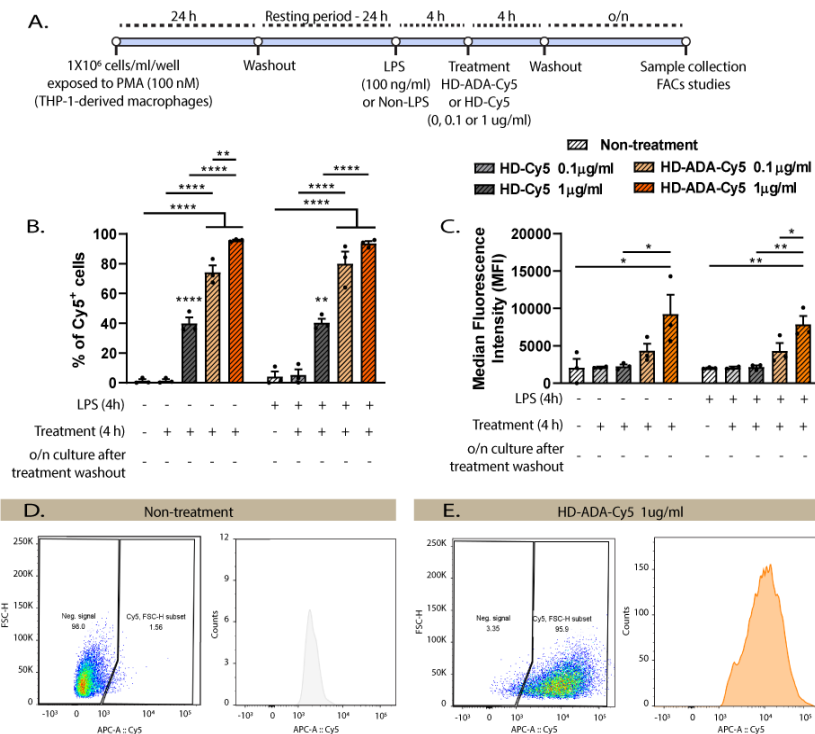


HD-ADA exhibited superior efficacy in reducing intracellular TNF- α levels in LPS-stimulated cells.

HD-ADA Significantly Reduced Intracellular TNF- α Levels and Secretion More Effectively than Free ADA in THP-1 Monocytes

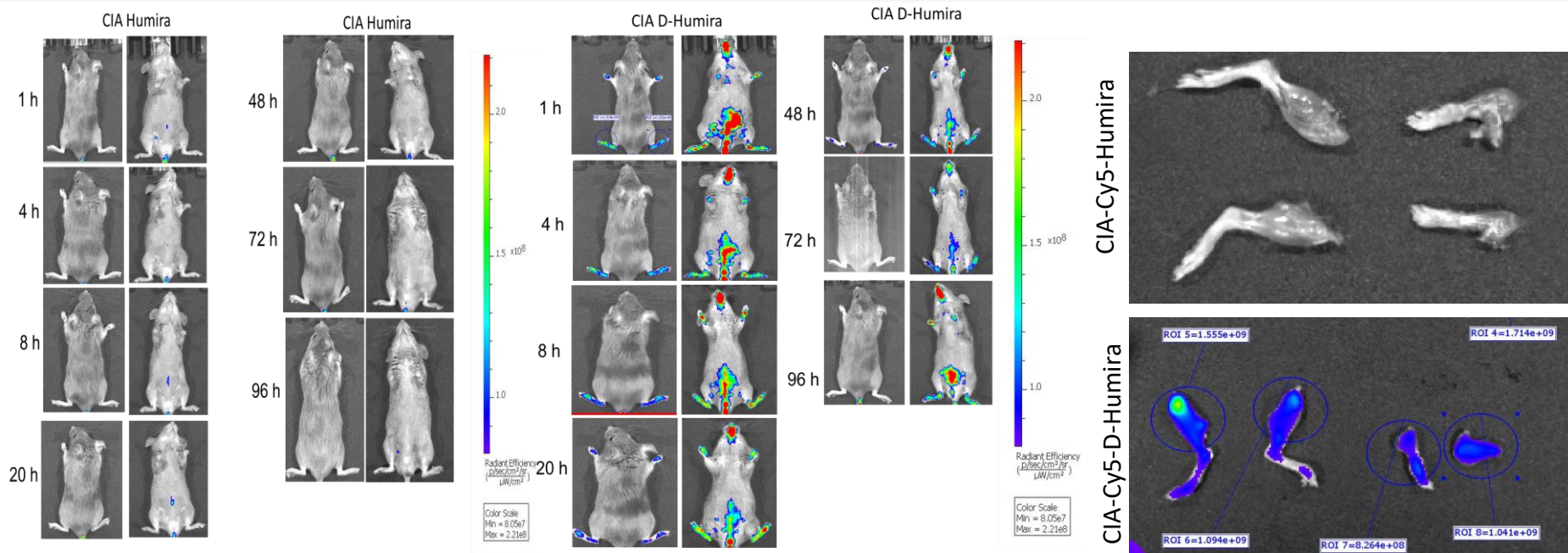


Evaluation of the *In Vitro* efficacy of HD-ADA in THP-1 derived-macrophages



Compared to ADA, the dendrimer-ADA conjugate more effectively reduced intracellular TNF-α levels at both tested concentrations, with superior statistical significance ($p < 0.0001$).

Cy5-HD-Ada Demonstrated Significantly Higher Accumulation Inflamed Joints Compared to Free Adalimumab



After 96 hours, Cy5-HD-Ada showed greater accumulation in inflamed joints compared to free Adalimumab

Conclusion/ Future perspective

- **HD-Adalimumab (HD-ADA) enhances targeting** of inflammatory cells, especially microglia/macrophages, monocyte.
- HD-ADA improves TNF- α suppression in comparison to free Adalimumab.
- **Reduces off-target effects**, enabling safer and more selective therapy.
- Promising therapeutic strategy to evaluate its efficacy in a humanized mice model of rheumatoid arthritis.



Acknowledgements & collaborations



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