

GNTI-932: A gut specific CAR-Engineered Regulatory T cell therapy to treat Inflammatory Bowel Disease

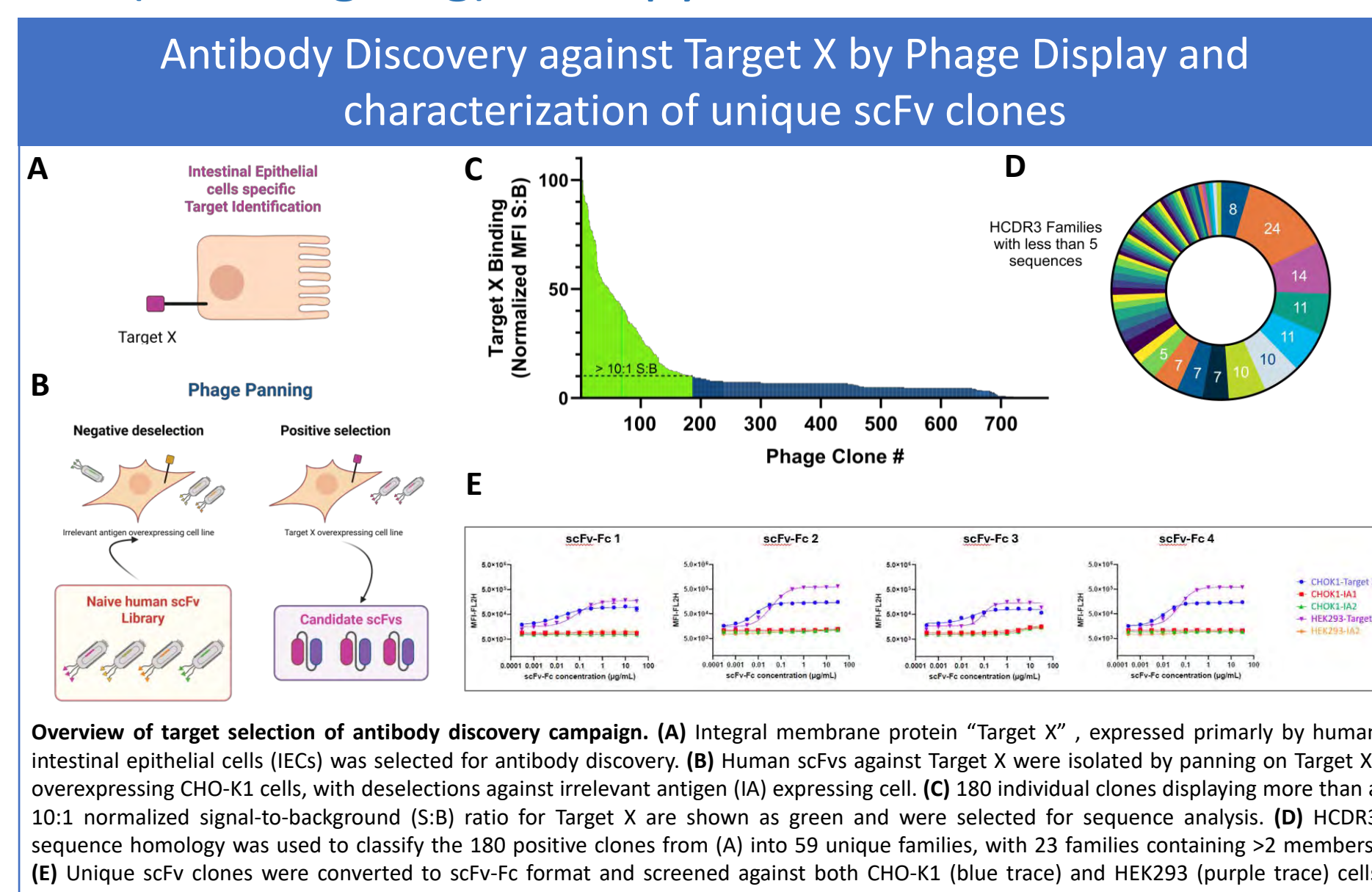
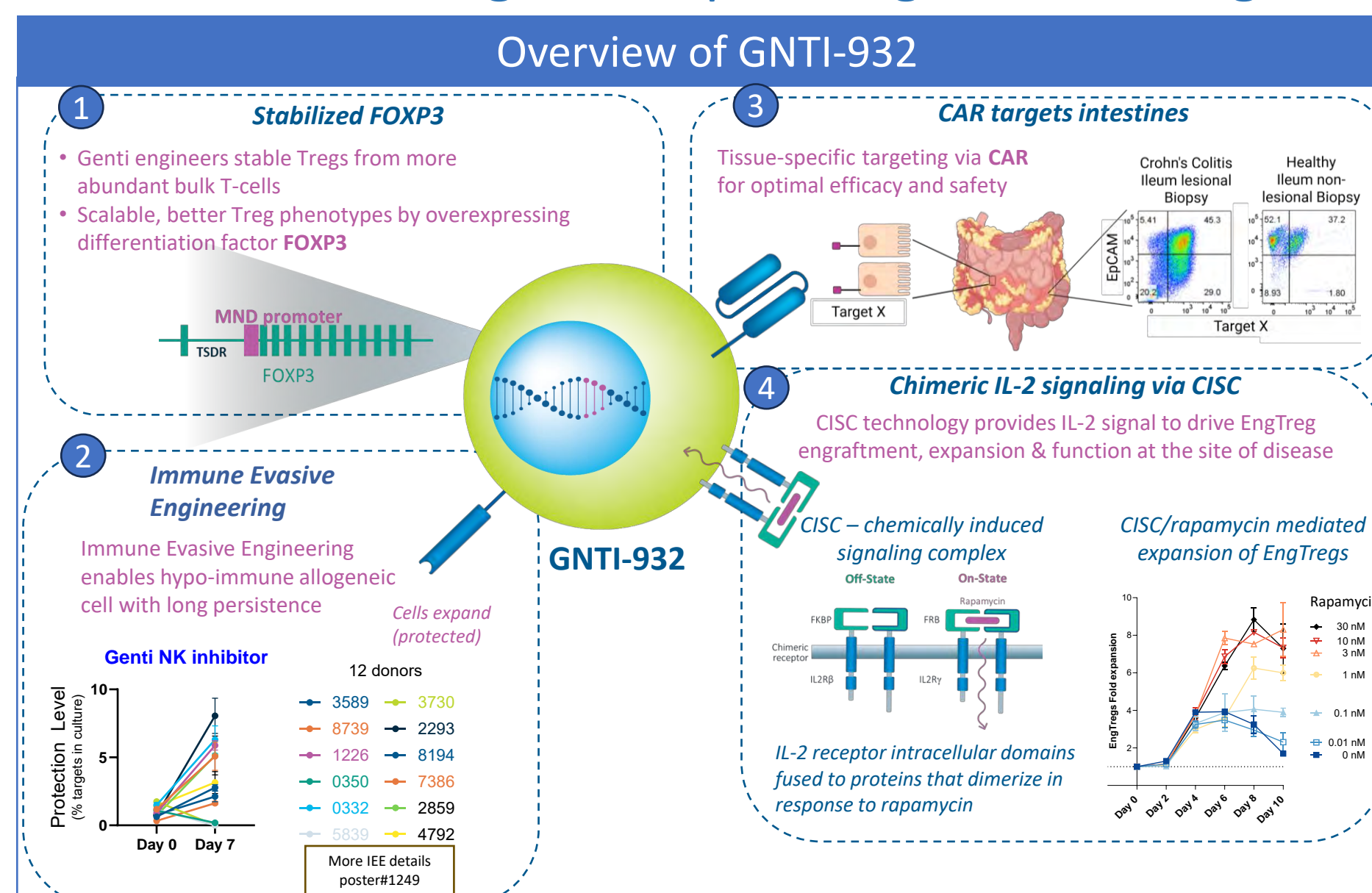
M Sassone-Corsi, D Tucker, J Yam, A Doherty, N Zammit, A Landyut, M Rashkovskii, S Verma, N Ngwenyama, G Uenishi, SA Hernandez, T Guo, A Burgess, P Rompikuntal, C Moore, D Gaddis, D Gopal, V Catala, H Kellog, Y Agarwal, T Chan, A Del Rio, J Mellen, Y Lao, V DeVault, A Singh, T Crevier, C Patel, T Wickham, TF Chen

GentiBio, Inc., Cambridge, MA, USA

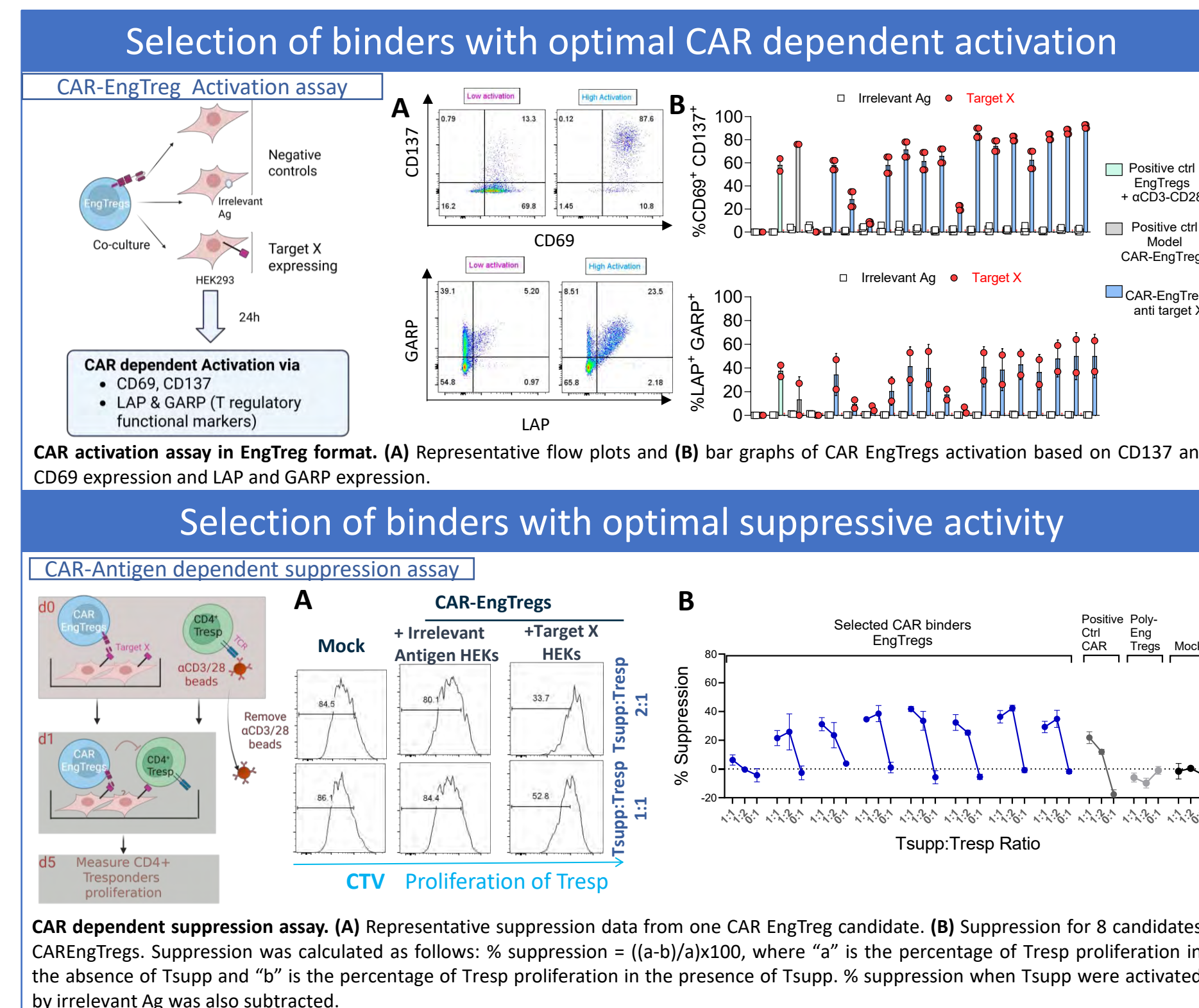
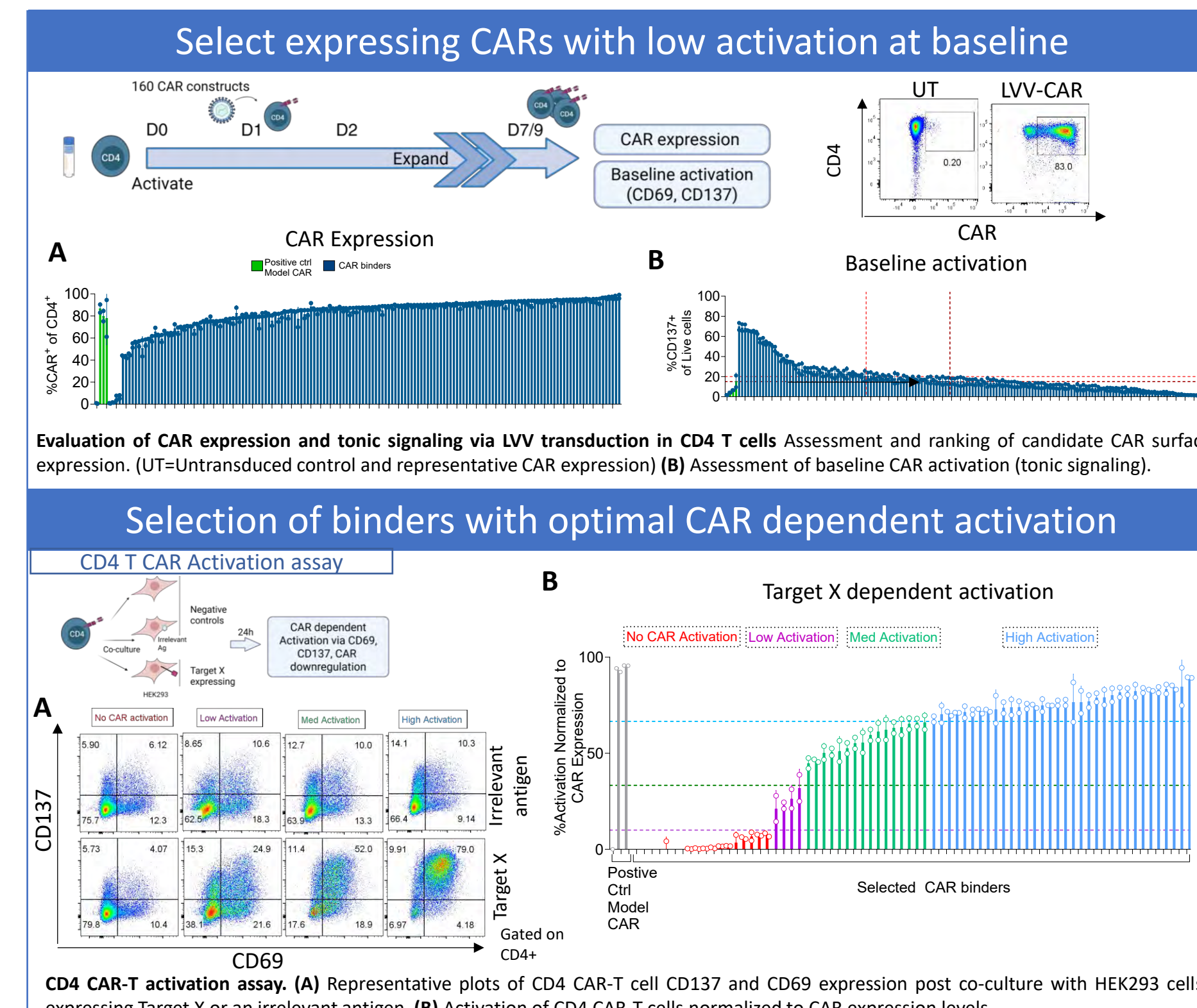
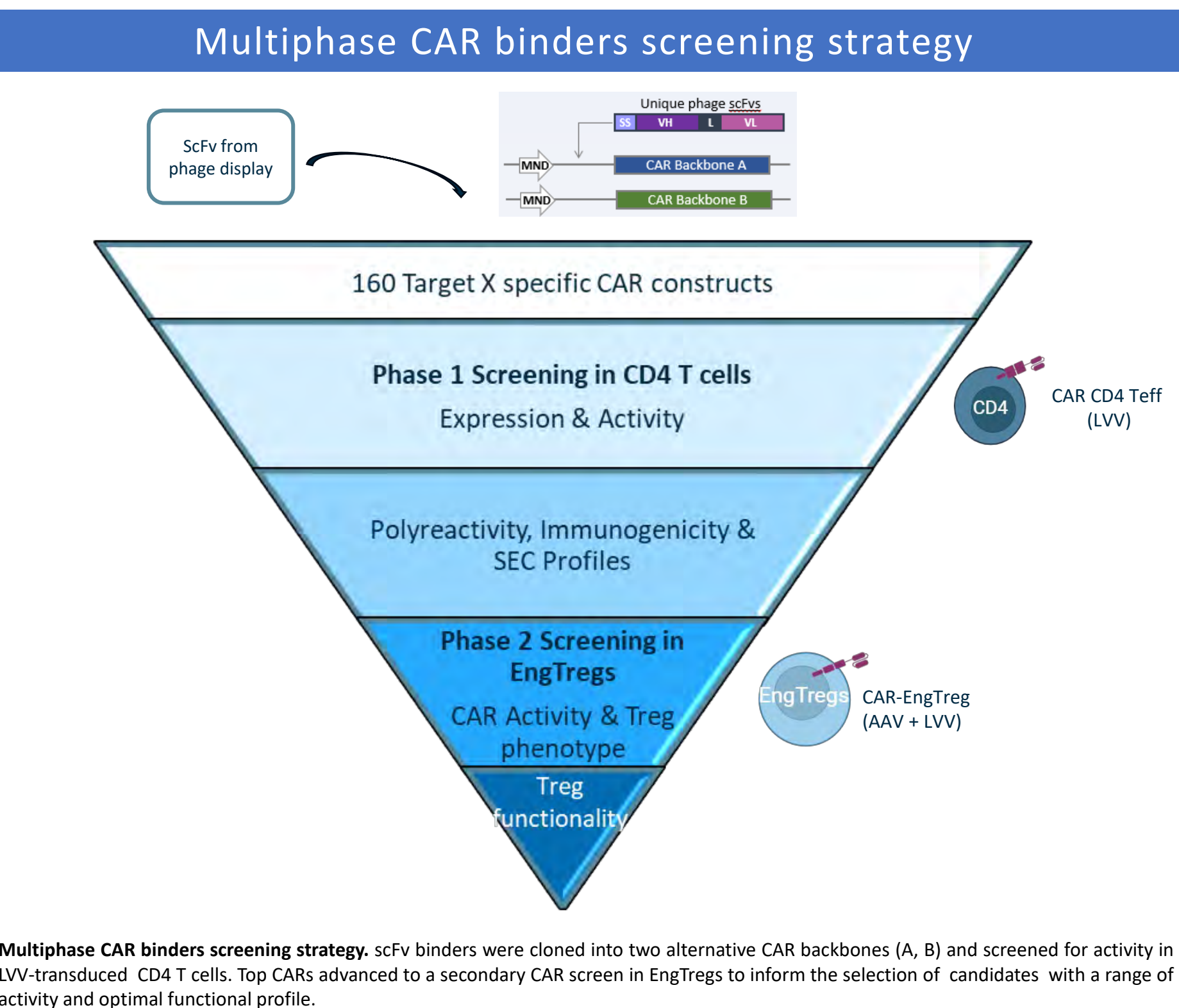
OVERVIEW | GNTI-932, a novel hypo-immune gut-specific chimeric antigen receptor engineered T regulatory cell (CAR-EngTreg) therapy

Summary

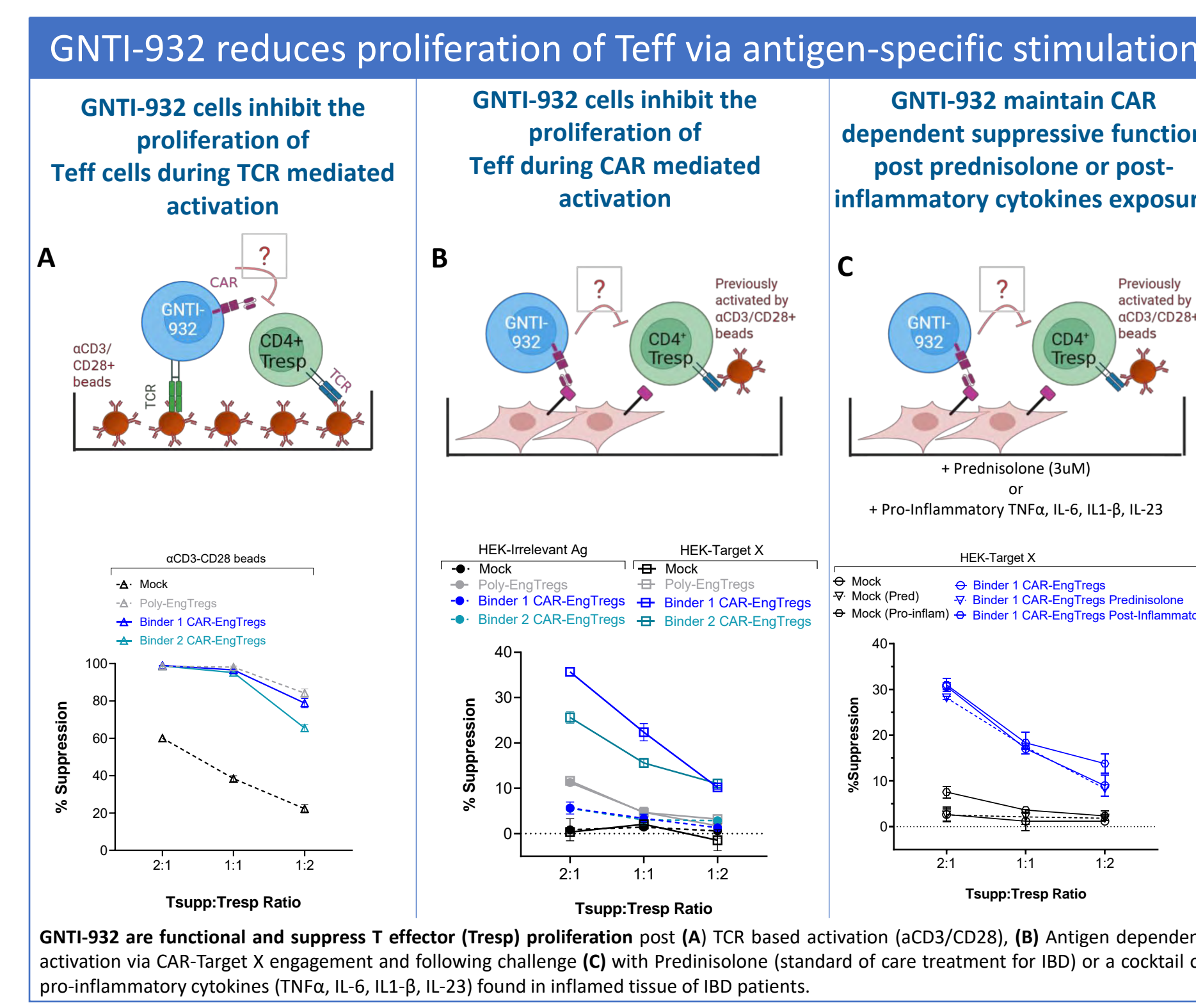
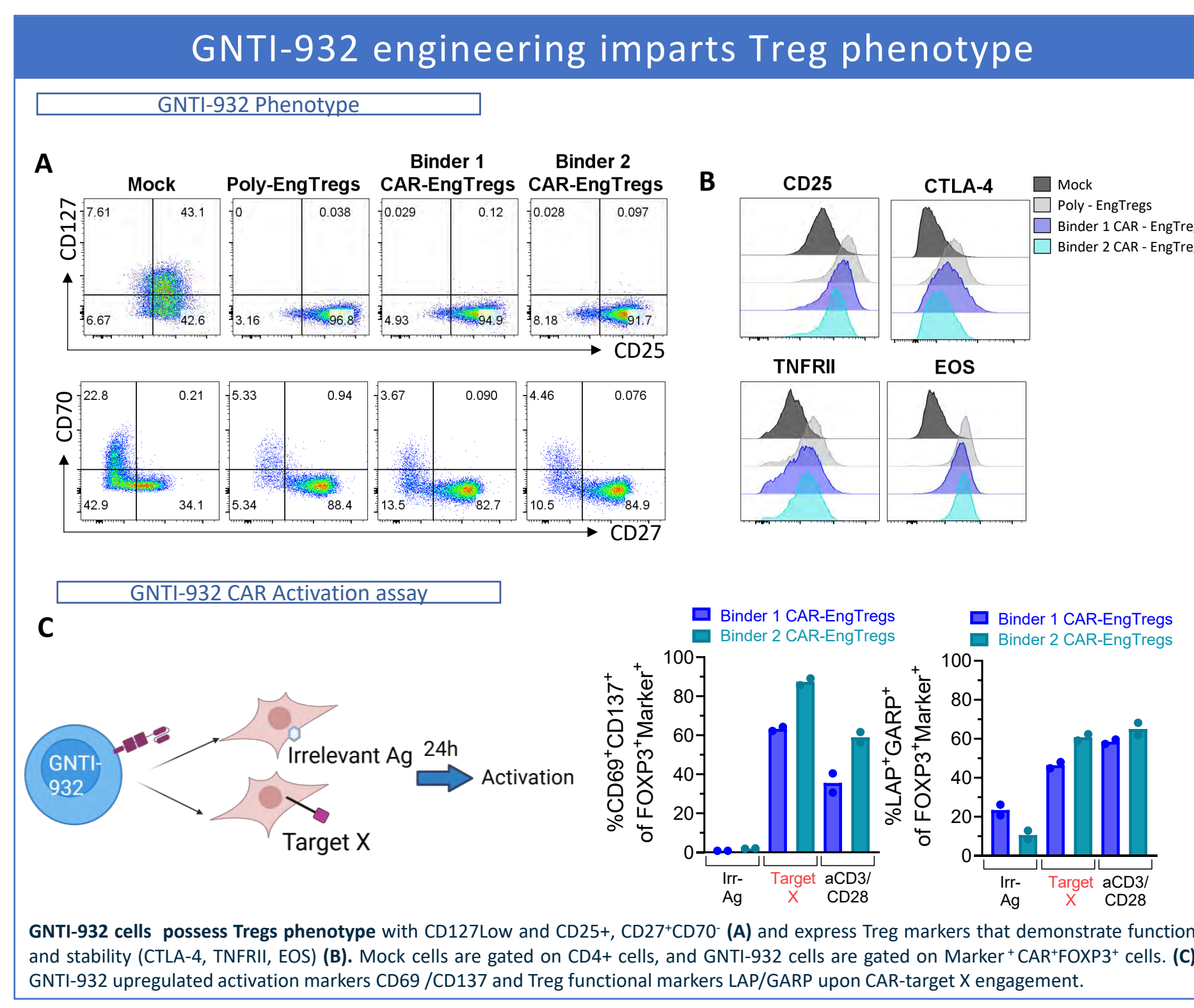
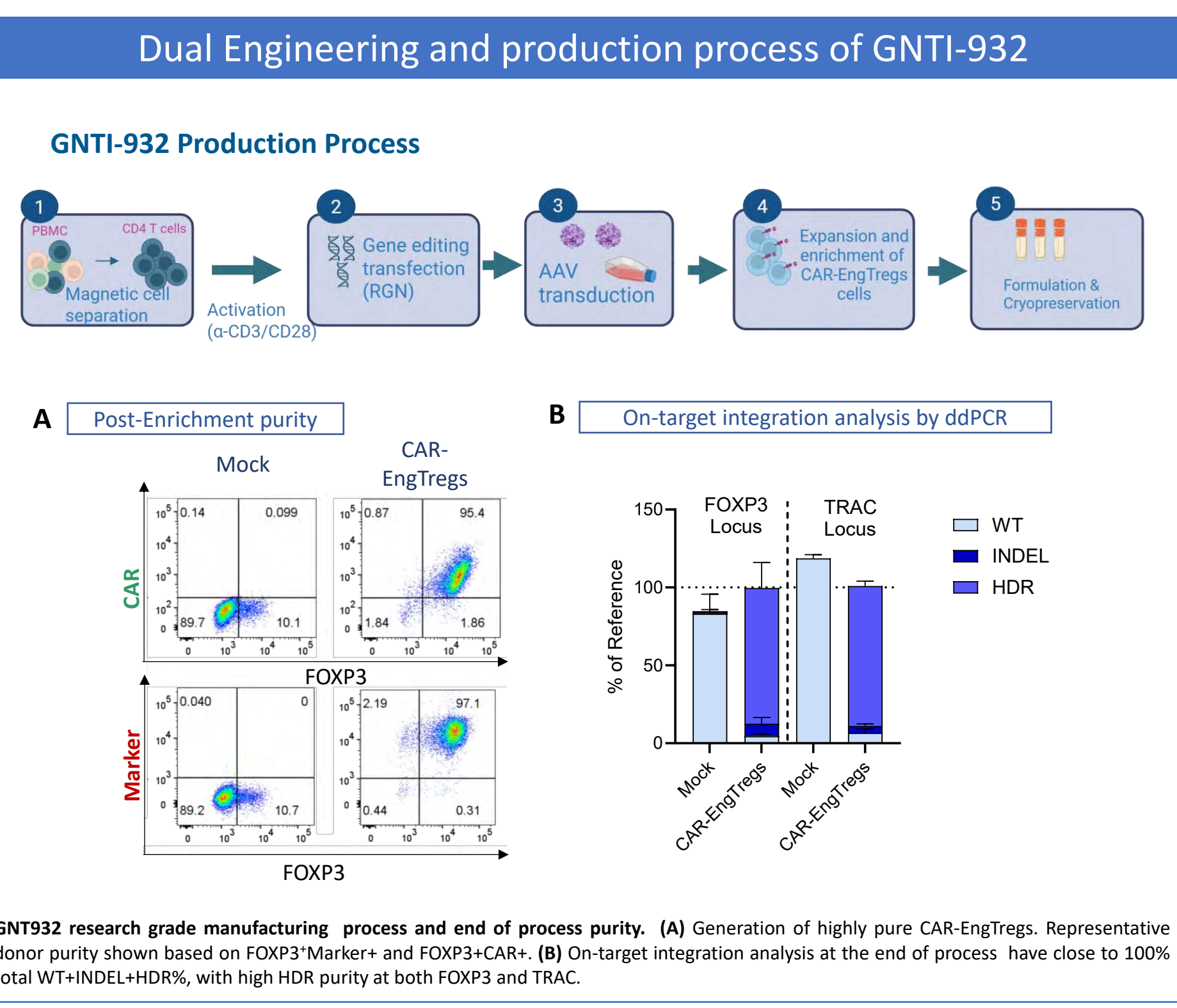
- GentiBio is advancing the development of GNTI-932, a novel hypo-immune gut-specific chimeric antigen receptor engineered T regulatory cell (CAR-EngTreg), to restore immune homeostasis in patients with Inflammatory bowel disease.
- GNTI-932 is designed with constitutive FOXP3 expression and a rapamycin-activated IL-2 signaling complex for stability and scalability, a potent immune evasive engineering technology (IEE) for persistence and a CAR to enhance gut localization and antigen-specific suppression.
- A multi-phase CAR screening strategy was implemented, to enable high throughput discovery and selection of the best binders that maintain Treg phenotype and functionality.
- Preclinical studies using murine CAR-EngTreg surrogates targeting the mouse ortholog of the human target gut antigen demonstrated preferential gut localization, proliferation, and significant therapeutic efficacy in colitis models.
- These findings suggest that CAR-EngTregs like GNTI-932, targeting tissue-specific antigens, hold promise for improving the effectiveness of Treg therapies for IBD.



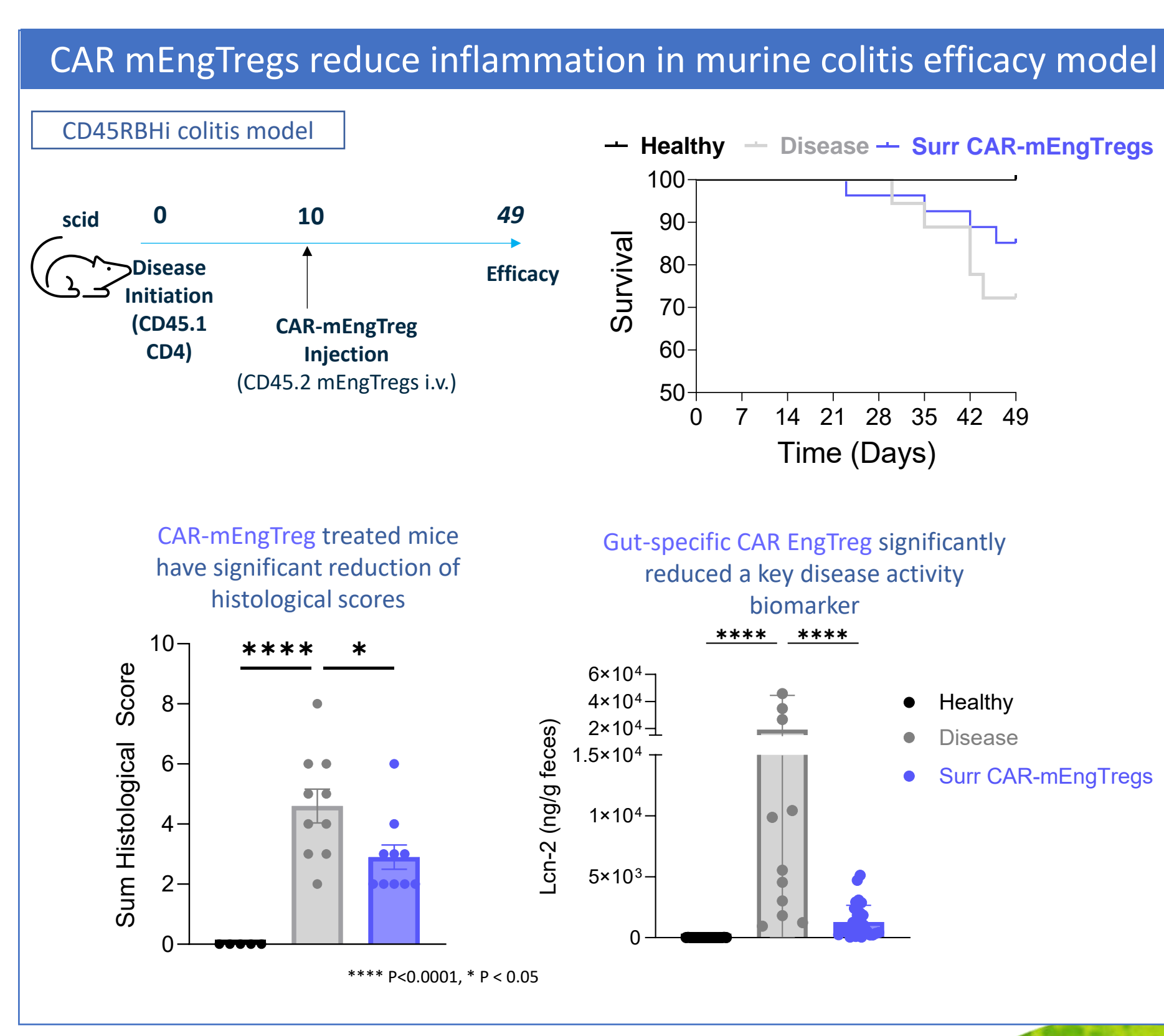
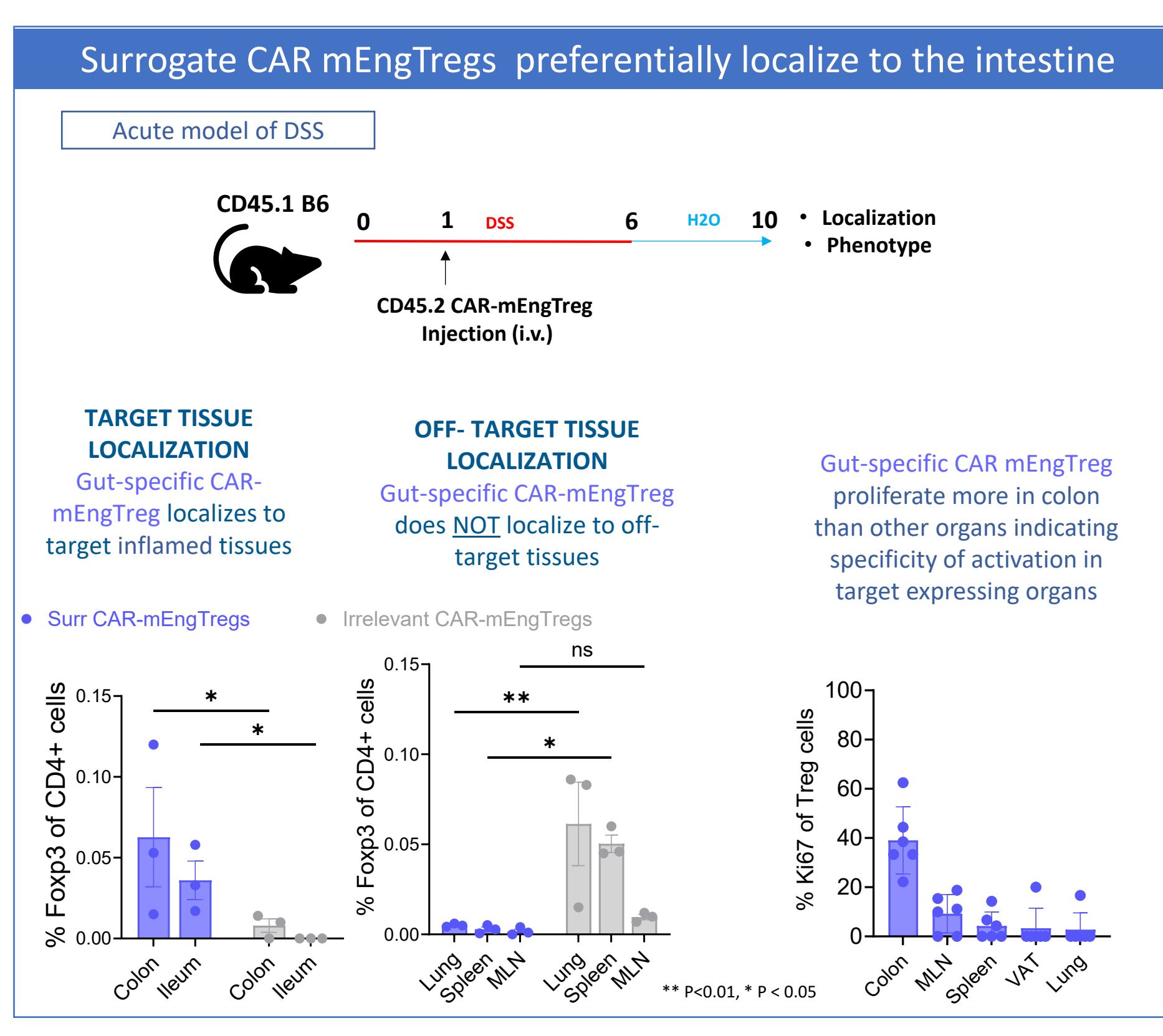
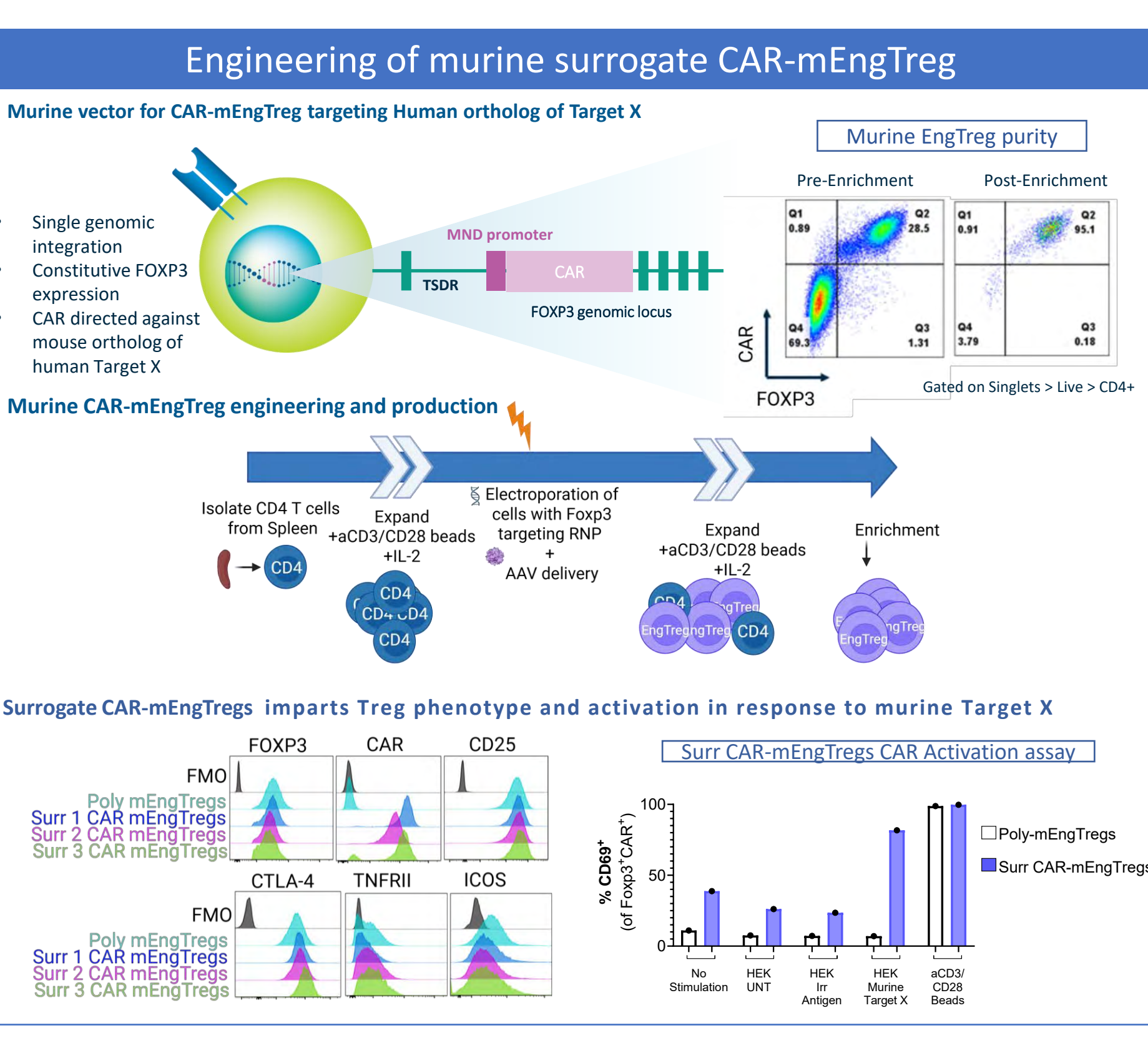
RESULTS | 1st Phase screening in CD4 T cells for CAR activity and 2nd Phase for selection of top CAR-EngTregs with optimal Treg phenotype and functionality



RESULTS | GNTI-932 is a Dual-Engineered Regulatory T Cell Therapy Product with T regulatory cell phenotype and function



RESULTS | Murine CAR-mEngTregs GNTI-932 surrogate localize in the intestine and improve outcomes in vivo efficacy models



CONCLUSIONS

- A multi-phase CAR screening strategy facilitated high-throughput discovery and selection of optimal binders for maintaining Treg phenotype and functionality.
- GNTI-932 exhibits key Treg characteristics and demonstrates antigen-dependent suppressive function against effector T cells while maintaining stability under inflammatory conditions and standard IBD treatment.
- Preclinical studies using murine surrogates of GNTI-932 demonstrated effective gut localization, proliferation at the site of inflammation, and significant therapeutic benefit in experimental colitis models, highlighting the potential for in vivo efficacy.
- In summary, Targeting IBD with CAR-engineered Tregs (GNTI-932) offers a novel approach to overcome the limitations of polyclonal Treg therapy by enhancing target specificity and persistence through its unique design.

