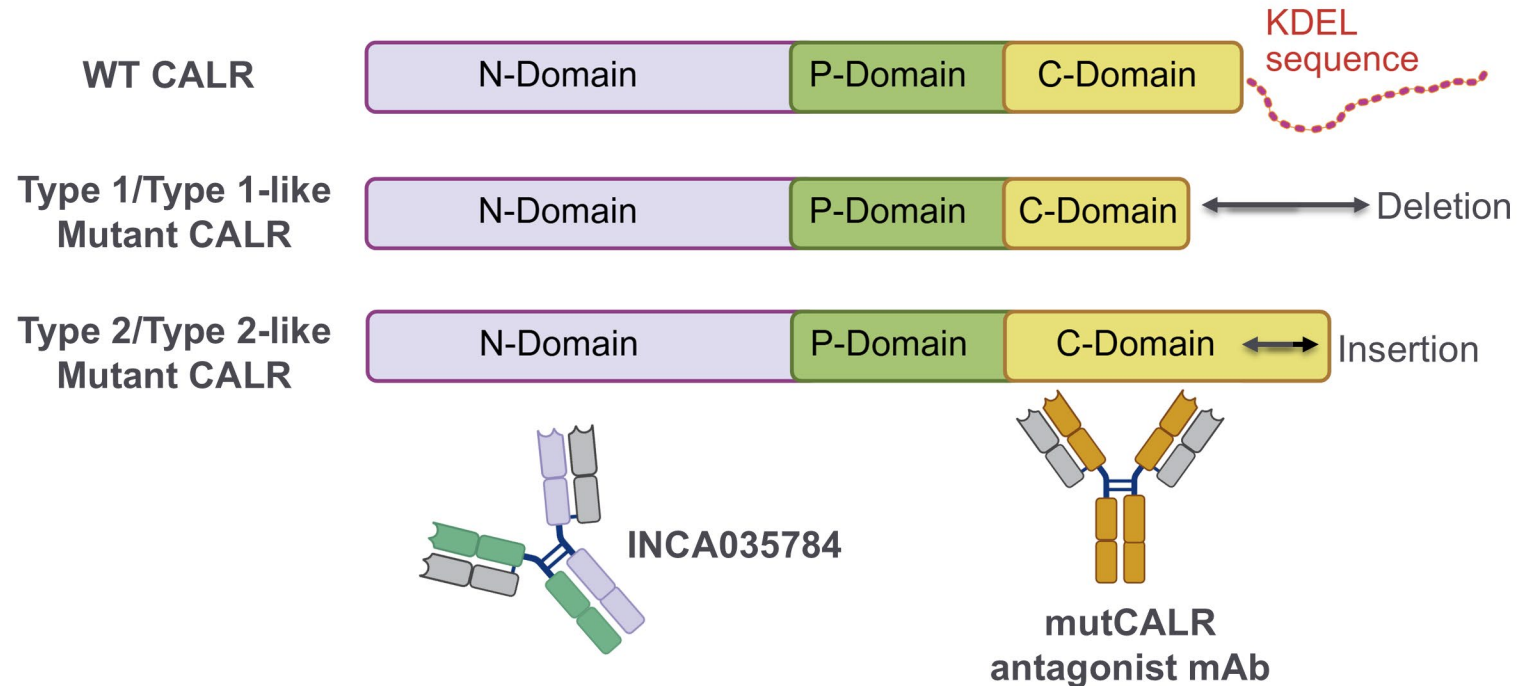
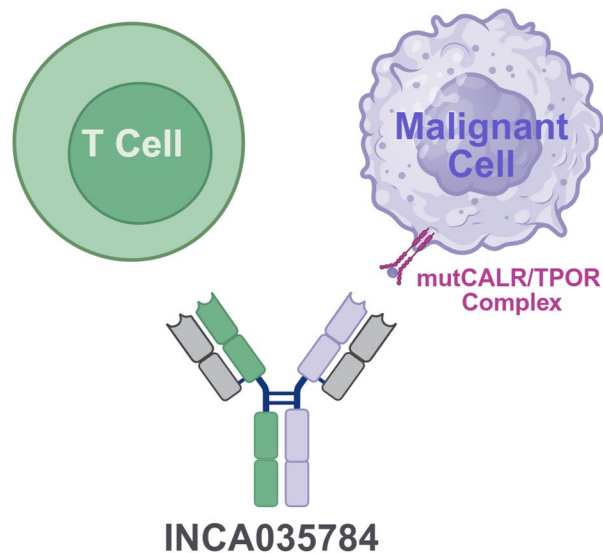


INCA035784, a Novel, Equipotent T Cell Redirecting Antibody for Patients With Myeloproliferative Neoplasms Carrying Different Types of Calreticulin Mutations

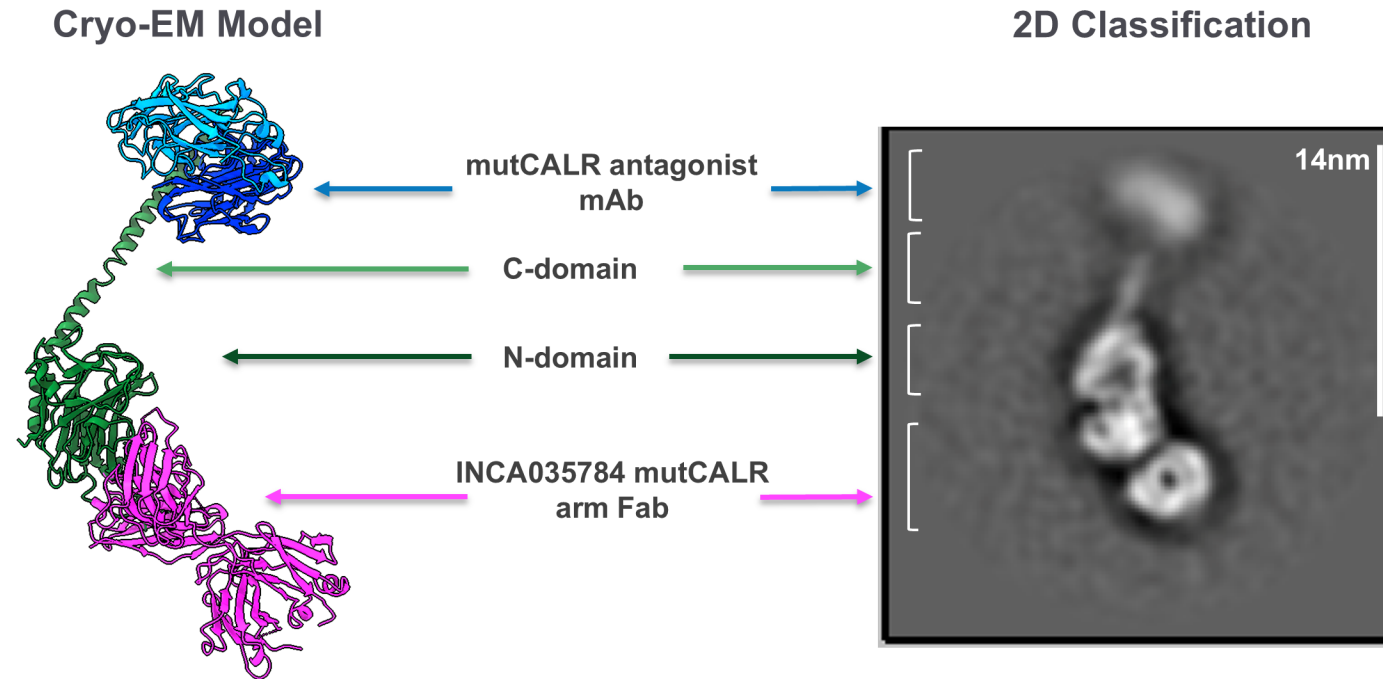
Veethika Pandey,¹ Liang-Chuan Wang,¹ Ashwini Kulkarni,¹ Linda Hendriks,² Tessa Steevels,² Daniel Merenich,¹ Jun Guan,¹ Emily Ren,¹ Niketa Langalia,¹ Karol Fiedorczuk,¹ Fatoumata Jobe,¹ Angelo Albertoni,¹ Hamza Celik,¹ Stephen Rudnick,¹ Rodrigo Hess,¹ Eleanor Murphy,³ Zoe Wong,³ Rinse Klooster,² David Maussang-Detaille,² Horacio Nasti,¹ Ricardo Macarron,¹ **Bethan Psaila**,³ Patrick A. Mayes¹

¹Incyte Research Institute, Wilmington, DE, USA; ²Merus NV, Utrecht, The Netherlands; ³Oxford University, Oxford, UK

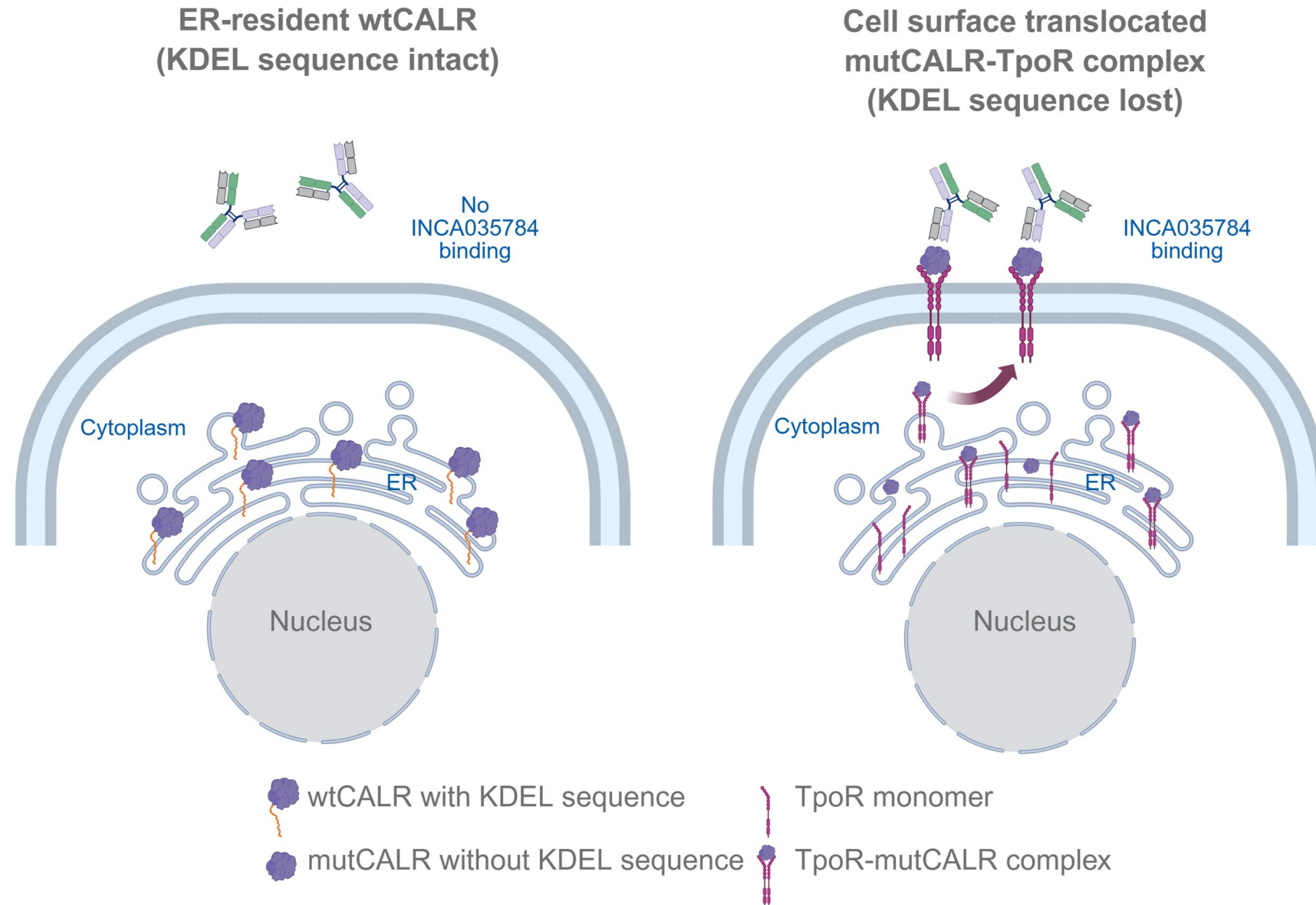
INCA035784: mutCALR-N-Domain-Specific T Cell Redirecting Antibody



INCA035784: mutCALR-N-Domain-Specific T Cell Redirecting Antibody

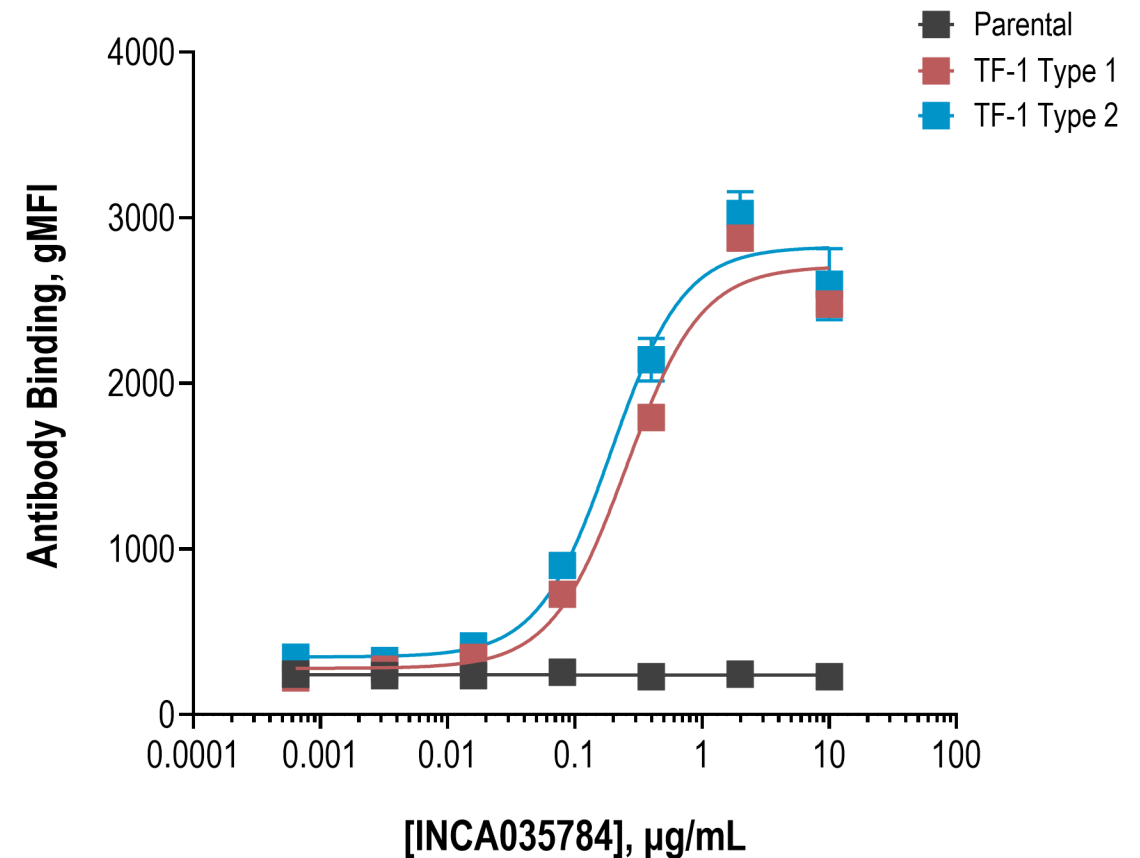
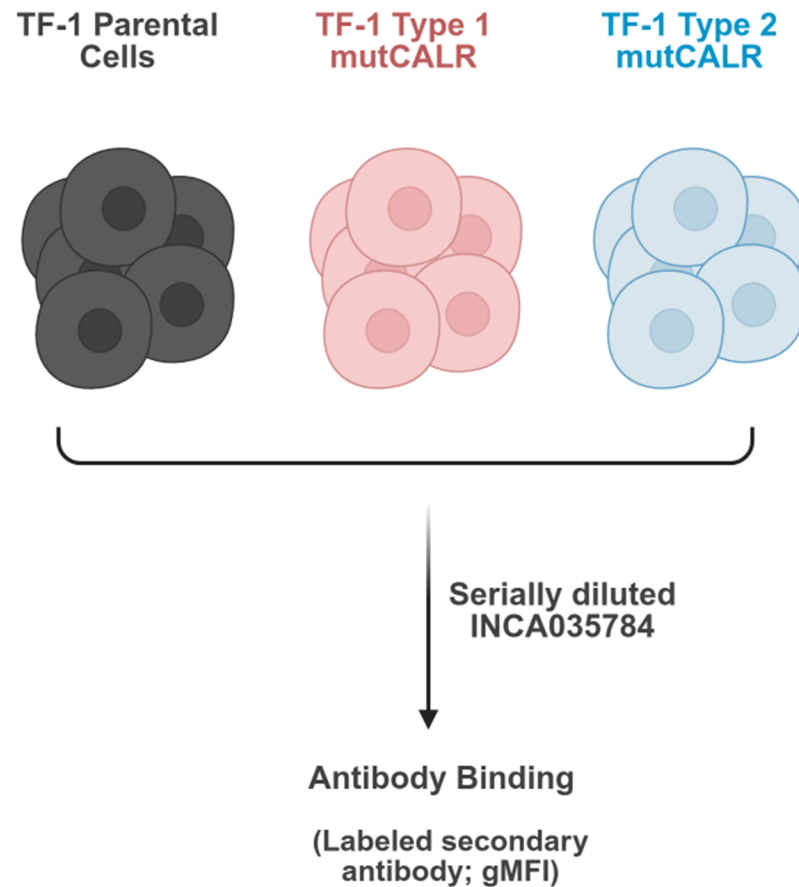


Cell Surface Translocation of Mutated CALR Upon Loss of KDEL Sequence (ER Retention Signal)



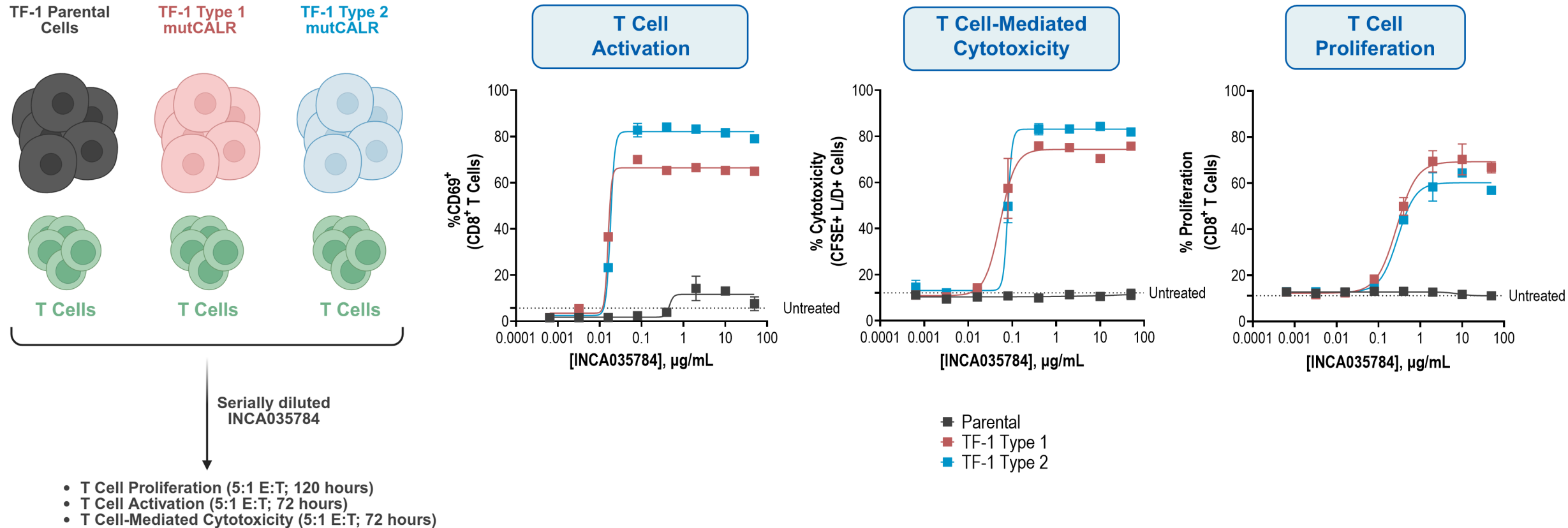
CALR, calreticulin;
ER, endoplasmic reticulum.

INCA035784 Selectively Binds to Type 1 and 2 mutCALR Expressing Engineered TF-1 Clones



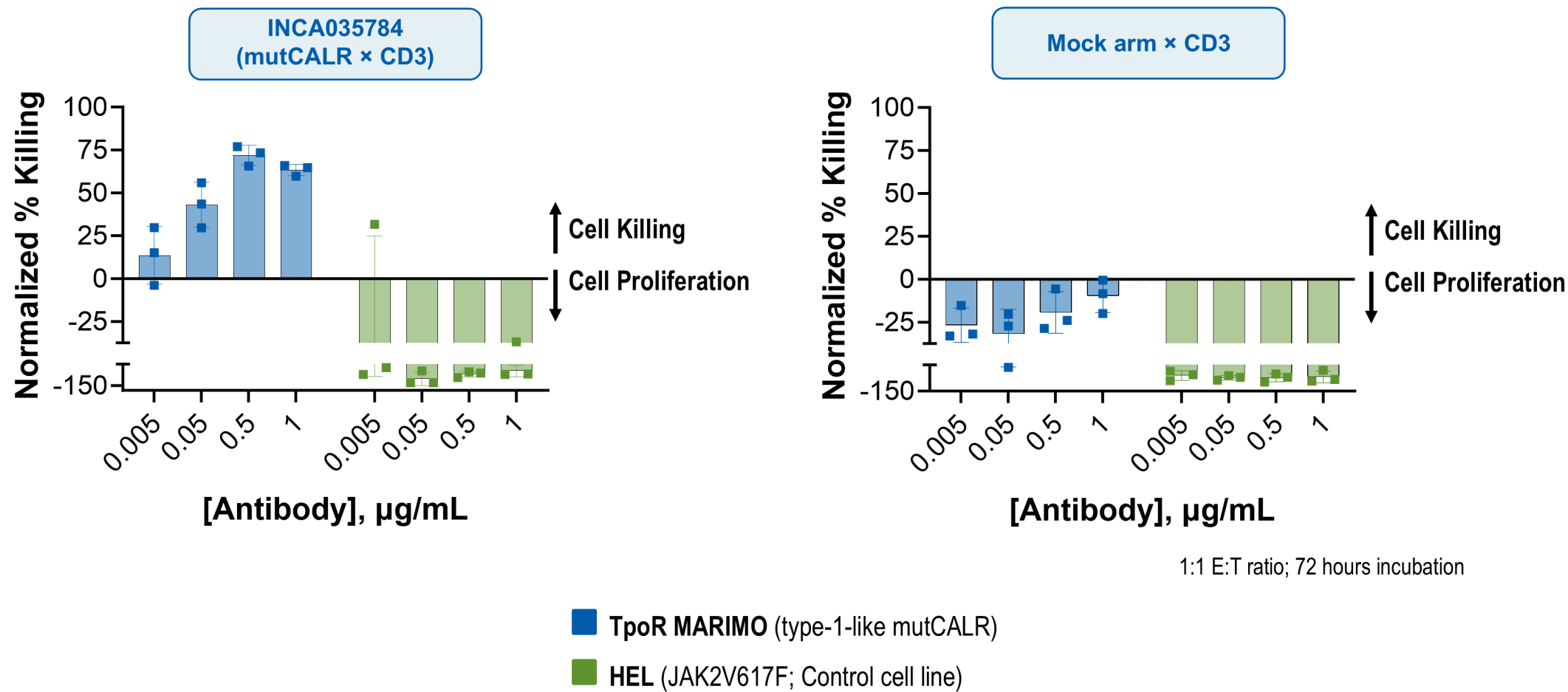
Data represents 2 independent experiments. Data points represent the mean and the error bars indicate standard deviation.
CALR, calreticulin; gMFI, geometric mean fluorescence intensity.

INCA035784 Shows T Cell-Mediated Functions Towards Type 1 and 2 mutCALR Expressing Engineered TF-1 Clones



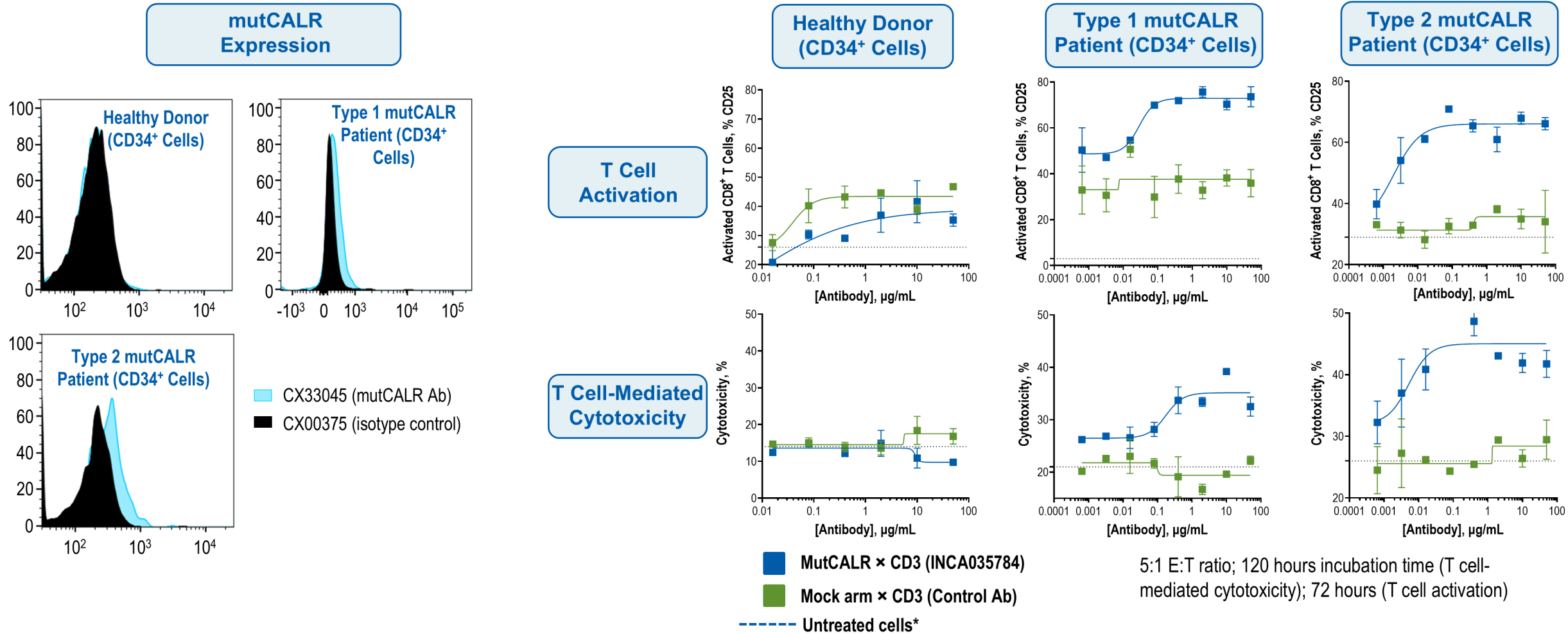
Data are representative of assays performed with 2 different healthy T cell donors. Data points represent the mean and the error bars indicate standard deviation. CALR, calreticulin; CFSE, carboxyfluorescein succinimidyl ester; E:T, effector to target ratio.

INCA035784 Shows Healthy Donor T Cell-Mediated Killing in Type-1-Like mutCALR Cells



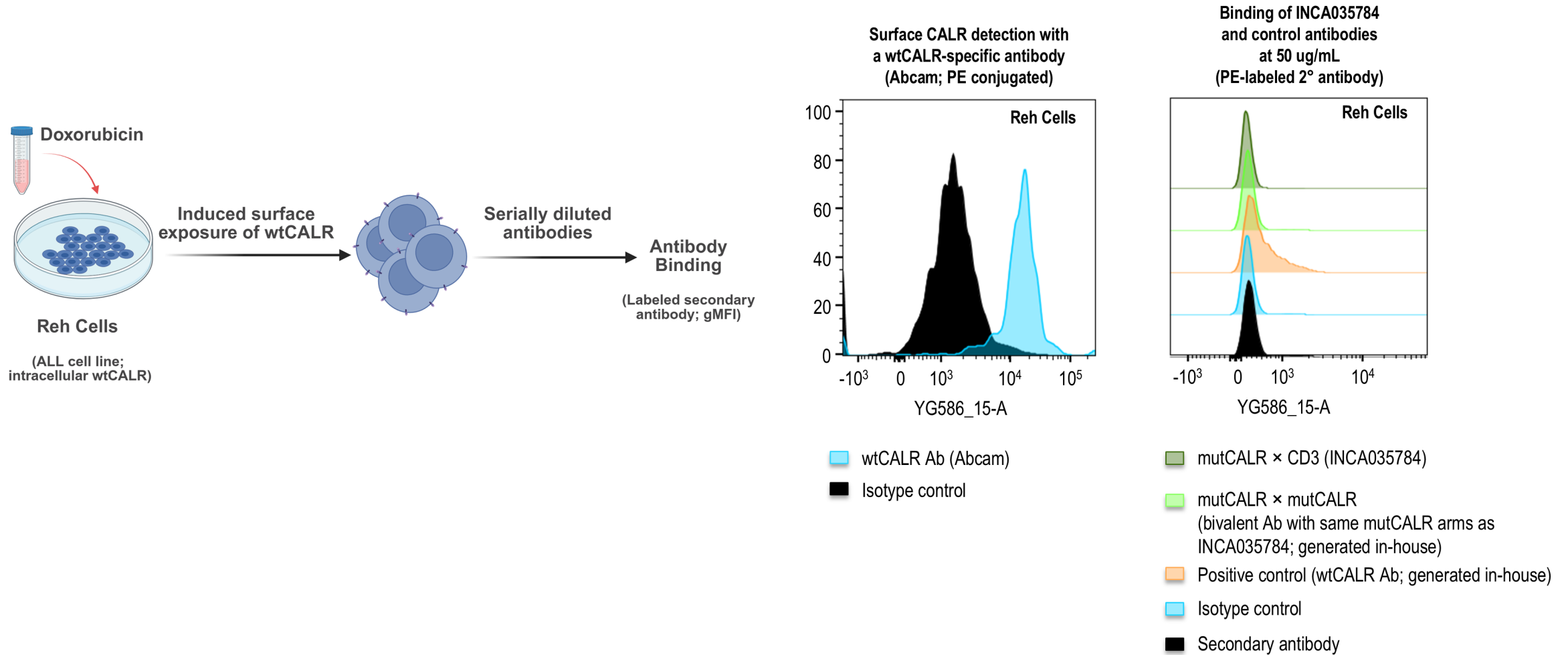
Data represents 3 independent experiments. Data points represent the mean and the error bars indicate standard deviation.
CALR, calreticulin; E:T, effector to target ratio.

INCA035784 Shows Healthy Donor T Cell-Mediated Functions Towards Type 1 and 2 mutCALR Patient-Derived CD34⁺ Cells



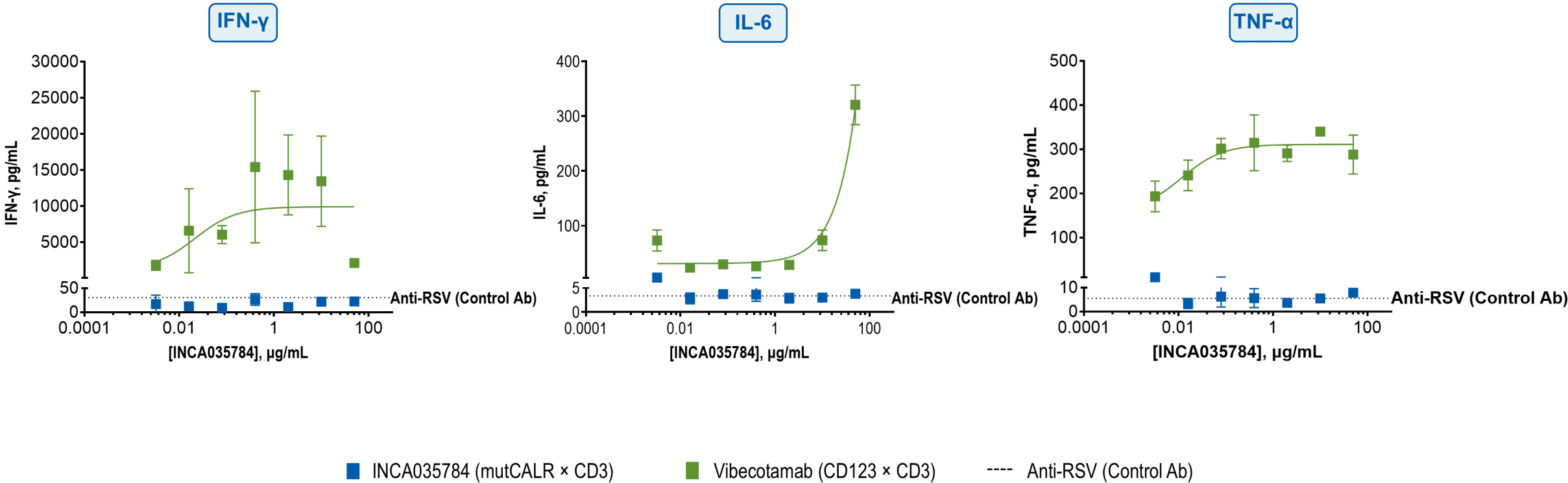
Flow cytometry analysis was performed and analyzed using FlowJo™ v10.8.1 Software (BD Life Sciences; Ashland, OR, USA). Data points represent the mean and error bars represent the standard deviation. *The dotted lines represent data from untreated cells (mean value of co-culture with no antibody treatment). Ab, antibody; CALR, calreticulin; E:T, effector to target ratio.

INCA035784 Does Not Bind Surface-Exposed Wild-Type CALR



Binding analysis was performed and analyzed using FlowJo™ v10.8.1 Software (BD Life Sciences; Ashland, OR, USA).
Ab, antibody; CALR, calreticulin; PE, phycoerythrin.

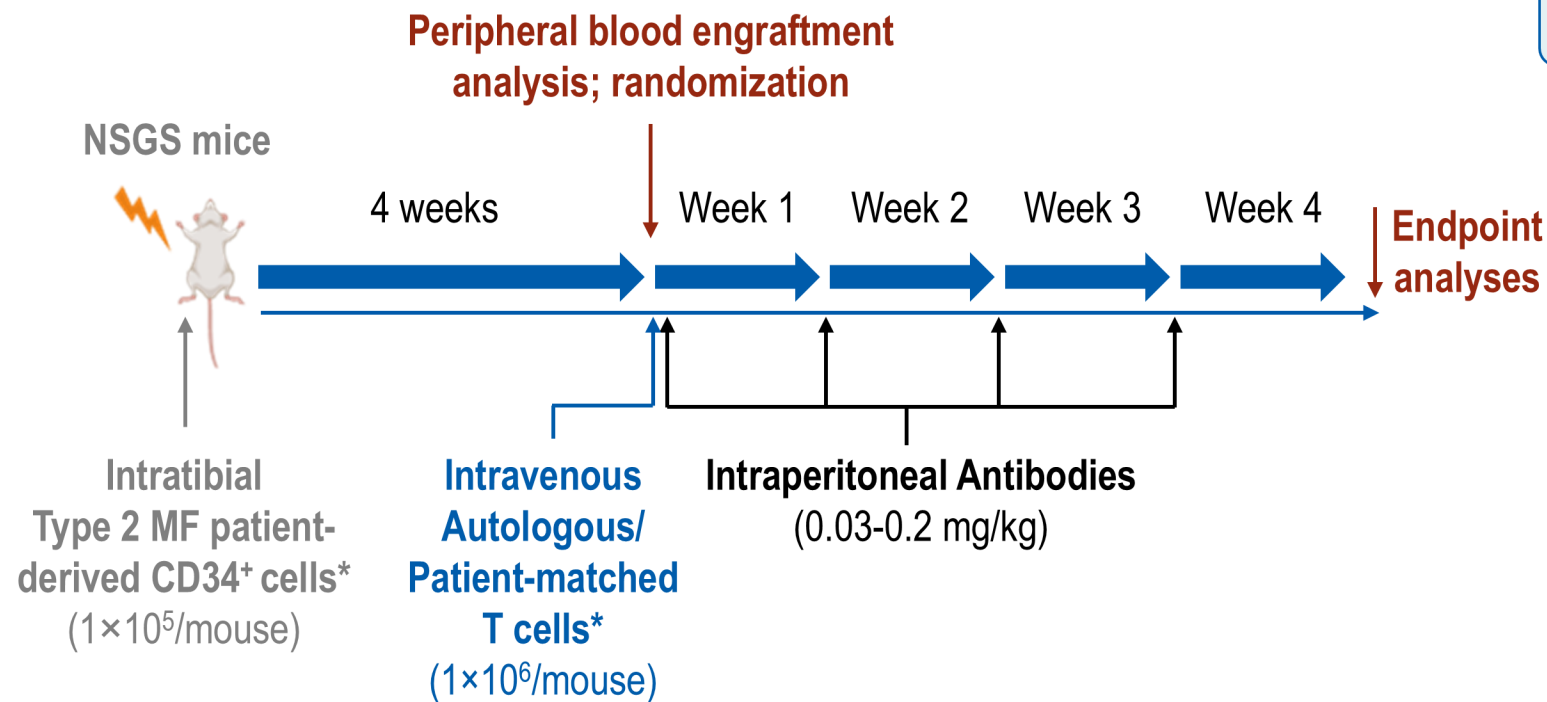
INCA035784 Does Not Induce Nonspecific Secretion of Cytokines Associated With CRS in Healthy Donor PBMCs



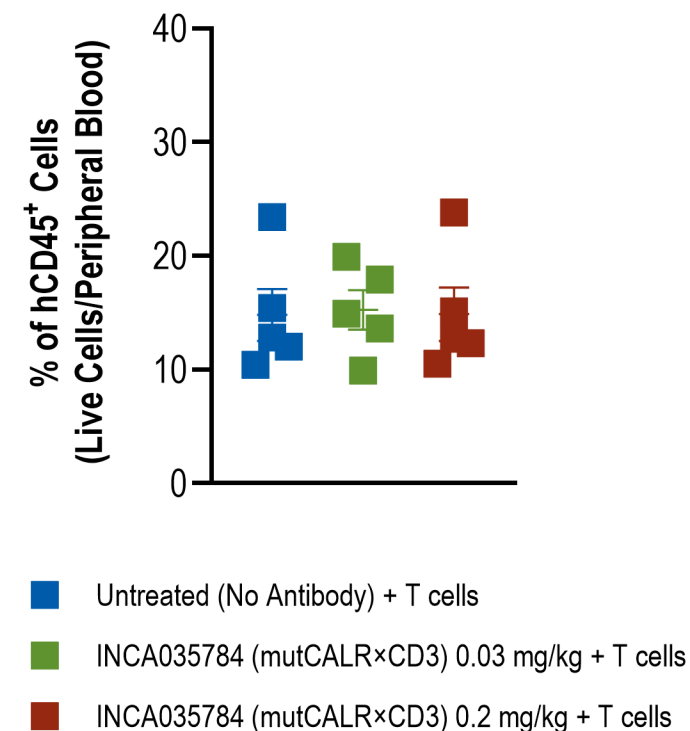
Graphs are representative of 3 independent experiments. Data points represent the mean and error bars represent the standard deviation. Anti-RSV line represents mean cytokine induction by anti-RSV control antibody.

Ab, antibody; CALR, calreticulin; CRS, cytokine release syndrome; IFN-γ, interferon gamma; IL-6, interleukin 6; PBMC, peripheral blood mononuclear cell; RSV, respiratory syncytial virus; TNF-α, tumor necrosis factor-alpha.

Autologous MF Patient-Derived Xenograft (PDX) Model



hCD45⁺ Cell Engraftment and Randomization

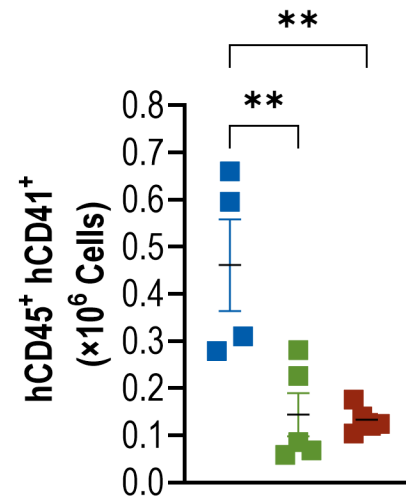


*Patient with Type 2 mutCALR MF (VAF, 89.6%). Data points represent the mean and error bars represent the standard error of the mean. CALR, calreticulin; MF, myelofibrosis; NSGS, NOD/SCID IL2RG knockout with cytokine expression.

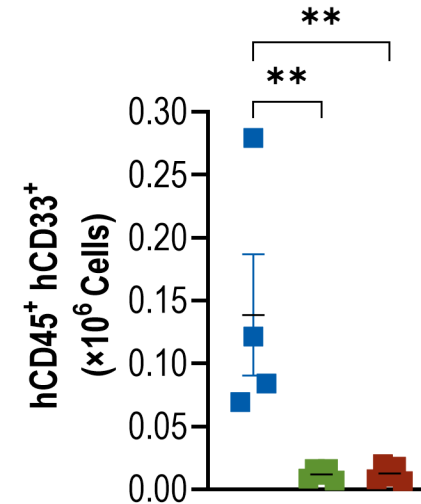
INCA035784 Exhibits Efficacy in an Autologous MF Patient-Derived Xenograft Model

- INCA035784 treatment causes reduction of myeloid cells (CD33⁺) and megakaryocytes (CD45⁺CD41⁺) in the bone marrow
- INCA035784 treatment does not affect the erythroid cell progenitor population (CD71⁺)

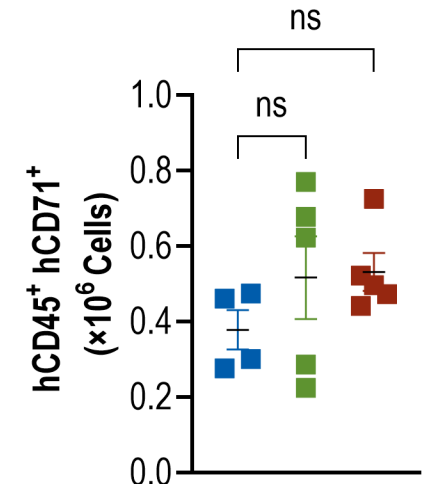
Megakaryocyte Progenitors



Myeloid Cells



Erythroid Cell Progenitors



- Untreated (No Antibody) + T cells
- INCA035784 (mutCALR x CD3) 0.03 mg/kg + T cells
- INCA035784 (mutCALR x CD3) 0.2 mg/kg + T cells

** $P < 0.01$ vs the untreated group (1-way ANOVA). Data points represent the mean and error bars represent the standard error of the mean. ANOVA, analysis of variance; CALR, calreticulin; MF, myelofibrosis; ns, not significant.

Summary

- INCA035784 is a T cell redirector with potent activity towards type 1 and type 2 mutCALR
 - Specifically binds to the conserved N-domain of surface-exposed mutCALR
 - Induces T cell activation, proliferation, and target cell cytotoxicity in co-culture of type 1 and type 2 mutCALR-expressing TF-1 cells and healthy donor T cells
 - Targets disease-initiating CD34⁺ progenitor cells from type 1 and type 2 mutCALR patients in co-cultures with healthy donor T cells
 - Demonstrates in vivo efficacy in an autologous MF patient-derived xenograft model
- INCA035784 binds to the N-domain of surface-exposed mutCALR which is conserved across all mutant types and an epitope distinct from mutCALR antagonist antibodies
- INCA035784 does not bind to stress-induced surface-exposed wild-type CALR
- Overall, INCA035784 represents a promising approach for patients with MPN who lack curative treatment options (NCT07008118)

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Disclosures

- **Veethika Pandey, Liang-Chuan Wang, Ashwini Kulkarni, Daniel Merenich, Jun Guan, Emily Ren, Niketa Langalia, Karol Fiedorczuk, Fatoumata Jobe, Angelo Albertoni, Hamza Celik, Stephen Rudnick, Rodrigo Hess, Horacio Nastri, Ricardo Macarron, Patrick A. Mayes:** *Incyte Corporation* - Employment and stock ownership
- **Linda Hendriks, Tessa Steevels, Rinse Klooster, David Maussang-Detaille:** *Merus NV* - Employment and stock ownership
- **Bethan Psaila:** *Incyte Corporation* - Research funding, consultancy, advisory board, travel support to attend EHA2025; *Blueprint Medicines* - Consultancy; *GSK* - Paid speaking engagements, advisory board; *BMS* - Consultancy; *Novartis* - Paid speaking engagements, advisory board, consultancy; *Alethiomics* - Major shareholder, consultancy, research funding