

Use of dasatinib for reversible control of CD123 CAR-T cells

Mantion *et al.*, Molecular Therapy Oncology, 2025, in press

<https://doi.org/10.1016/j.omton.2025.201097>

Charles-Frédéric Mantion, PhD Student

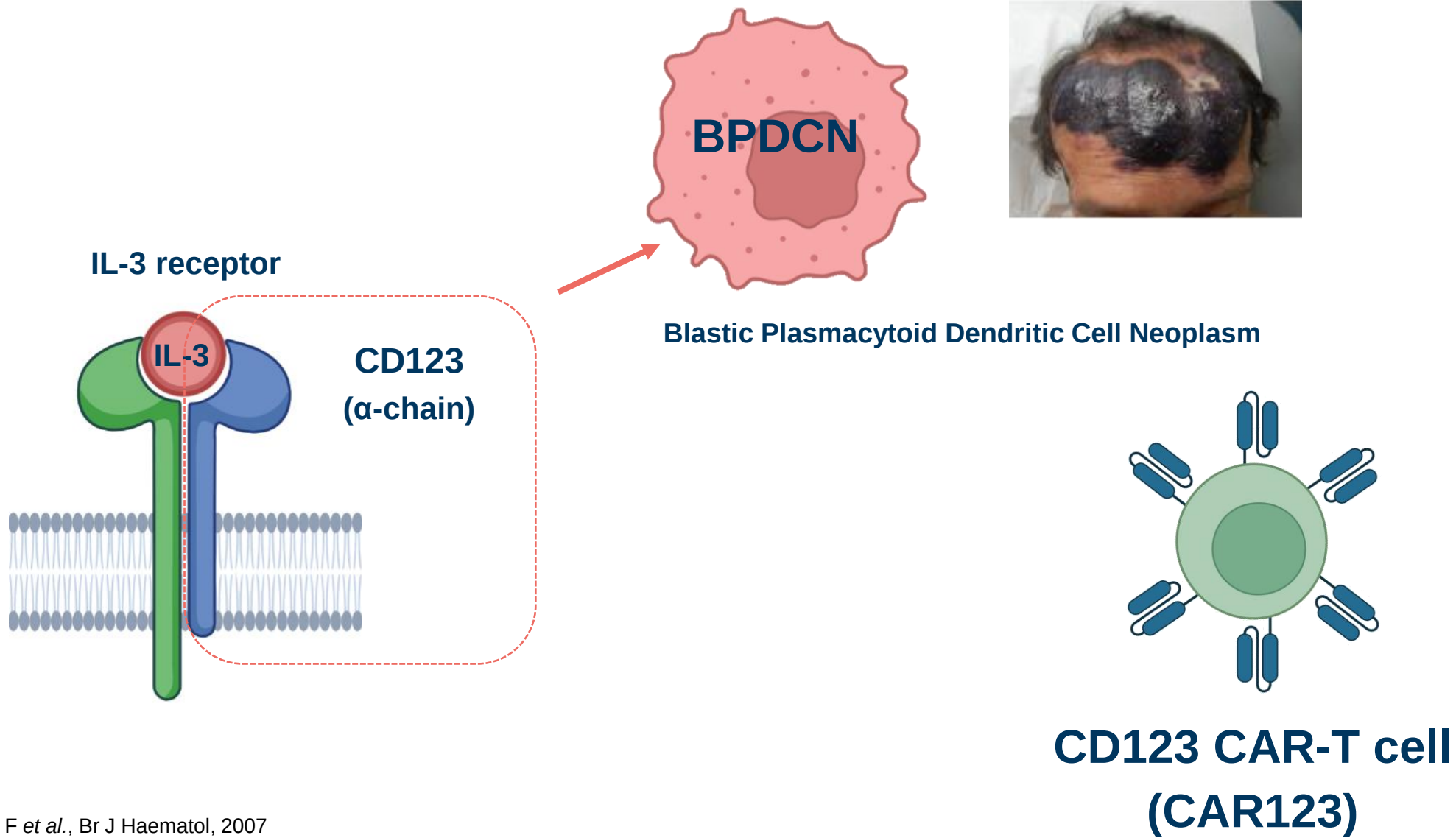
Université Marie et Louis Pasteur, EFS, INSERM, UMR1098 RIGHT

Pr. Francine Garnache-Ottou (PU-PH)

Dr. Maxime Fredon (CSO, CARLA Biotherapeutics)

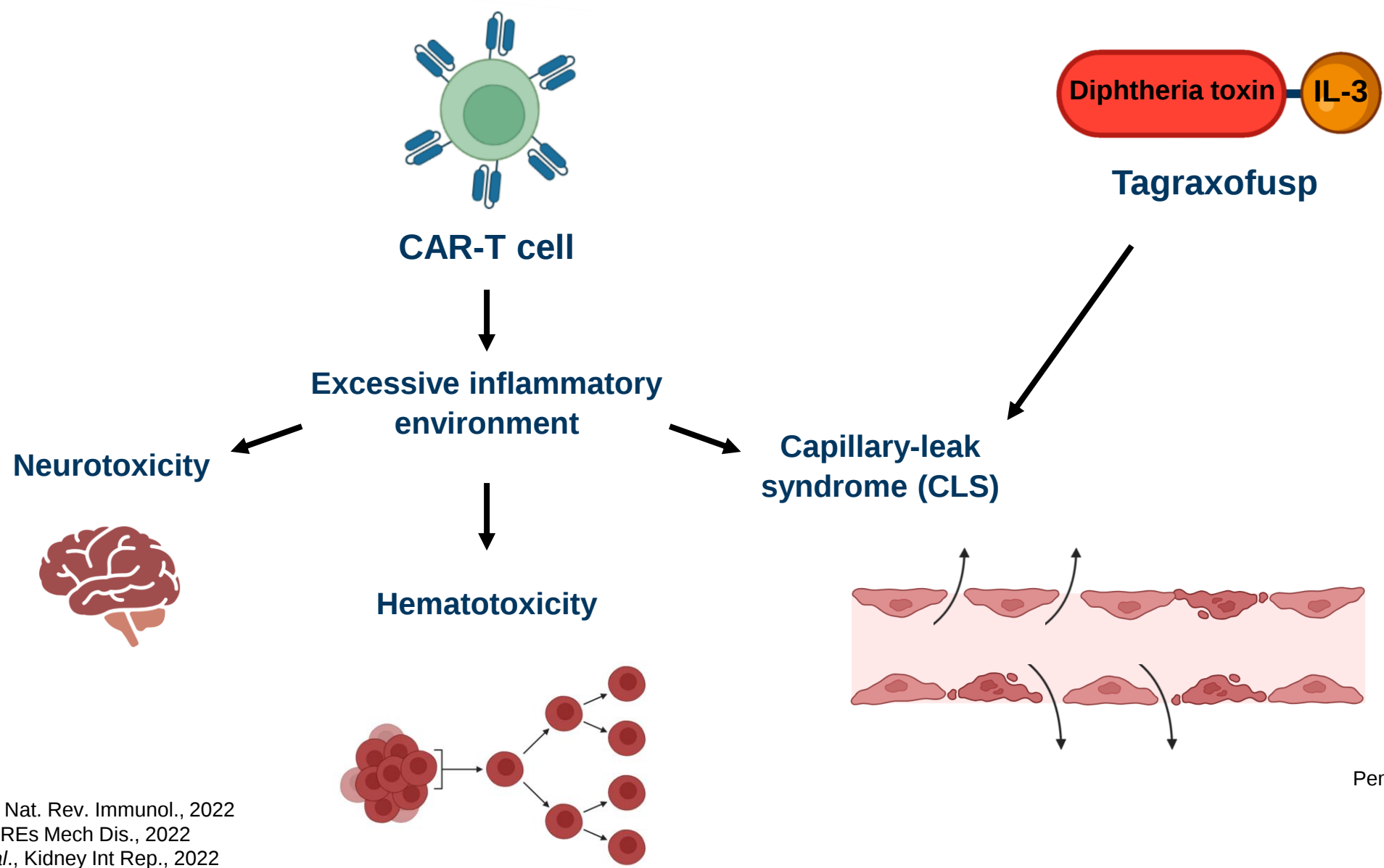


CD123 is a target in BPDCN



Garnache-Ottou F *et al.*, Br J Haematol, 2007
Garnache-Ottou *et al.*, Blood Advances, 2019
Angelot-Delettre & Garnache-Ottou. Blood, 2012
Bôle-Richard *et al.*, Leukemia, 2020
Fredon *et al.*, Cancer Immunol. Res., 2024

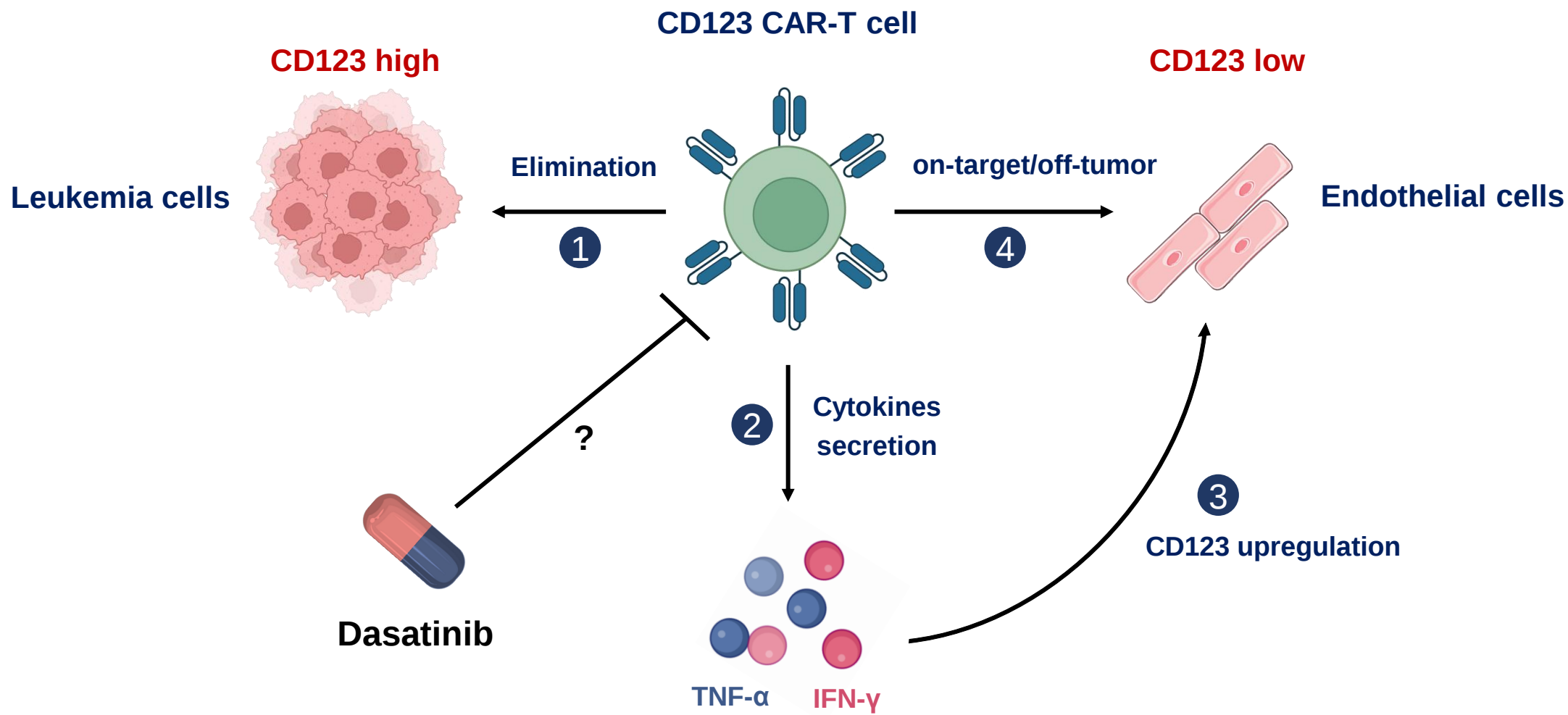
CD123-targeted therapies and CAR-T cell therapies are associated with toxicities



Morris *et al.*, Nat. Rev. Immunol., 2022
Gu *et al.*, WIREs Mech Dis., 2022
Izzedine *et al.*, Kidney Int Rep., 2022

Frankel *et al.*, Blood, 2014
Pemmaraju *et al.*, N Engl J Med., 2019

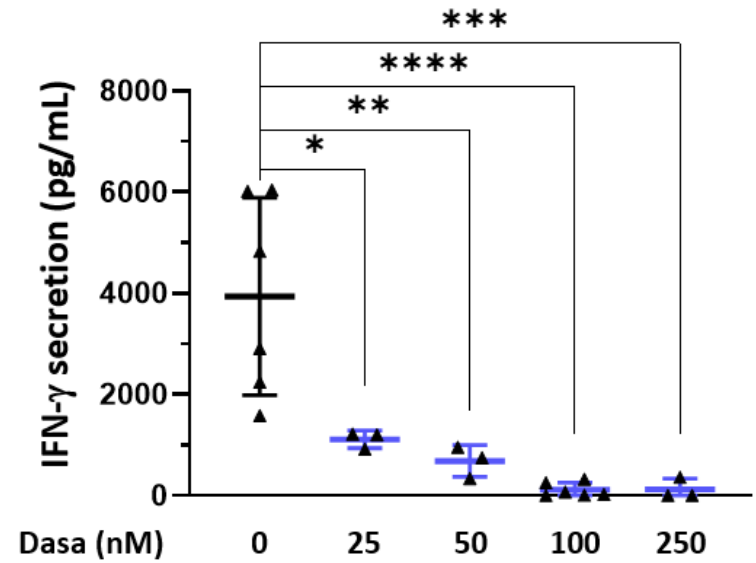
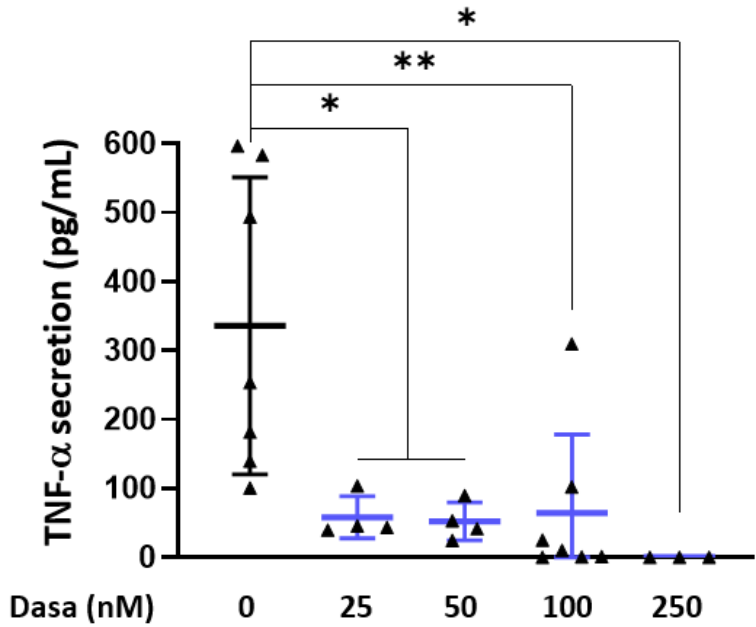
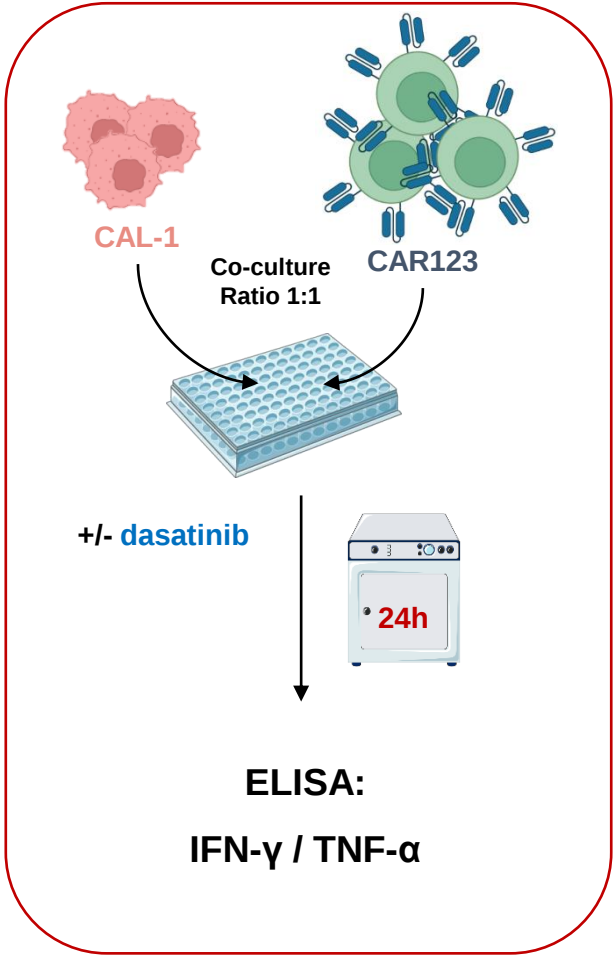
TNF- α and IFN- γ induce an overexpression of CD123 on endothelial cells



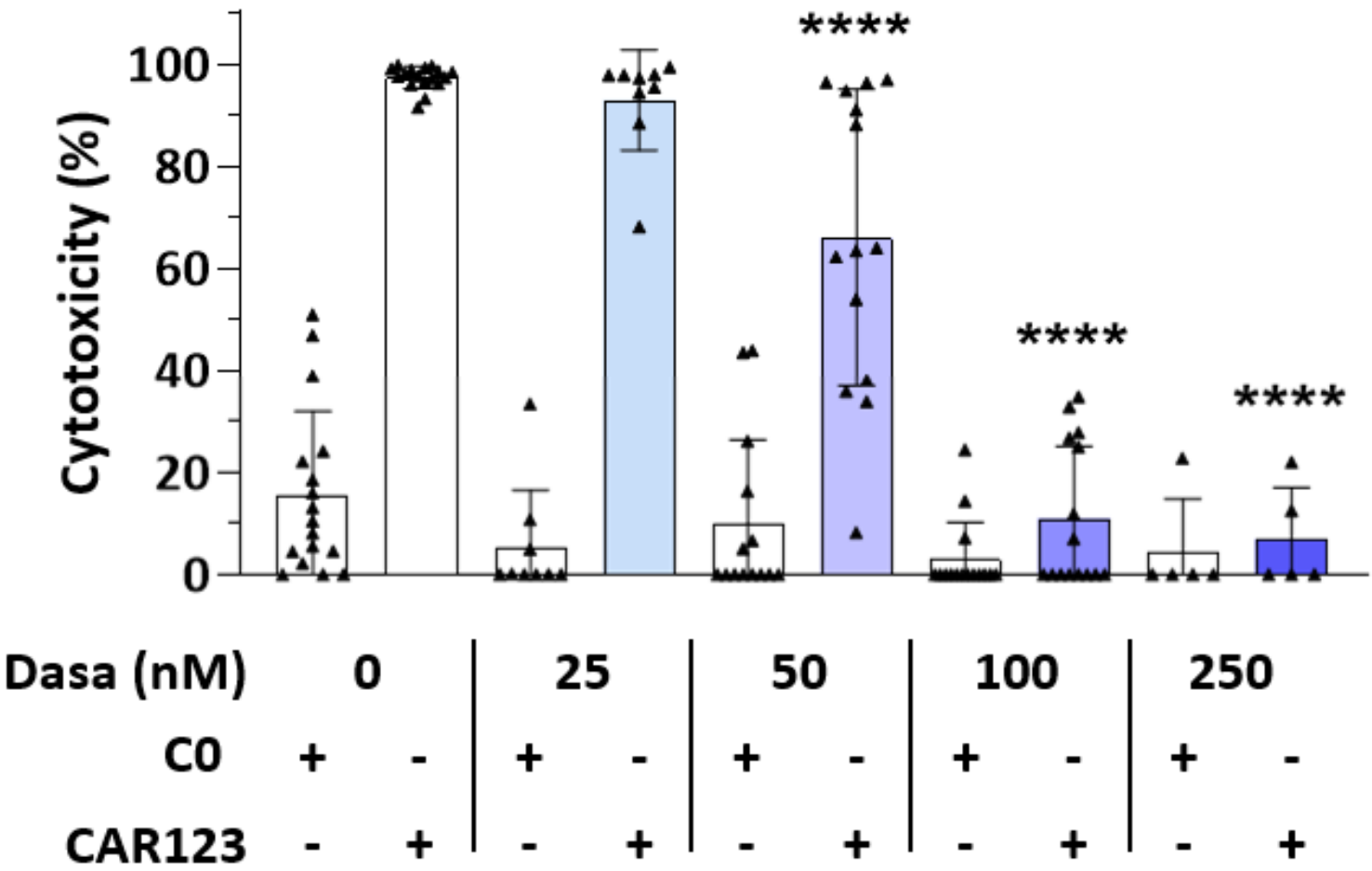
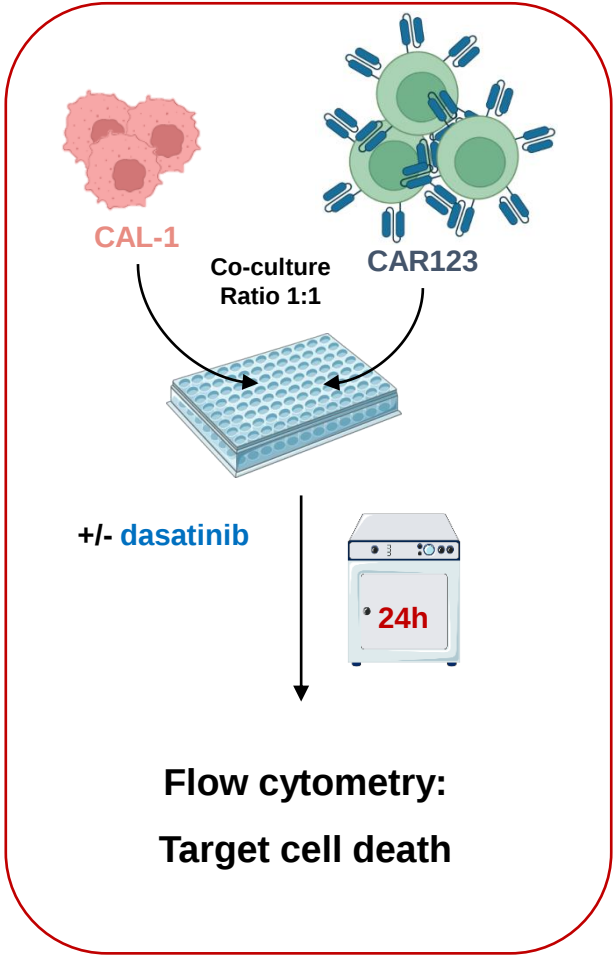
(Sun *et al.*, OncoTargets Ther., 2019)
(Fredon *et al.*, Cancer Immunol Res., 2024)

(Mantion *et al.*, Mol. Ther. Oncol., in press)

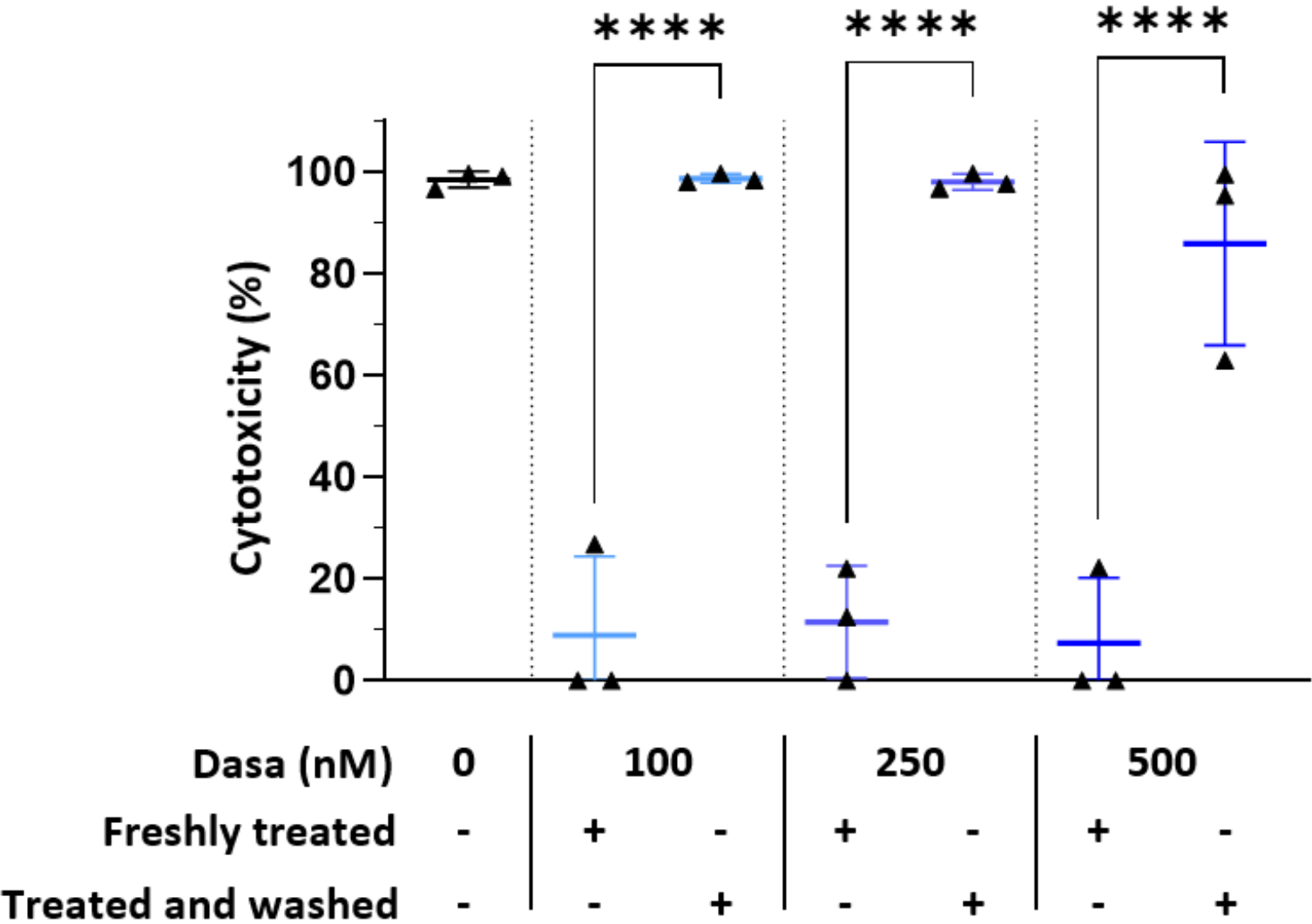
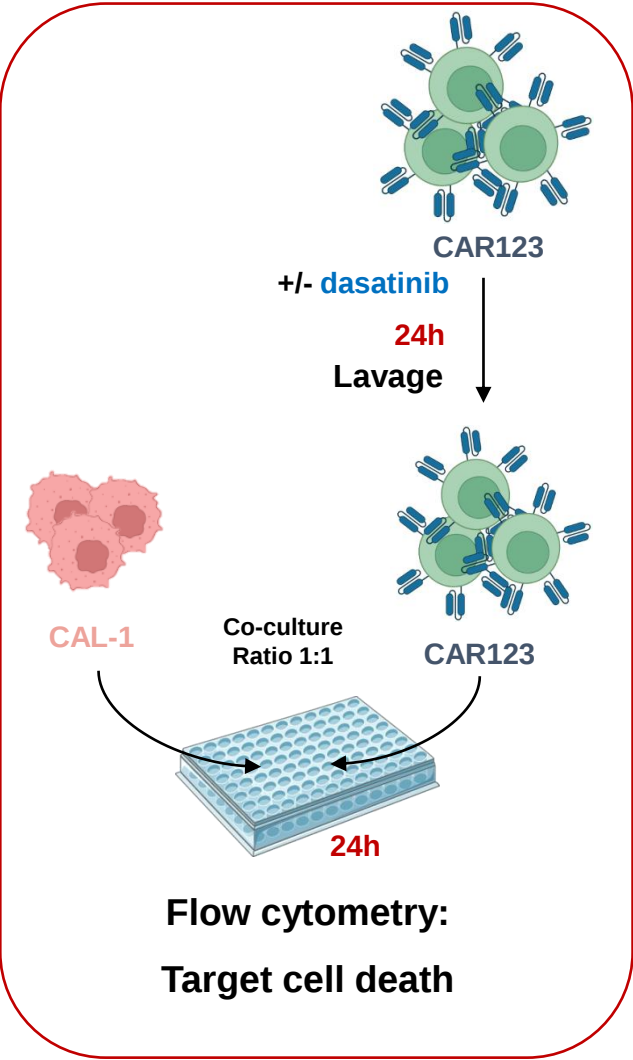
Dasatinib 25 nM inhibits TNF-α and IFN-γ secretion by CAR123



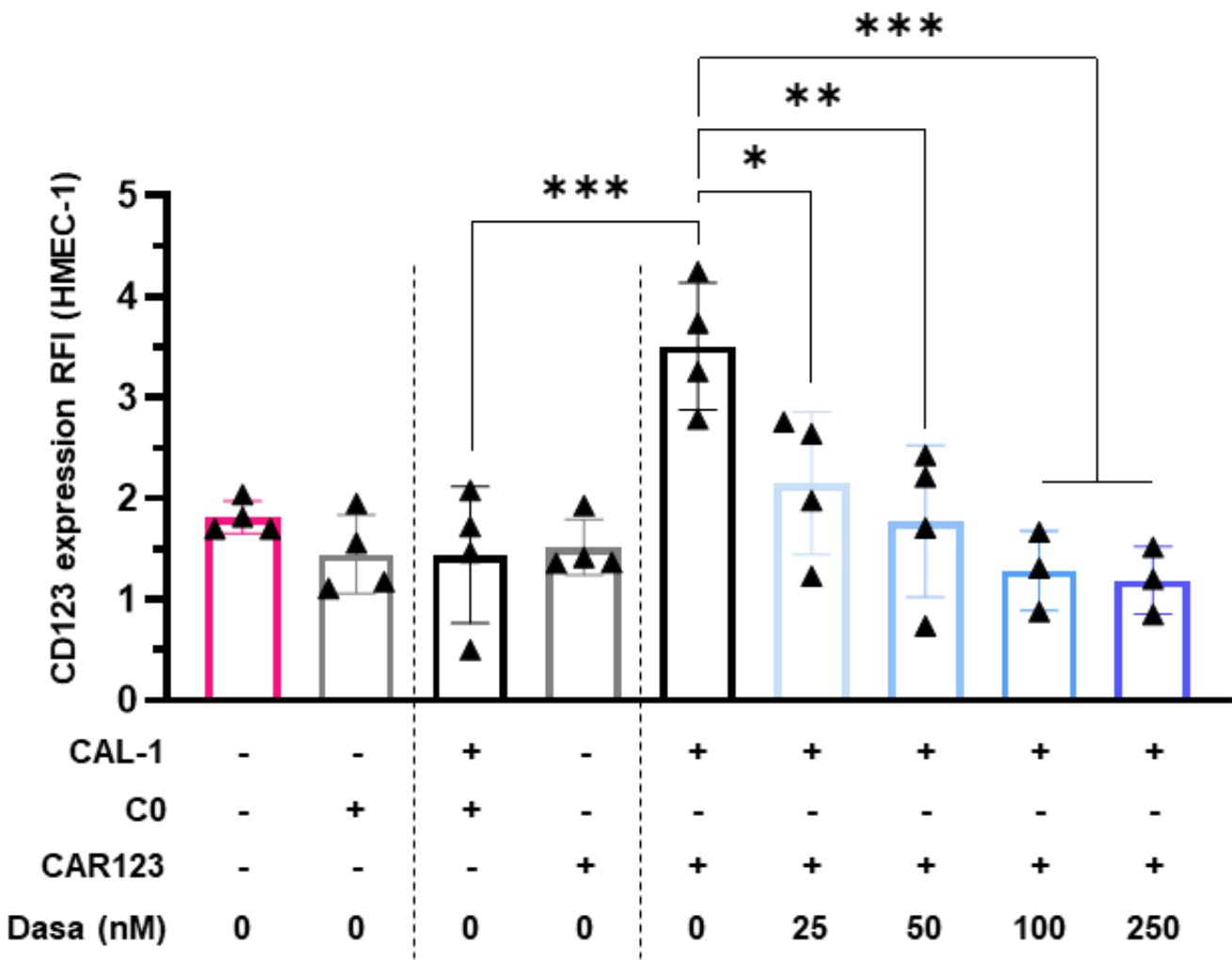
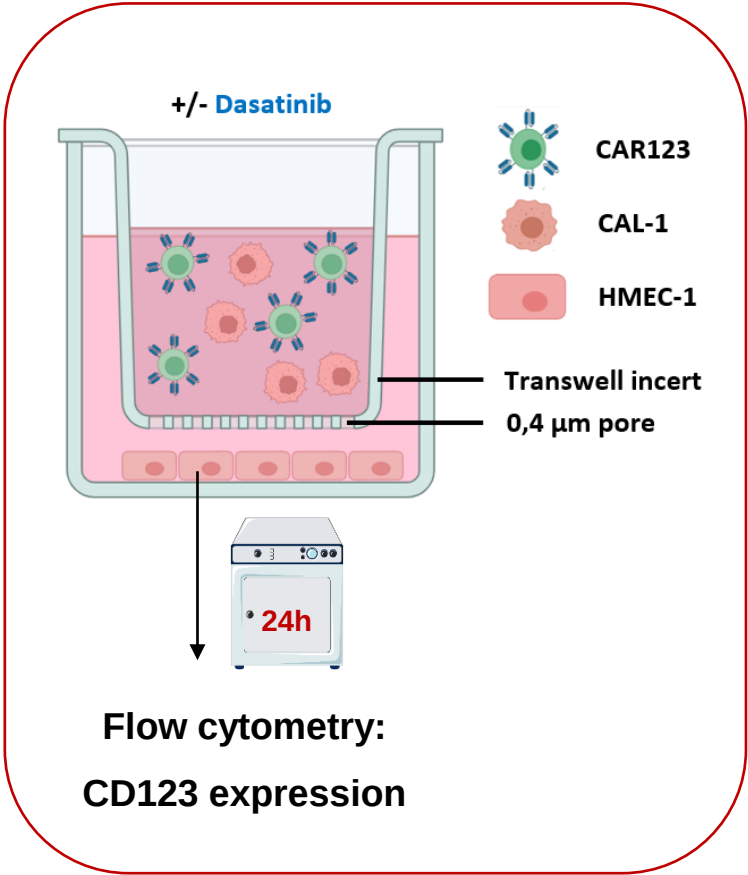
Dasatinib 25 nM does not impact CAR123 anti-tumor effect



Dasatinib inhibition of cytotoxicity is reversible



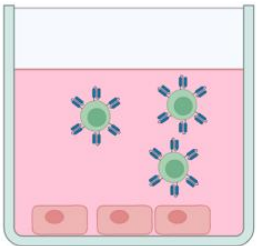
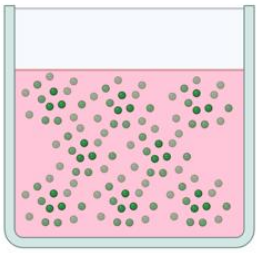
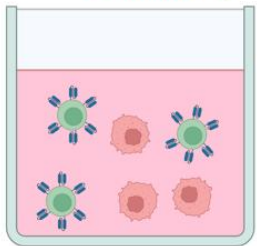
Dasatinib reduces CAR123-induced CD123 overexpression by HMEC-1 endothelial cell line



Dasatinib controls on-target/off-tumor effect of CAR123 on HMEC-1 endothelial cell line

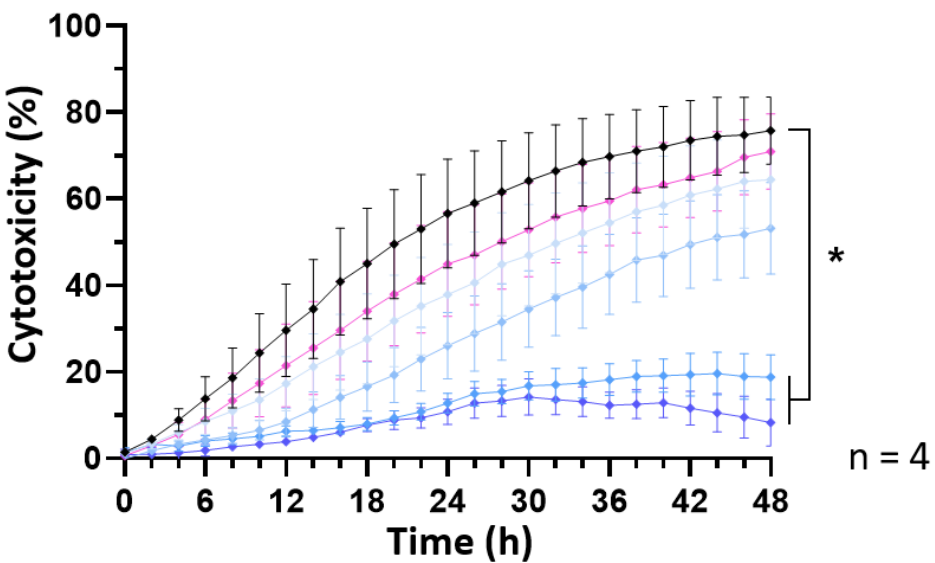
Incucyte cytotoxicity assay
in conditioned media

+/- Dasatinib
+/- anti-TNF- α
+ anti-IFN- γ

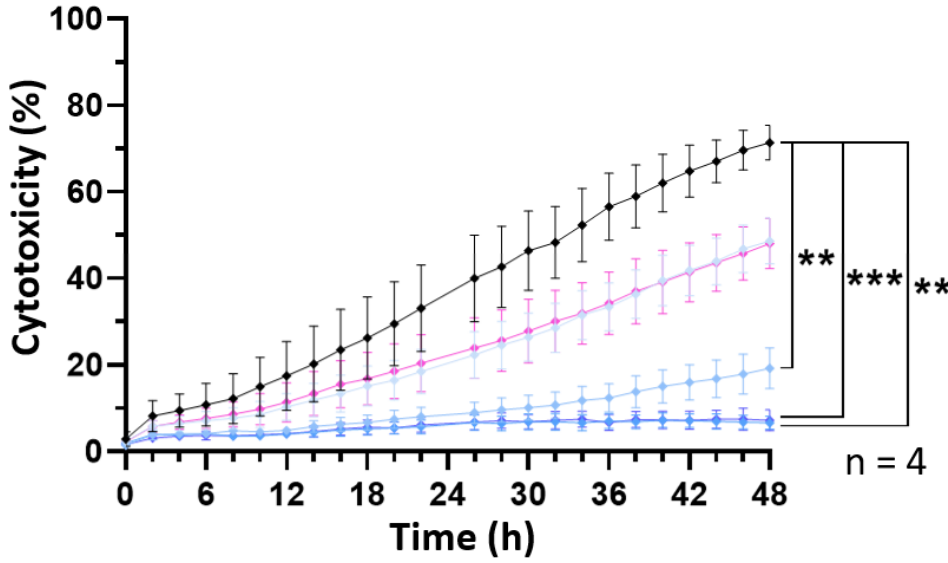


Incucyte S3 microscopy:
Target cell death

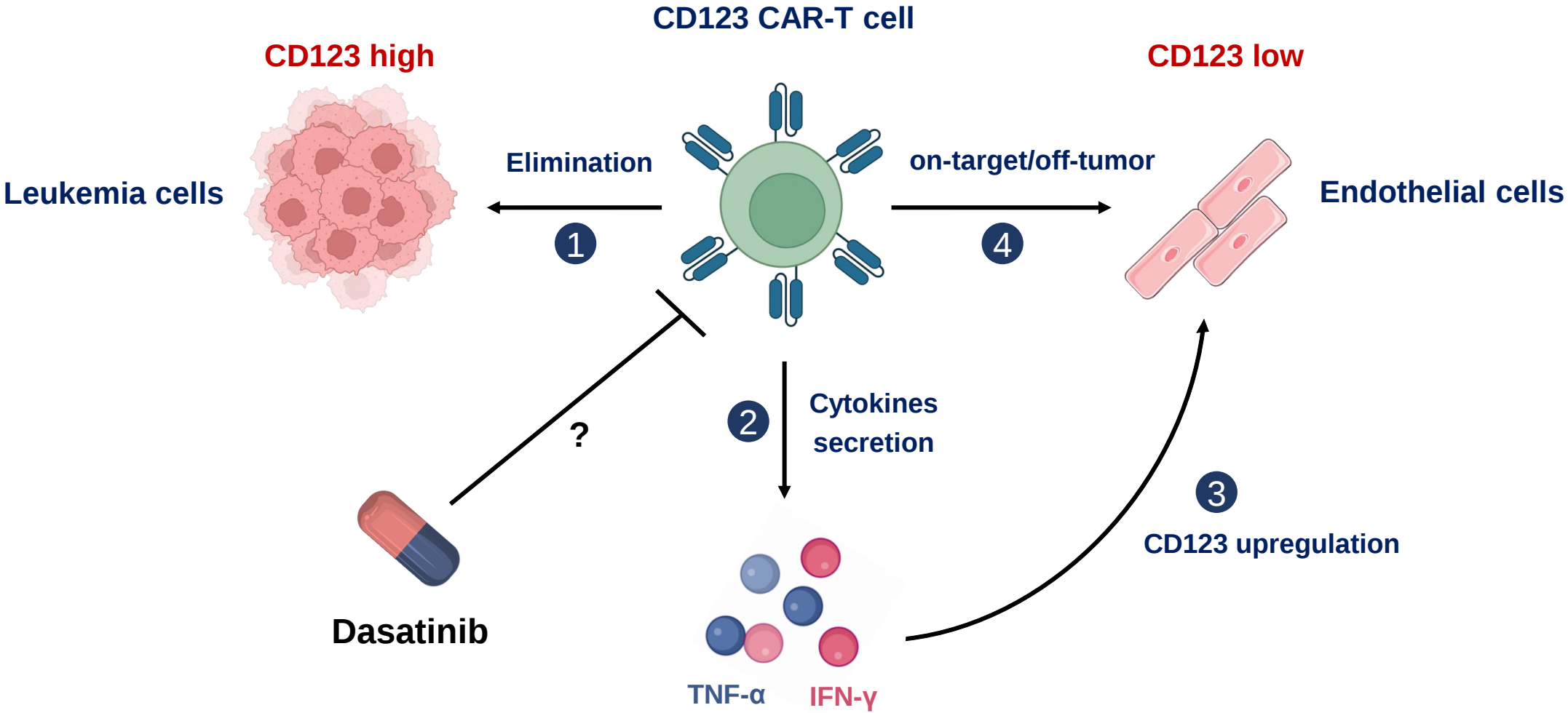
CAL-1 + CAR123



HMEC-1 + CAR123



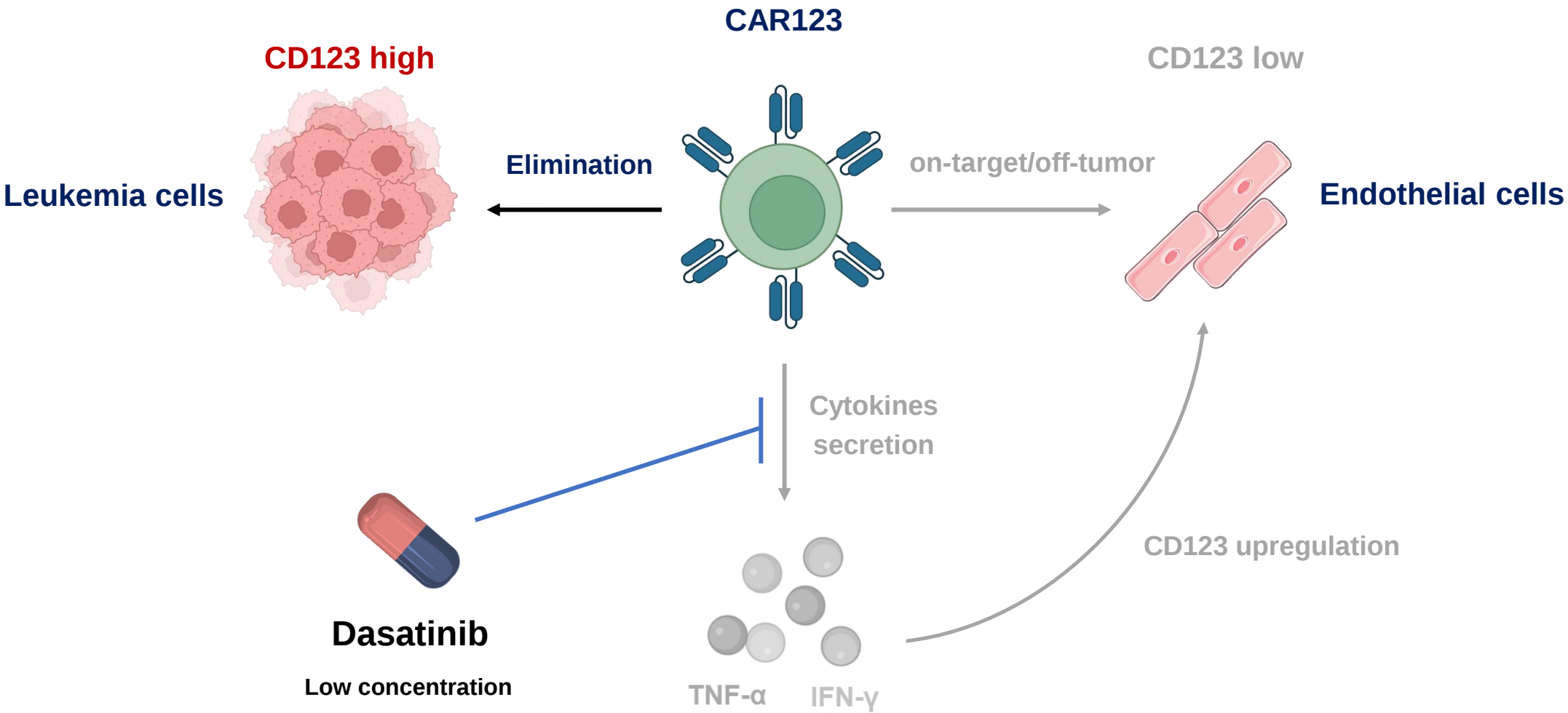
TNF-α and IFN-γ induce an overexpression of CD123 on endothelial cells



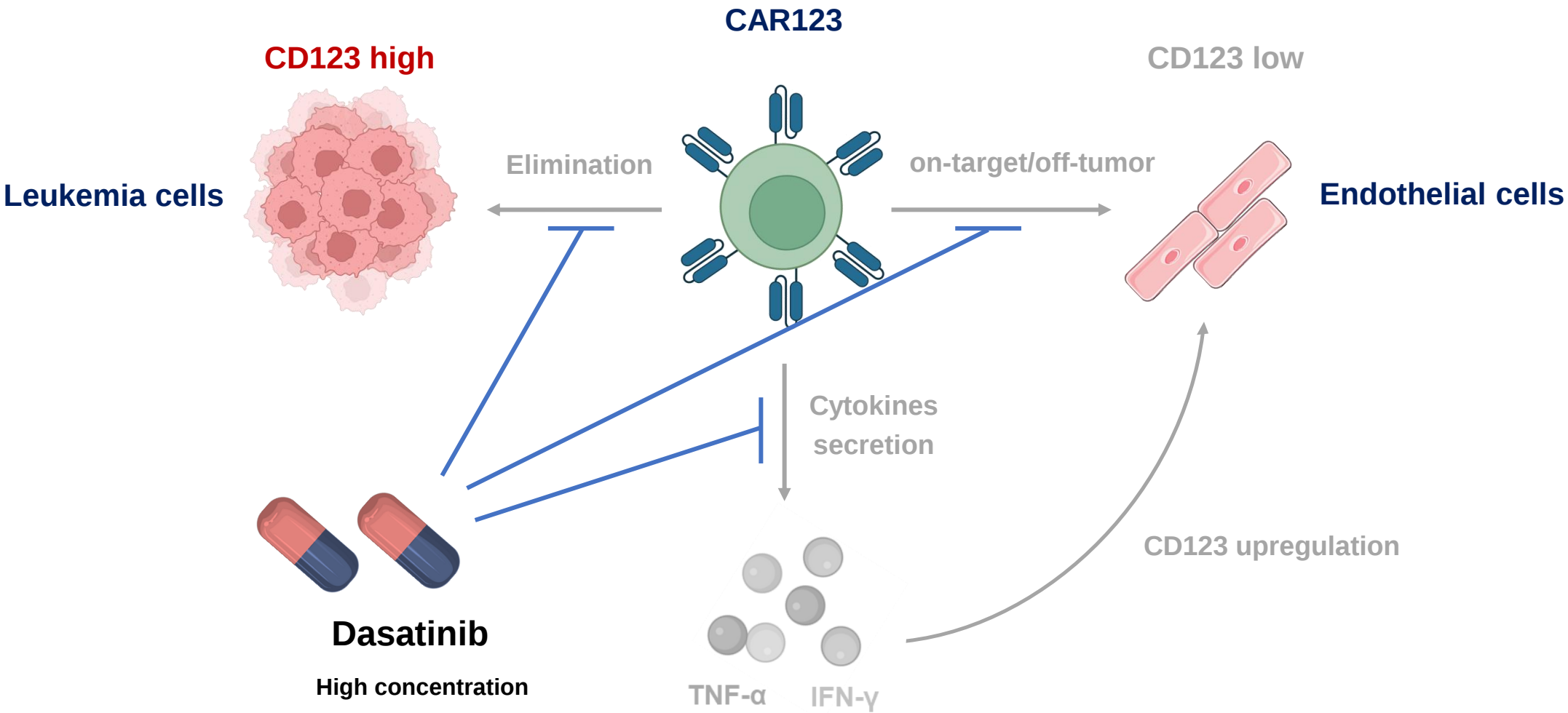
(Sun *et al.*, OncoTargets Ther., 2019)
(Fredon *et al.*, Cancer Immunol Res., 2024)

(Mantion *et al.*, Mol. Ther. Oncol., in press)

Low concentration dasatinib reduces CAR123 toxicity on endothelial cells



High concentration dasatinib reversibly inhibits CAR123 functionality





Pr. Francine Garnache-Ottou

Pr. Olivier Adotevi

Dr. Romain Loyon

Dr. Bernard Royer

Dr. Xavier Roussel

Dr. Gwenaël Rolin

Dr. Tony Labaigt

Dr. Florian Renosi

Dr. Elodie Bôle-Richard

Sabeha Biichlé

Agathe Lejeune

All the UMR RIGHT members



Dr. Maxime Fredon



Thank you

fgarnache@chu-besancon.fr

Seeking postdoctoral
opportunities starting 03/2026:

charles-frederic.mansion.ext@efs.sante.fr
charlesmansion@icloud.com