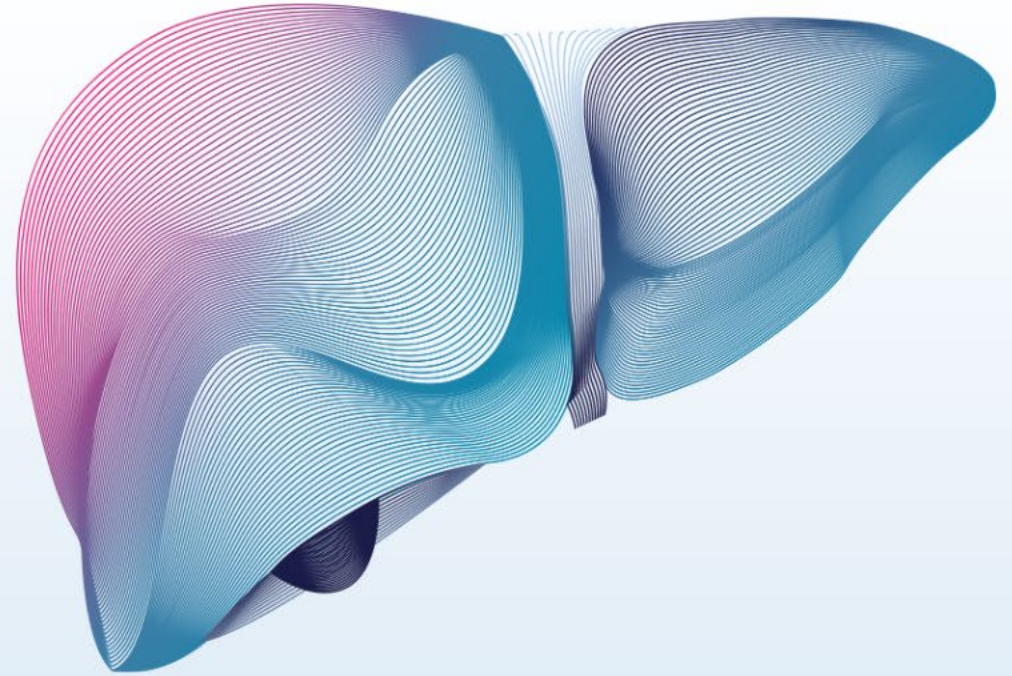




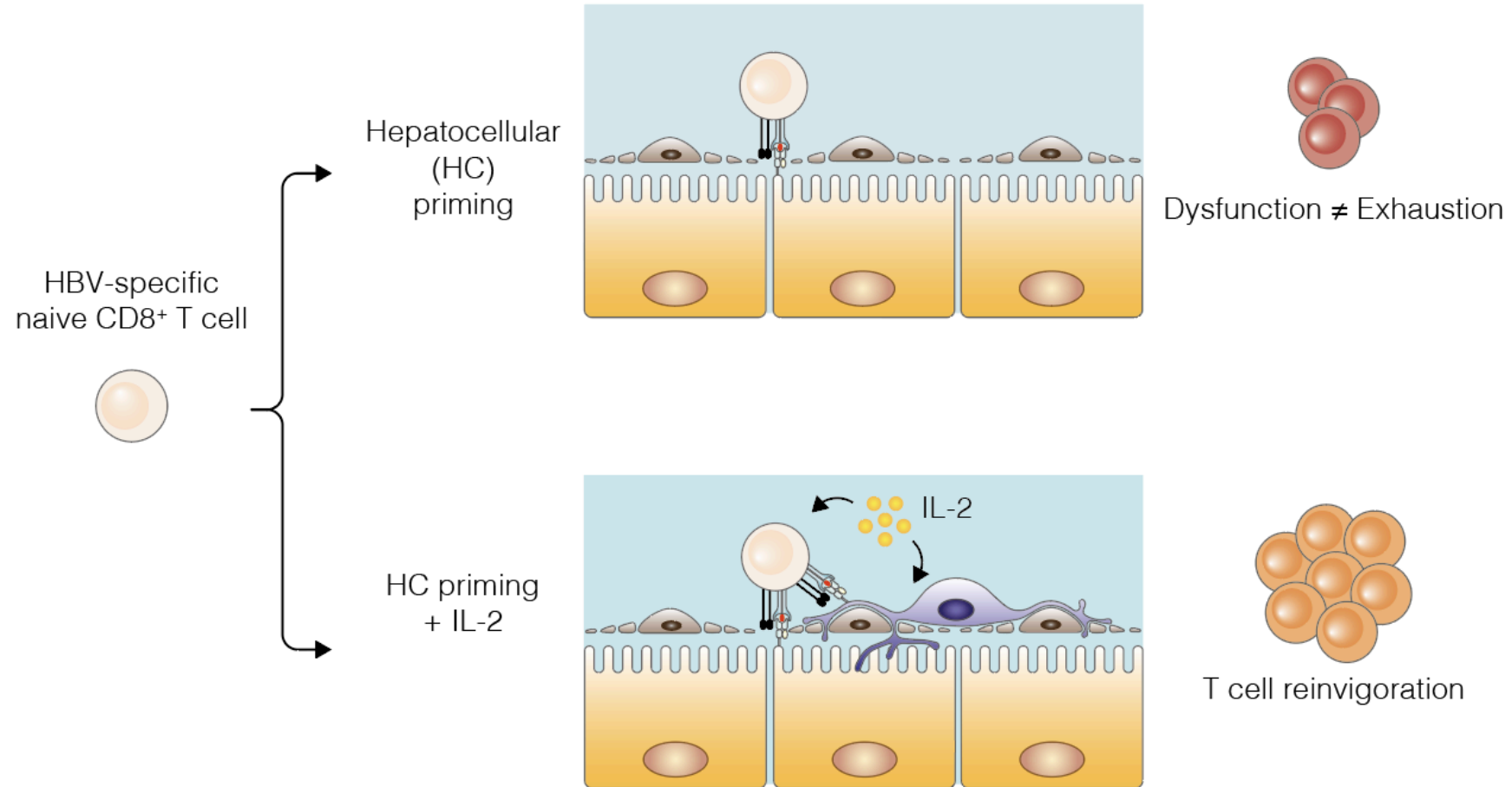
The International Liver Congress™



# CD8 *cis*-targeted IL-2 drives potent antiviral activity against hepatitis B virus

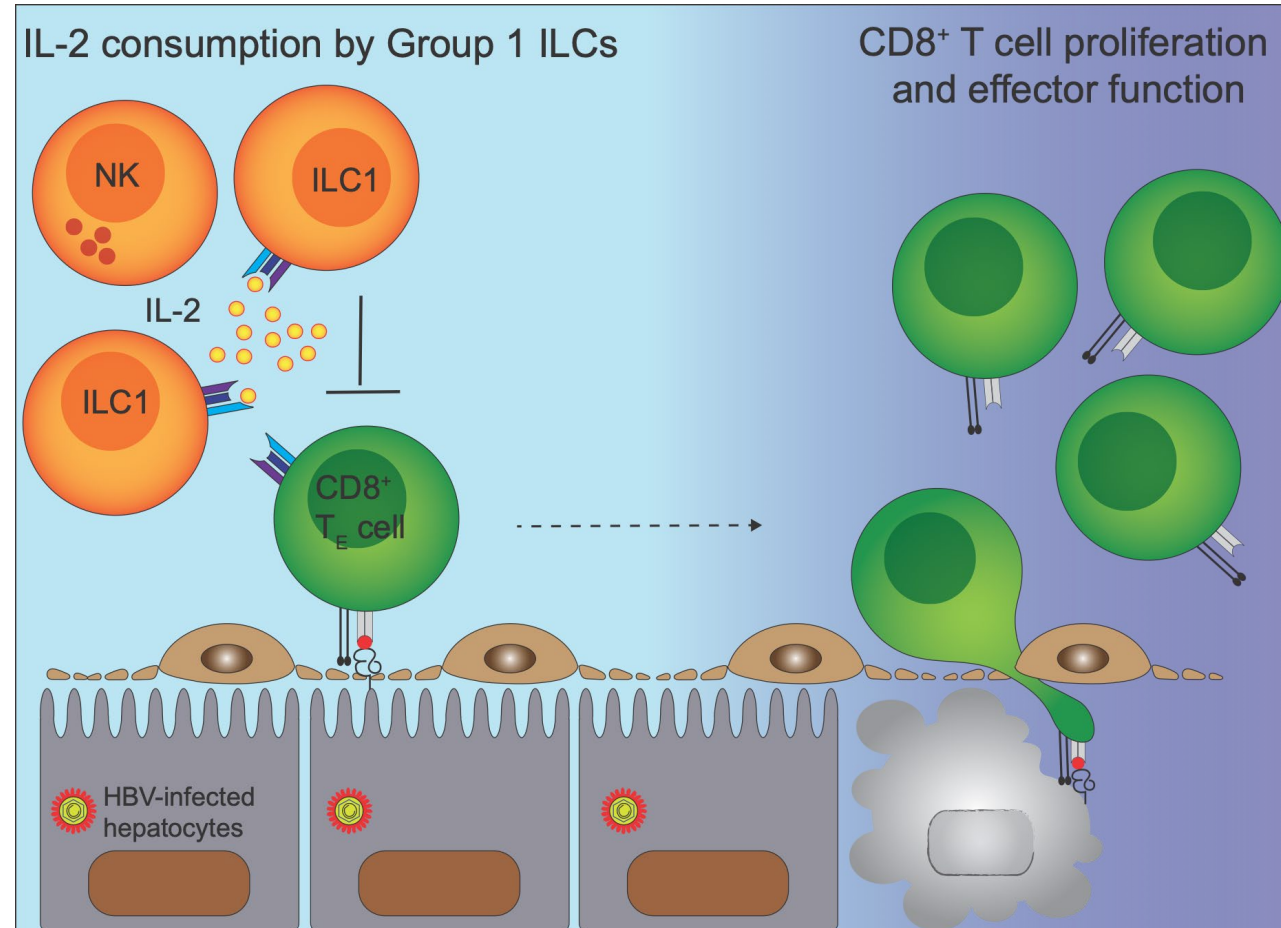
Matteo Iannacone M.D., Ph.D.

# Intrahepatically primed, dysfunctional CD8<sup>+</sup> T cells can be rescued by IL-2



Bén  chet et al., *Nature*. 2019

# Group 1 ILCs compete with CD8<sup>+</sup> T cells for local IL-2 availability

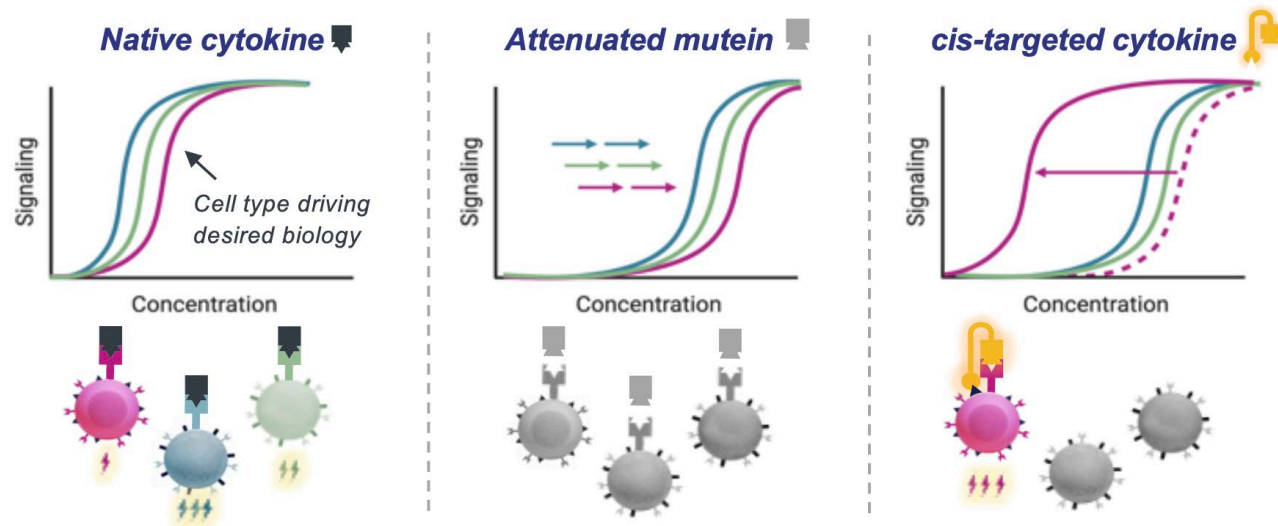
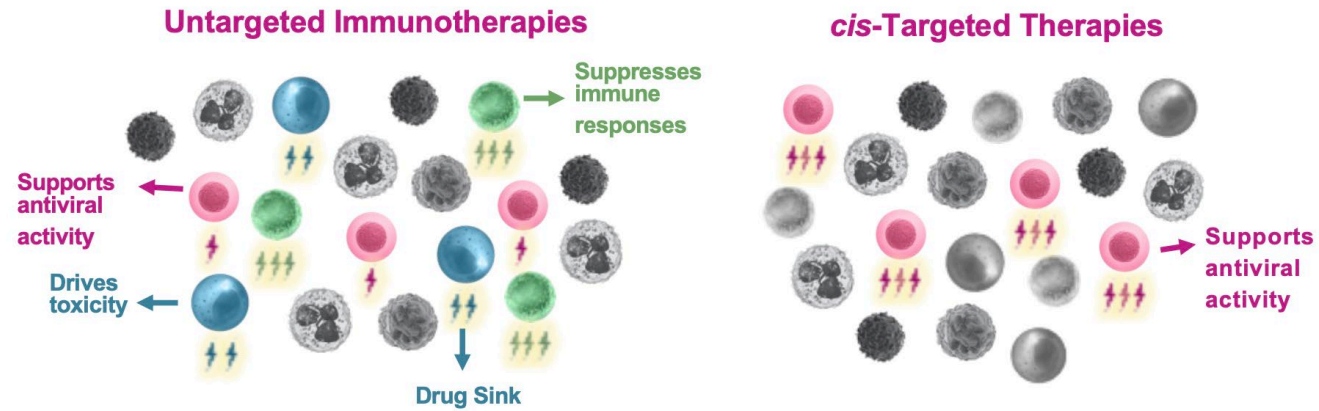


Valeria  
Fumagalli

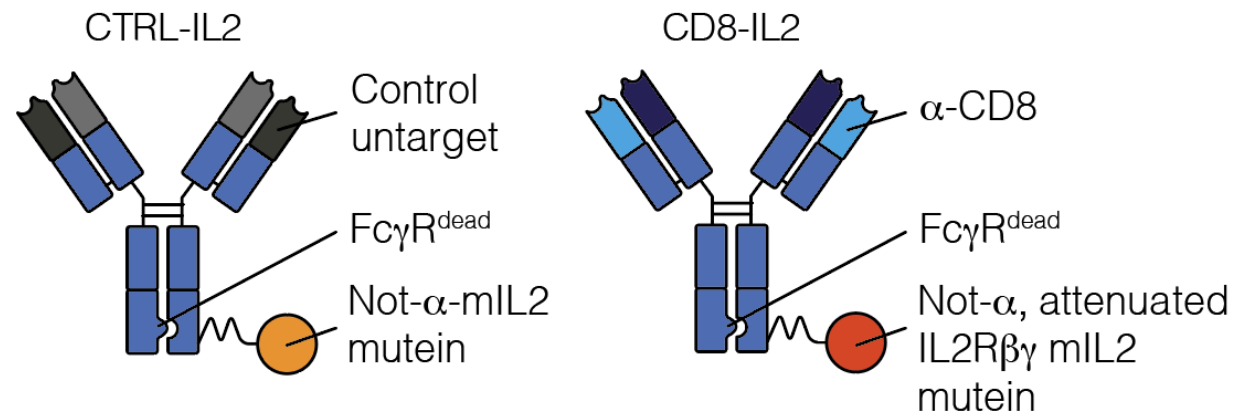
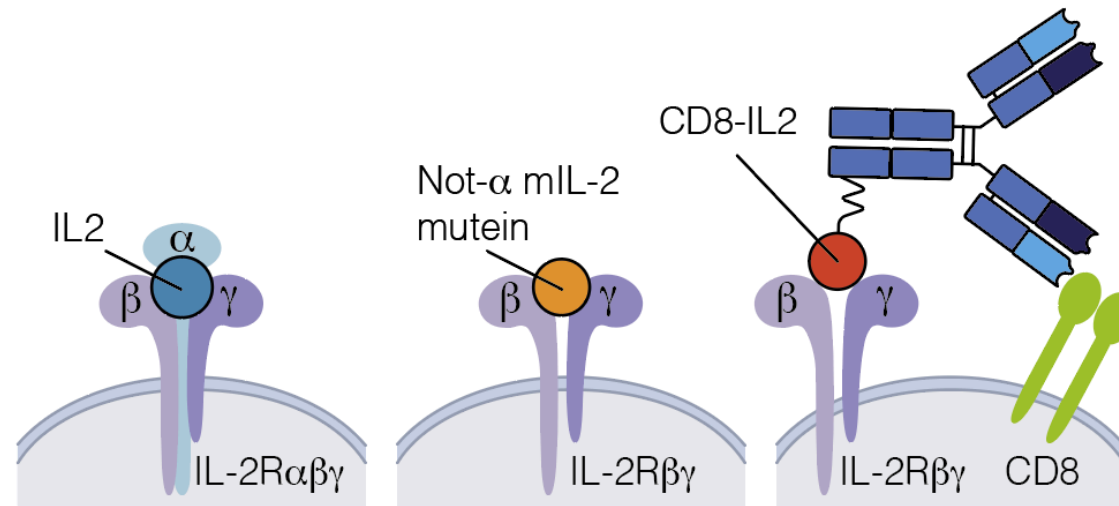
*Fumagalli et al., Science Immunology 2022*



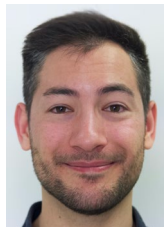
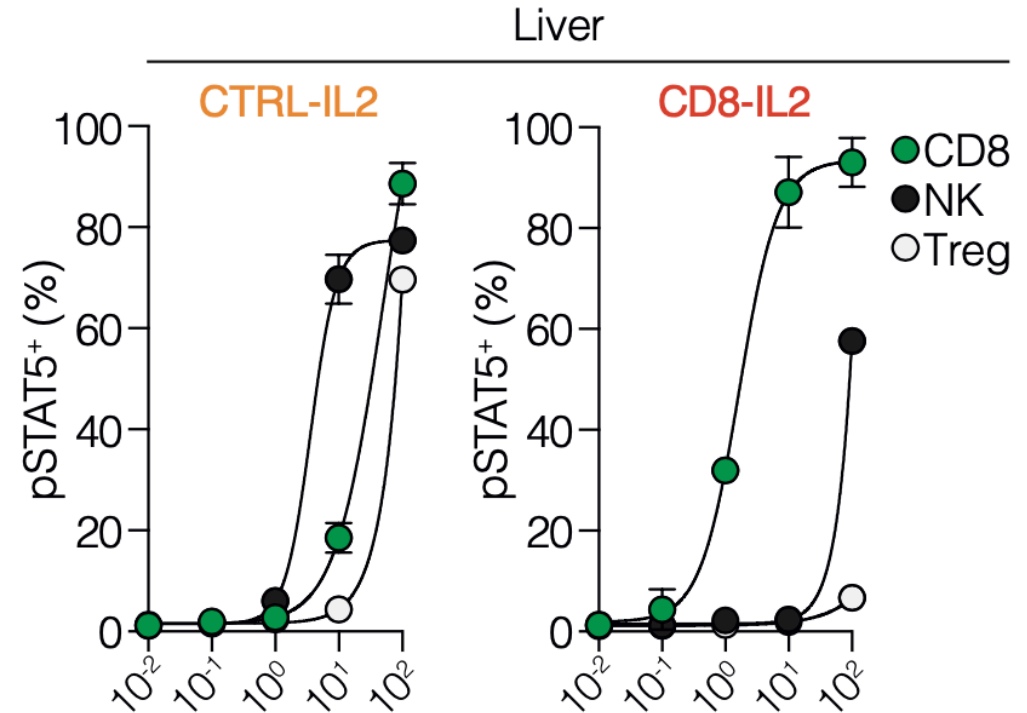
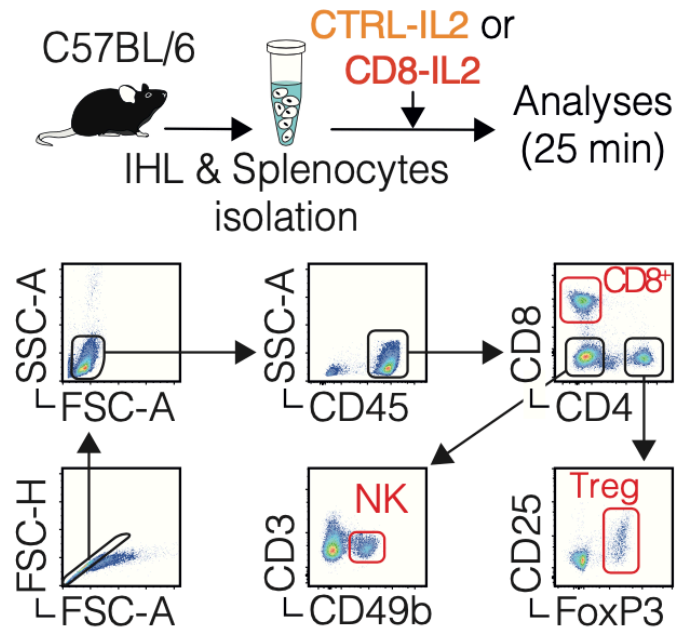
# *Cis*-targeting may address the pleiotropy associated with WT cytokines



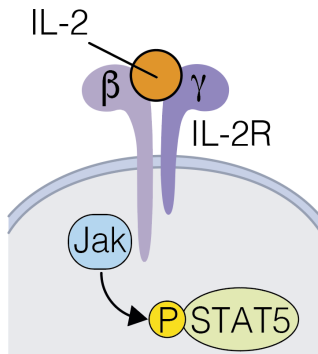
# Generation of a CD8 cis-targeted IL-2



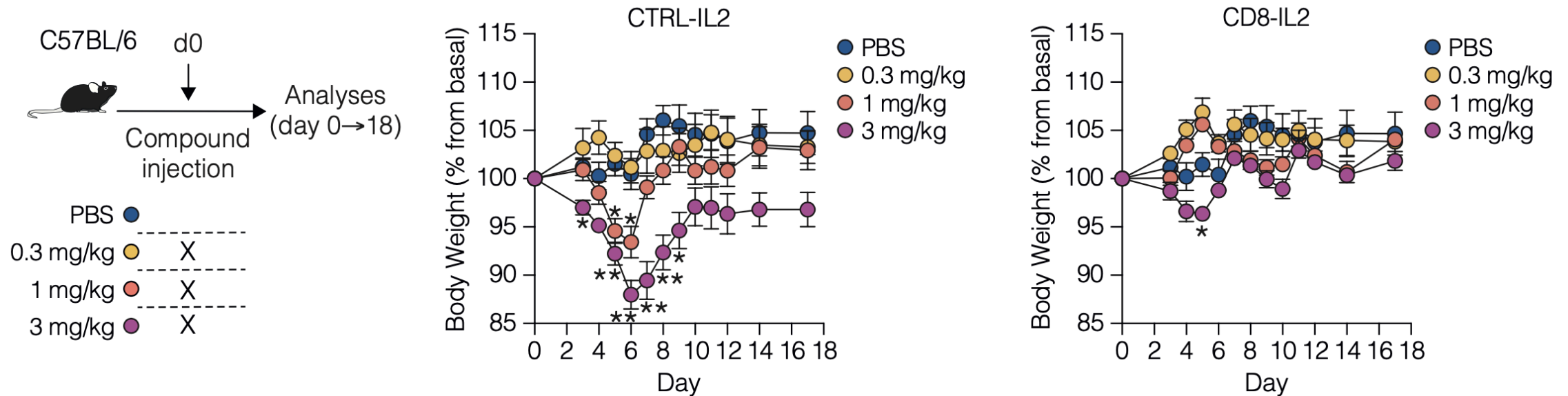
# A mouse CD8 cis-targeted IL-2 shows selective intrahepatic CD8<sup>+</sup> T cell activation *in vitro*



Francesco  
Andreata

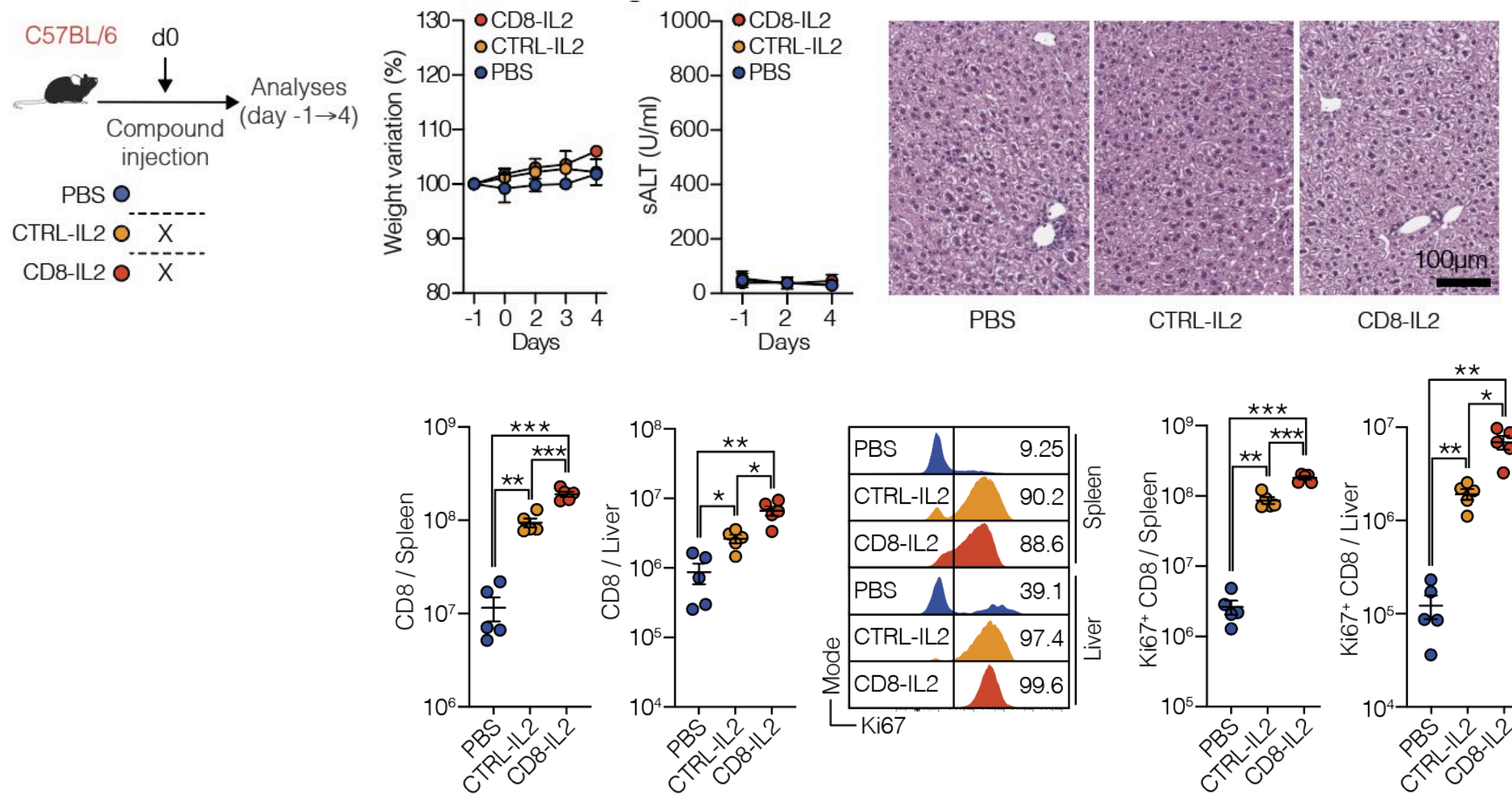


# A mouse CD8 *cis*-targeted IL-2 shows an acceptable safety profile *in vivo*



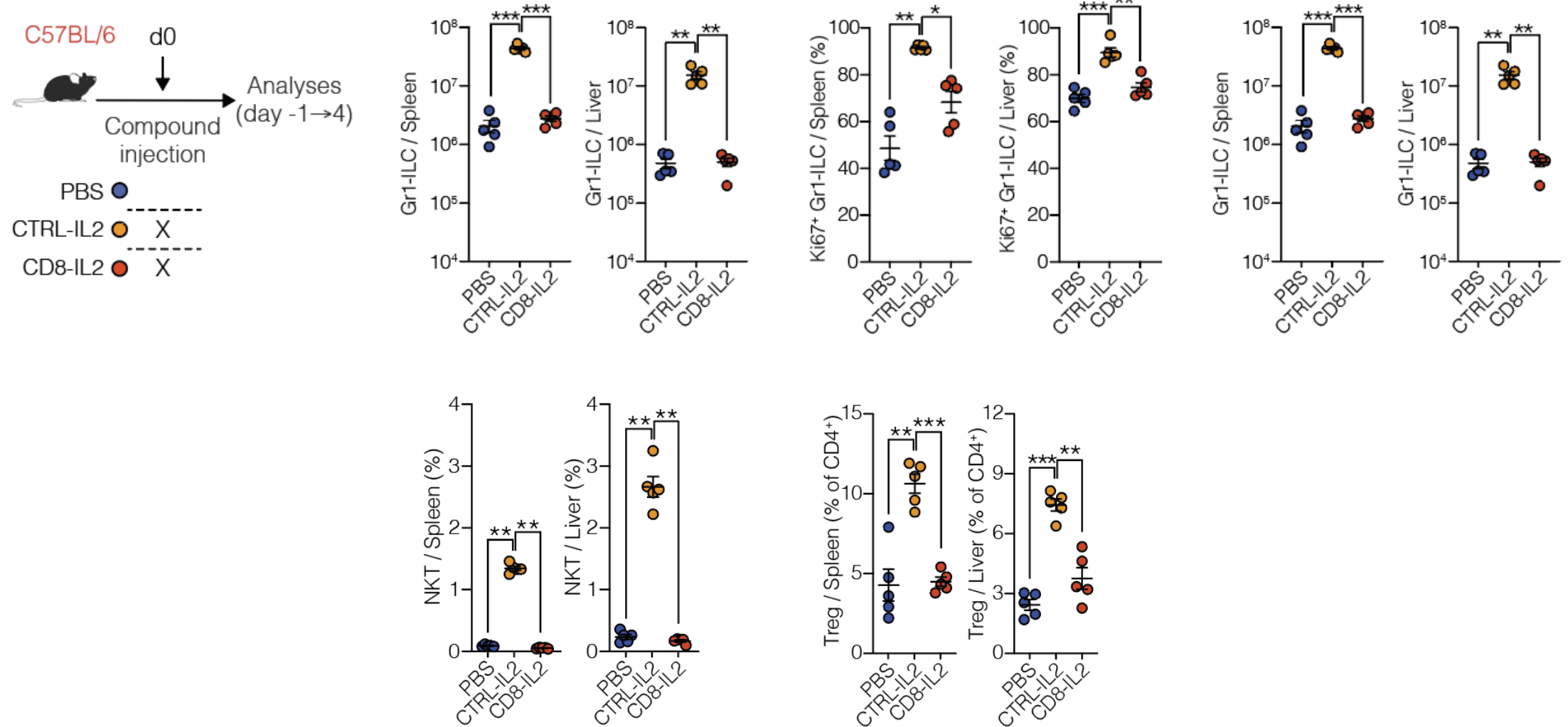


## CD8-IL2 selectively expands CD8<sup>+</sup> T cells without evidence of liver toxicity in WT mice

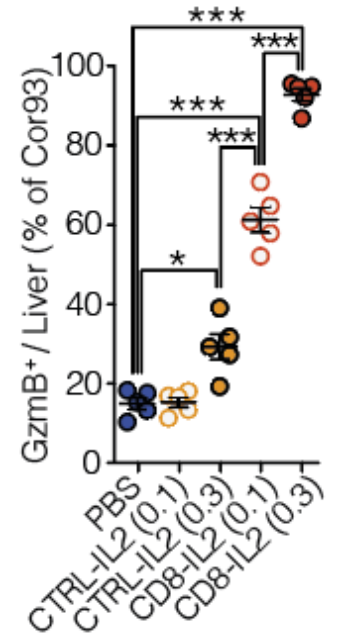
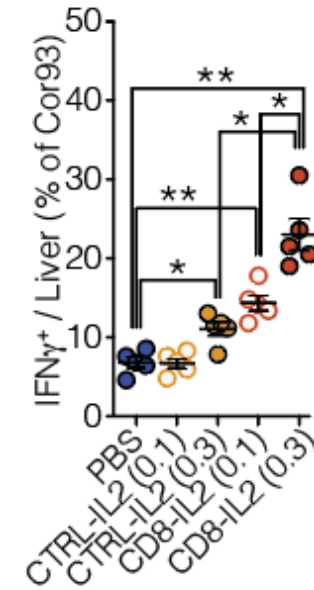
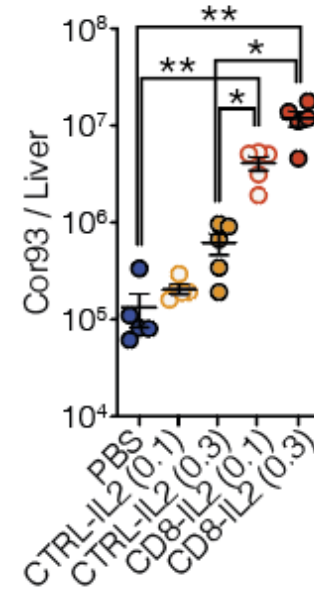
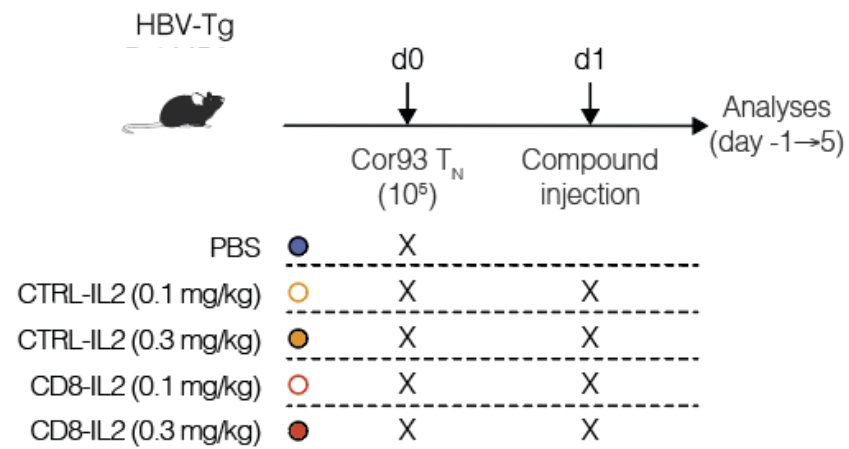




# Untargeted control not- $\alpha$ IL-2 predominantly activates Group 1 ILCs and Tregs

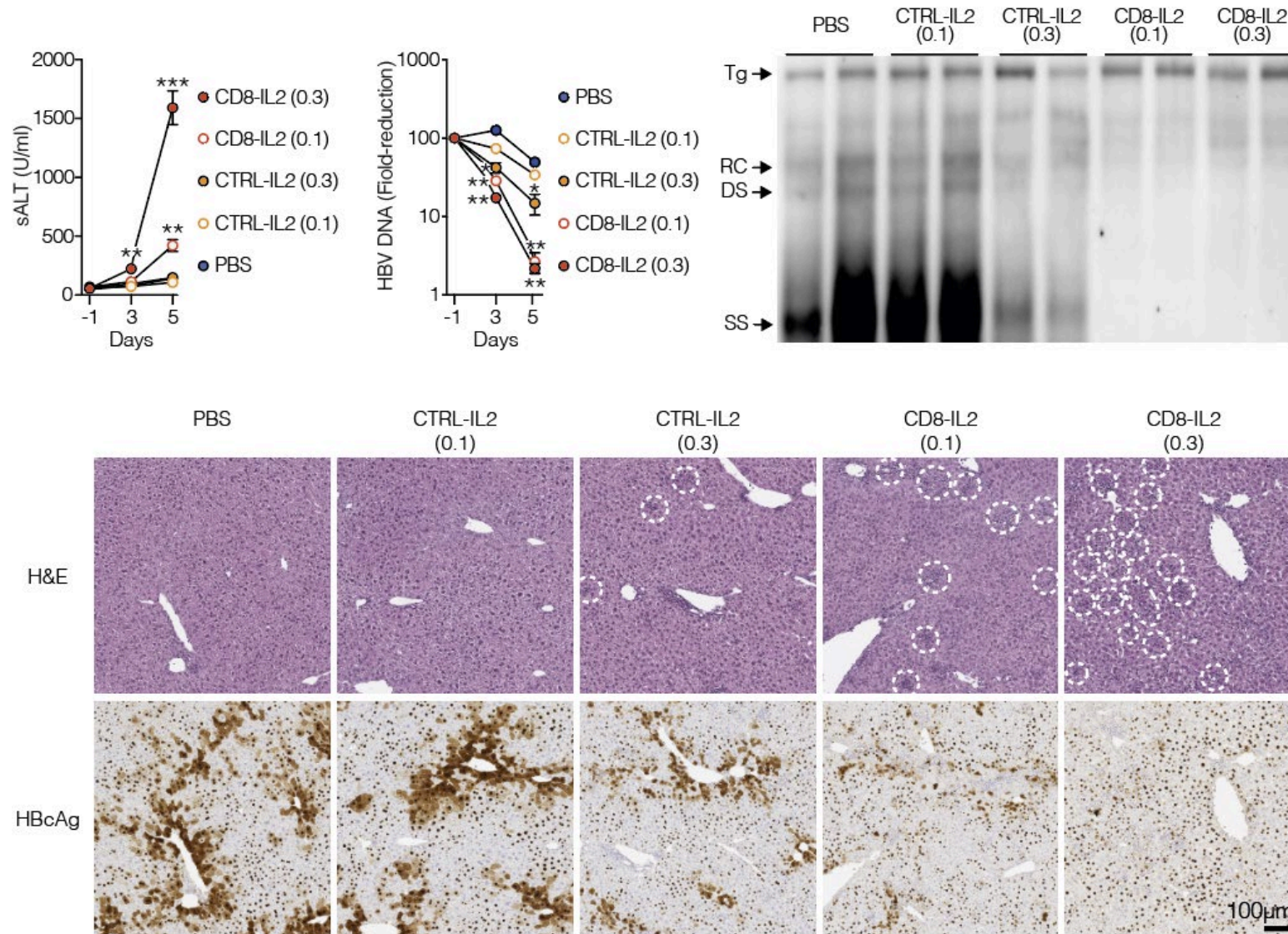


# In a mouse model of hepatitis B, CD8-IL2 demonstrates strong antiviral activity, outperforming an untargeted not- $\alpha$ IL-2



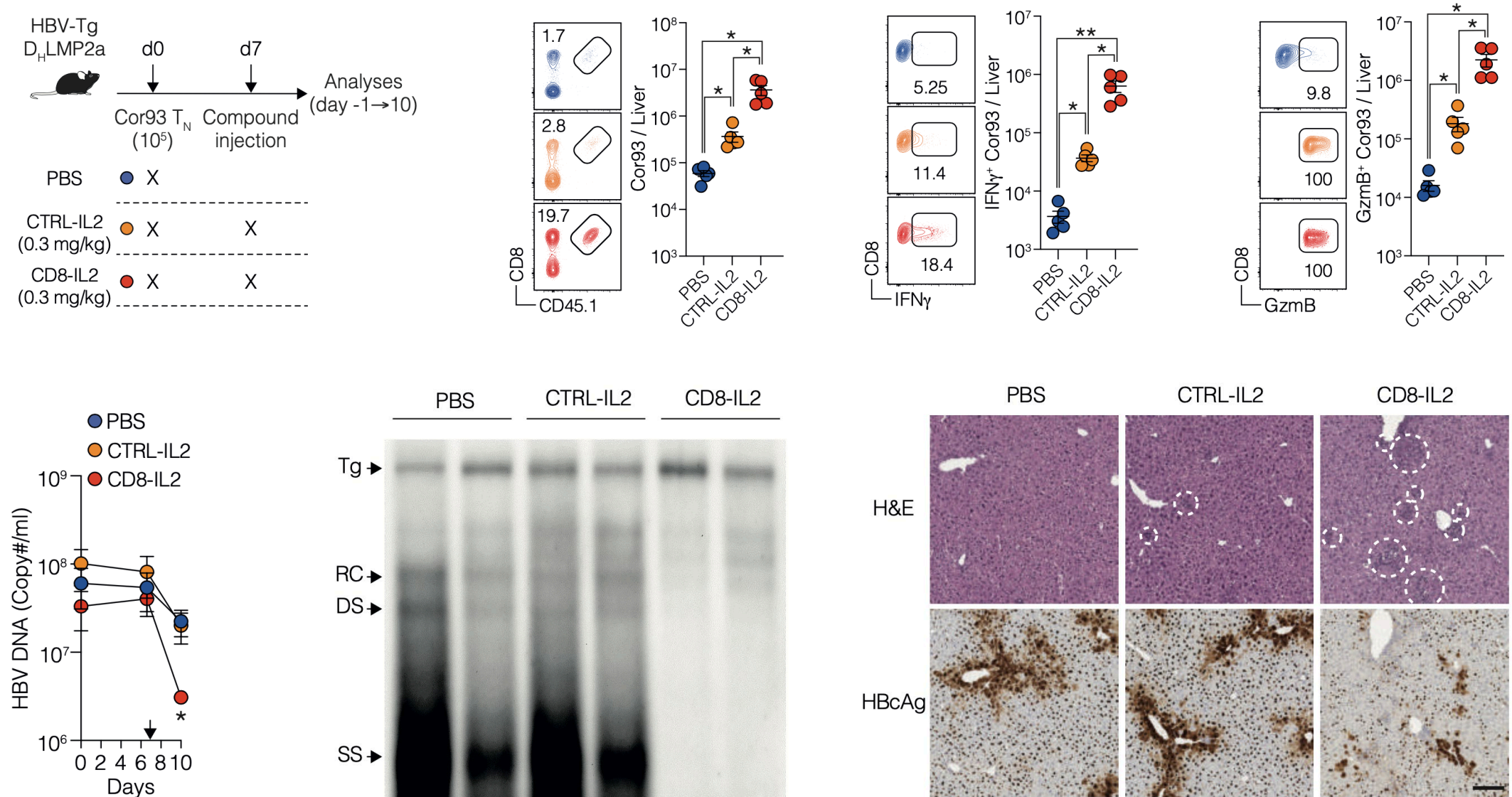


# In a mouse model of hepatitis B, CD8-IL2 demonstrates strong antiviral activity, outperforming an untargeted not- $\alpha$ IL-2

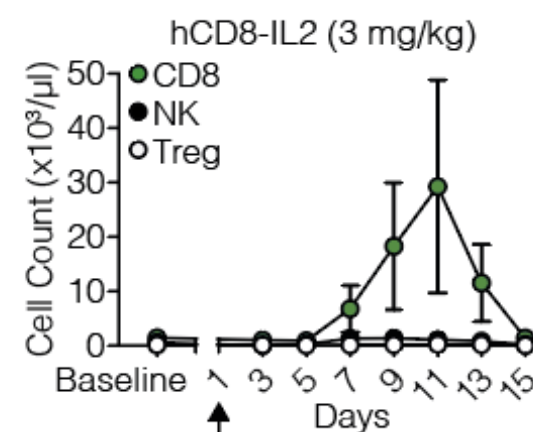
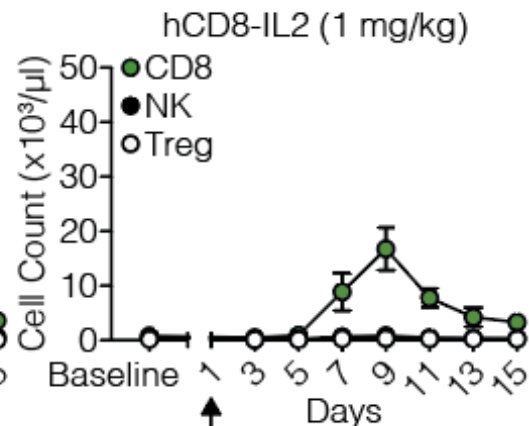
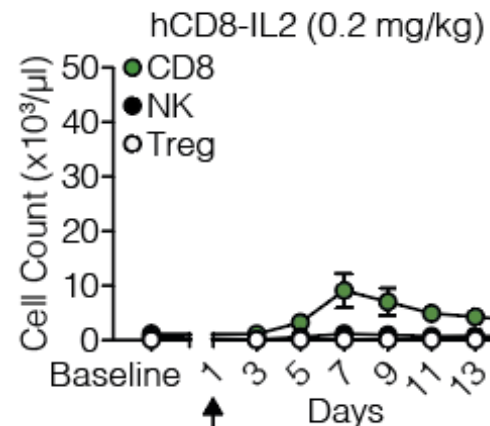
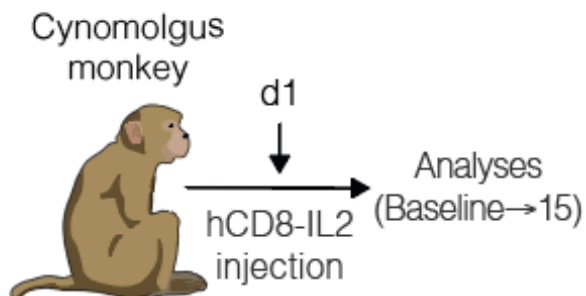
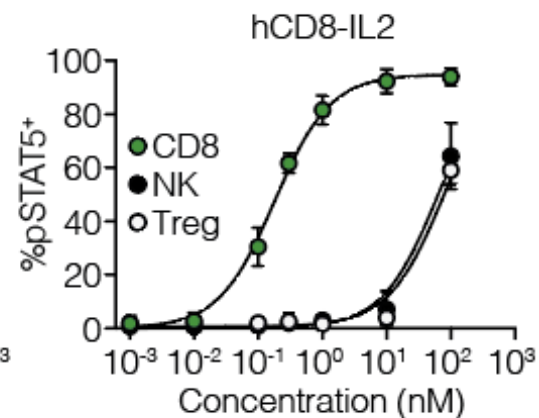
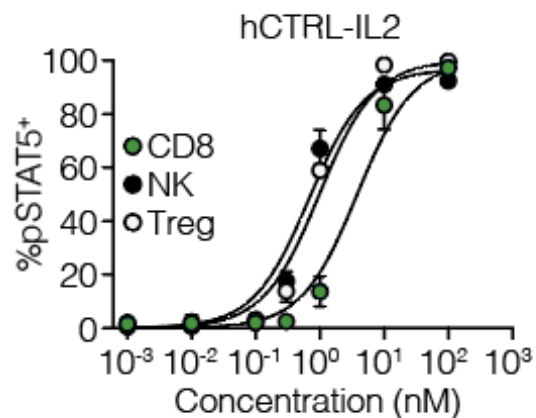
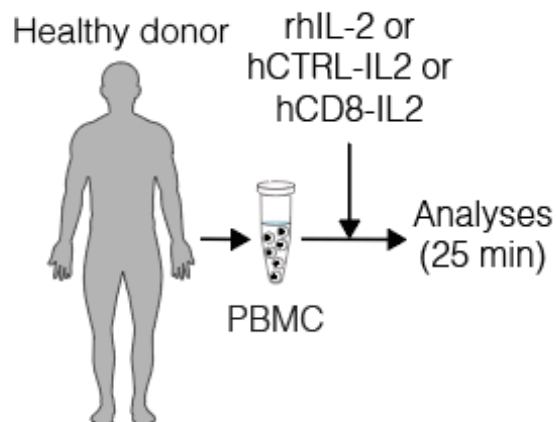




# CD8-IL2 rescues HBV-specific CD8<sup>+</sup> T cells with established dysfunction

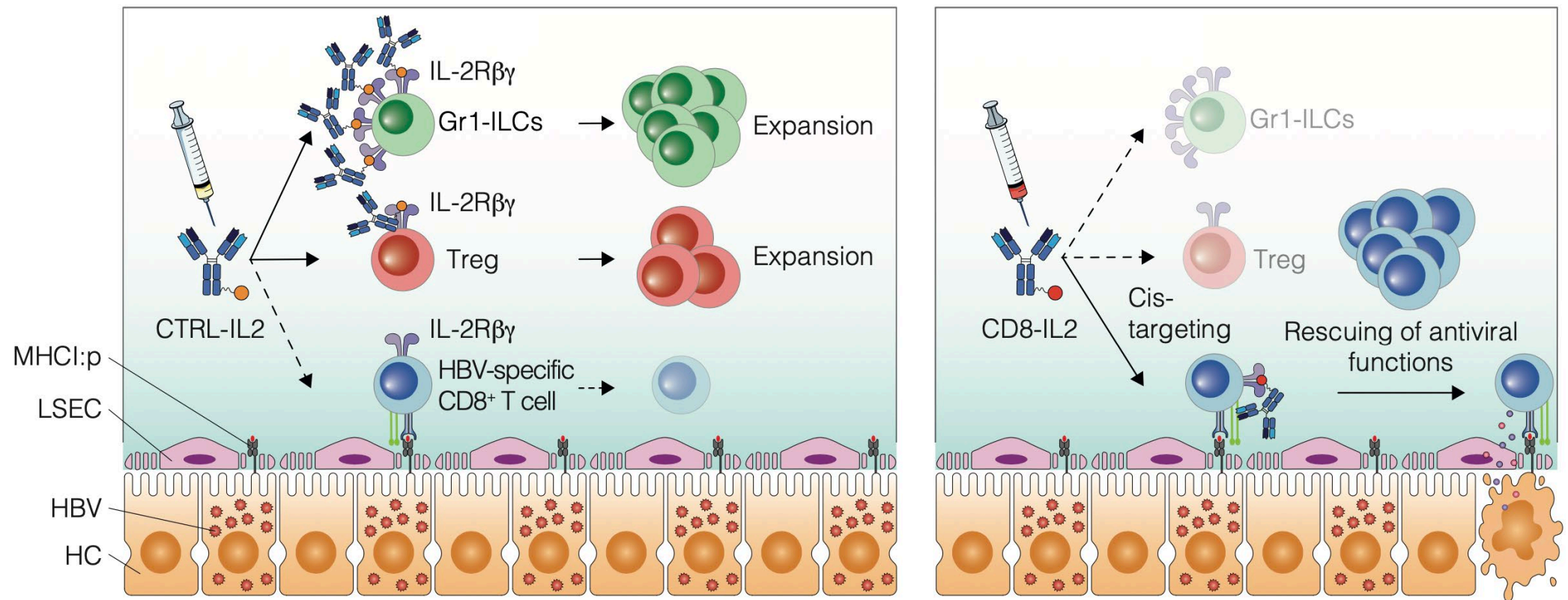


# A human CD8-IL2 molecule drives CD8<sup>+</sup> T cell-selective IL-2 signaling in cynomolgus monkey peripheral blood cells





# CD8 *cis*-targeted IL-2 drives potent antiviral activity against HBV





# ACKNOWLEDGMENTS



@iannaconelab



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