Title: Development of a novel humanized mouse model for improved evaluation of in vivo anti-cancer effects of anti-PD-1 antibody

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Saline

100µm

Nivolumab

Saline

Nivolumab



- 100µm

HSC4

HCC827



huNOG

huNOG-FcyR KO



p=0.008

Nivo.

Saline

huNOG

**

Nivo.

huNOG-FcγR KO

Saline

hPD-L1⁺ Area / Spleen area (%) 0 0 0 0 0 0

100µm 100µm

NCI-H1975

RKO





*____

p=0.032





Anti-hPD-L1 Ab



N ivolum ab



а













CD8 CD4 GZMB $\mathsf{TNF}\text{-}\alpha$ GZMB $\mathsf{TNF}\text{-}\alpha$ IL-2 IFN-γ IFN-γ 100 100₁ 100₁ 100₁ 100₁ 100₁ 100₁ 80-80-80-80 80-80--80 huNOG-FcγR KO Freq. of cytokine producing cells (%) 60 60 60 60 60-60 60. 40-40--40 40 40 40 40 Ŧ 20-20-20--20-20-20 20-----0 0 0 0 0 0 n Saline-Saline-Nivo.-Saline-Nivo.-Saline-Nivo.-Saline-Nivo.-Saline-Nivo. Nivo. Saline[.] Nivo. 100₁ 100₁ 100₁ 100 100₁ 100 100₁ 80-80-80 80-80-80-80-• 60 60-60-60-60-60 60. huNOG Ŧ 40 40 40 40-40-40 40 20-20 20-20-20 20 20-Ţ 0 0 0 0 C Nivo.-Saline-Saline-Saline-Saline-Nivo.-Saline-Nivo.-Saline-Saline-Nivo. Nivo. Nivo. Nivo.

HSC4 TIL

CD8 CD4 GZMB $\mathsf{TNF-}\alpha$ $\mathsf{TNF}\text{-}\alpha$ IL-2 IFN-γ GZMB IFN-γ 1001 100₁ 100₁ 100₁ 100₁ 100₁ 100 80-80 80-80 80-80 80huNOG-FcγR KO 60-60 60. Freq. of cytokine producing cells (%) 60 60-60 60 Ŧ Ŧ 40-40 40 40 40-40 40 20-20-20. Ŧ 20-Ŧ 20-₽ 20-20-Ŧ 0 0 0 0 0 n Saline-Nivo.-Saline-Nivo.-Saline-Saline-Nivo. Saline-Nivo.-Saline-Saline-Nivo.-Nivo.-Nivo.-100₁ 100₁ 100₁ 100₁ 100 100₁ 100 80-80-80-80-80-80 80-60-60-60 60-60 60. 60 huNOG 40 40 40 40 40-40 40 ÷ 20-20-20. 20-20 20--20 -+ -0 0 0 n 0 Nivo.-Saline-Saline-Saline-Saline-Saline-Nivo.-Saline-Saline-Nivo.-Nivo.-Nivo.-Nivo. Nivo.

NCI-H1975 TIL



RKO Spl

HSC4 HCC827 NCI-H1975 Saline 100µm Anti-hGZMB Ab Nivolumab Saline Anti-hPerforin Ab 100µm 100µn 100µm 100µm Nivolumab 100µm 100µm huNOGhuNOGhuNOGhuNOG huNOG huNOG FcyR KO FcyR KO FcyR KO



