



COLUMBIA UNIVERSITY
MEDICAL CENTER

Discover. Educate. Care. Lead.



Molecular genotyping in PTCL

Teresa Palomero, PhD

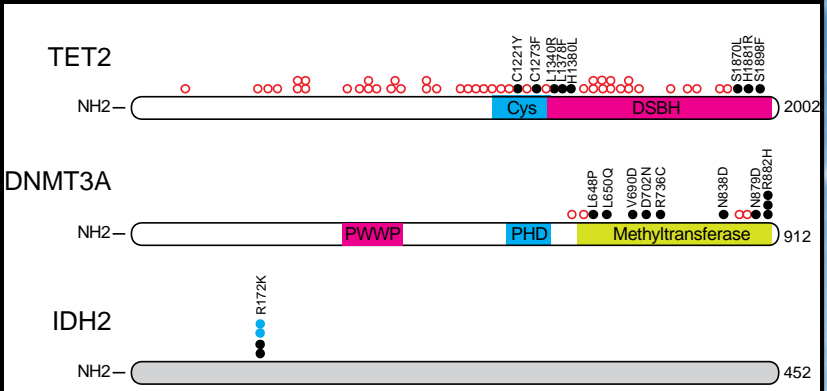
Institute for Cancer Genetics
Department of Pathology and Cell Biology
Herbert Irving Comprehensive Cancer Center

Columbia University Medical Center

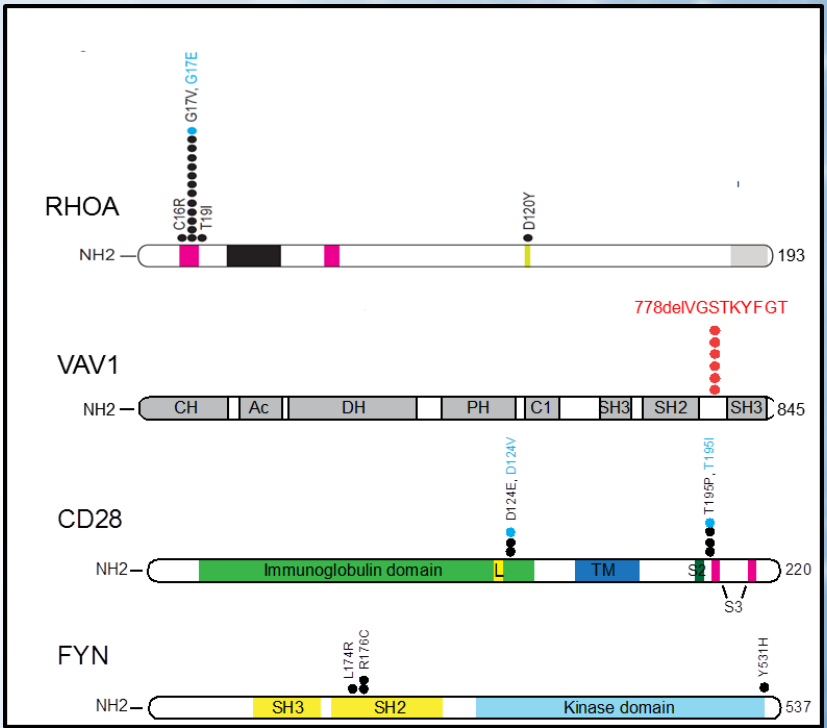
Recurrent mutations in AITL and PTCL, NOS



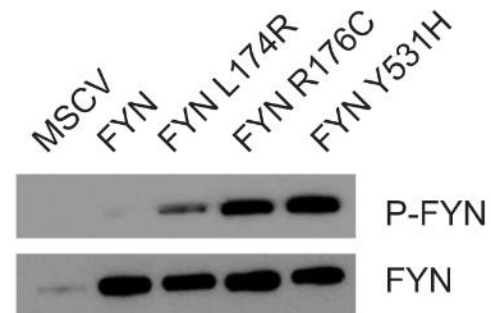
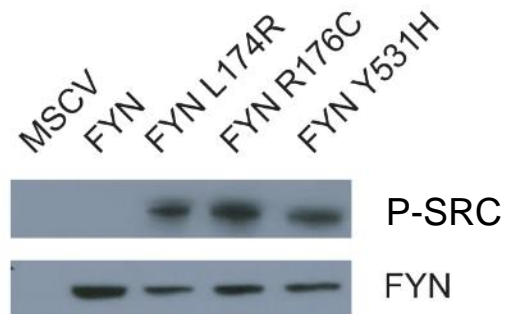
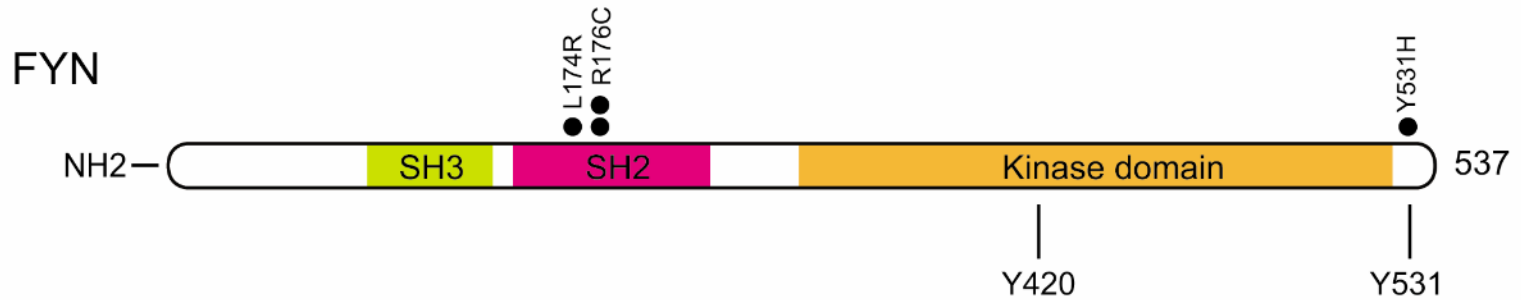
Epigenetic regulators



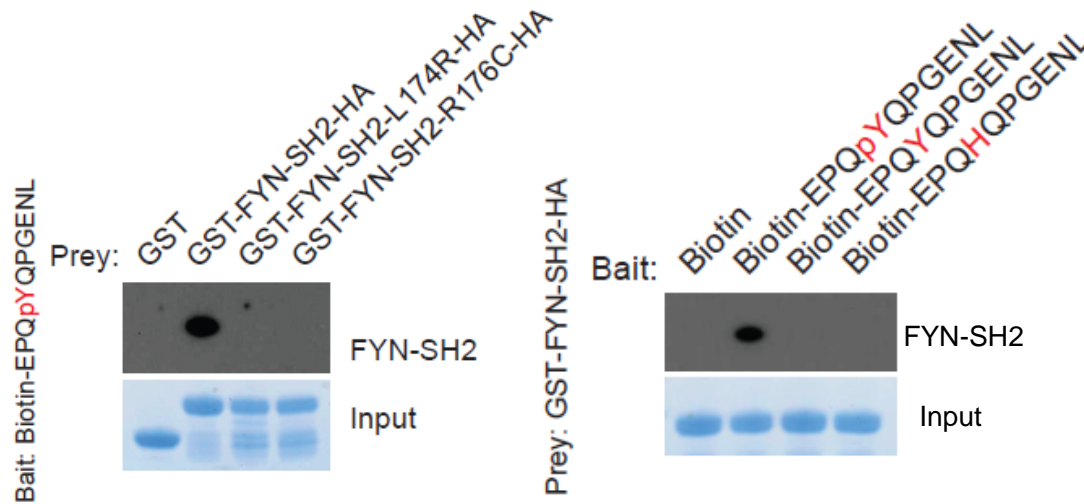
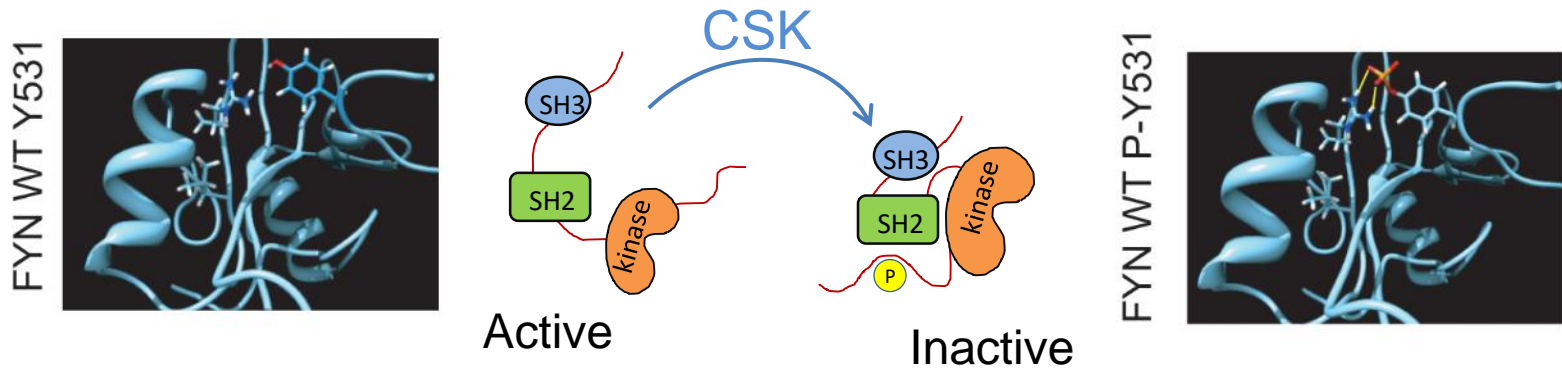
TCR signaling pathway



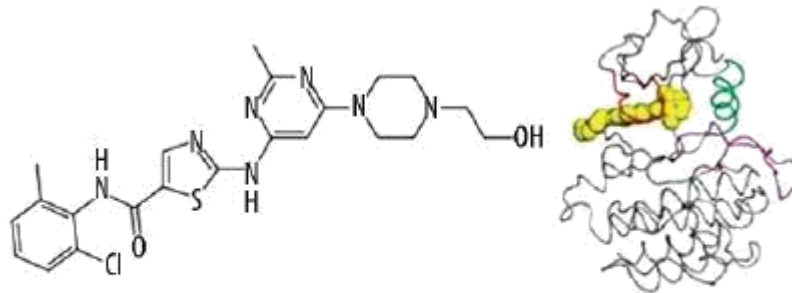
Recurrent activating FYN kinase mutations in PTCL



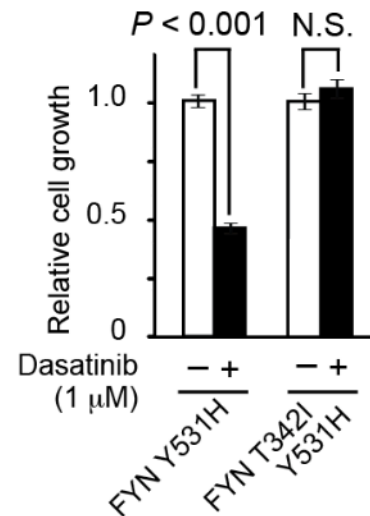
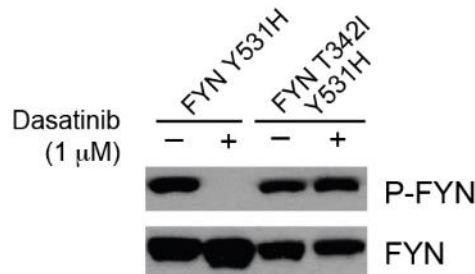
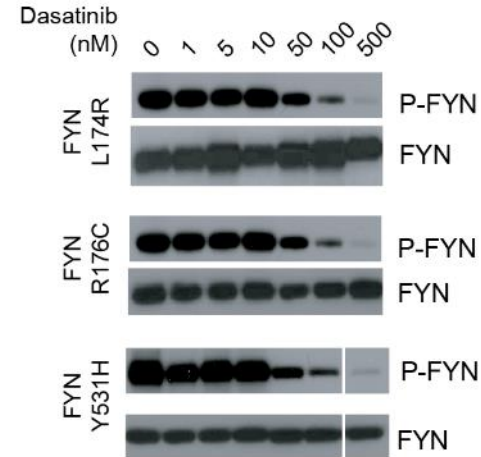
Mechanisms of FYN constitutive activation in PTCL



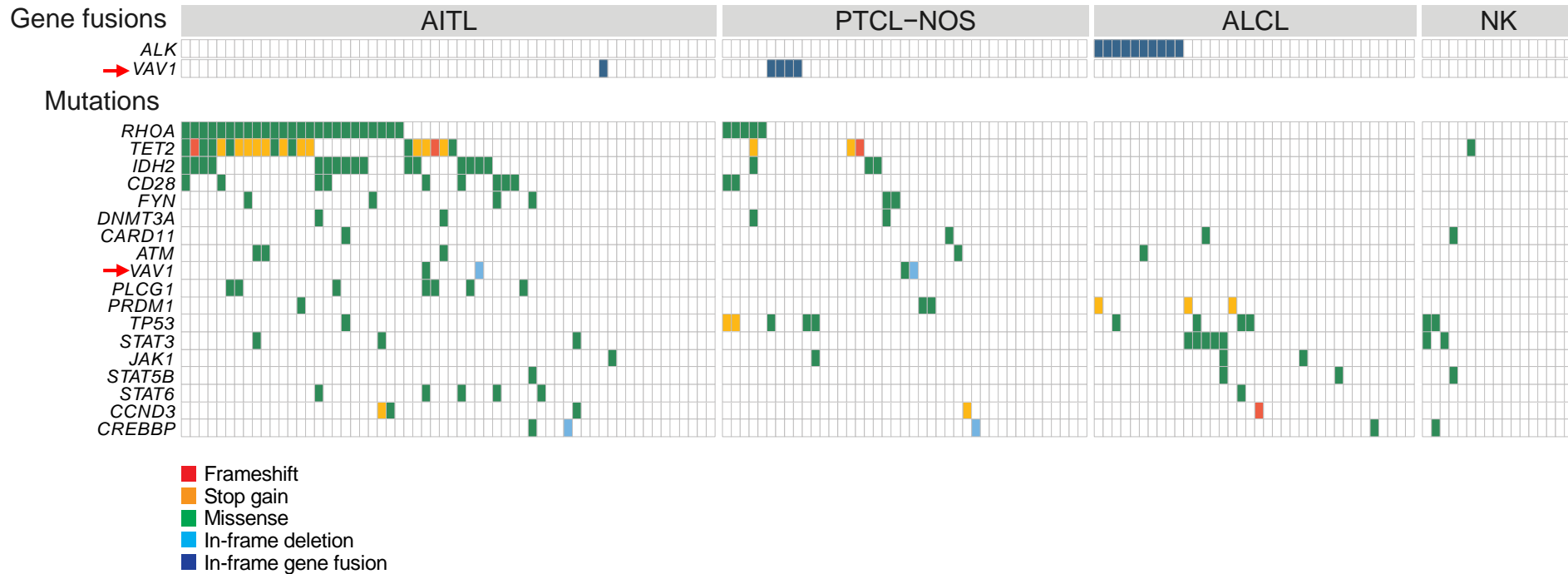
Inhibition of oncogenic mutant FYN activity by Dasatinib



Dasatinib (BMS-354825)



Identification of frequent alterations in *VAV1* in PTCL

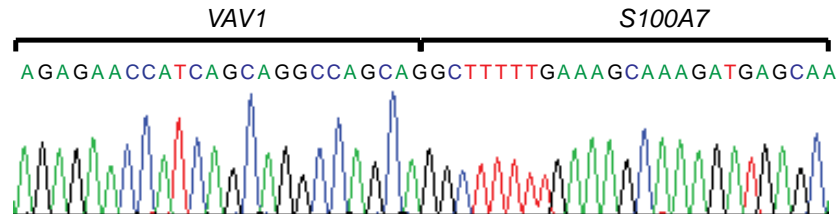


C-terminal *VAV1* gene fusions in PTCL

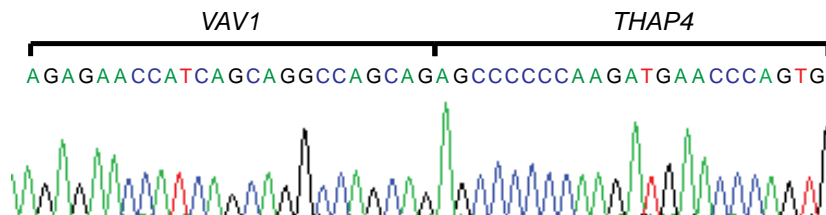
A



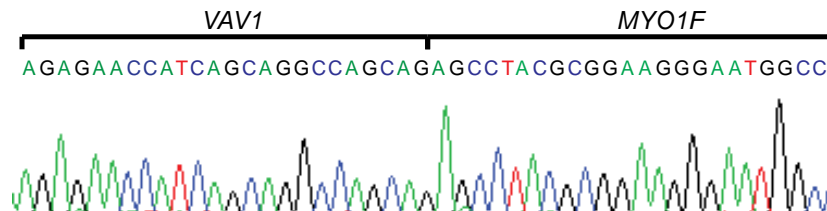
B



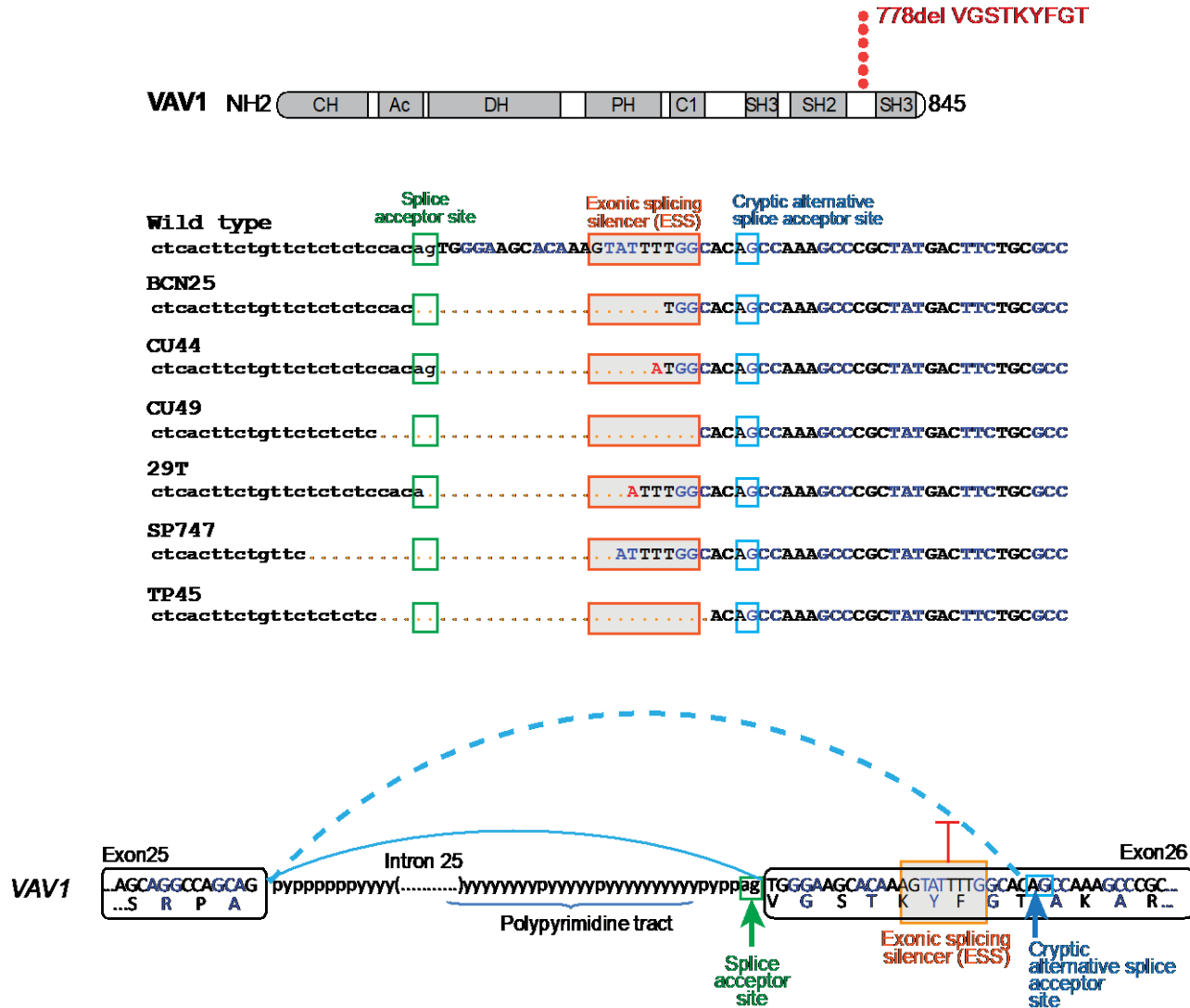
C



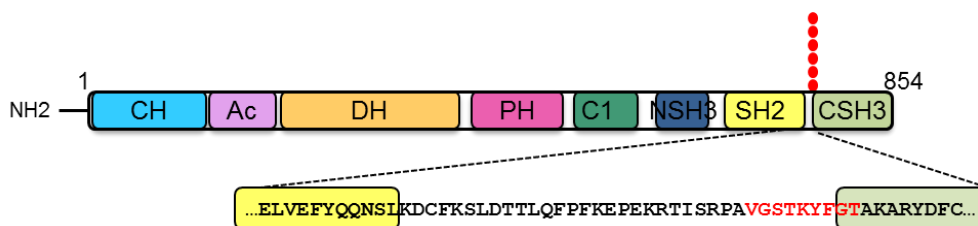
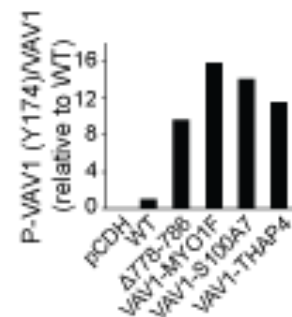
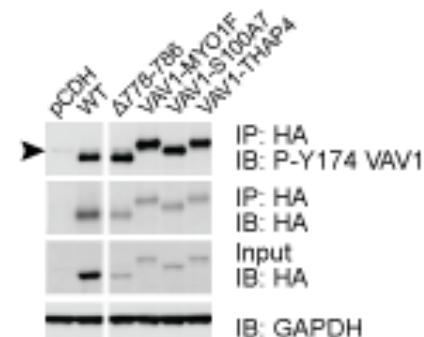
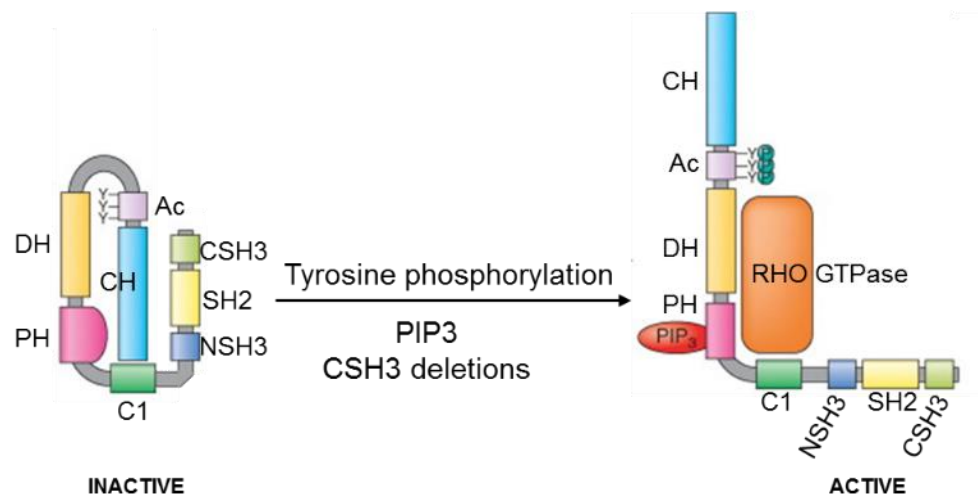
D



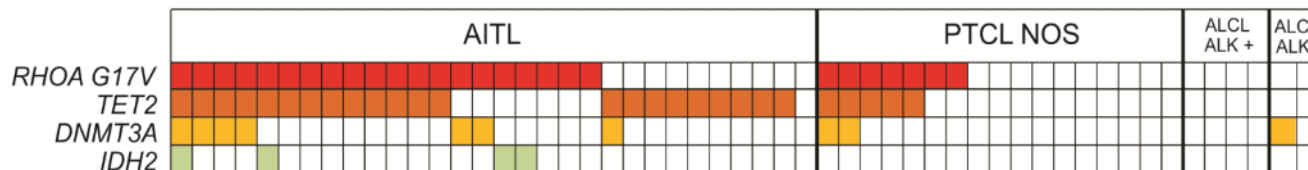
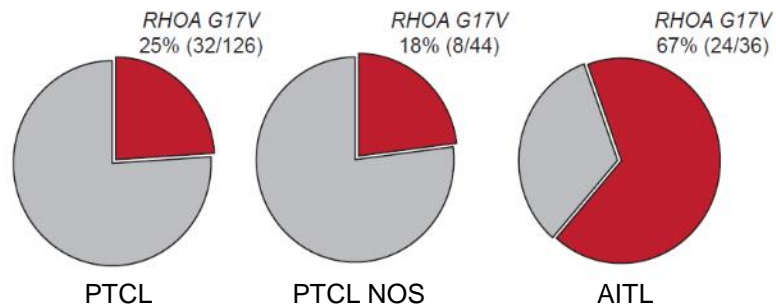
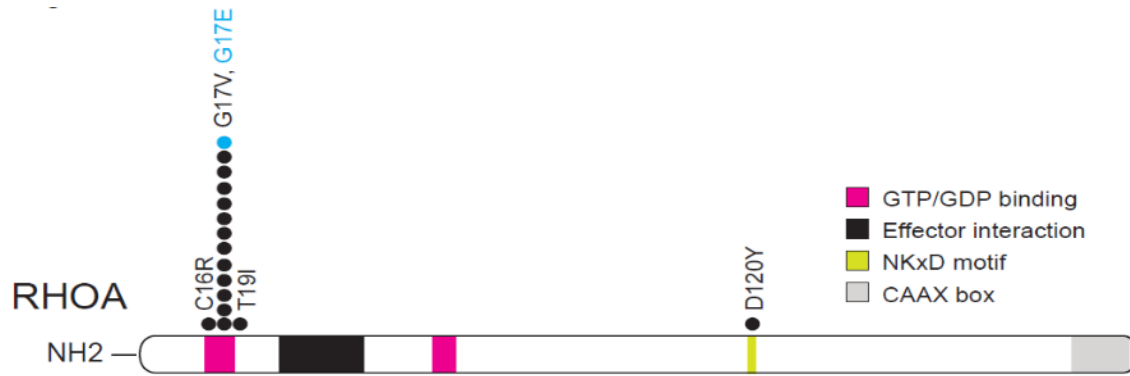
VAV1 splice site deletions induce alternative splicing by eliminating an exonic silencer



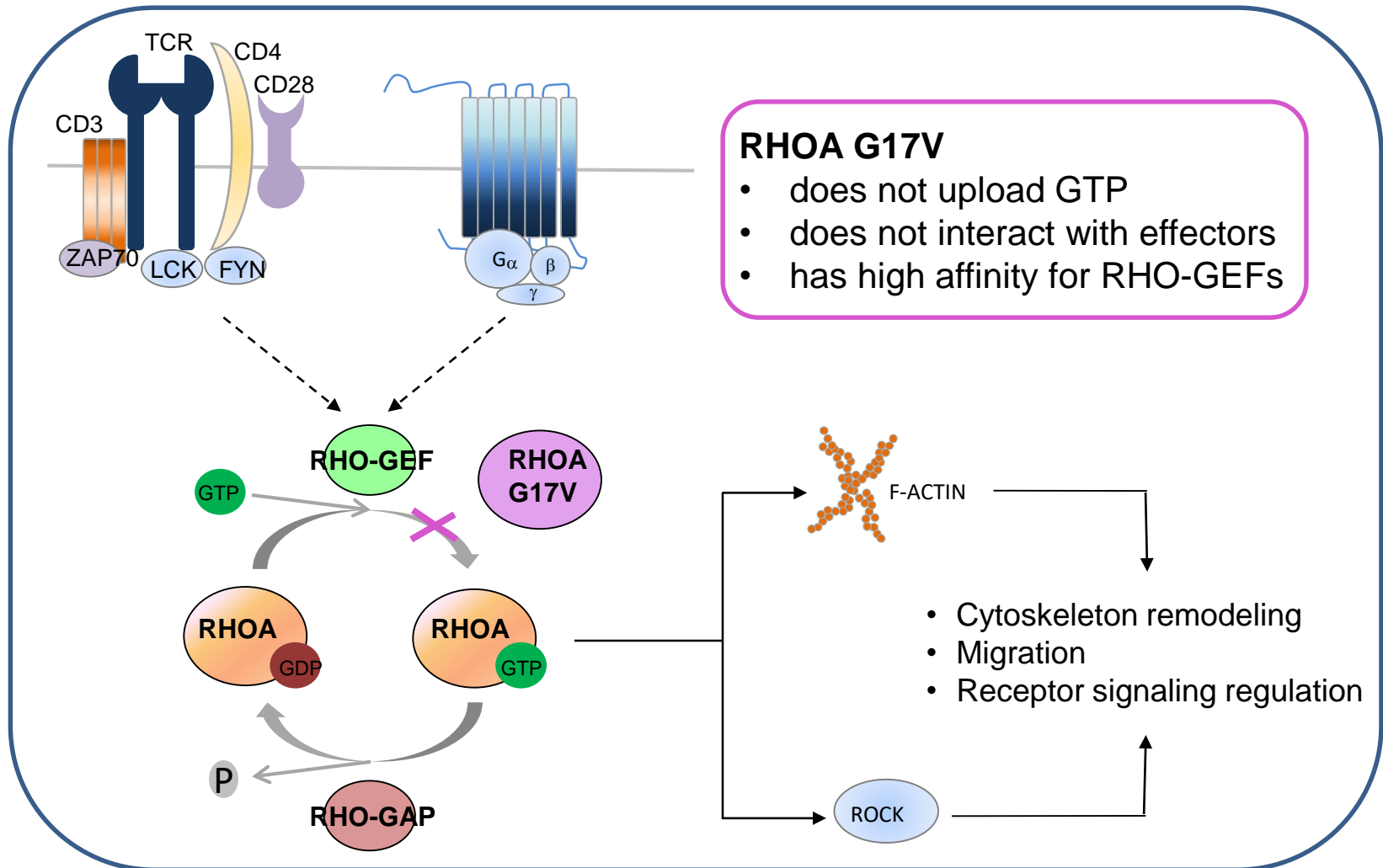
Deletions affecting the c-terminal SH3 domain of VAV1 induce an open active conformation of the protein



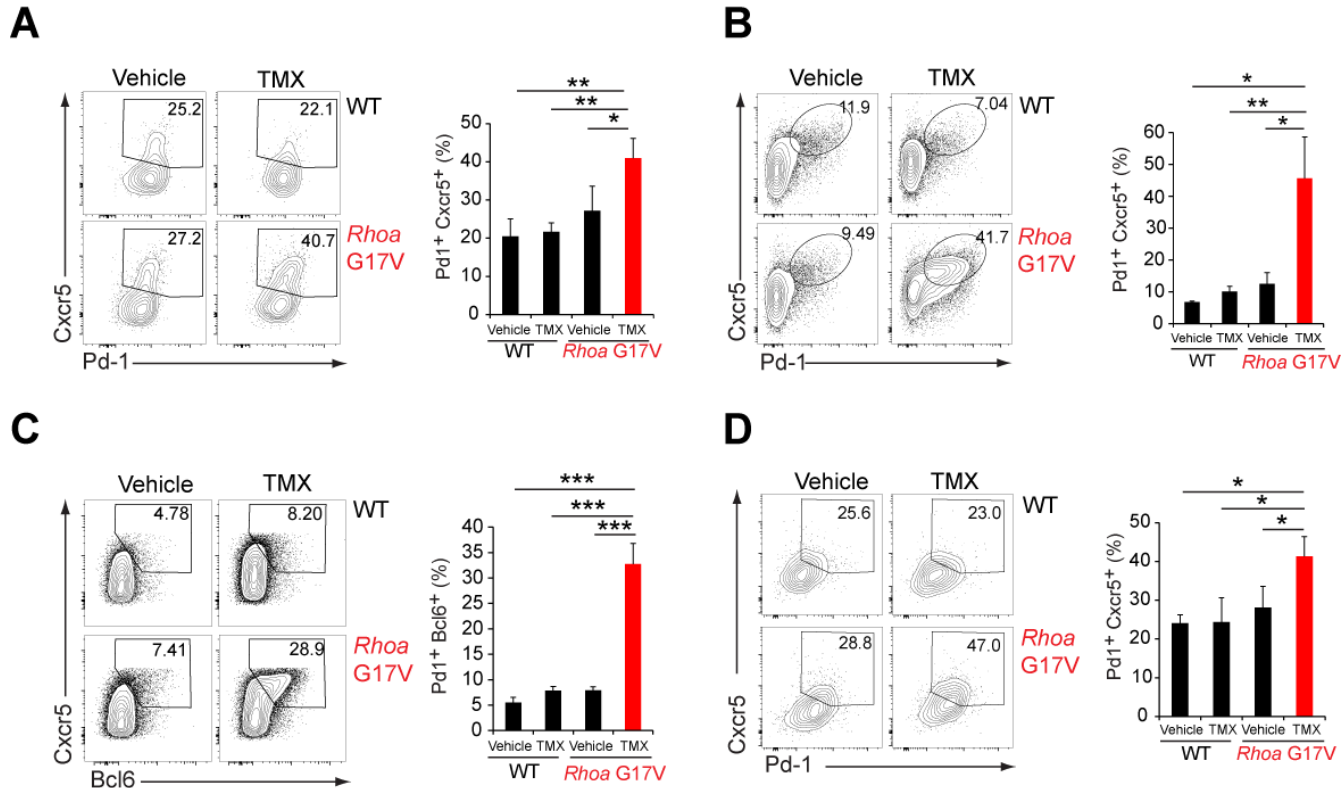
Recurrent mutations in RHOA in PTCL



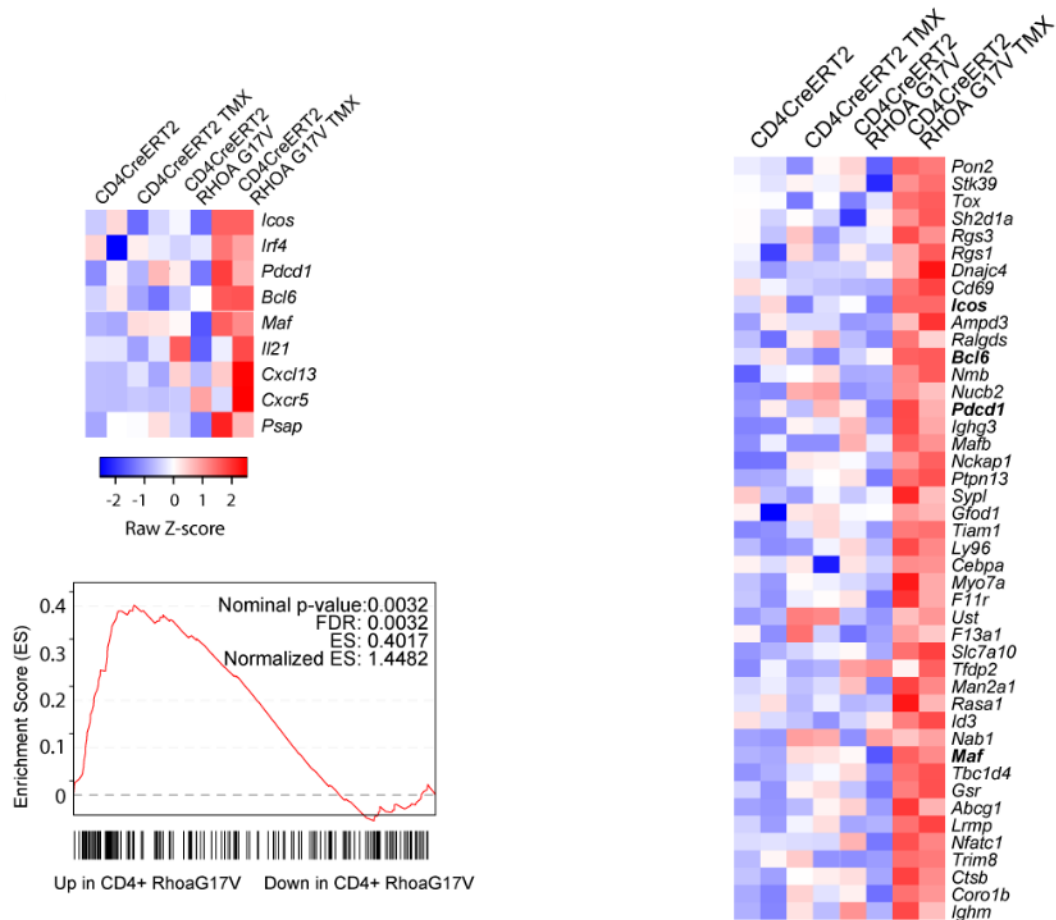
RHOA G17V impairs RHOA activation by interfering with RHOA pathway activation



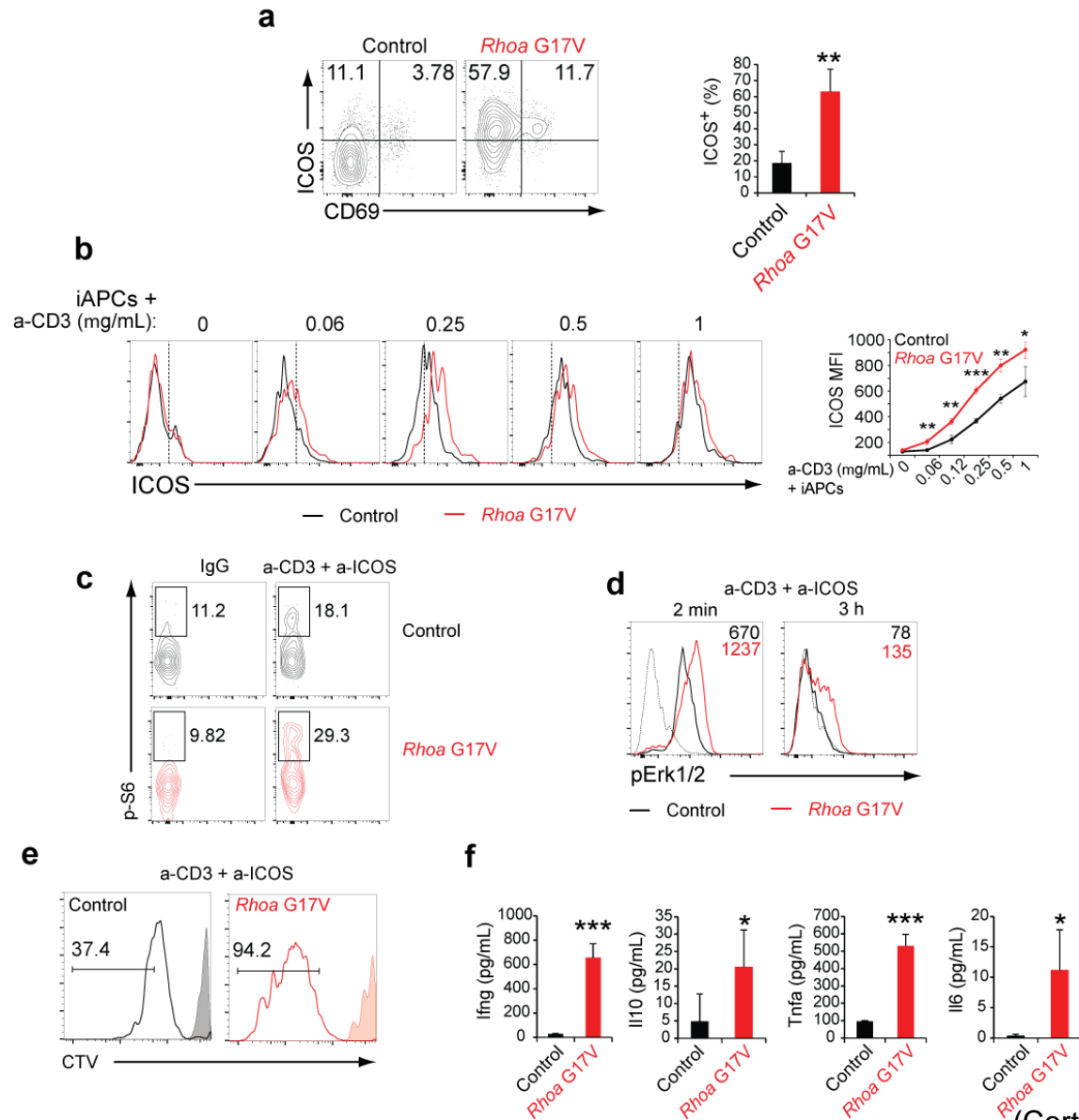
Tamoxifen-induced expression of *Rhoa G17V* in CD4+ cells leads to TFH differentiation



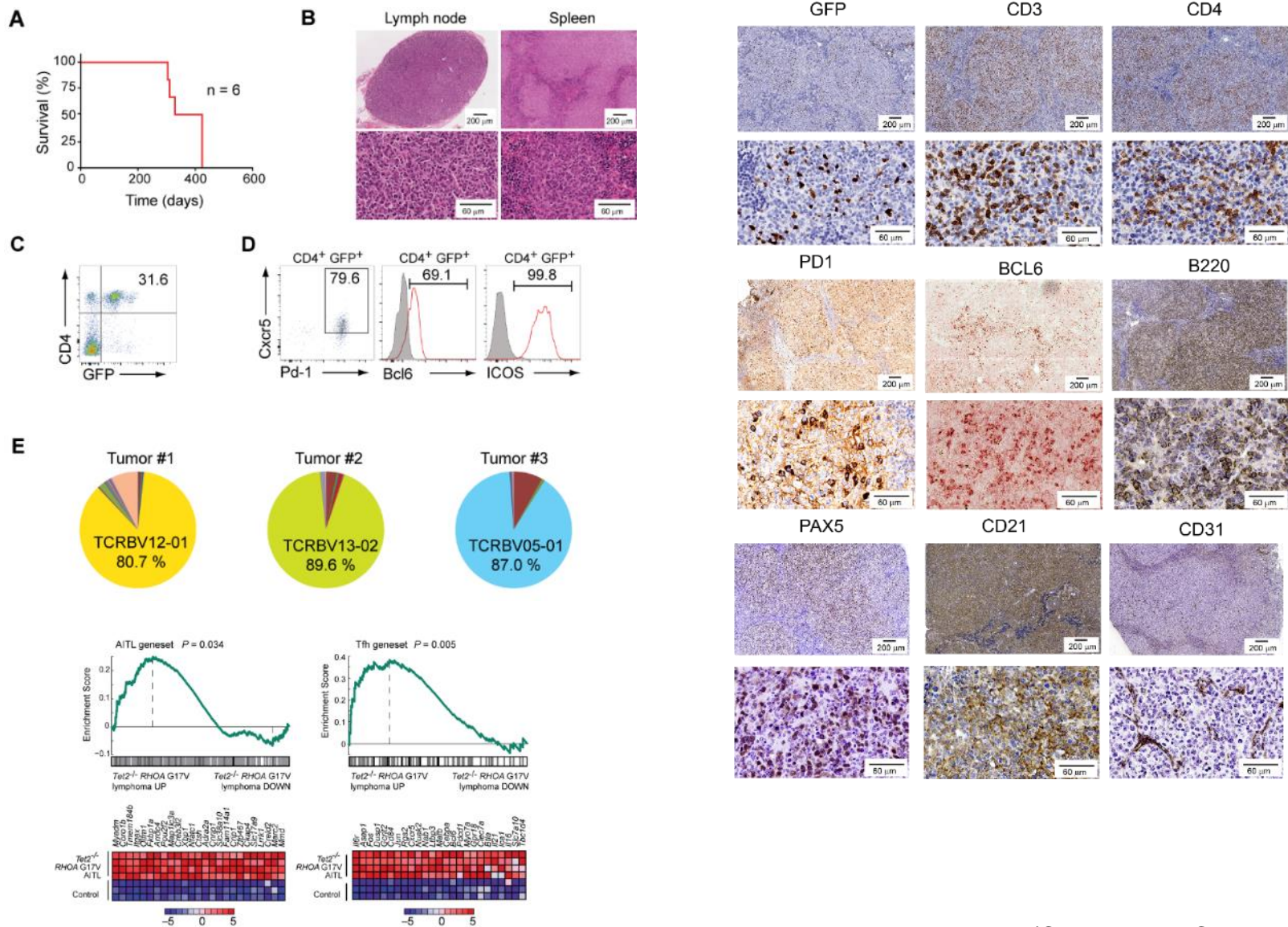
Rhoa G17V CD4+ T-cells show increased expression of Tfh markers



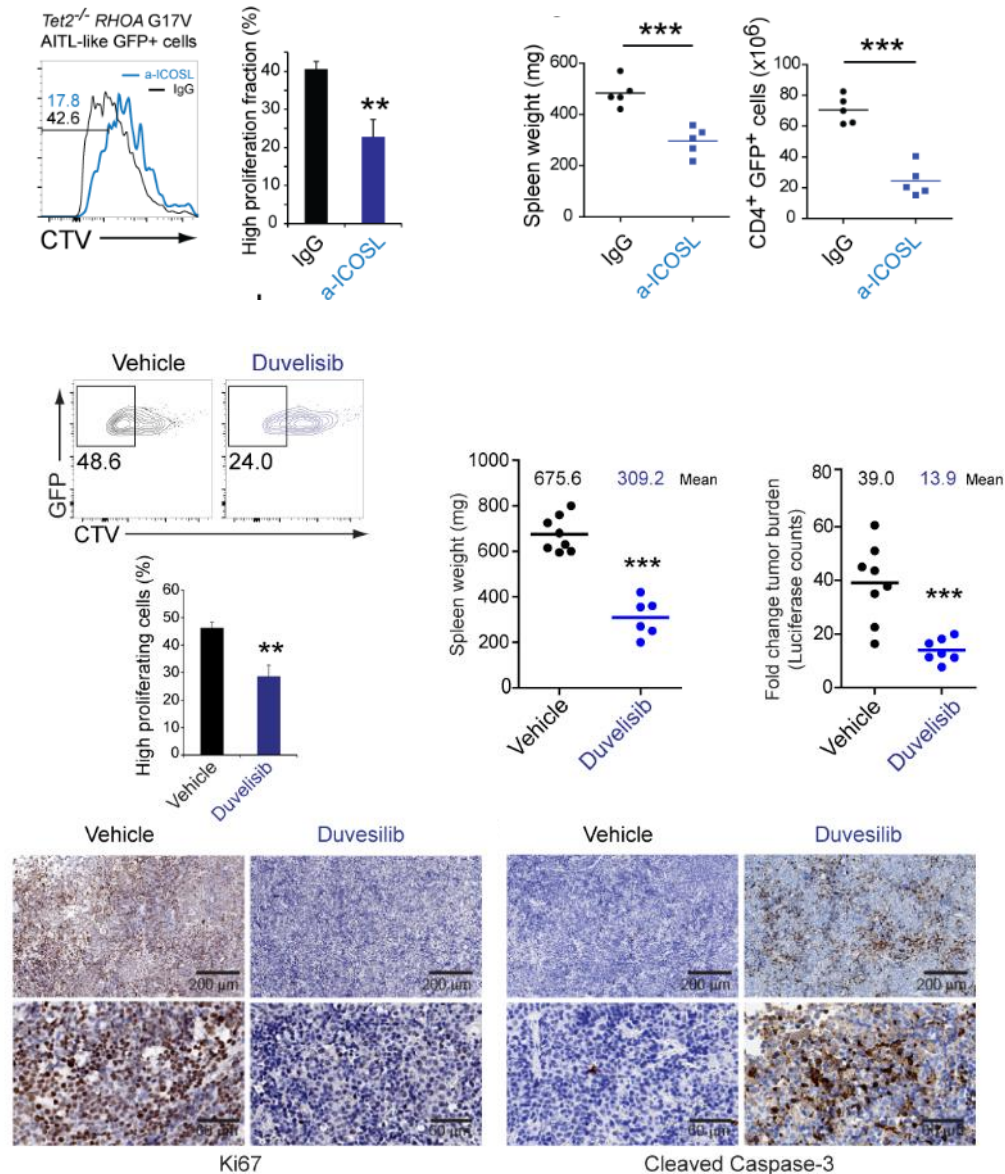
Rhoa G17V increases the activity of ICOS-regulated signaling pathways *in vitro*

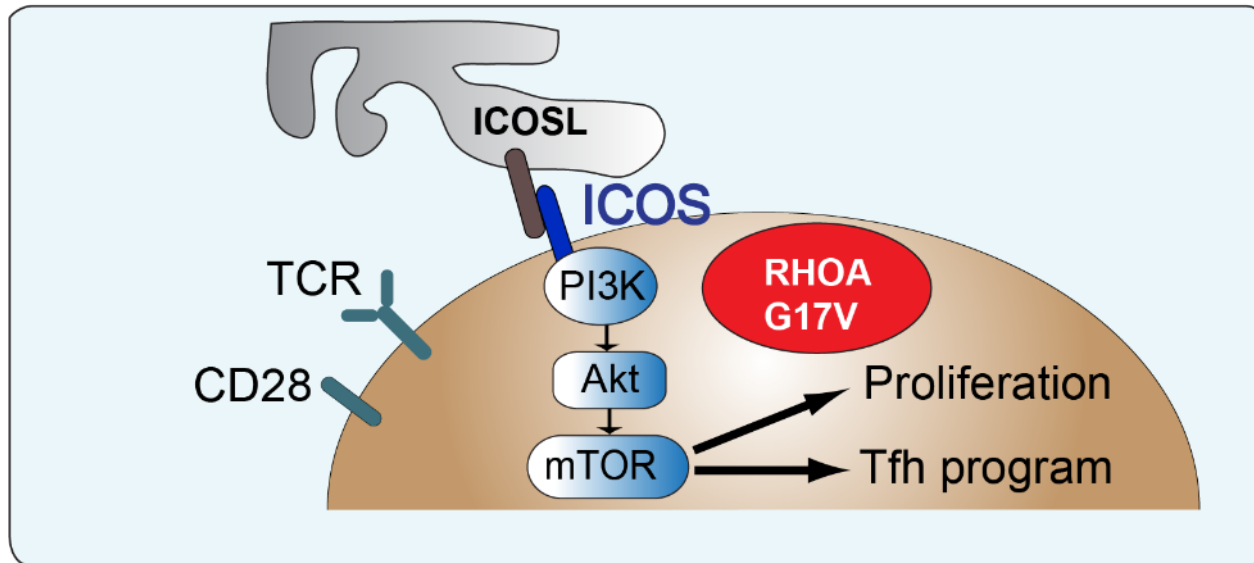
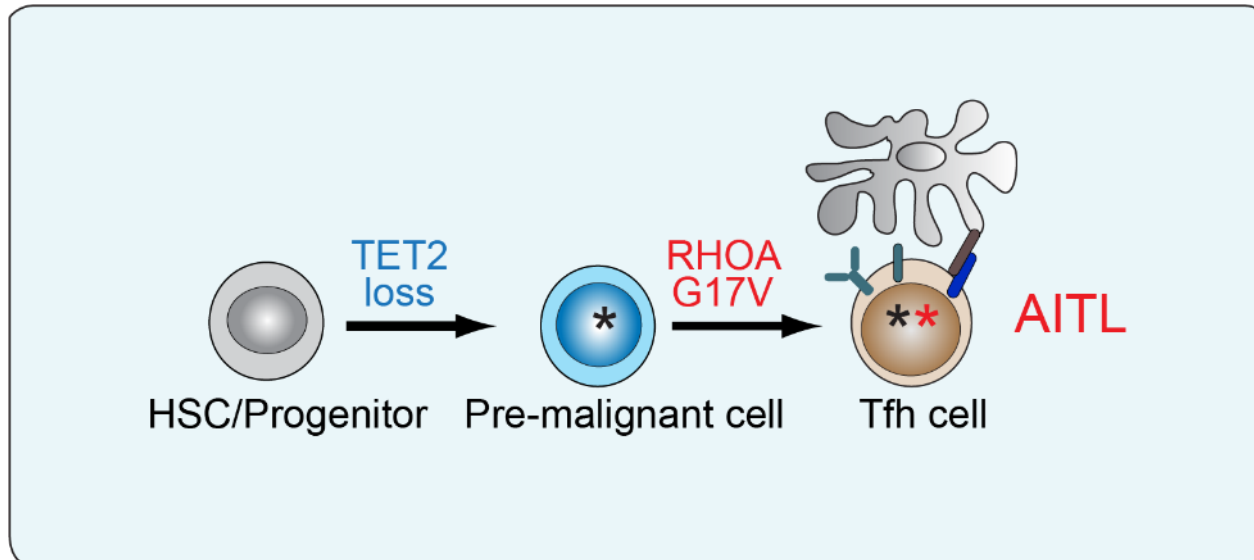


Expression of *RHOA G17V* in a *Tet2* null background leads to AITL development

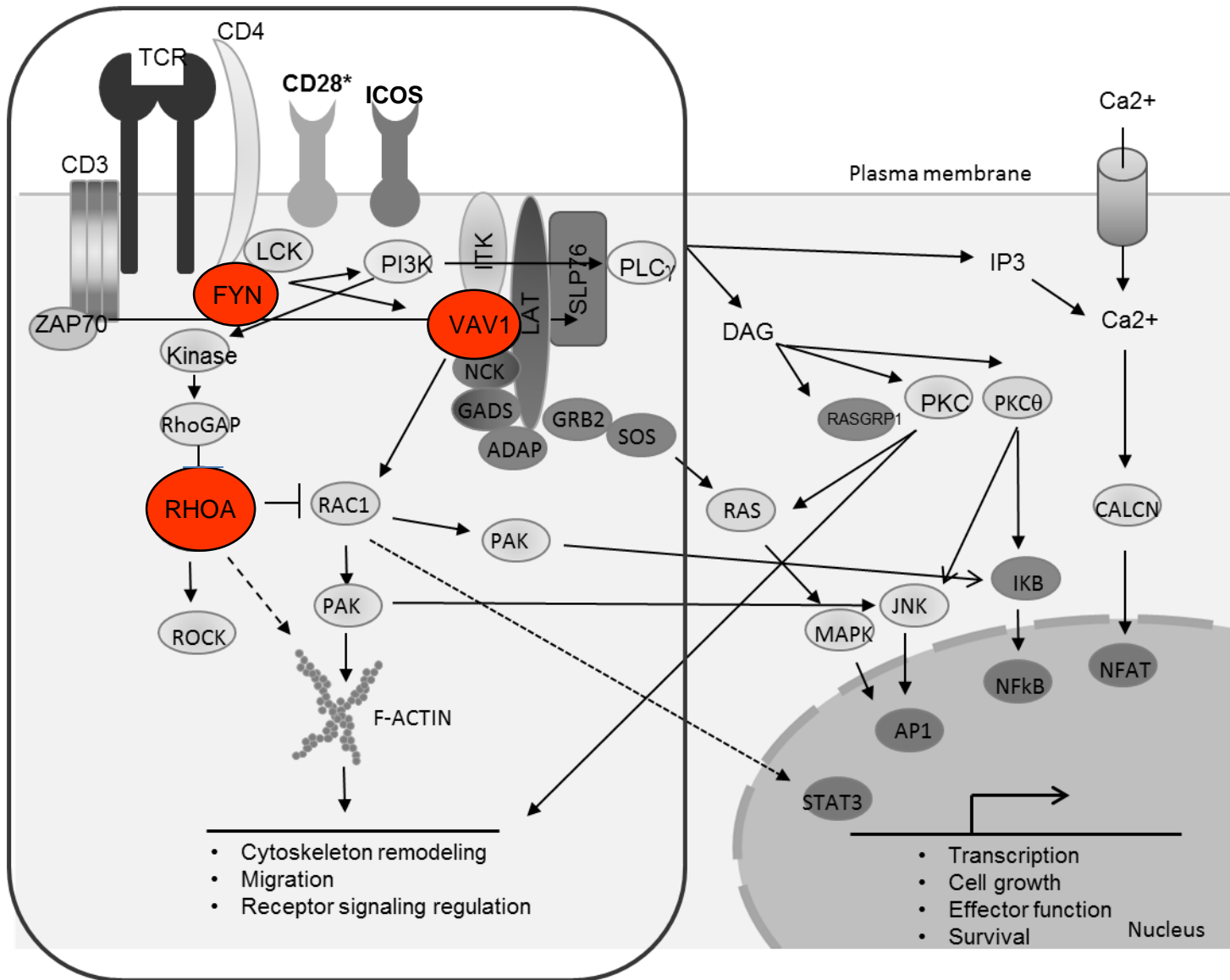


Inhibition of ICOS signaling blocks AITL growth *in vivo*





RHO GTPases pathways play a key role in PTCL



Acknowledgements

Dr. Jose R. Cortes
Dr. Ana da Silva Almeida
Anisha Cooke



Dr. Adolfo Ferrando
Dr. Lucile Couronne
S. Aidan Quinn
Dr. Marta Sanchez Martin
Christine S. Kim
Dr. Mi-Yeon Kim



Dr. Raul Rabadan
Dr. Francesco Abate
Sakellarios Zairis
Dr. Hossein Khiabani



Dr. Larisa Geskin
Christina Patrone

Dr. Xosé R Bustelo
Javier Robles-Valero



Dr. Stefano Pileri
Dr. Maria Antonella Laginestra



Dr. Ross Levine



Memorial Sloan Kettering
Cancer Center

Dr. Iannis Aifantis



Dr. Ari Melnick
Dr. Giorgio Inghirami
Dr. Danilo Fiore



Dr. Joan Guitart
Dr. Estela Martinez



Dr. Govind Bhagat
Dr. Olivier A. Bernard
Dr. Elias Campo

Dr. Miguel Angel Piris

Dr. Izidore Lossos



COLUMBIA UNIVERSITY
MEDICAL CENTER

Herbert Irving Comprehensive Cancer Center