

# Targeting MDSCs in CLL-bearing mice by suppressing the synthesis of secretory IgM via activation of RIDD

Chih-Chi Andrew Hu

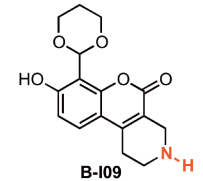
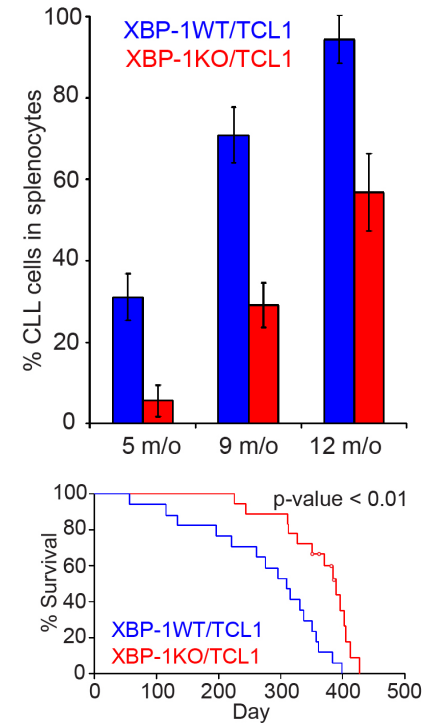
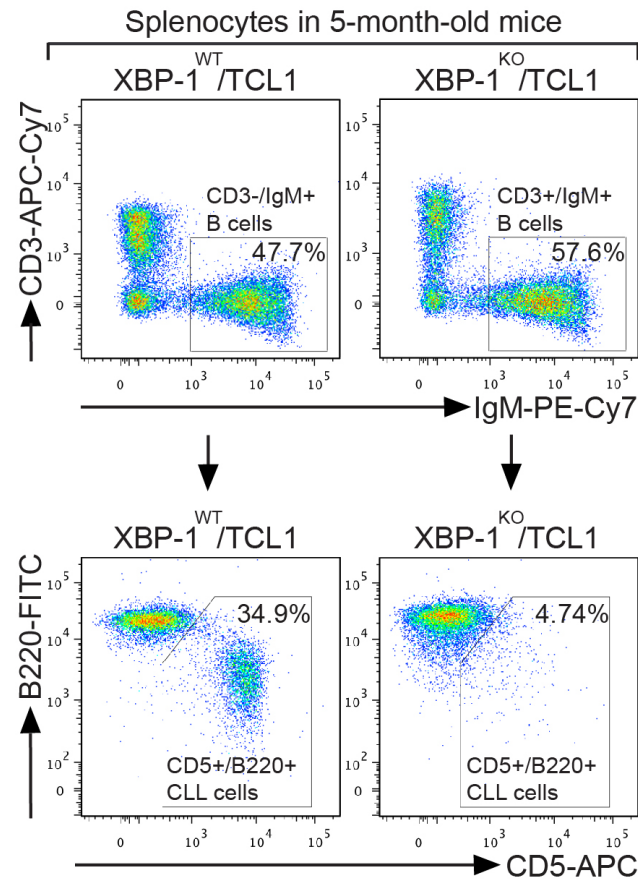
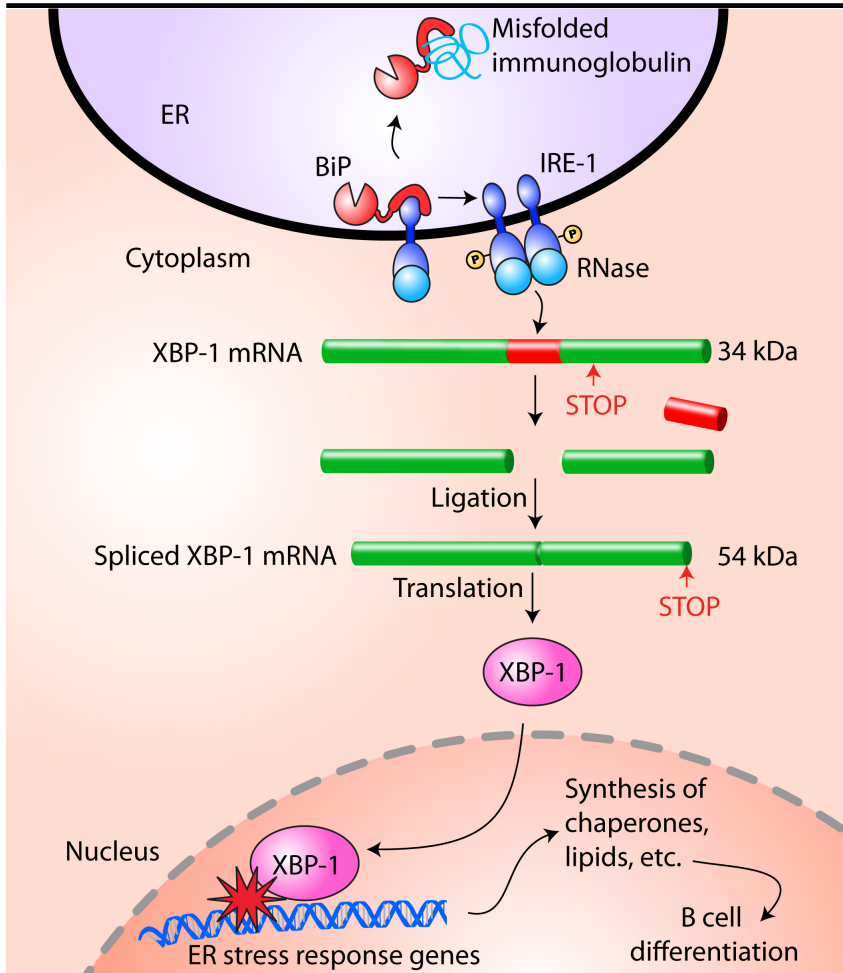
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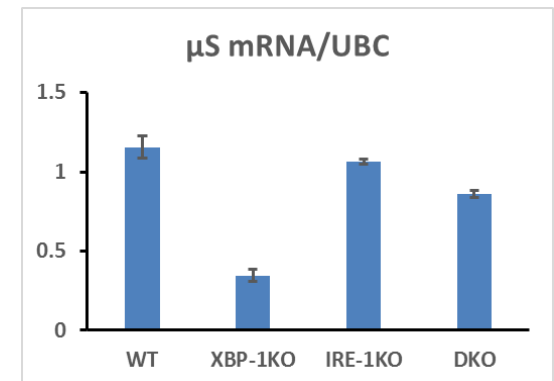
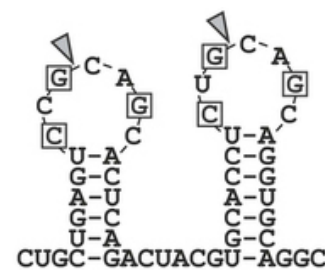
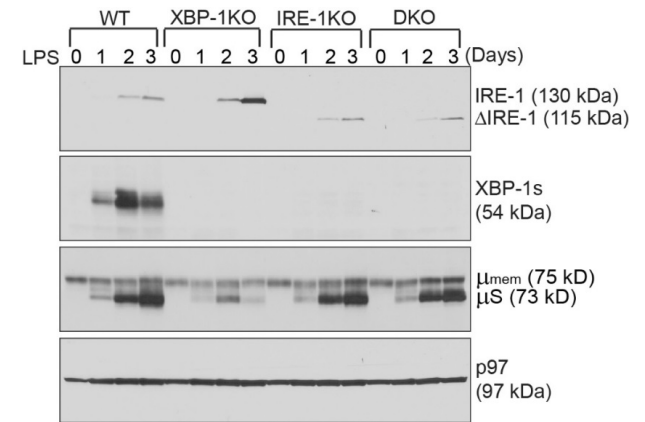
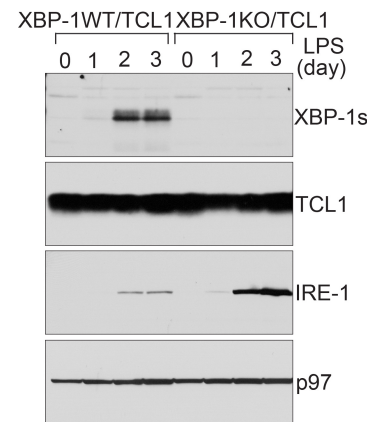
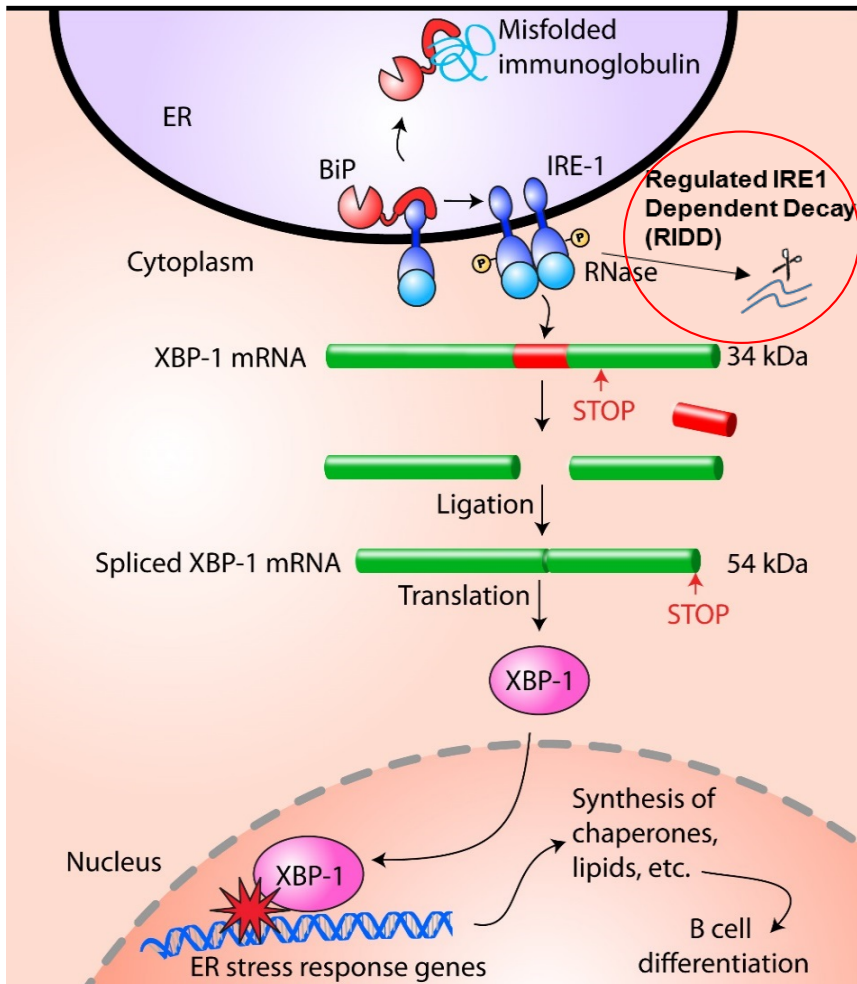
**I have nothing to disclose.**

For more information and discussion, please visit us at Poster # 1987 or e-mail us at [chu@wistar.org](mailto:chu@wistar.org)

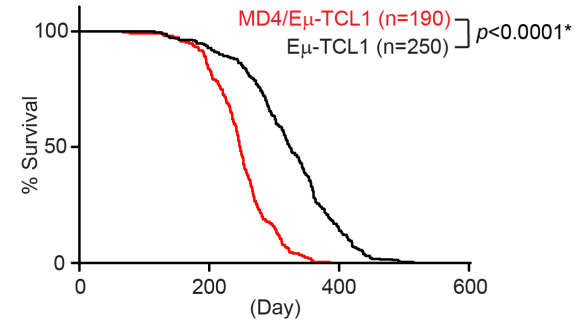
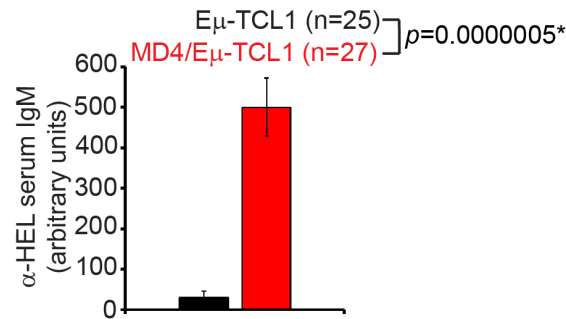
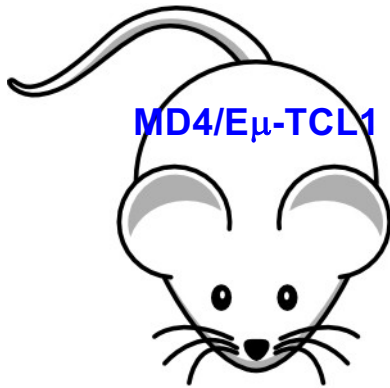
# The IRE-1/XBP-1 pathway of the ER stress response supports the growth and survival of CLL



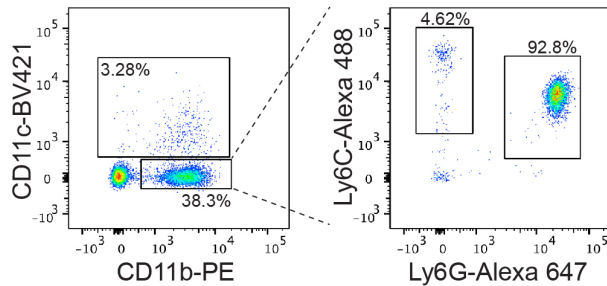
# XBP-1 deficiency triggers hyperactivated IRE-1, which can cleave the mRNAs of secretory Ig $\mu$ heavy chains (**RIDD**)



# MD4/E $\mu$ -TCL1 mice produce higher levels of sIgM and increased numbers of MDSCs, and exhibit shorter survival

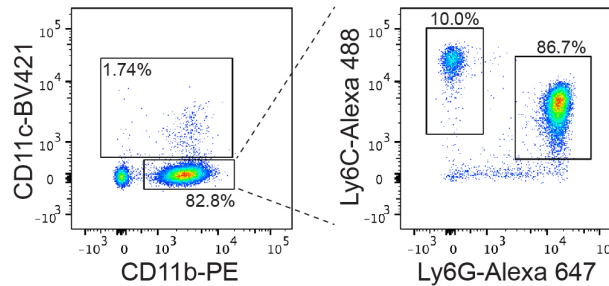


6-month-old E $\mu$ -TCL1



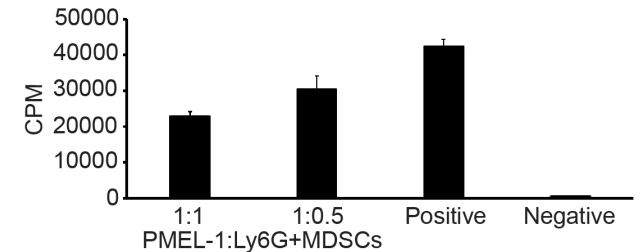
% CD11b+ myeloid cells  
 E $\mu$ -TCL1 (n=15)  
 MD4/E $\mu$ -TCL1 (n=14)  $p=0.0013^*$

6-month-old MD4/E $\mu$ -TCL1

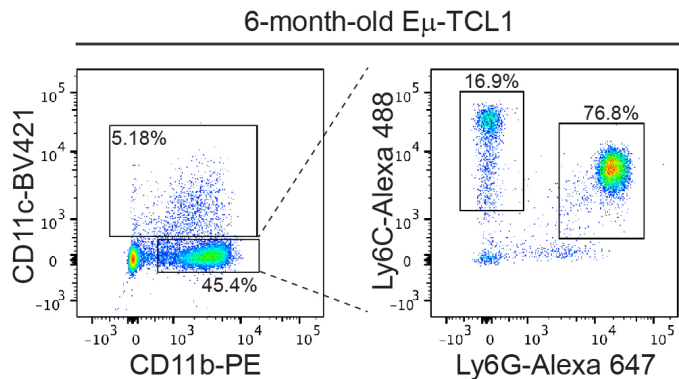
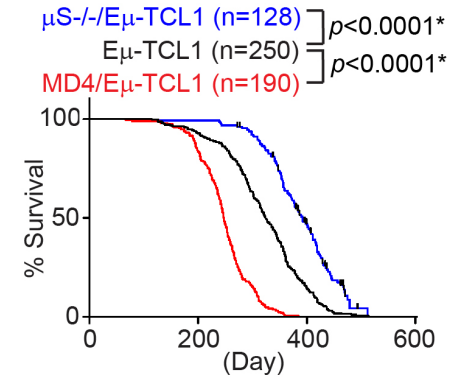
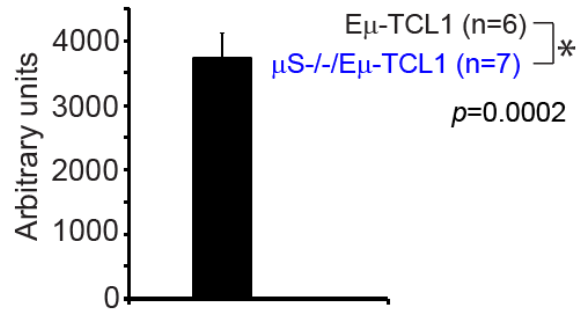
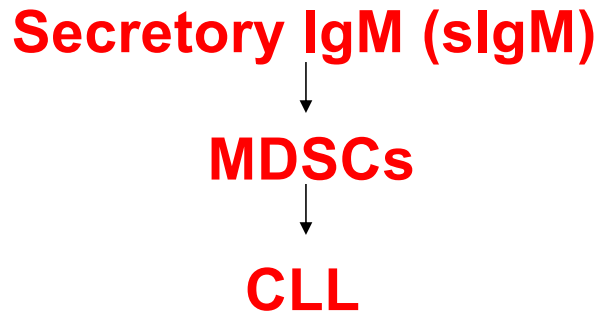


% CD11b+/Ly6G+ PMN-MDSCs  
 E $\mu$ -TCL1 (n=15)  
 MD4/E $\mu$ -TCL1 (n=14)  $p=0.0009^*$

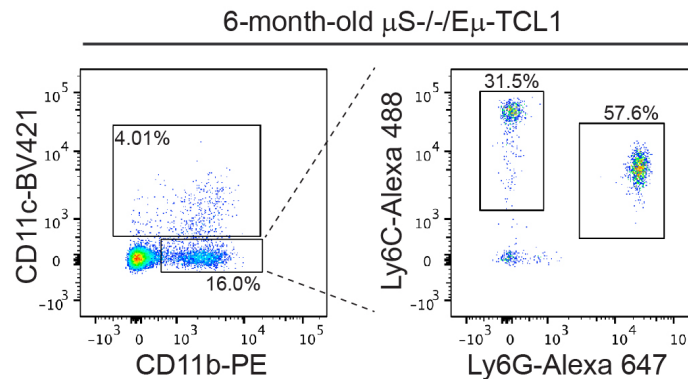
% CD11b+/Ly6C+ M-MDSCs  
 E $\mu$ -TCL1 (n=15)  
 MD4/E $\mu$ -TCL1 (n=14)  $p=0.08$



# Deleting the capability of E $\mu$ -TCL1 mice in producing sIgM leads to decreased MDSCs and prolonged survival

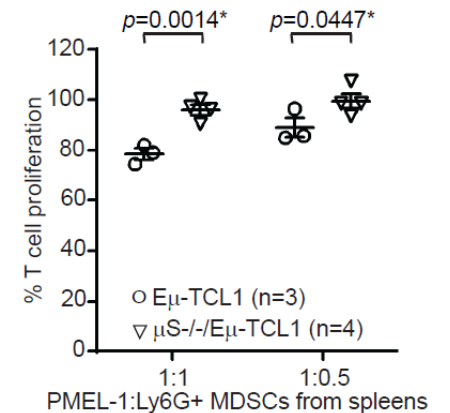


% CD11b<sup>+</sup> myeloid cells  
 E $\mu$ -TCL1 (n=15)  
 $\mu$ S<sup>-/-</sup>/E $\mu$ -TCL1 (n=10)  $p=0.0004^*$



% CD11b<sup>+</sup>/Ly6G<sup>+</sup> PMN-MDSCs  
 E $\mu$ -TCL1 (n=15)  
 $\mu$ S<sup>-/-</sup>/E $\mu$ -TCL1 (n=10)  $p=0.006^*$

% CD11b<sup>+</sup>/Ly6C<sup>+</sup> M-MDSCs  
 E $\mu$ -TCL1 (n=15)  
 $\mu$ S<sup>-/-</sup>/E $\mu$ -TCL1 (n=10)  $p=0.16$



# Targeting XBP-1s in B and CLL cells leads to reduced sIgM and decreased numbers and functions of MDSCs

