

Data S1. Original Images of Representative Western blot. Related to Figures 1-7 and S1-S7.

Fig 1A)

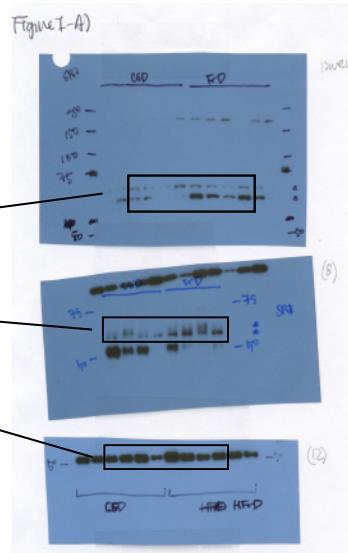
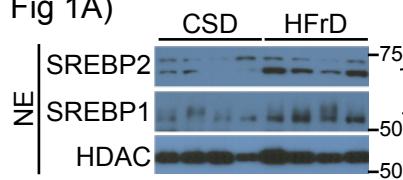


Figure 1 - B)

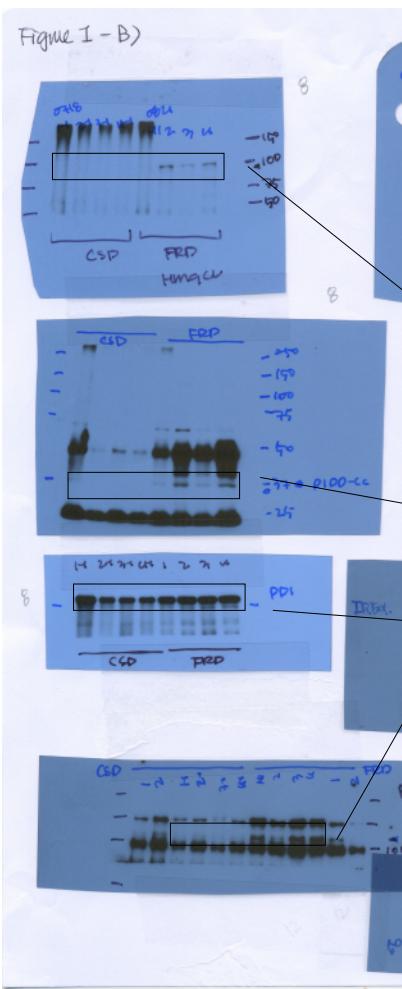


Fig 1B)

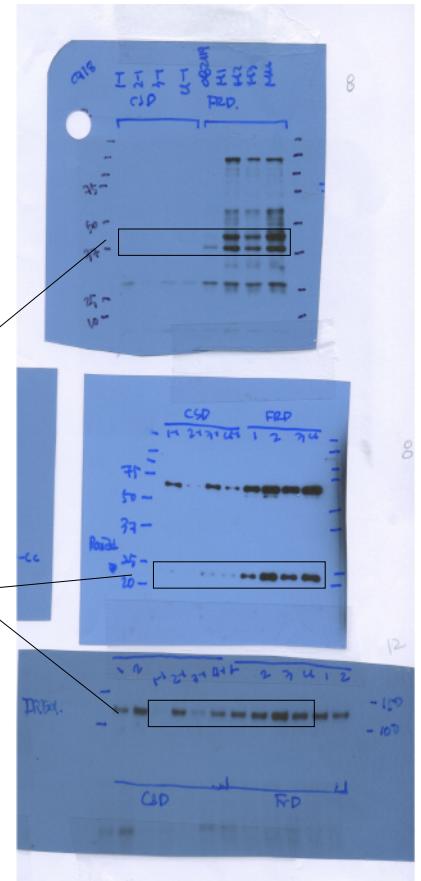
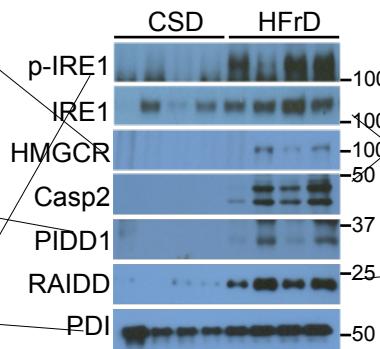
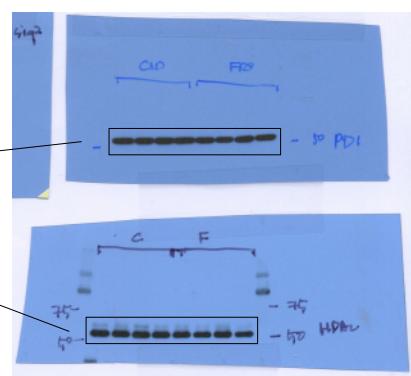
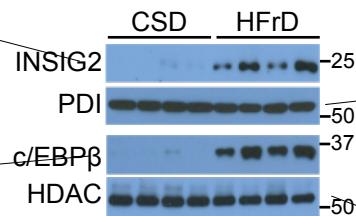


Fig 1C)



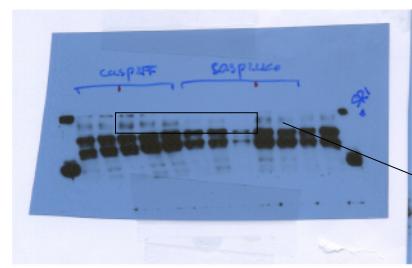


Fig 1E)

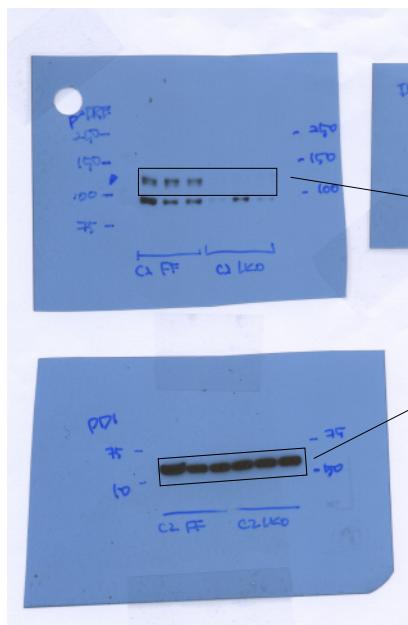
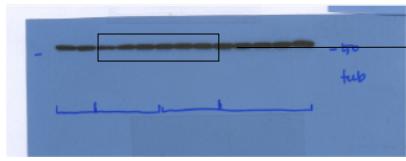
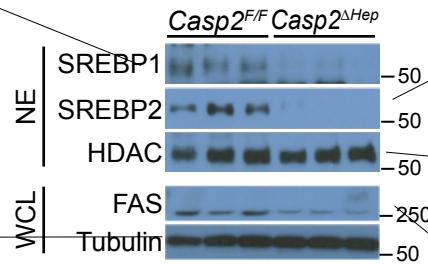


Fig 1F)

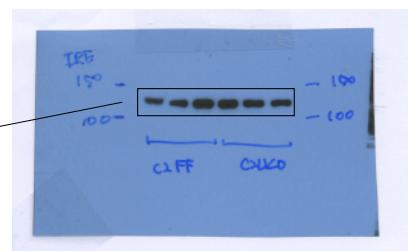
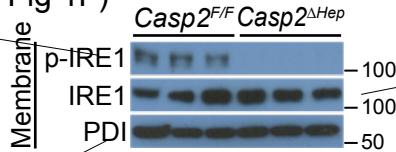


Fig 2C)

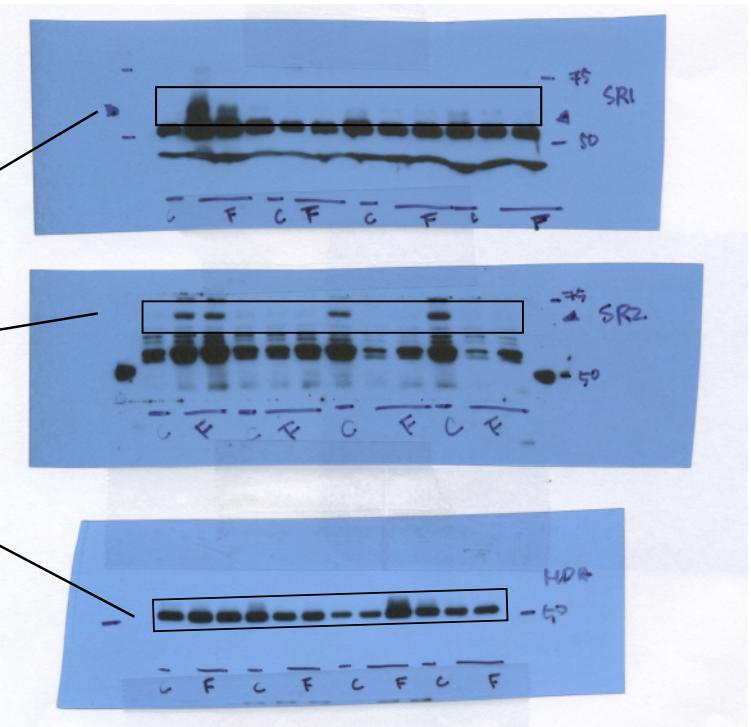
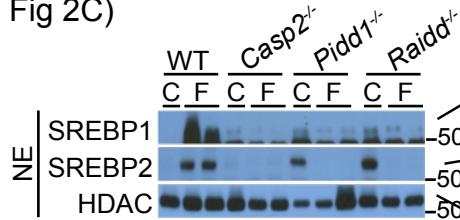


Figure 2 -D

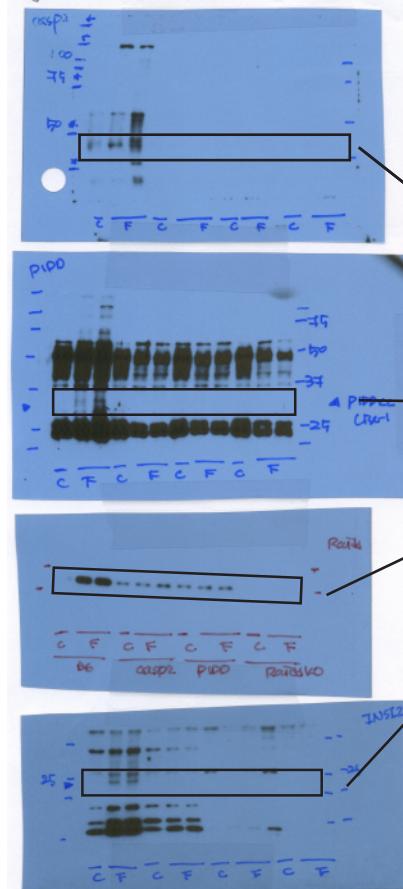
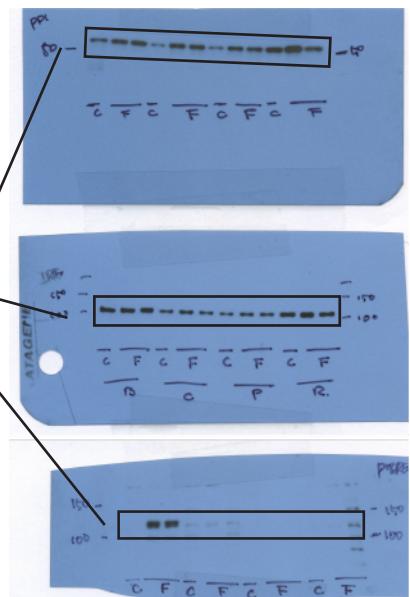
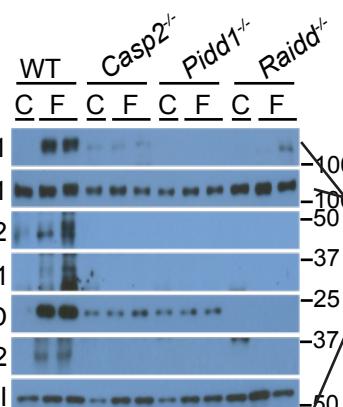


Fig 2D)



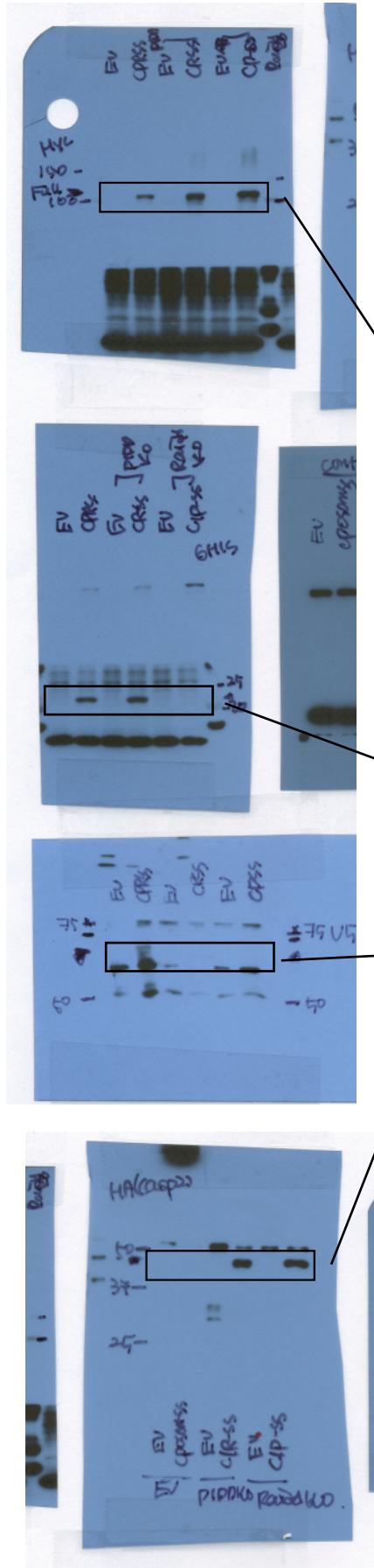
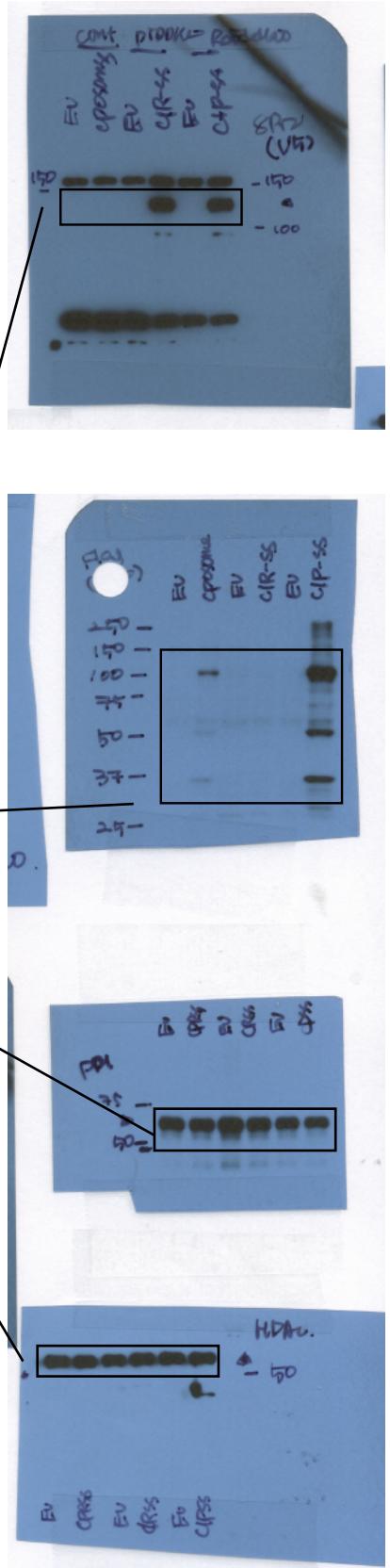


Fig 4A)

Western blot analysis showing protein expression and co-localization of various proteins in HEK293T cells. The blot is probed with antibodies against Myc, HA, Flag, V5, PDI, V5, and HDAC. Molecular weight markers (50, 45, 35, 25, 15 kDa) are indicated on the right.

	EV <sup>Δ</sup>			PIDD1 <sup>Δ</sup>			RAIDO <sup>Δ</sup>		
	+	+	+	+	+	+	+	+	+
V5-SREBP2	++	++	++	+	+	+	+	+	+
Myc-S1P	++	++	++	+	+	+	+	+	+
RAIDO-6HIS	++	++	++	+	+	+	+	+	+
PIDD1-Flag	++	++	++	+	+	+	+	+	+
Casp2-HA	++	++	++	+	+	+	+	+	+
EV	++	++	++	+	+	+	+	+	+

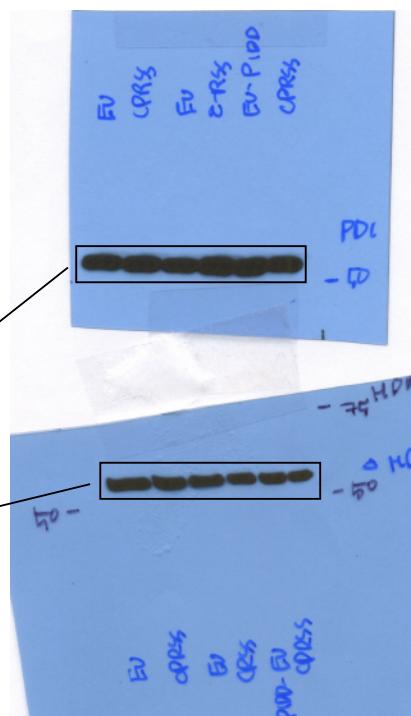


**Fig 4B)**

EV $^{\Delta}$  PIDD1 $^{\Delta}$

	+	+	+
V5-SREBP2	+	+	+
Myc-S1P	+	+	+
RAIDD-6HIS	+	+	+
PIDD1-Flag			
Casp2-HA	+	+	+
EV	+	+	+

Western blot analysis showing expression of V5, PDI, V5, and HDAC. Red arrowheads indicate bands at 150 kDa (labeled (P)) and 75 kDa (labeled (C)). Molecular weight markers (150, 100, 50) are indicated on the right.

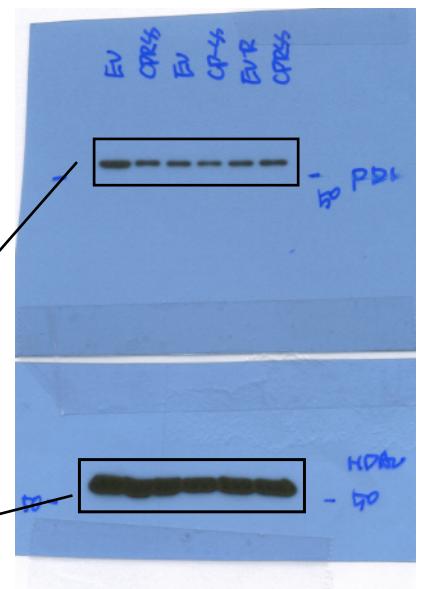


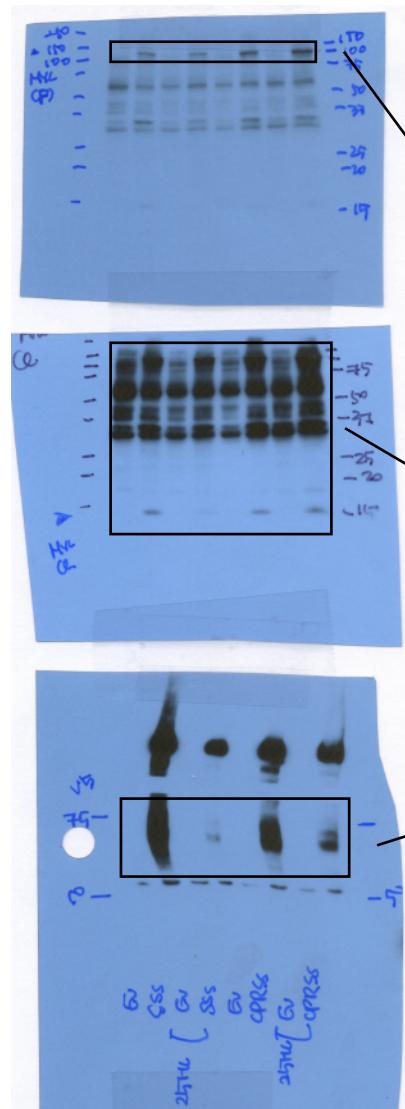
**Fig 4C)**

EV $^{\Delta}$  RAIDD $^{\Delta}$

	+	+	+
V5-SREBP2	+	+	+
Myc-S1P	+	+	+
RAIDD-6HIS	+		
PIDD1-Flag			
Casp2-HA	+	+	+
EV	+	+	+

Western blot analysis showing expression of V5, PDI, V5, and HDAC. Red arrowheads indicate bands at 150 kDa (labeled (P)) and 75 kDa (labeled (C)). Molecular weight markers (150, 100, 50) are indicated on the right.





**Fig 4D)**

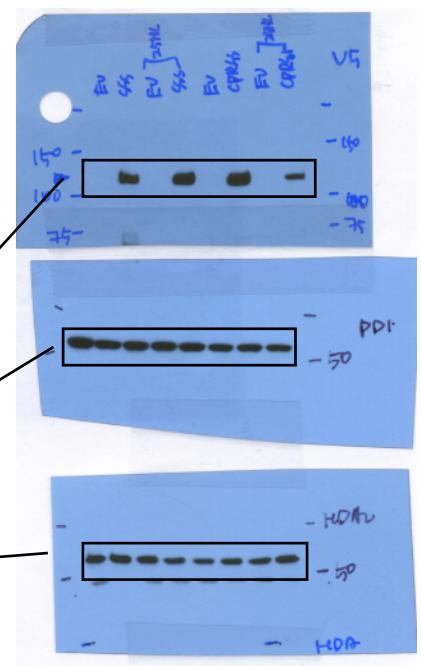
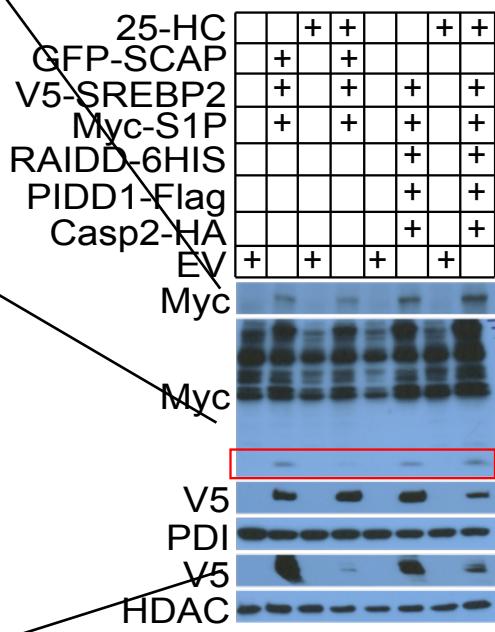


Fig 5B)

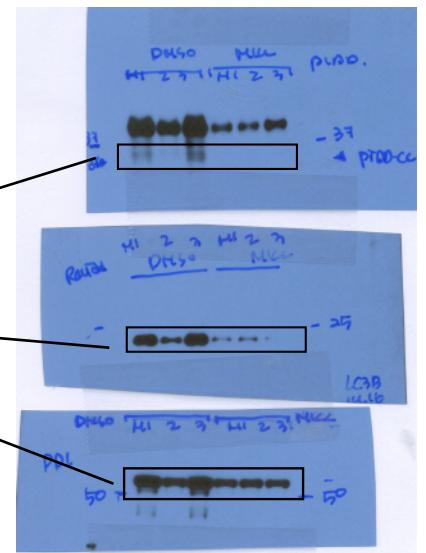
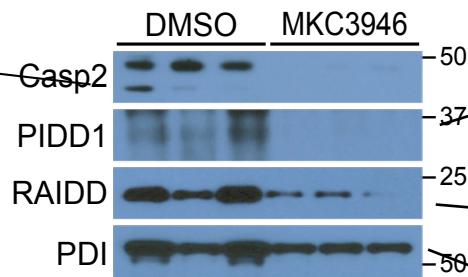


Fig 5C)

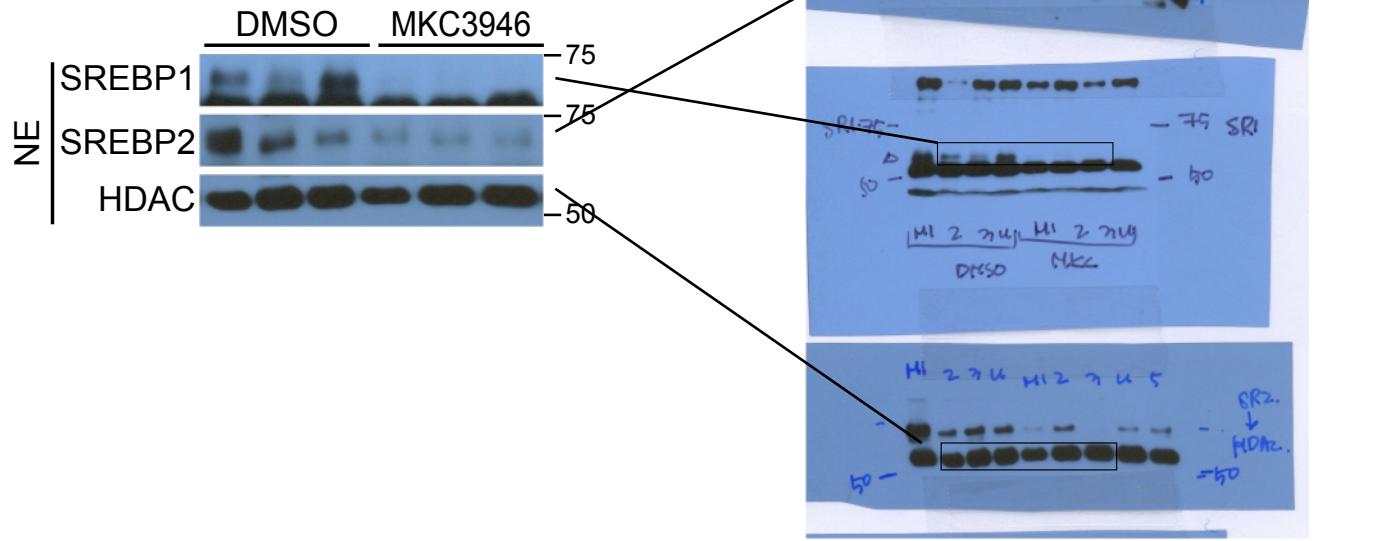


Fig 5E)

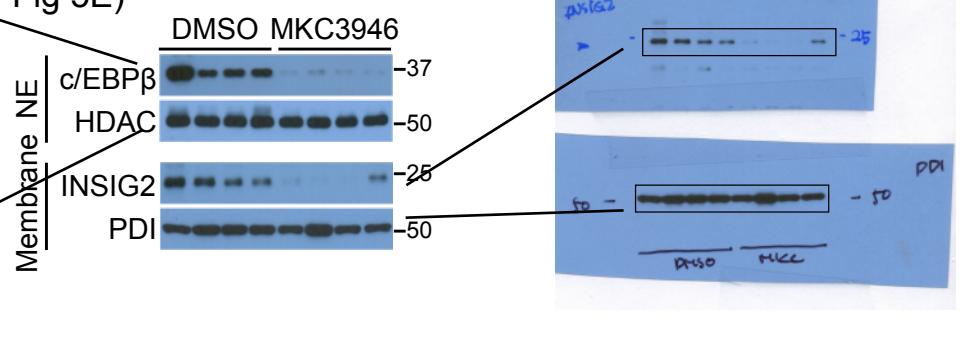


Fig 6A)

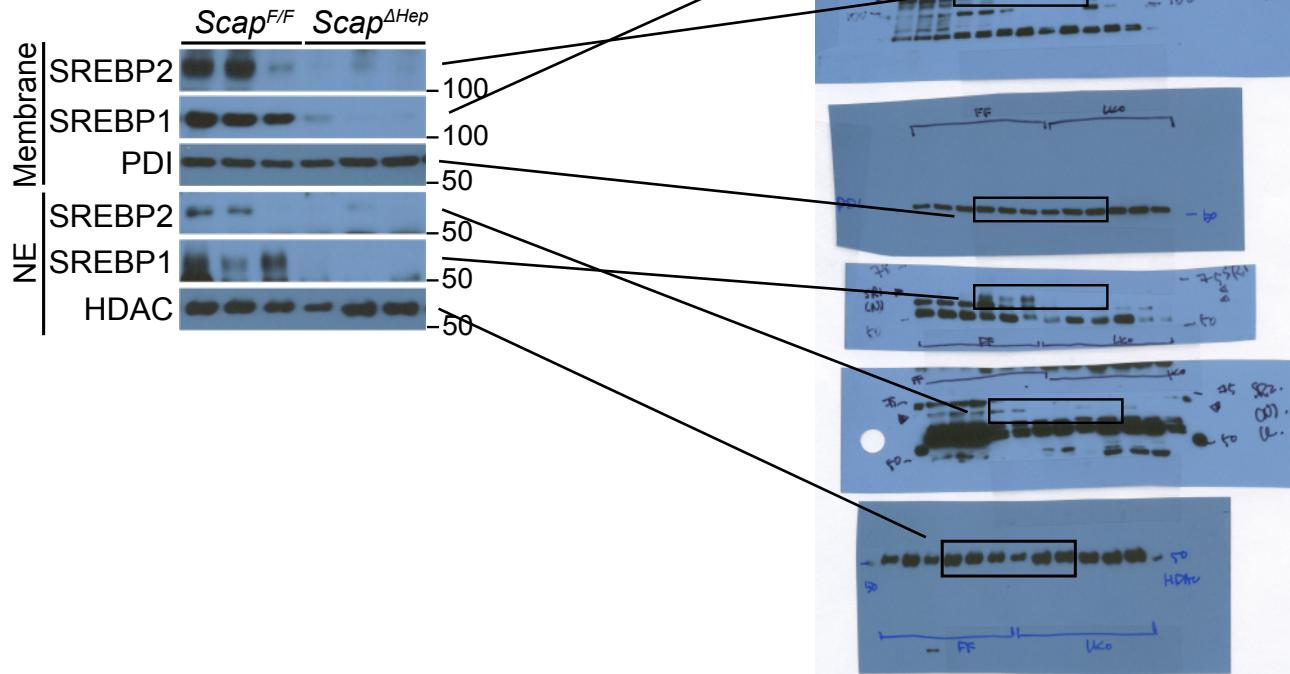


Fig 6D)

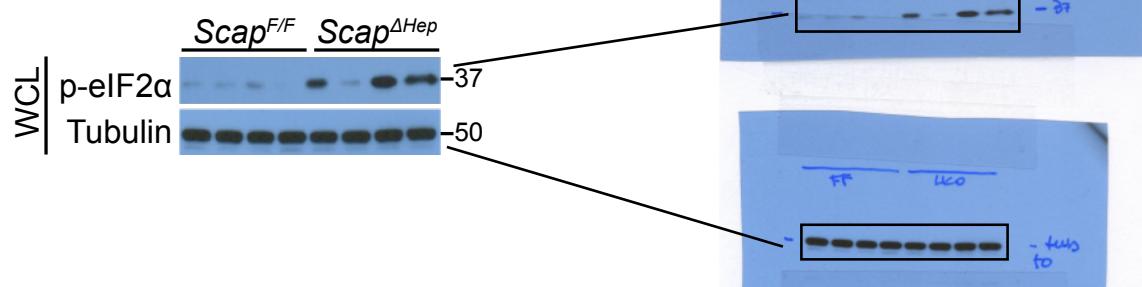


Fig 6C)

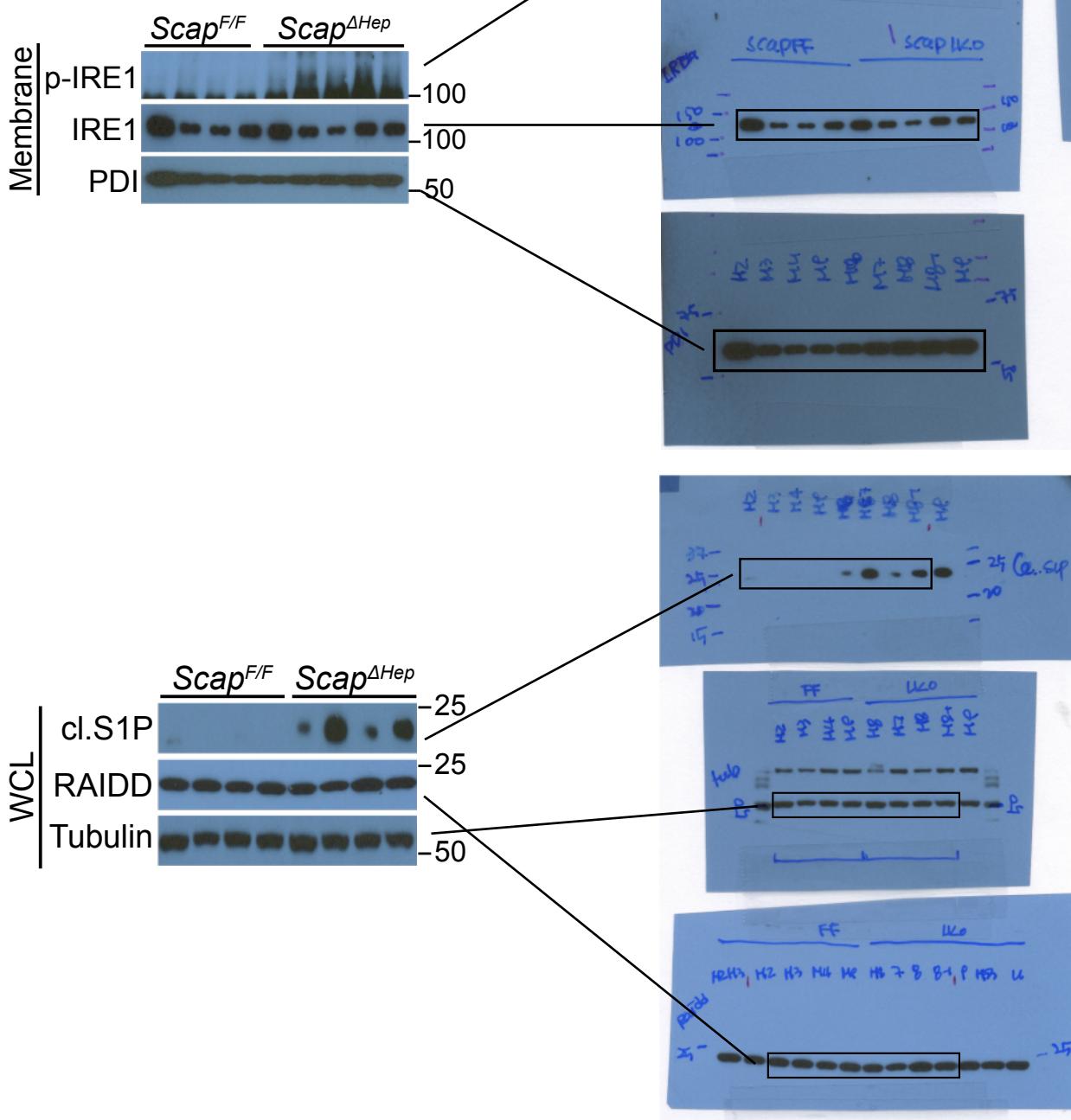


Fig 7B)

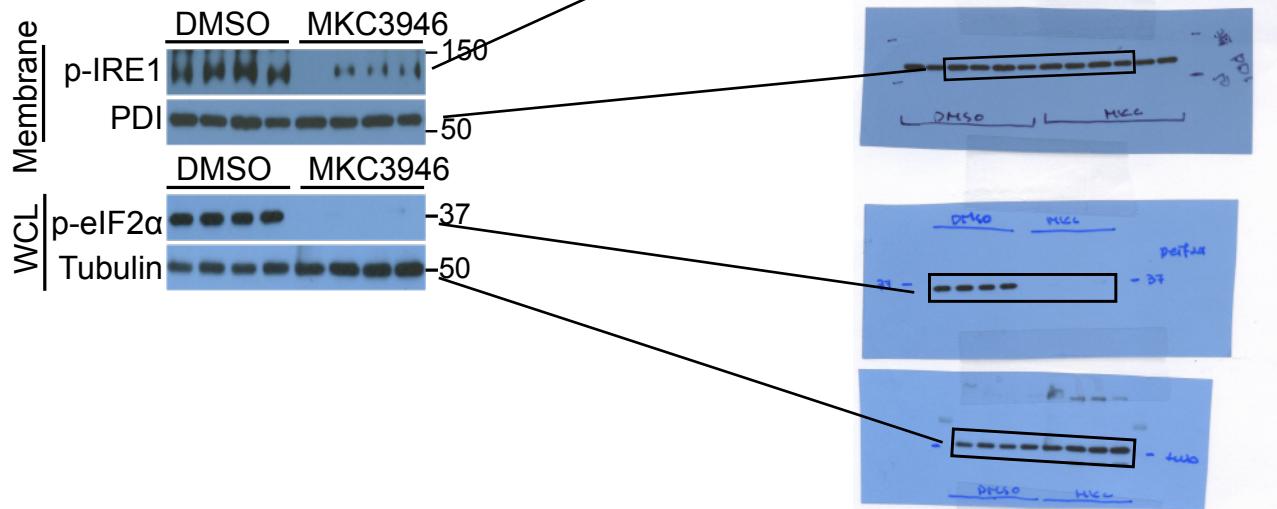
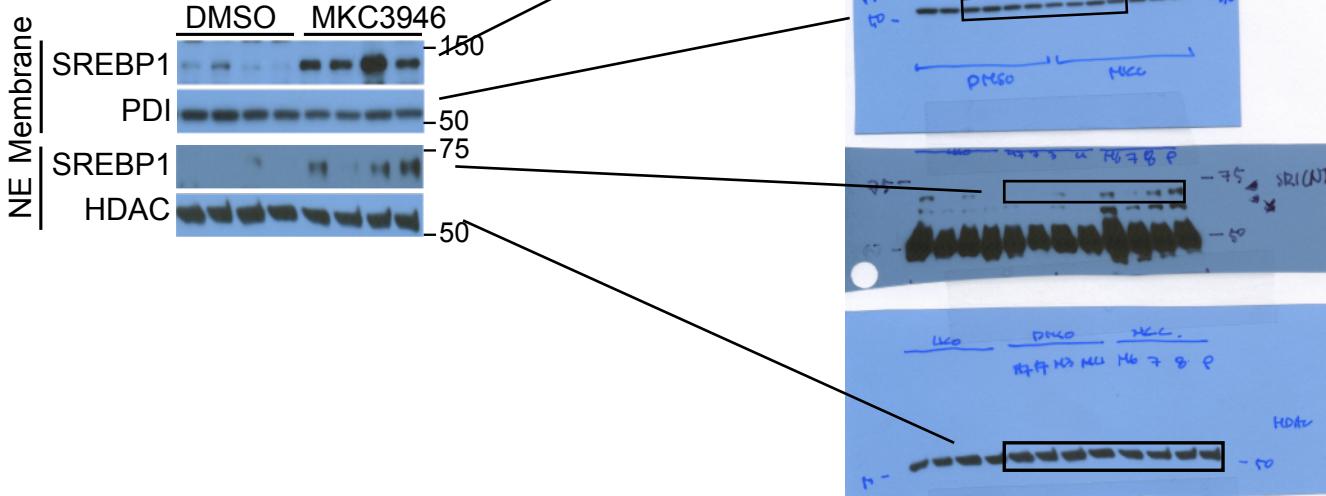
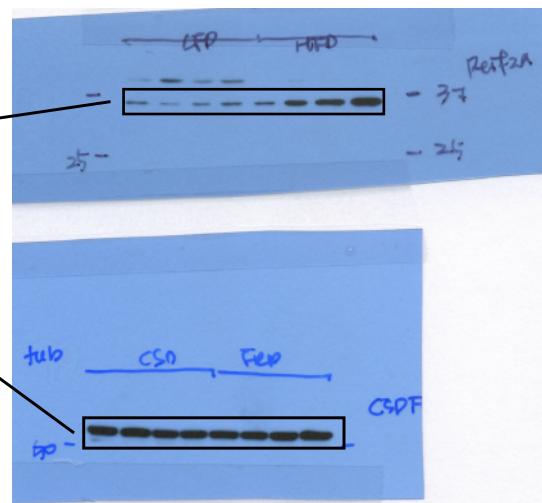
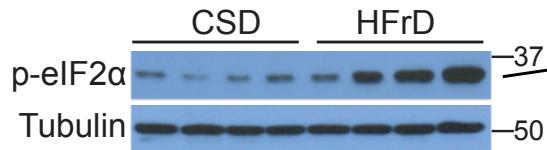


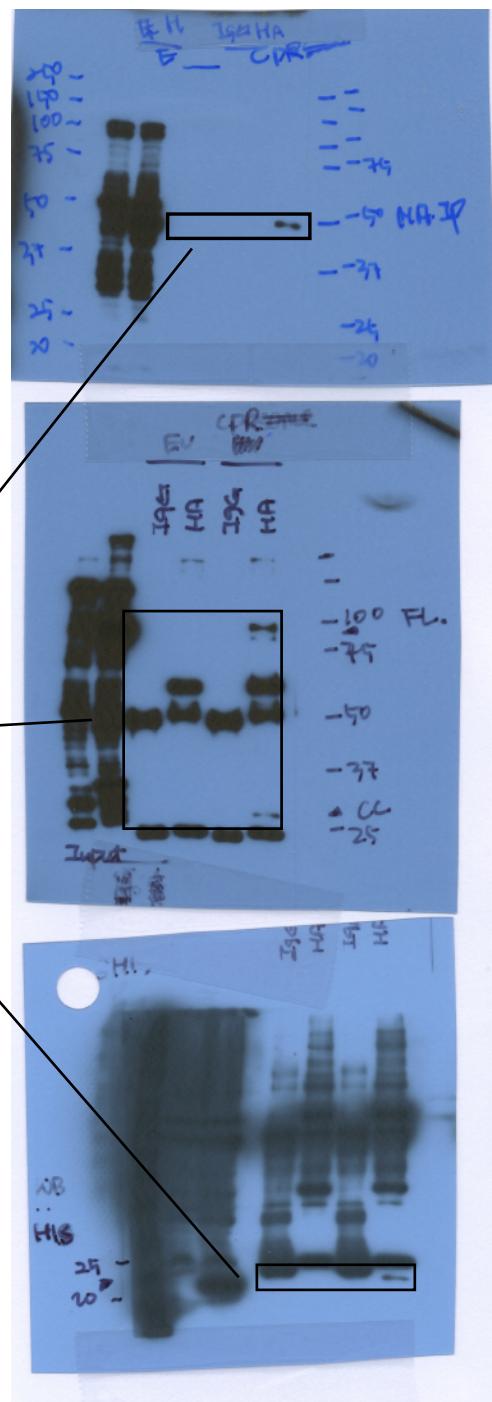
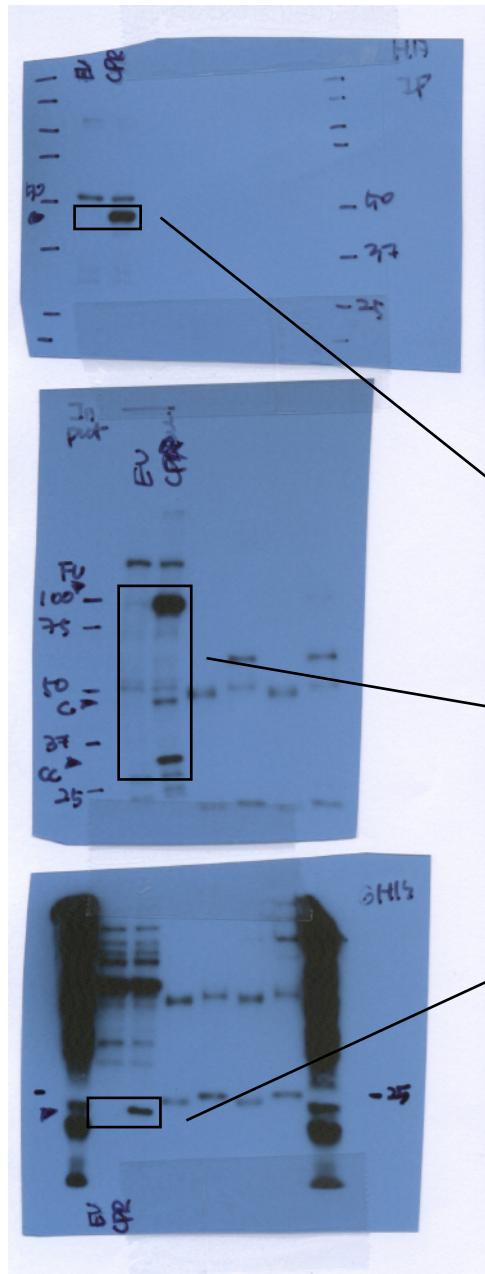
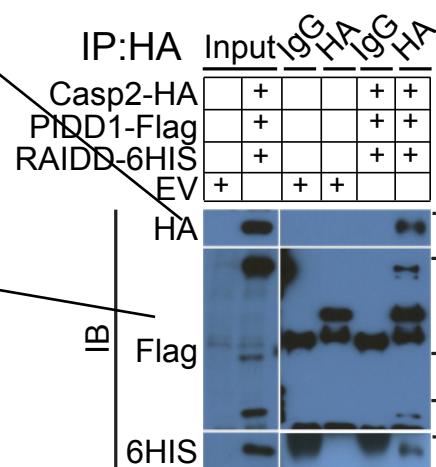
Fig 7C)



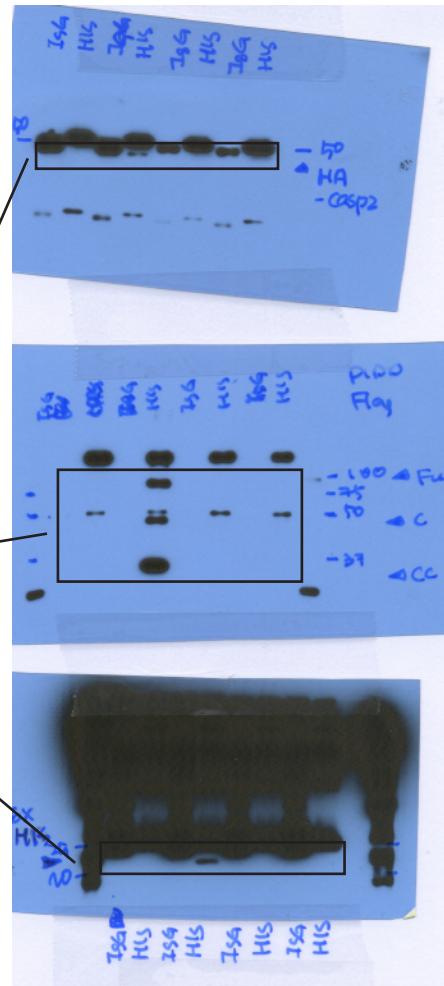
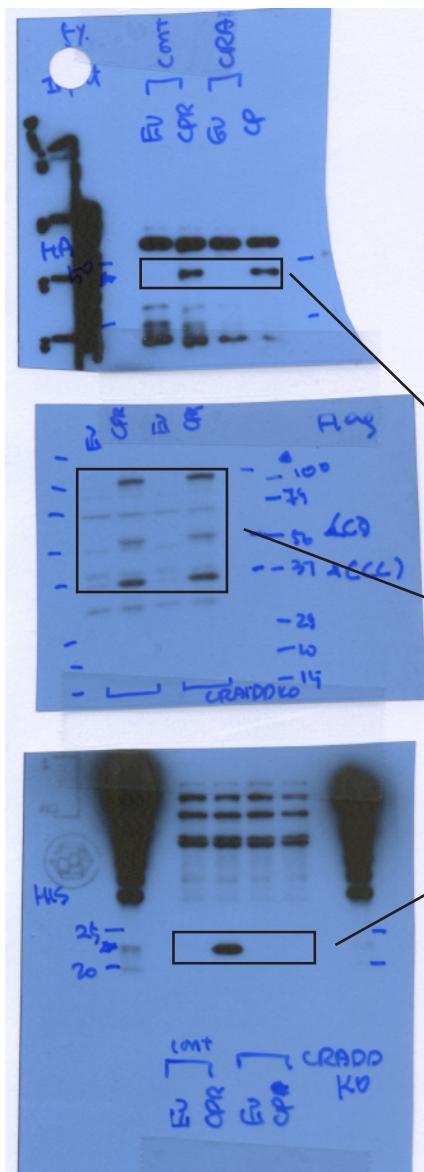
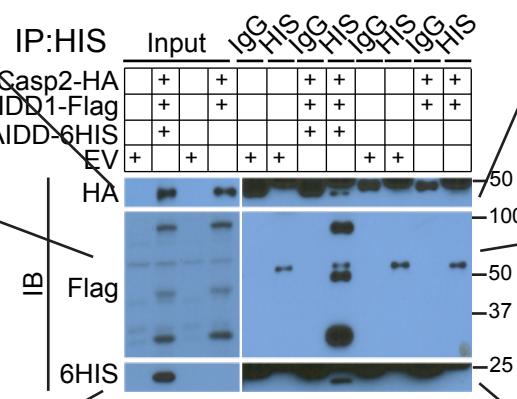
Sup, Fig 1D)



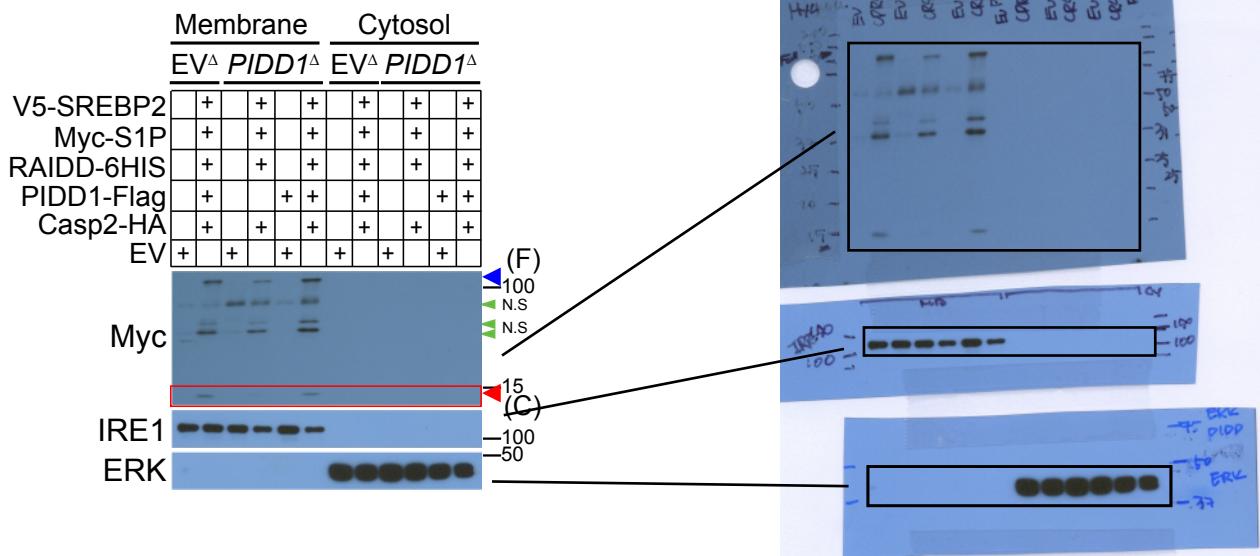
Sup Fig4 A)



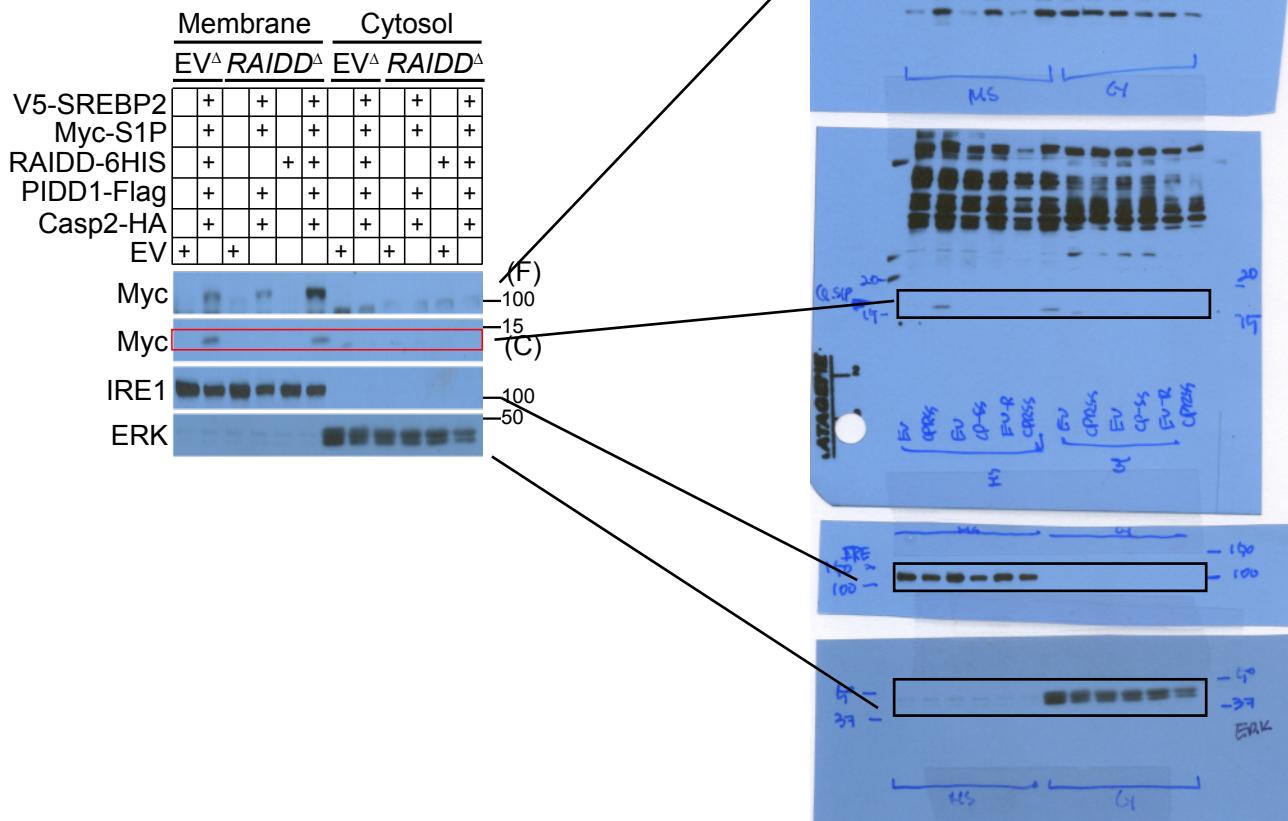
Sup Fig 4B)



Sup Fig 4C)



Sup Fig 4D)



Sup Fig 4F)

	Membrane			Cytosol		
	+	+	+	+	+	+
V5-SREBP2	+	+	+	+	+	+
Myc-S1P	+	+	+	+	+	+
RAIDD-6HIS	+	+	+	+	+	+
PIDD1 <sup>ΔDD</sup> -Flag			+			++
PIDD1-Flag		+	+		+	+
Casp2-HA		+	+	+	+	+
EV	+	+	+	+	+	+

Myc

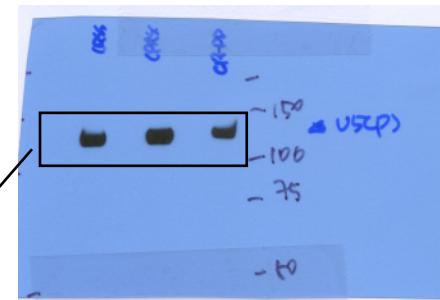
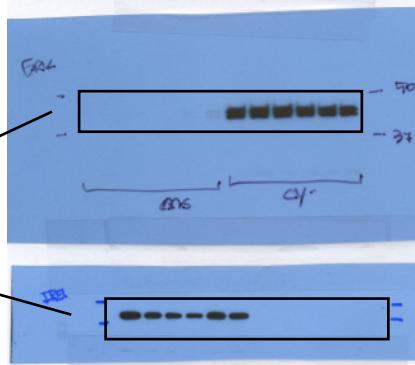
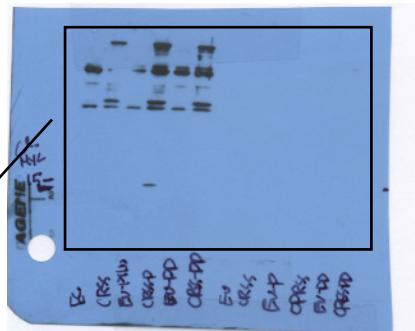
100

IRE1

15

ERK

50



	+	+	+
	+	+	+
V5-SREBP2	+	+	+
Myc-S1P	+	+	+
RAIDD-6HIS	+	+	+
PIDD1 <sup>ΔDD</sup> -Flag			++
PIDD1-Flag		+	+
Casp2-HA	+	+	+
EV	+	+	+

Mem

NE  
brane

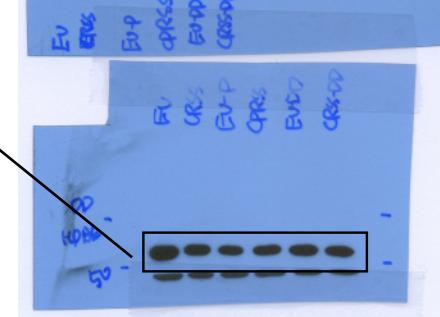
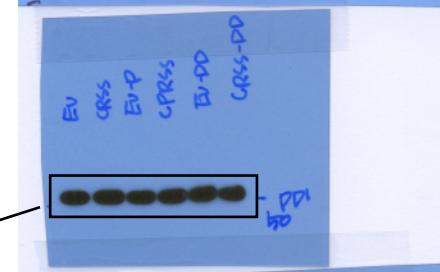
V5  
PDI  
V5  
HDAC

150

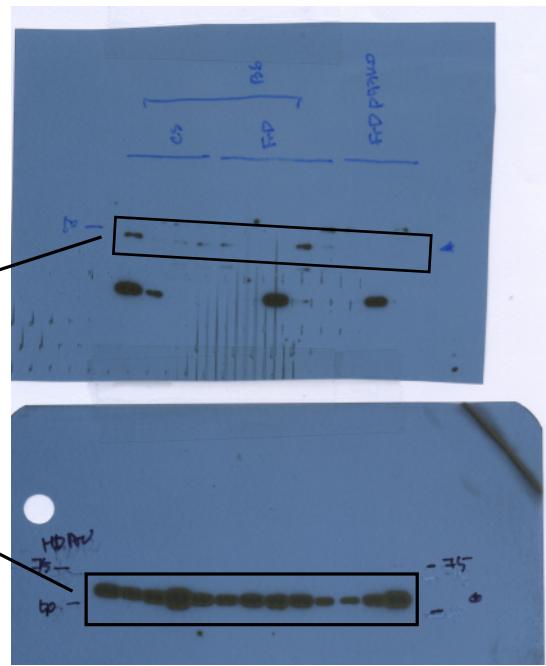
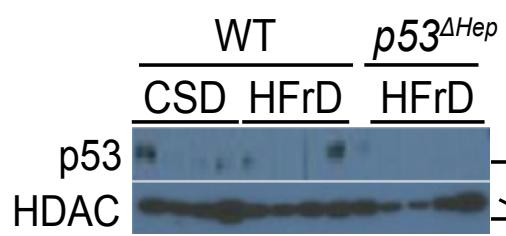
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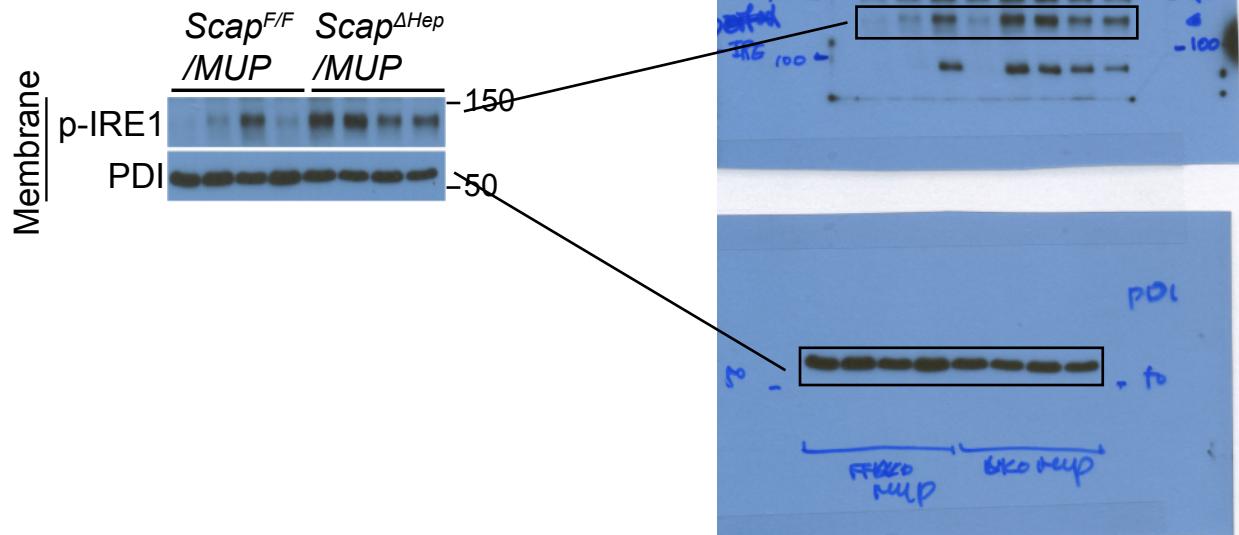
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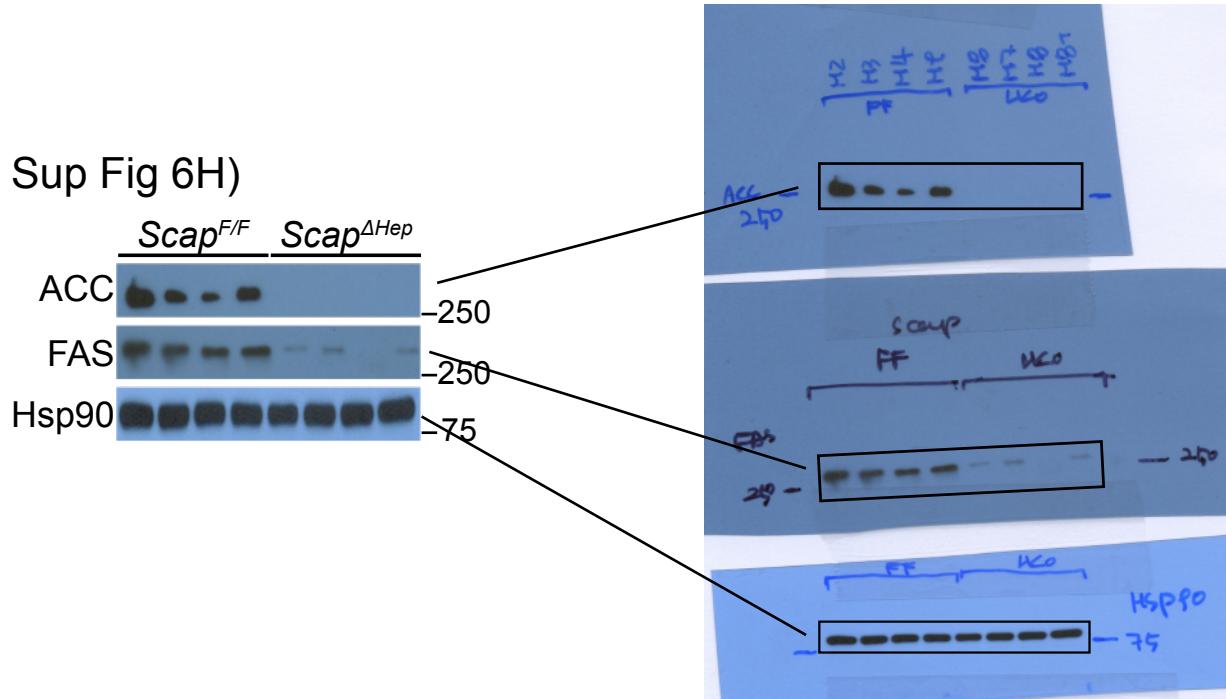
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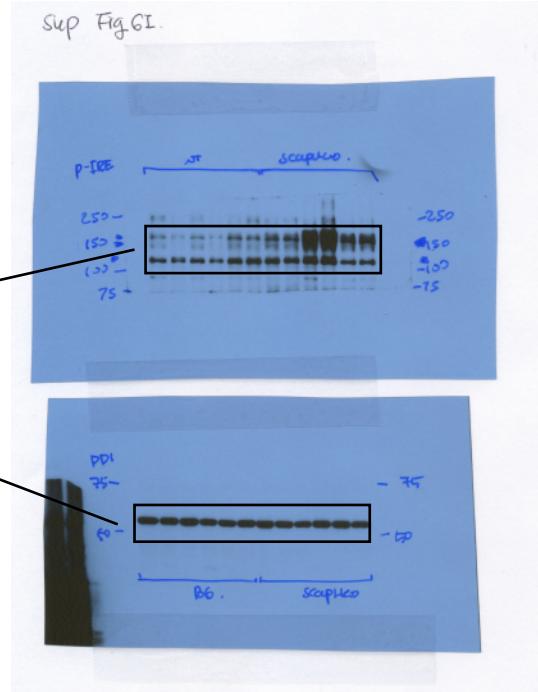
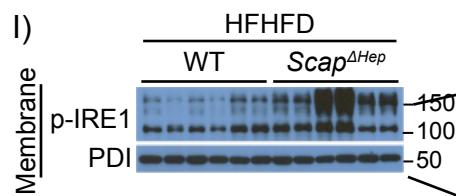
Sup Fig 6B)



Sup Fig 6H)



Sup Fig 6I.



Sup Fig 7A)

