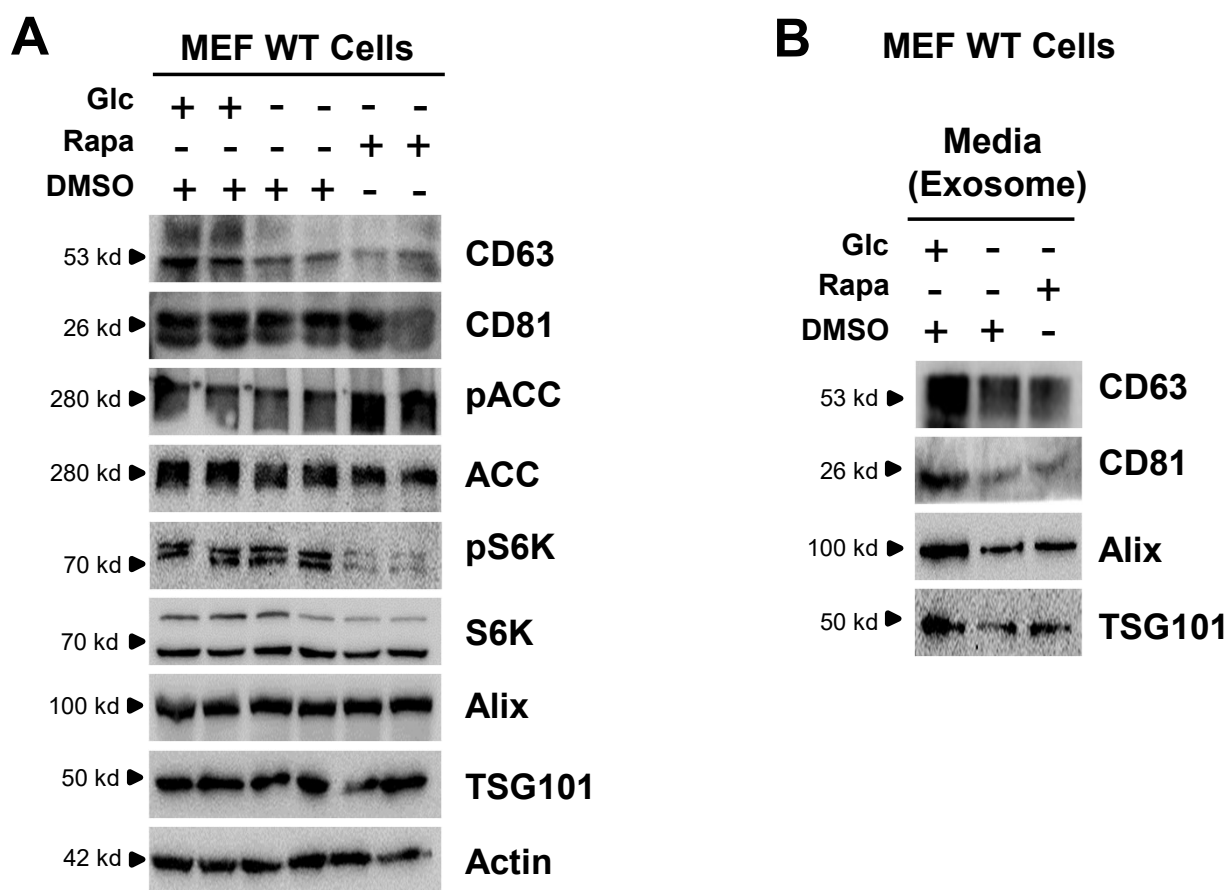
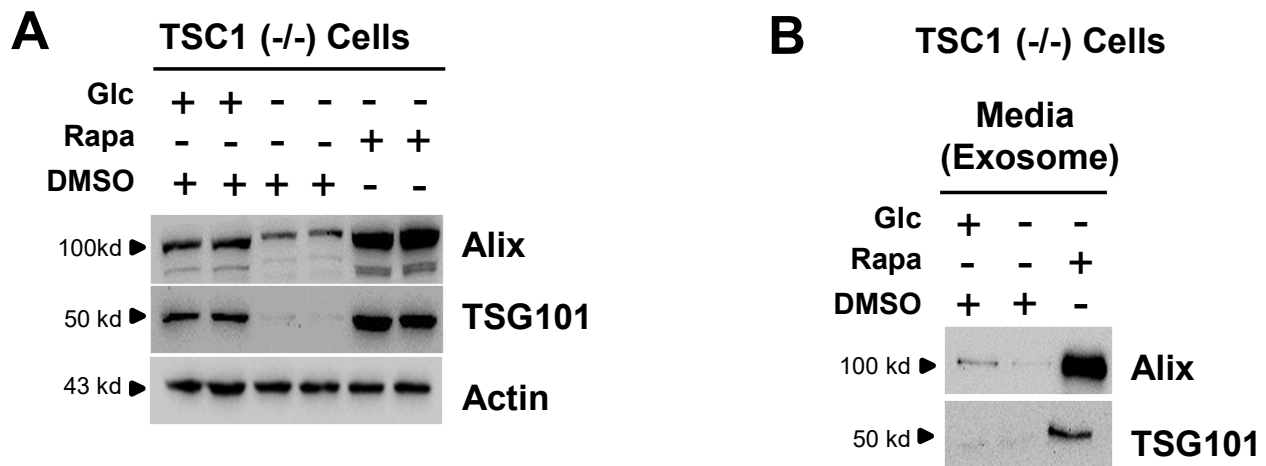


Supple. Figure S1. Effects of exosome release by mTORC1 inhibition in TSC2-null cells. (A) TSC2 (-/-) MEF cells were cultured with completed media. During serum starvation, cells were cultured in the absence or presence of glucose for 48 h. Rapamycin (100 nM) was treated in the absence of glucose for 24 h. The cells were harvested, lysed, and analyzed by immunoblotting with the indicated antibodies such as Alix, and TSG101. Actin was used as a loading control. (B) TSC2 (-/-) MEF cells were cultured with completed media. During serum starvation, cells were cultured in the absence or presence of glucose for 48 h. Rapamycin (100 nM) was treated in the absence of glucose for 24 h. After the collection of medium from cells, the media were subjected to ultracentrifugation to harvest the exosome fraction, as according to the materials and methods. The samples were analyzed by immunoblotting with antibodies for exosome marker proteins, such as Alix, and TSG101. Glucose (Glc), Rapamycin (Rapa), Dimethyl Sulfoxide (DMSO).



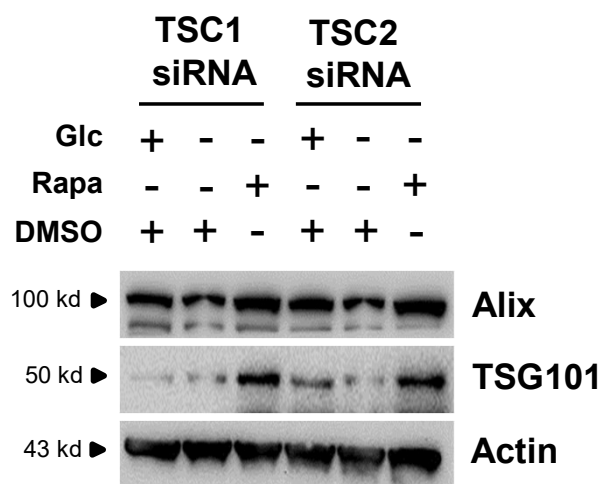
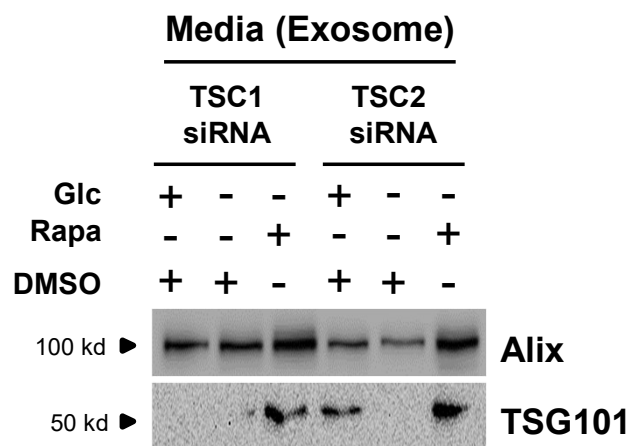
Supple. Figure S2. Effects of exosome release by mTORC1 inhibition in MEF-WT cells.

(A) MEF-WT cells were cultured with completed media. During serum starvation, cells were cultured in the absence or presence of glucose for 48 h. Rapamycin (100 nM) was treated in the absence of glucose for 24 h. The cells were harvested, lysed, and analyzed by immunoblotting with the indicated antibodies. Actin was used as a loading control. (B) MEF-WT cells were cultured with completed media. During serum starvation, cells were cultured in the absence or presence of glucose for 48 h. Rapamycin (100 nM) was treated in the absence of glucose for 24 h. After the collection of medium from cells, the media were subjected to ultracentrifugation to harvest the exosome fraction, as according to the materials and methods. The samples were analyzed by immunoblotting with antibodies for exosome marker proteins, such as CD63, CD81, Alix, and TSG101. Glucose (Glc), Rapamycin (Rapa), Dimethyl Sulfoxide (DMSO).



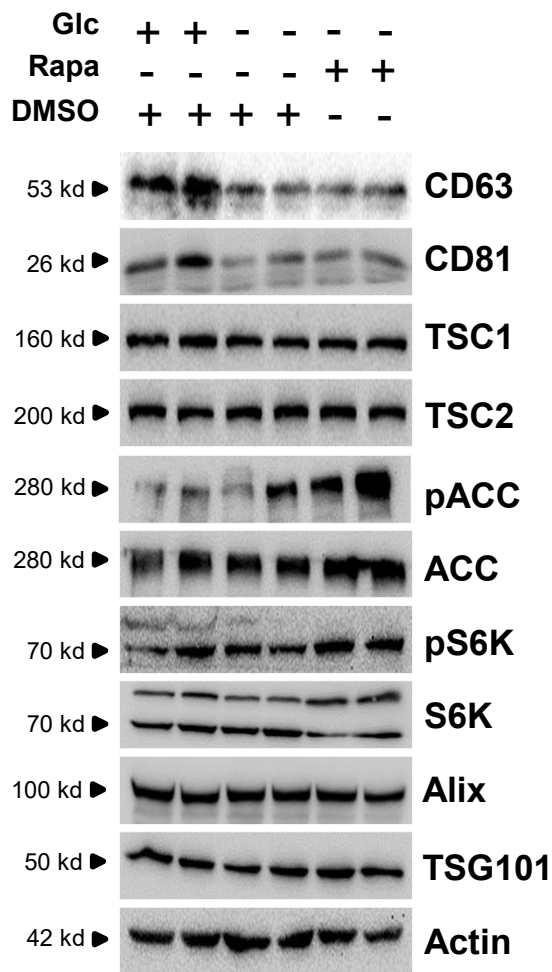
Supple. Figure S3. Effects of exosome release by mTORC1 inhibition in TSC1-null cells.

(A) TSC1 (-/-) MEF cells were cultured with completed media. During serum starvation, cells were cultured in the absence or presence of glucose for 48 h. Rapamycin (100 nM) was treated in the absence of glucose for 24 h. The cells were harvested, lysed, and analyzed by immunoblotting with the indicated antibodies such as Alix, and TSG101. Actin was used as a loading control. (B) TSC1 (-/-) MEF cells were cultured with completed media. During serum starvation, cells were cultured in the absence or presence of glucose for 48 h. Rapamycin (100 nM) was treated in the absence of glucose for 24 h. After the collection of medium from cells, the media were subjected to ultracentrifugation to harvest the exosome fraction, as according to the materials and methods. The samples were analyzed by immunoblotting with antibodies for exosome marker proteins, such as Alix, and TSG101. Glucose (Glc), Rapamycin (Rapa), Dimethyl Sulfoxide (DMSO).

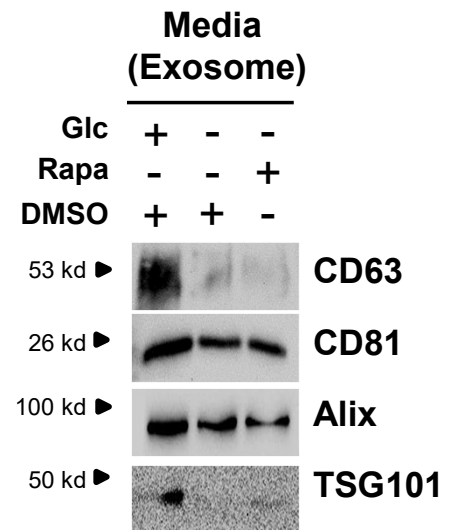
A**HEK293 cells****B****HEK293 cells**

Supple. Figure S4. Effects of exosome release by mTORC1 inhibition in TSC1- or TSC2-silencing cells.

(A) HEK293 cells transfected with either TSC1 siRNA or TSC2 siRNA were cultured with completed media, and then incubated in the absence or presence of glucose for 48 h during serum starvation. The cells incubated in the absence of glucose were treated with 100 nM rapamycin for 24 h. The cells were harvested and lysed, and analyzed by immunoblotting with the indicated antibodies. Actin was used as a loading control. (B) HEK293 cells transfected with either TSC1 siRNA or TSC2 siRNA were cultured with completed media, and then incubated in the absence or presence of glucose for 48 h during serum starvation. After the collection of medium from cells, the media were subjected to ultracentrifugation to harvest the exosome fraction, according to the materials and methods. The samples were analyzed by immunoblotting with antibodies for exosome marker proteins, such as Alix, and TSG101. Glucose (Glc), Rapamycin (Rapa), Dimethyl Sulfoxide (DMSO).

A

**HEK293 cells transfected cells
with scrambled siRNA**

B

**HEK293 cells transfected cells
with scrambled siRNA**

Supple. Figure S5. Effects of exosome release by mTORC1 inhibition in HEK293 cell transfected with scrambled siRNA.

(A) HEK293 cells transfected with scrambled siRNA were cultured with completed media, and then incubated in the absence or presence of glucose for 48 h during serum starvation. The cells incubated in the absence of glucose were treated with 100 nM rapamycin for 24 h. The cells were harvested and lysed, and analyzed by immunoblotting with the indicated antibodies. Actin was used as a loading control. (B) HEK293 cells transfected with scrambled siRNA were cultured with completed media, and then incubated in the absence or presence of glucose for 48 h during serum starvation. After the collection of medium from cells, the media were subjected to ultracentrifugation to harvest the exosome fraction, according to the materials and methods. The samples were analyzed by immunoblotting with antibodies for exosome marker proteins, such as CD63, CD81, Alix, and TSG101m. Glucose (Glc), Rapamycin (Rapa), Dimethyl Sulfoxide (DMSO).

Figure 1A

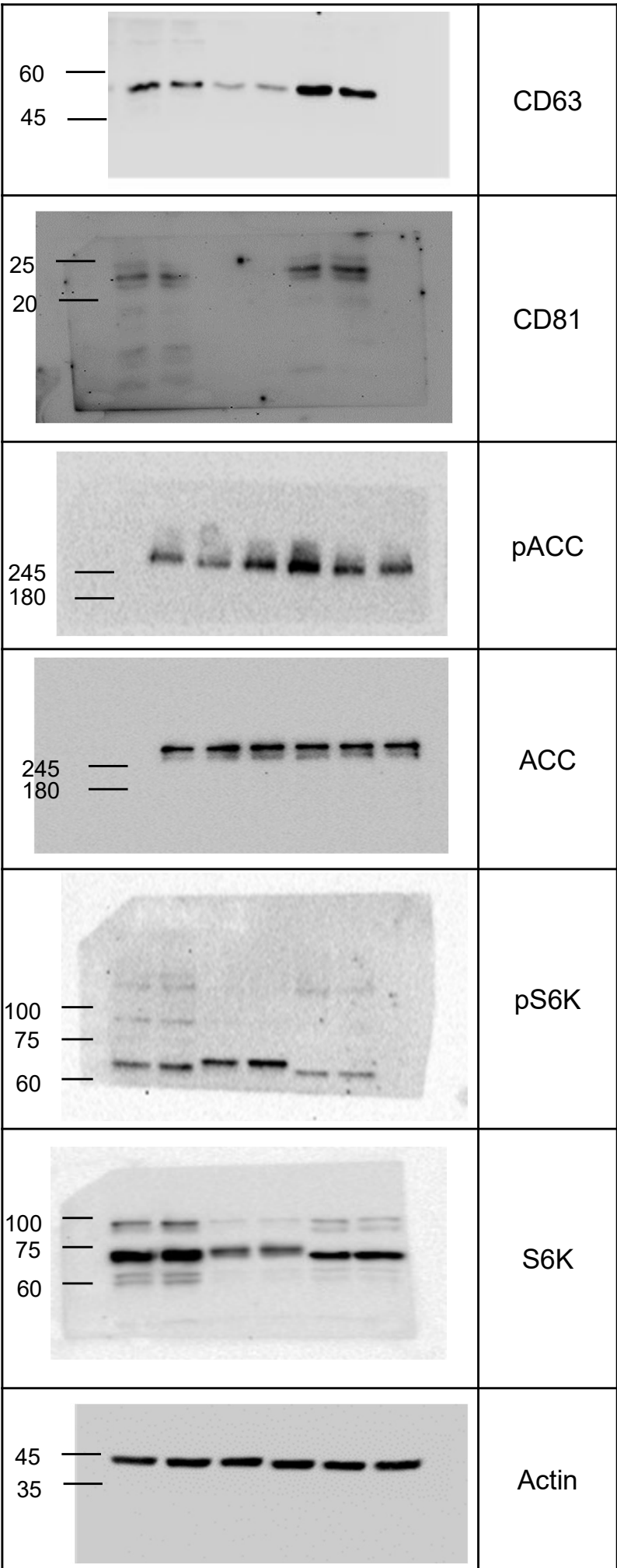


Figure 1C

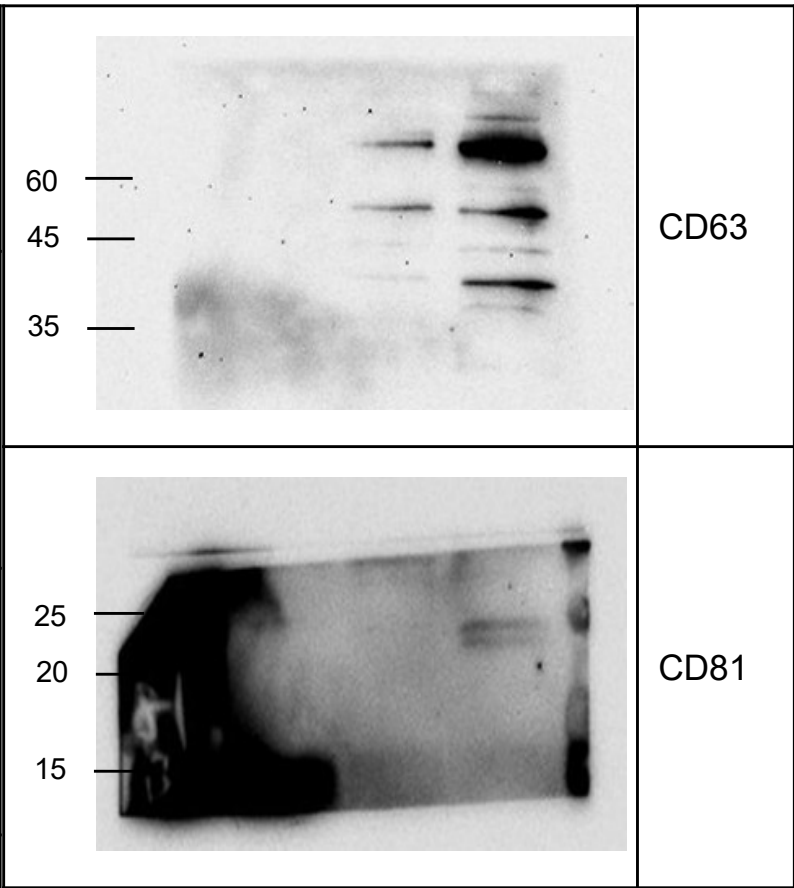


Figure 2A

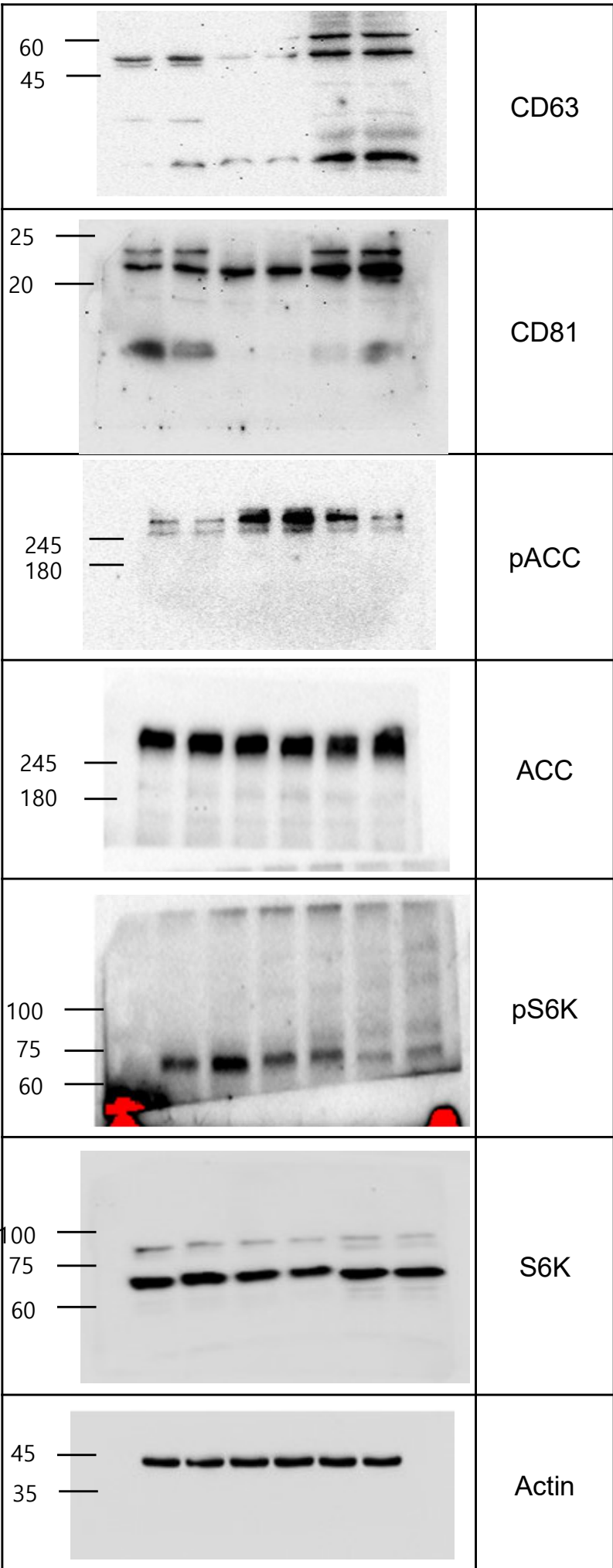


Figure 2C

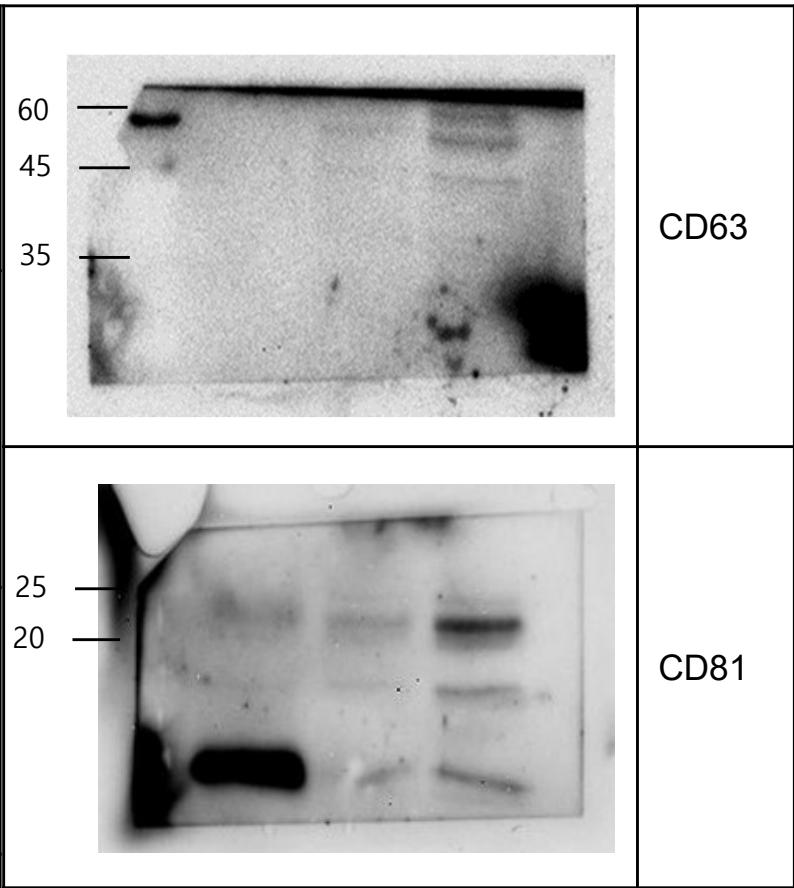
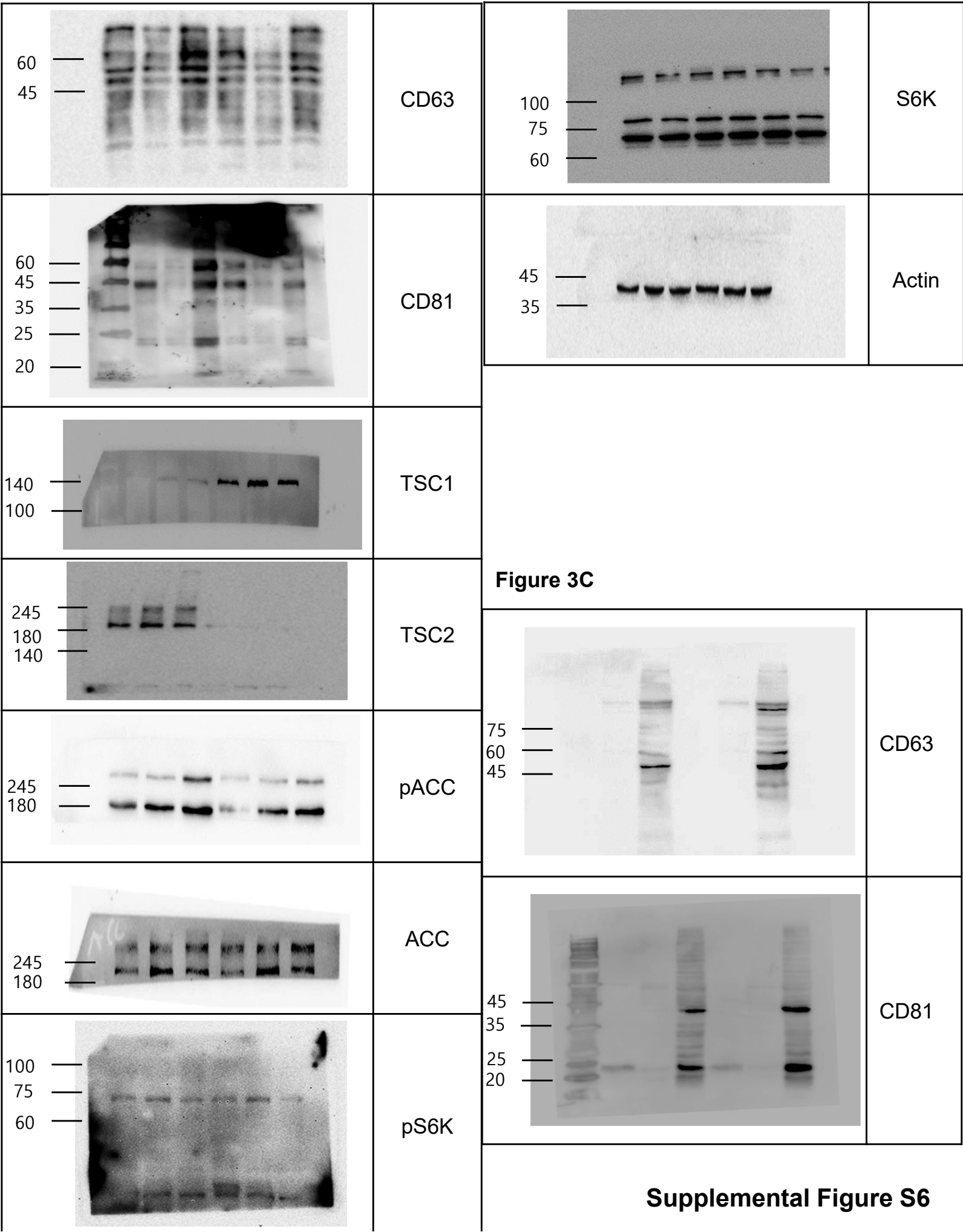
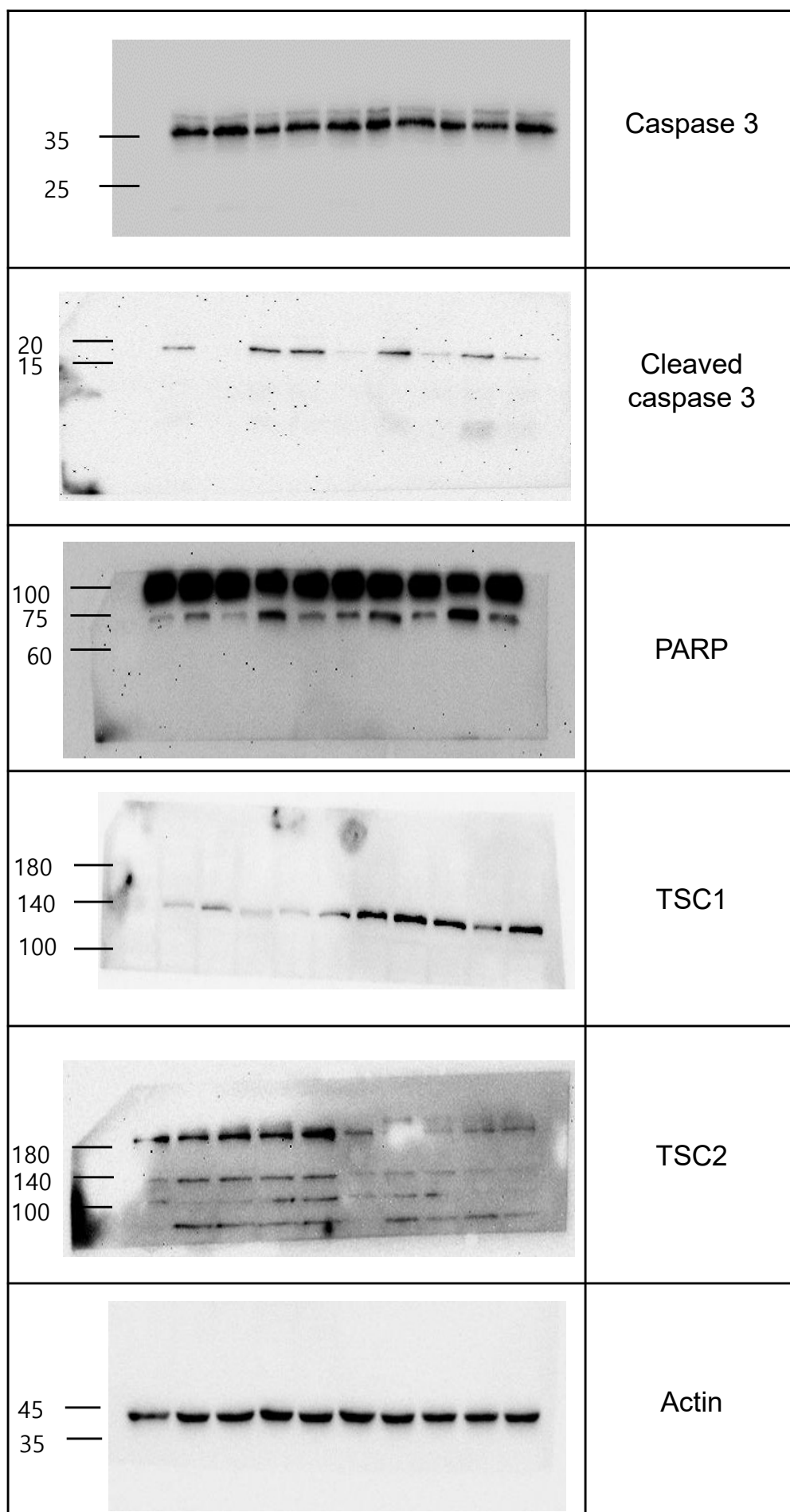


Figure 3A

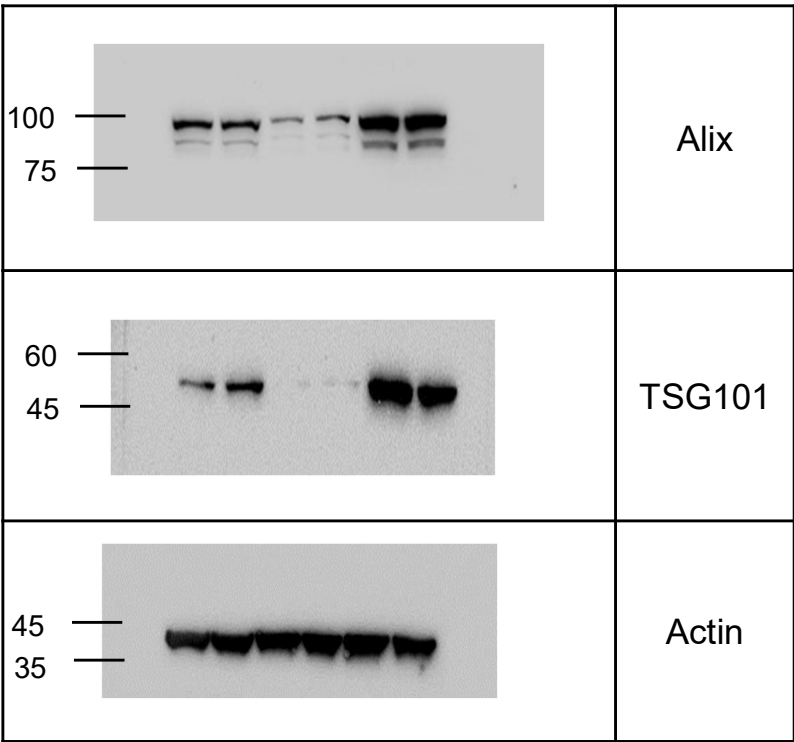


Supplemental Figure S6

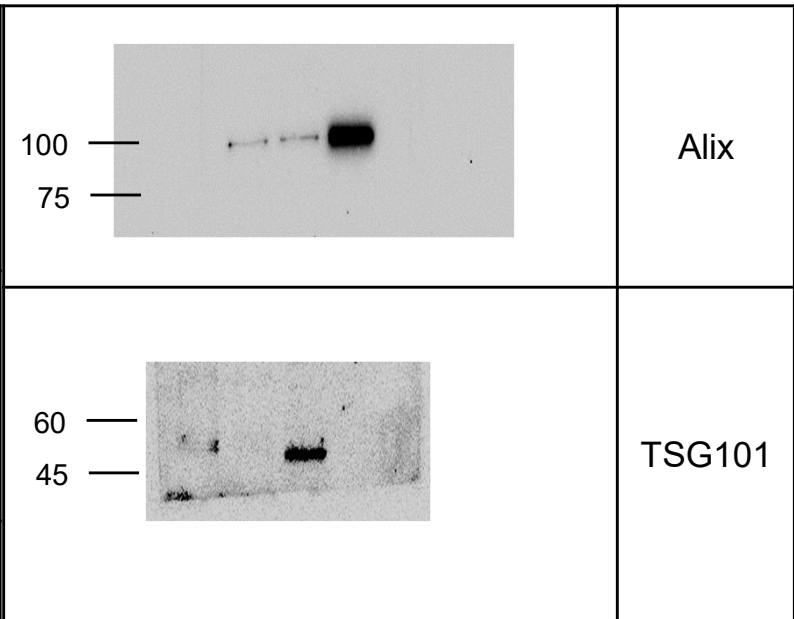
Figure 4F



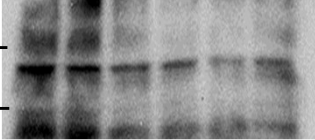
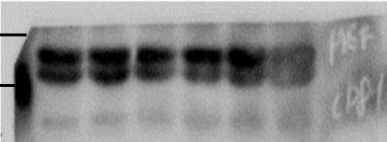
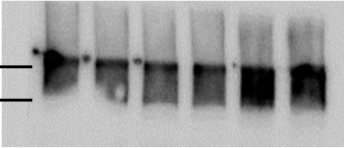
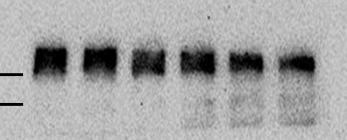
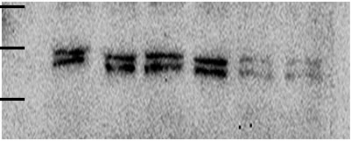
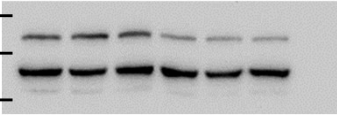
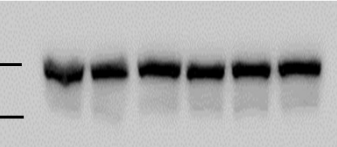
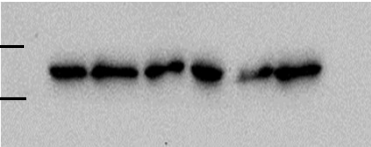
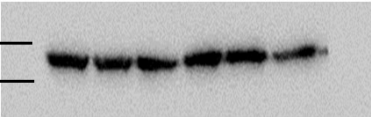
Supple. Figure S1A



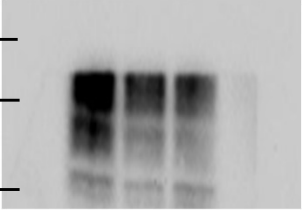
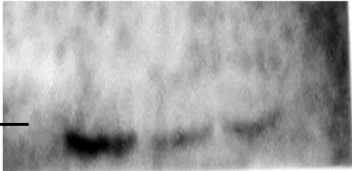
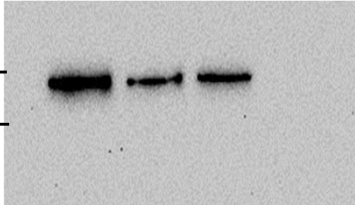
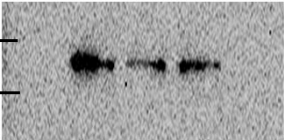
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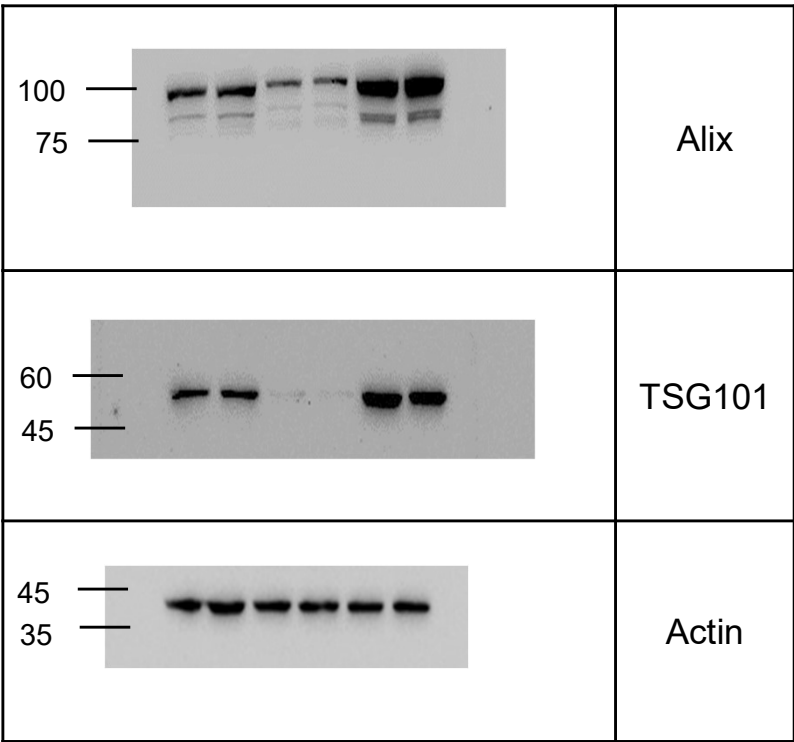
Supple. Figure S2A

	CD63
	CD81
	pACC
	ACC
	pS6K
	S6K
	Alix
	TSG101
	Actin

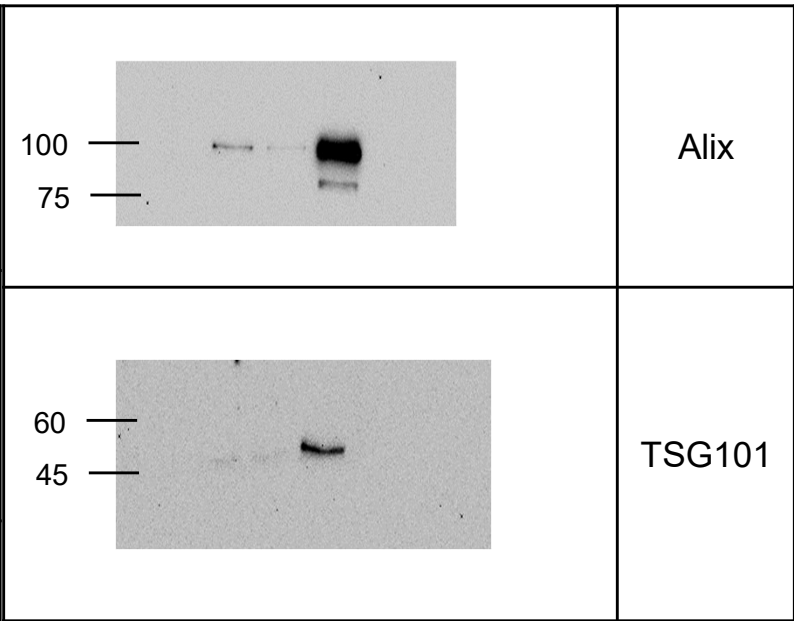
Supple. Figure S2B

	CD63
	CD81
	Alix
	TSG101

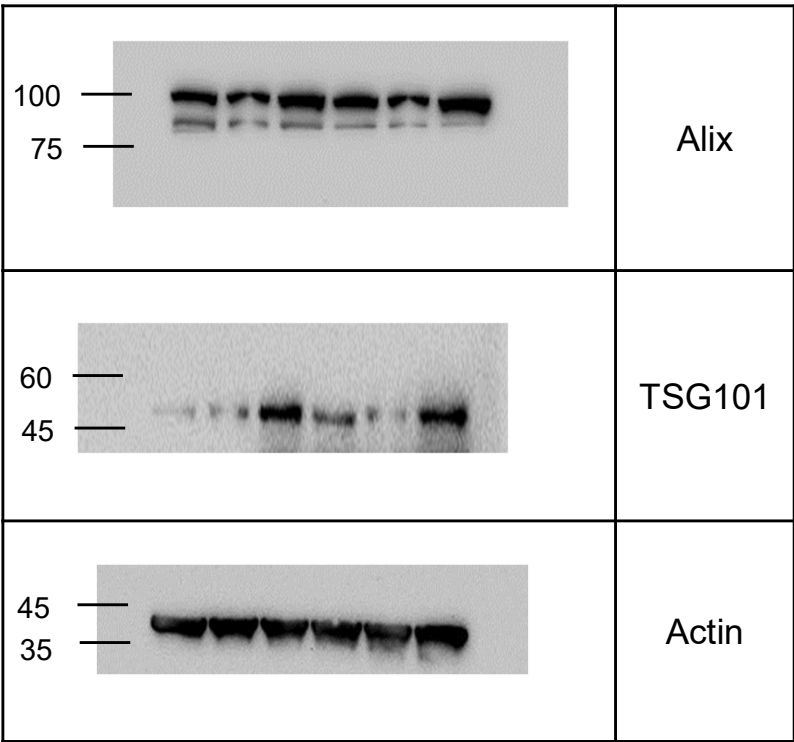
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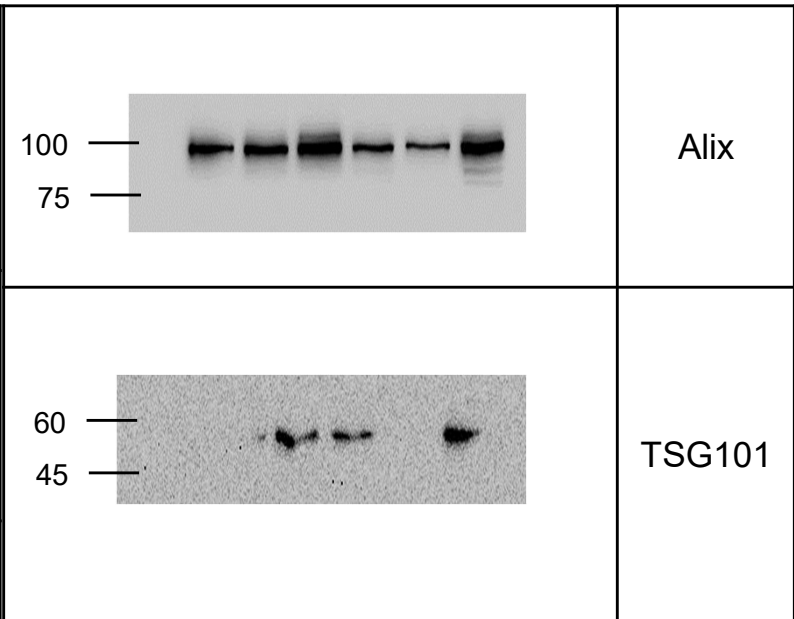
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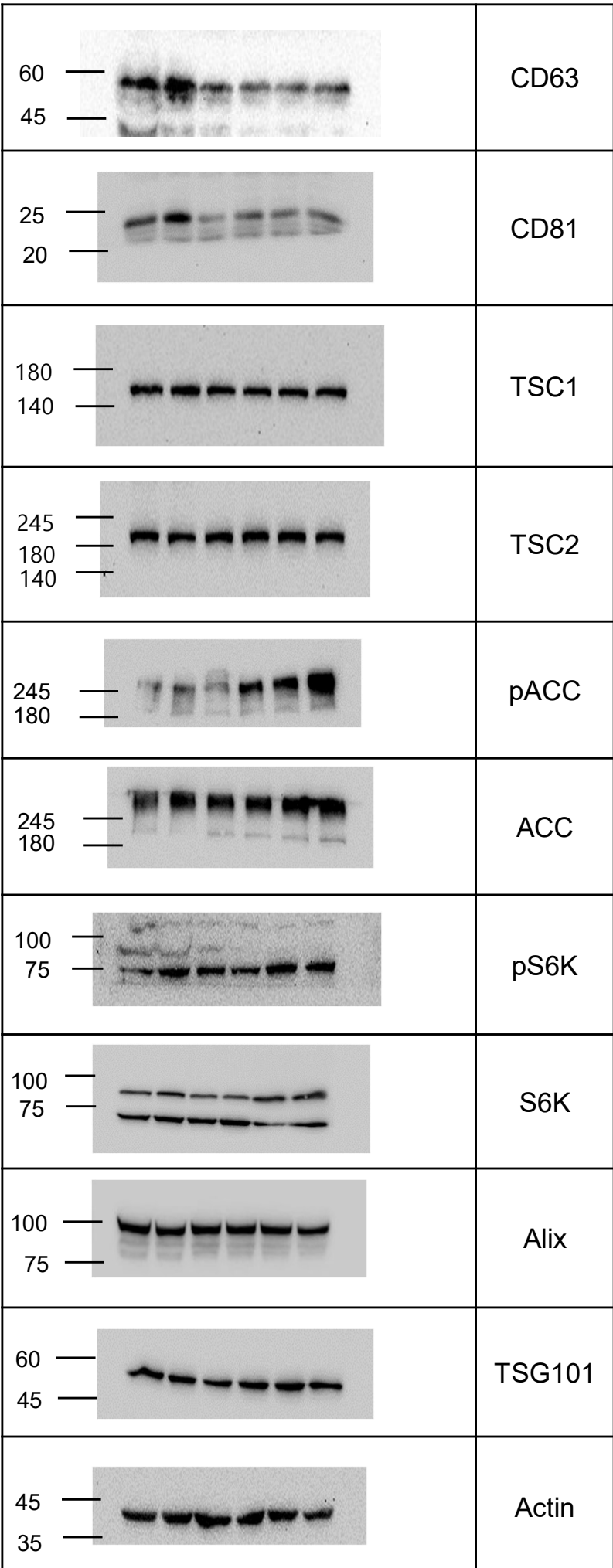
Supple. Figure S4A



Supple. Figure S4B



Supple. Figure S5A



Supple. Figure S5B

