

Supporting Information

Interaction of Calmodulin with the cSH2 Domain of the p85 Regulatory Subunit

Guanqiao Wang,[†] Mingzhen Zhang,[‡] Hyunbum Jang,[‡] Shaoyong Lu,[†] Shizhou Lin,[§] Guoqiang Chen,[†] Ruth Nussinov,^{‡,||,*} Jian Zhang,^{†,*} and Vadim Gaponenko^{⊥,*}

[†]Department of Pathophysiology, Key Laboratory of Cell Differentiation and Apoptosis of Ministry of Education, Shanghai Jiao-Tong University School of Medicine, Shanghai, 200025, China.

[‡]Cancer and Inflammation Program, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, National Cancer Institute at Frederick, Frederick, MD 21702, U.S.A.

[§]Obstetrics and Gynecology Hospital, Fudan University, Shanghai 200011, China

^{||}Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine, Tel Aviv University, Tel Aviv 69978, Israel

[⊥]Department of Biochemistry and Molecular Genetics, University of Illinois at Chicago, IL 60607, USA

Corresponding Authors:

*Vadim Gaponenko, University of Illinois at Chicago, E-mail: vadimg@uic.edu; *Jian Zhang, Shanghai Jiaotong University, E-mail: jian.zhang@sjtu.edu.cn; *Ruth Nussinov, National Cancer Institute at Frederick, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, E-mail: NussinoR@mail.nih.gov

Title Running Head: Calmodulin binding to cSH2-p85 α

nSH2 ³²⁵WYWGDISREEVNEKLRDTADG**TF**LVRDASTKMHGDYTLTLR**K**GN**N**KL**IKI**FHRDGKY**GF**
cSH2 ⁶¹⁴WNVGSSNRNKAENLLRGKRDG**TF**LVRES**SKQ**--G**CY**ACSVV**V**DGE**V**K**HCV**INKTATGY**GF**
nSH2 SDPLT**F**-**SSV**VEL**IN**H**YR**NE**SLA**QYNPKLDV**KLL**YPVSKY**QQ**⁴³⁵
cSH2 AEPYN**L**Y**SSL**KEL**LV**L**HY**QHT**SLV**QH**NDS**LN**V**TLAYPVYA**QQR**⁷²⁴

Figure S1. Protein sequence information obtained from the basic local alignment search tool (BLAST) algorithm in the National Center for Biotechnology Information (NCBI) webserver (<https://blast.ncbi.nlm.nih.gov/Blast.cgi>). Bold highlights the residues conserved in both nSH2 and cSH2 domains, box denotes the residues used for mutation, and light blue represents the residues containing the 1-5-10 CaM-binding motif.

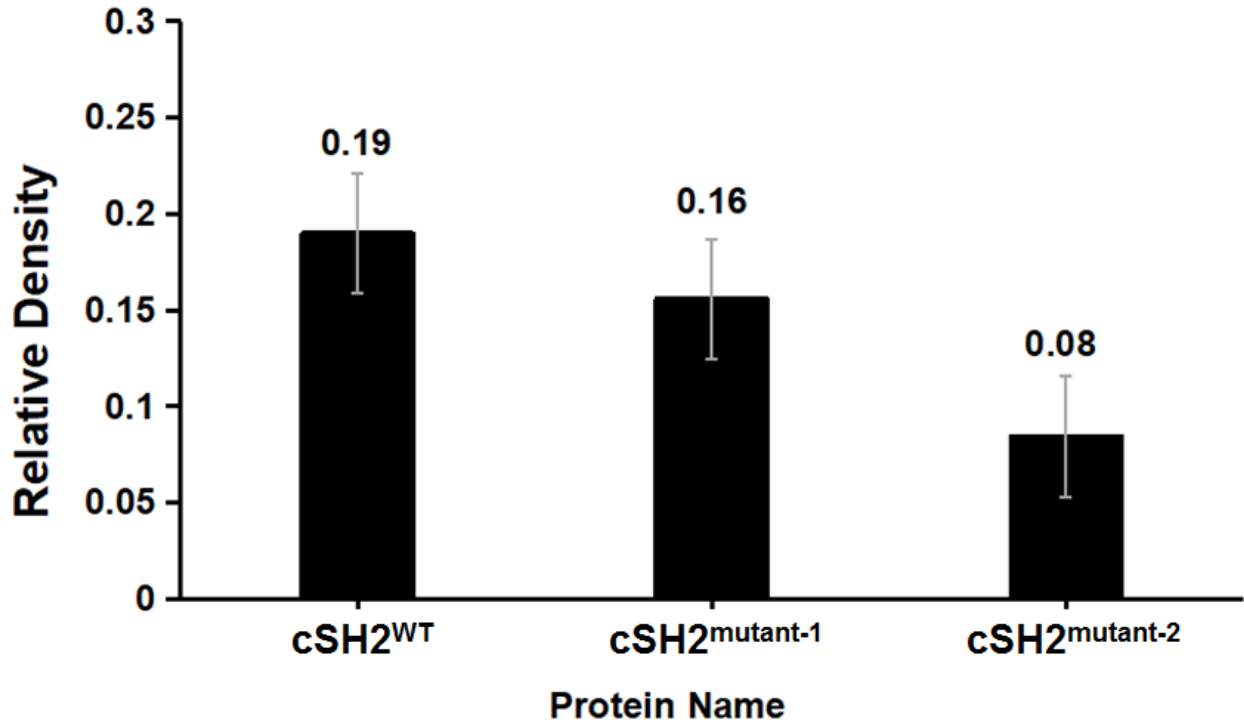


Figure S2. Relative quantitative analysis of the CaM–cSH2 EDC crosslinking experiment for the wild type (cSH2^{WT}) and two cSH2 mutants; cSH2^{mutant-1} (cSH2^{V663K/V667N}) and cSH2^{mutant-2} (cSH2^{V663K/V667N/L687F/L691V/L696N}).

Table S1. Identified residue pairs of intermolecular interactions by NOEs. In the residue names, hydrophobic, polar/glycine, positively charged, and negatively charged residues are colored black, green, blue, and red, respectively.

CaM residue	cSH2 residue
Ala147	Lys674, Thr675, Tyr657
Glu127	Asn673
Glu114	Lys653, Gln654
Met109	Gln654
Asp80	Leu687
Thr79	Tyr688
Gly40	Tyr685
Ile9	Glu614, Leu616