Supporting Information For:

Criterion for amino acid composition of defensins and antimicrobial peptides based on geometry of membrane destabilization

Nathan W. Schmidt,[†,‡] Abhijit Mishra,[‡,§] Ghee Hwee Lai,[†,‡] Matthew Davis,[§] Lori K. Sanders,[§] Dat Tran,[] Angie Garcia,[] Kenneth P. Tai,[] Paul B. McCray, Jr.,[#] André J. Ouellette,[] Michael E. Selsted,[] Gerard C. L. Wong,[,†,‡,§]*

[†]Department of Physics, University of Illinois, Urbana-Champaign, IL 61801

[‡]Department of Bioengineering, University of California, Los Angeles, CA 90095

[§]Department of Materials Science, University of Illinois, Urbana-Champaign, IL 61801

[]Department of Pathology & Laboratory Medicine, USC Norris Cancer Center, Keck School of Medicine of the University of Southern California, Los Angeles, CA 90089-9601

[#]Department of Pediatrics, Carver College of Medicine, University of Iowa, Iowa City, IA 52242

Email: gclwong.ucla@gmail.com

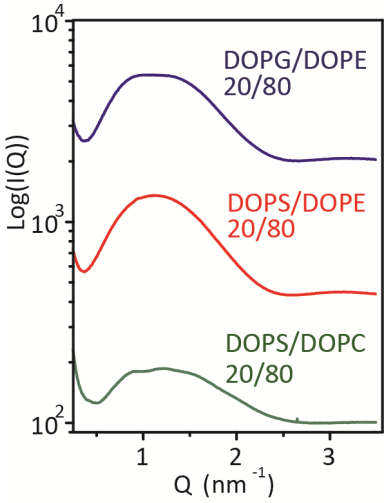

Figure S1: SAXS measurements on membranes used in this study show broad features consistent with the form factor from lipid bilayers indicating the presence of SUVs. Samples are in 100mM NaCl solution.

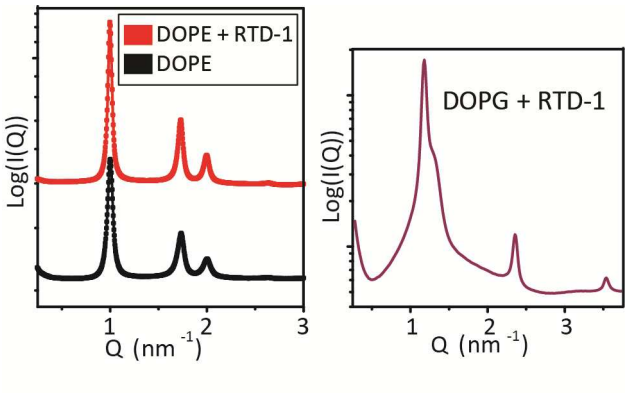

Figure S2: RTD-1 interacts differently with different lipid species. Virtually identical scattering profiles for DOPE only and DOPE+RTD-1 demonstrate RTD-1 weakly interacts with DOPE, and does not drastically reorganize DOPE lipids. RTD-1 strongly interacts with DOPG, and mediates adhesion between DOPG membranes into a L_α lamellar phase with d = 5.3nm. Replacement of DOPG with DOPS gives similar results. Since RTD-1 generates a Pn3m cubic phase only in composite DOPG:DOPE membranes this indicates both lipids play an essential role in curvature generation.

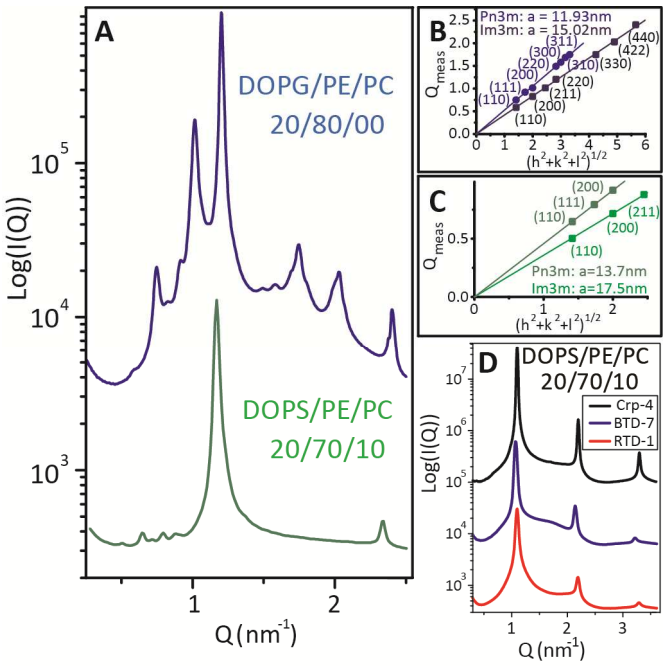

Figure S3: Generation of negative Gaussian curvature by protegrin-1 requires less membrane PE content. Protegrin-1 (PG-1) is an 18 amino acid amphipathic cathelicidin which resembles θ-defensins both sequentially and structurally. All six of its cationic residues are arginine, and its sheet structure is largely conferred from two intra-disulfide bonds from four cysteine residues. (A) PG-1 restructures vesicles with high amounts of PE, DOPG/DOPE = 20/80, and reduced amounts, DOPS/DOPE/DOPC = 20/70/10, into coexisting Pn3m and Im3m cubic phases. For the 80% PE condition (B), a_{Pn3m} = 11.91 nm and a_{Im3m} = 15.02 nm, with ratio a_{Im3m}/ a_{Pn3m} = 1.26, which is close to the Bonnet ratio of 1.279 for coexisting cubic phases, and (C) a_{Pn3m} = 13.7 nm and a_{Im3m} = 17.5 nm, for the 70% PE condition (C). The calculated lattice parameters, *a*, for the coexisting cubic phases show *a* increases with decreasing PE. Since *a* is inversely related with the amount of negative Gaussian curvature, *K*, this implies large *K* is easier to produce in PE rich membranes. (D) None of the defensins measured at DOPS/DOPE/DOPC = 20/70/10 induced a cubic phase. Crp-4, BTD-7, and RTD-1 generate lamellar phases, d = 5.7nm, 5.9nm, and 5.7nm, respectively, with zero Gaussian curvature in membranes with reduced PE. The lower threshold PE concentration necessary for PG-1 to generate cubic phases may explain its reduced specificity compared with defensins. P/L = 1/30, for PG-1, RTD-1, and BTD-7, and 1/45 for Crp-4.