

## Supplementary Information

# Size and Flexibility Define the Inhibition of the H3N2 Influenza Endonuclease Enzyme by Calix[n]arenes

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## Supplementary Materials:

**Figure S1:** Coomassie-stained gel SDS-PAGE of the PA protein purified from bacterial extract. Molecular weight (MW) ladder (kDa) is shown on the right.

**Figure S2:** Agarose gel electrophoresis shows the digestion activity of PA endonuclease protein. A concentration range of PA endonuclease protein has been mixed with  $\lambda$ -DNA phage. Molecular weight (MW) ladder (1kb) is shown on the right. Reaction products were run in a 0.6 % agarose gel stained with Ethidium Bromide.

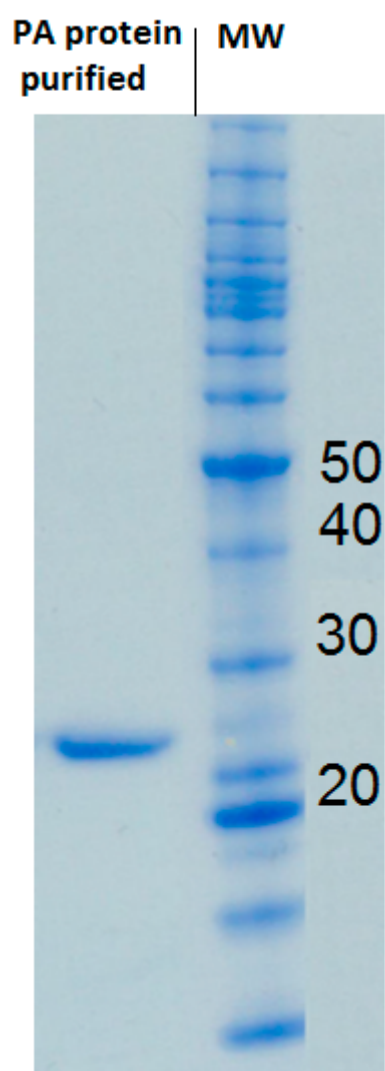
**Figure S3.** IC50 determination of H3N2 influenza PA endonuclease at 6.4  $\mu$ M of SC8a on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.

**Figure S4.** IC50 determination of H3N2 influenza PA endonuclease at 14  $\mu$ M of SC8b on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.

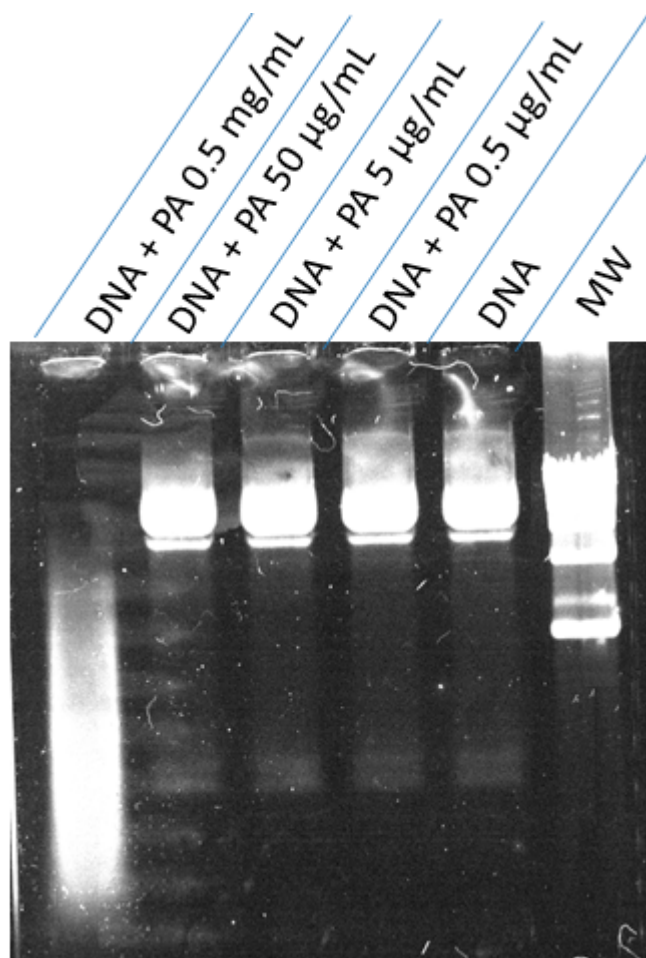
**Figure S5.** IC50 determination of H3N2 influenza PA endonuclease at 18.7  $\mu$ M of SC8c on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.

**Figure S6.** IC50 determination of H3N2 influenza PA endonuclease at 11.2  $\mu$ M of SC6a on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.

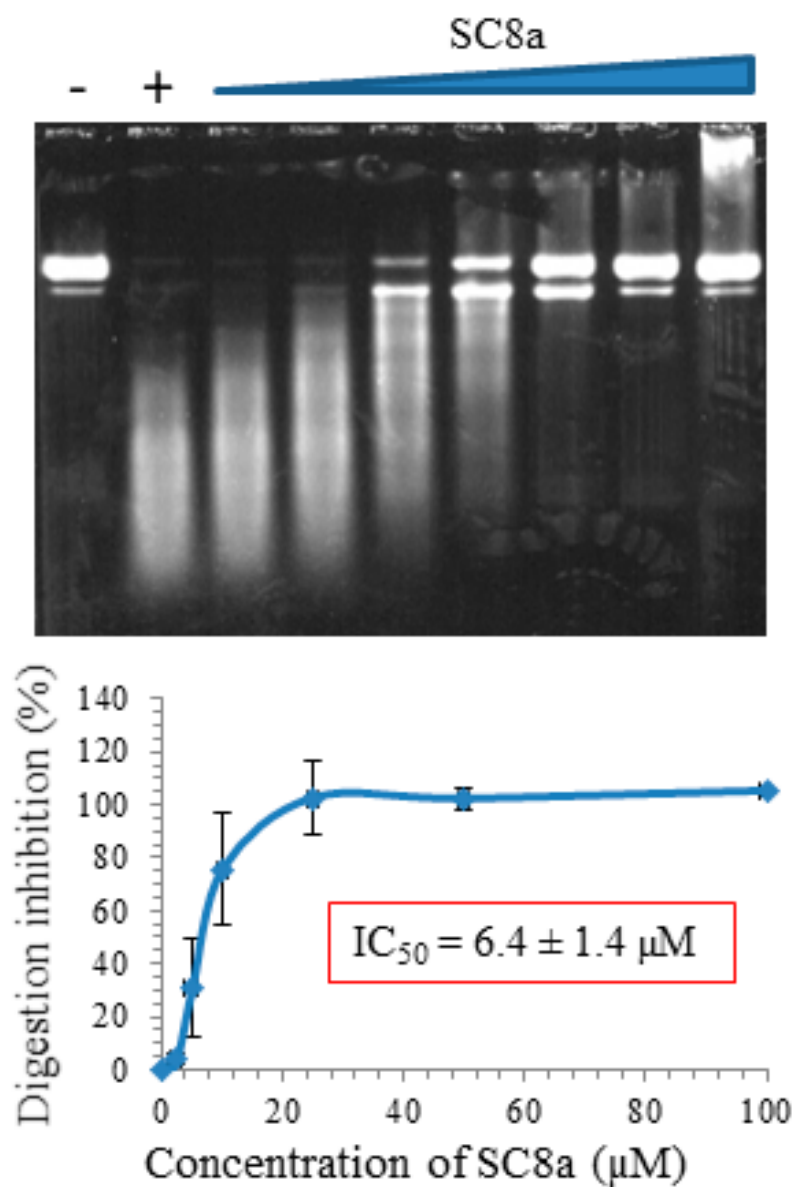
**Figure S7:** Histogram obtained from blind docking results. Estimated binding energy in Kcal/mol is shown on X-axis, while the number of poses or occurrences with binding energy values corresponding to a given interval is shown on Y axis.



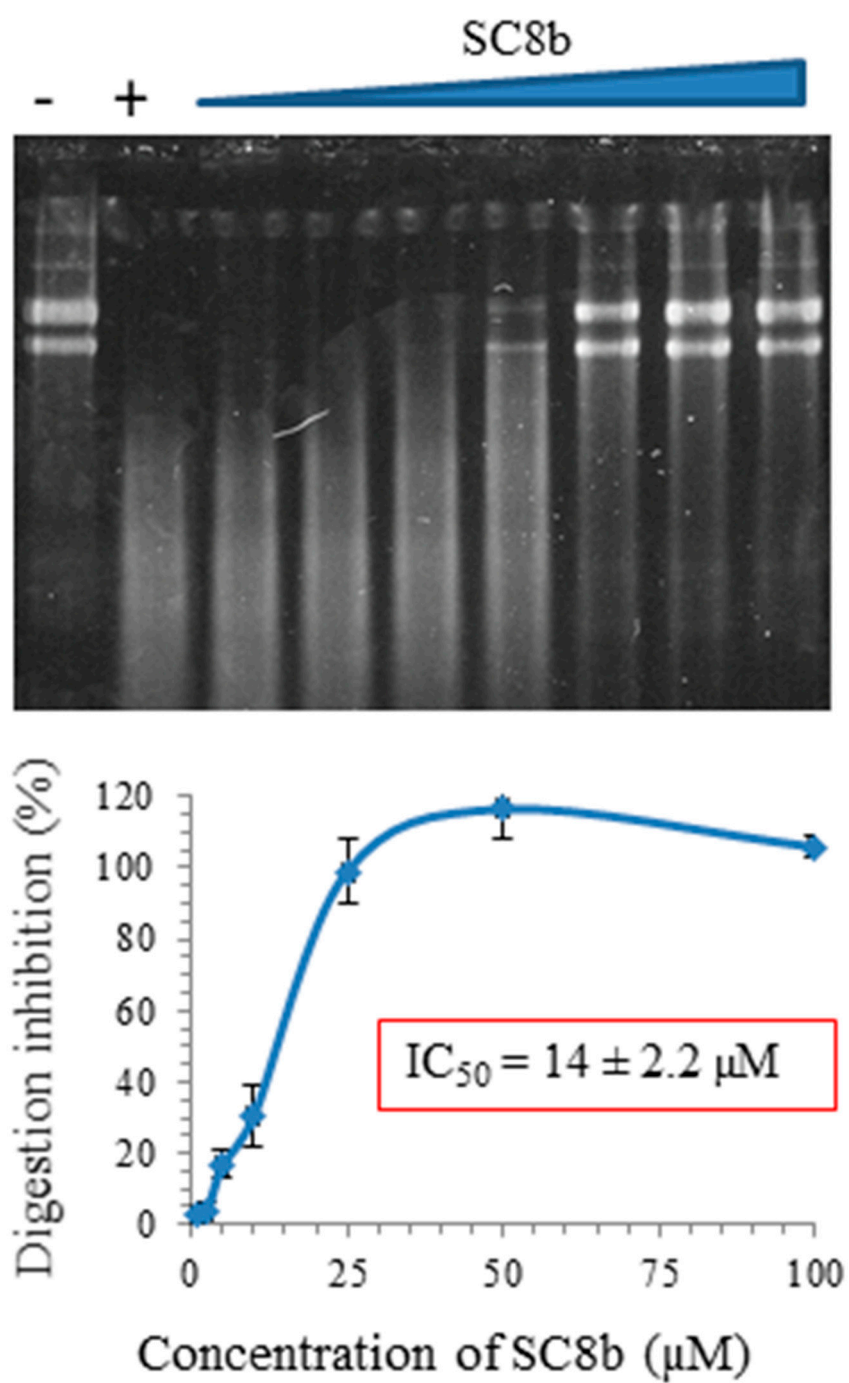
**Figure S1.** Coomassie-stained gel SDS-PAGE of the PA protein purified from bacterial extract. Molecular weight (MW) ladder (kDa) is shown on the right.



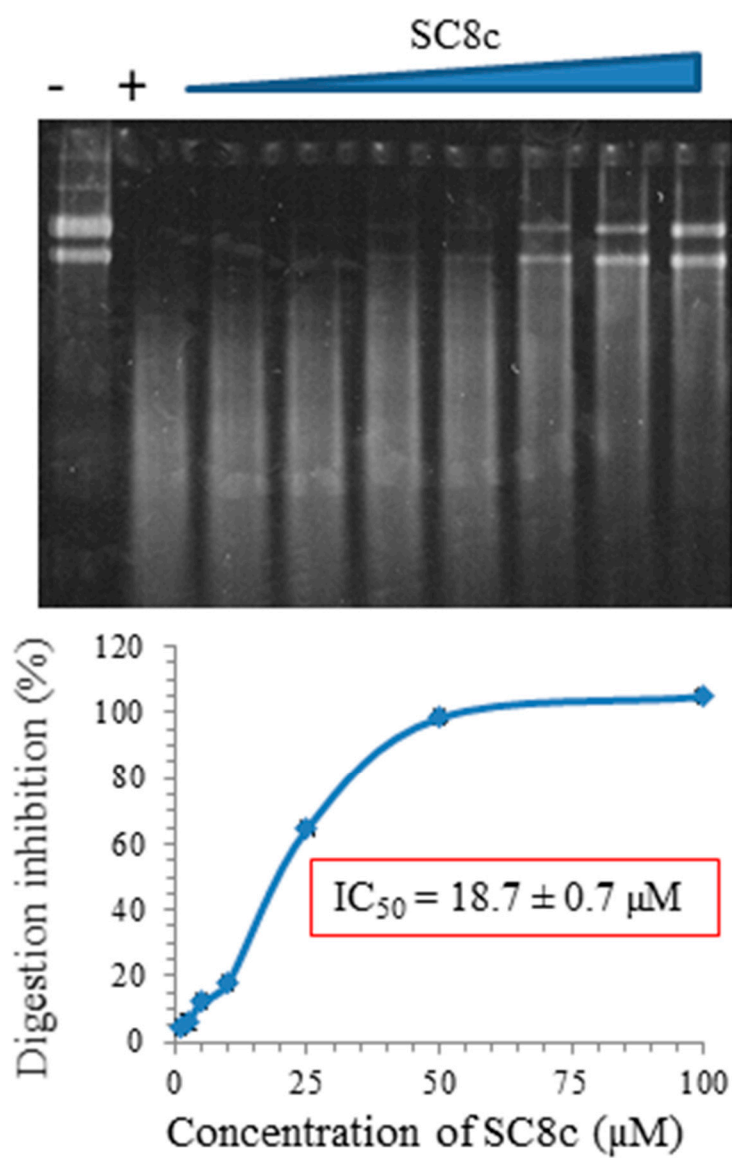
**Figure S2.** Agarose gel electrophoresis shows the digestion activity of PA endonuclease protein. A concentration range of PA endonuclease protein has been mixed with  $\lambda$ -DNA phage. Molecular weight (MW) ladder (1kb) is shown on the right. Reaction products were run in a 0.6 % agarose gel stained with Ethidium Bromide.



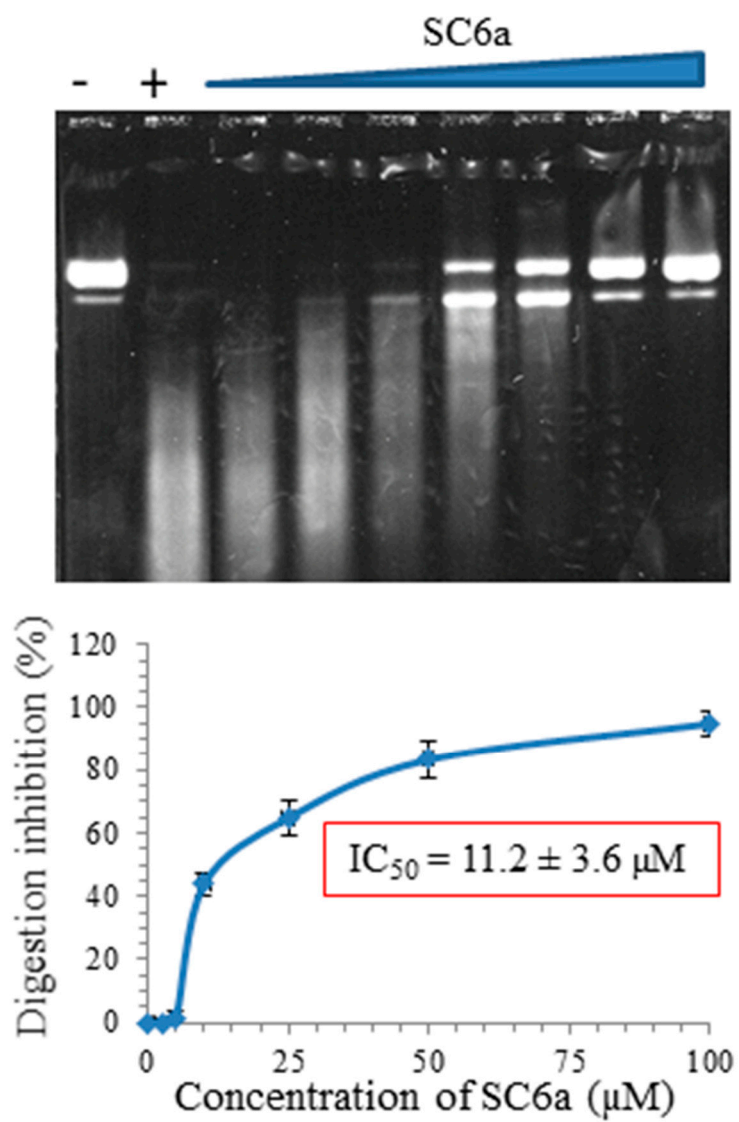
**Figure S3.**  $\text{IC}_{50}$  determination of H3N2 influenza PA endonuclease at  $6.4 \mu\text{M}$  of SC8a on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.



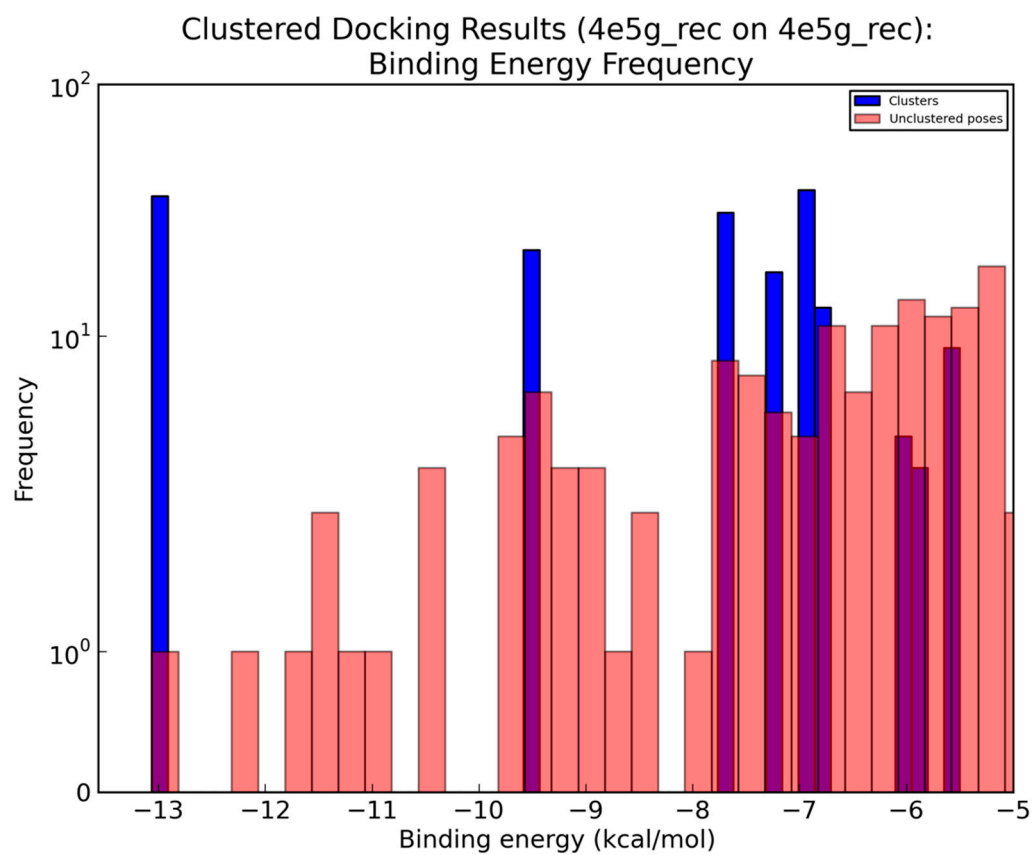
**Figure S4.** IC<sub>50</sub> determination of H3N2 influenza PA endonuclease at 14 μM of SC8b on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.



**Figure S5.** IC<sub>50</sub> determination of H3N2 influenza PA endonuclease at 18.7 μM of SC8c on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.



**Figure S6.** IC<sub>50</sub> determination of H3N2 influenza PA endonuclease at 11.2 µM of SC6a on PA endonuclease. '+' means DNA and '-' corresponds to DNA and PA endonuclease.



**Figure S7.** Histogram obtained from blind docking results. Estimated binding energy in Kcal/mol is shown on X-axis, while the number of poses or occurrences with binding energy values corresponding to a given interval is shown on Y axis.



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