Supporting Information

Mechanisms of Fumonisin B1 Toxicity: A Computational Perspective beyond the Ceramide Synthases Inhibition

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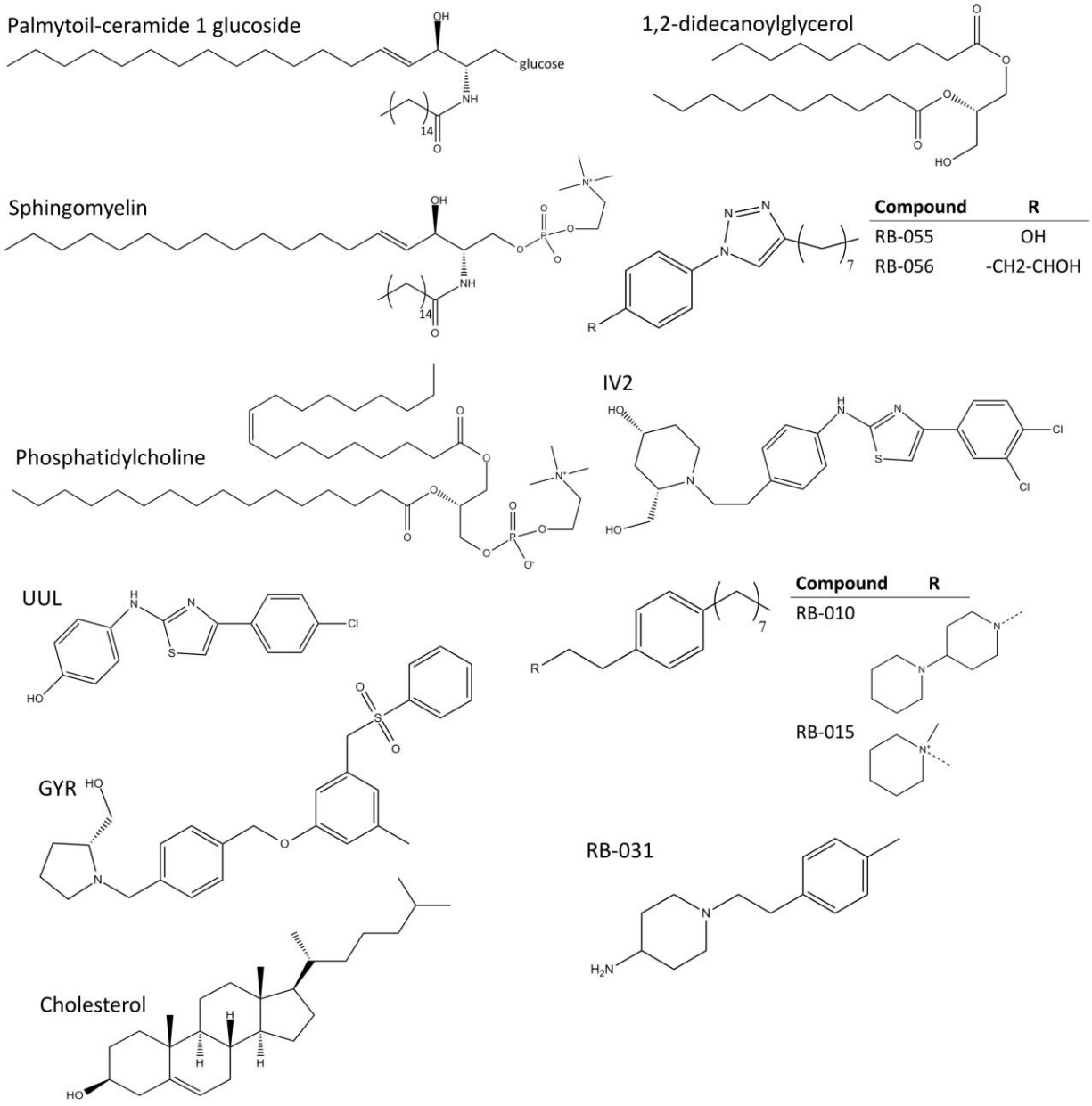

Figure S1. Chemical structures of compounds belonging to reference sets

Assessment of procedural reliability

The procedure proved to be reliable in calculating the interaction of reference compounds with the CERT START domain and SPK1 as: i) reference compounds were significantly categorized in qualitative terms according to the experimental activity reported in the literature (Figure S2); ii) it succeeded in calculating the binding architecture of reference compounds (Figure S3).

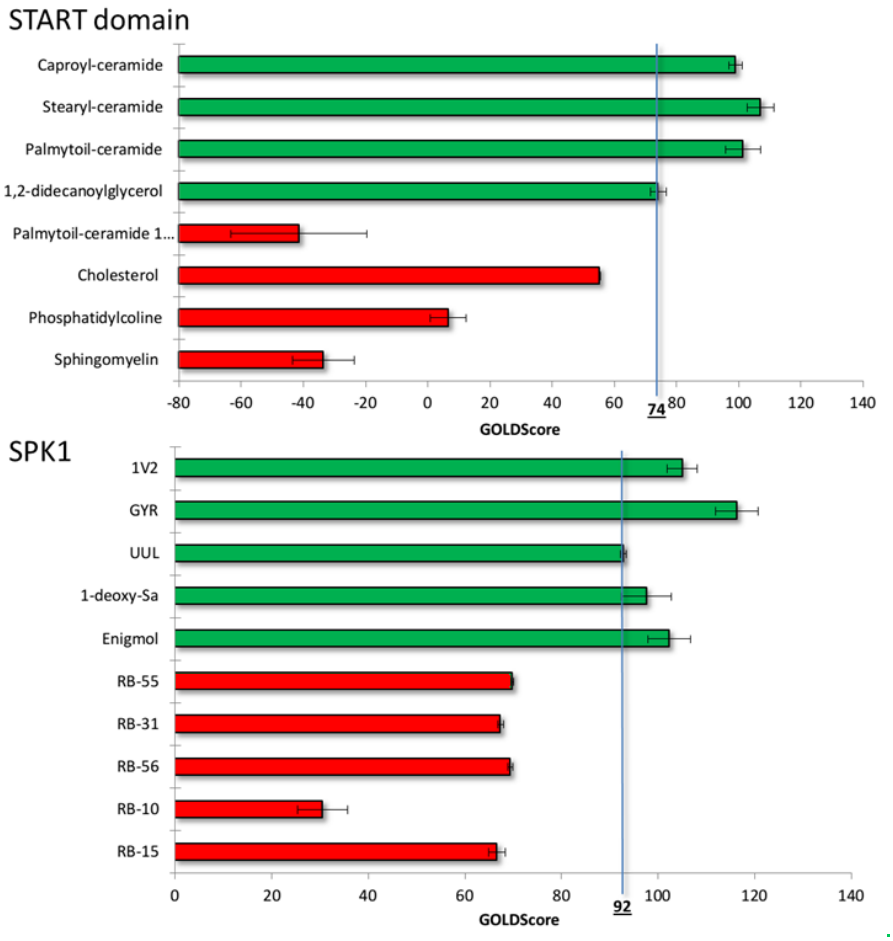

Figure S2. Computed scores of reference compounds. START ligands and SPK1 inhibitors are indicated by green bars, while compounds unable to bind START or inhibit SPK1 are indicated in red bars. All the START ligands and SPK1 inhibitors recorded scores significantly different from those of compounds unable to bind START or inhibit SPK1 ($p < 0.05$, according to Fisher'LSD *post hoc* test; $\alpha = 0.05$). The lowest score recorded among the known ligands and inhibitors (i.e. 74 and 92 units for START and SPK1, respectively) was set as threshold value to infer the capability of fumonisins and derivatives to positively interact with the models.

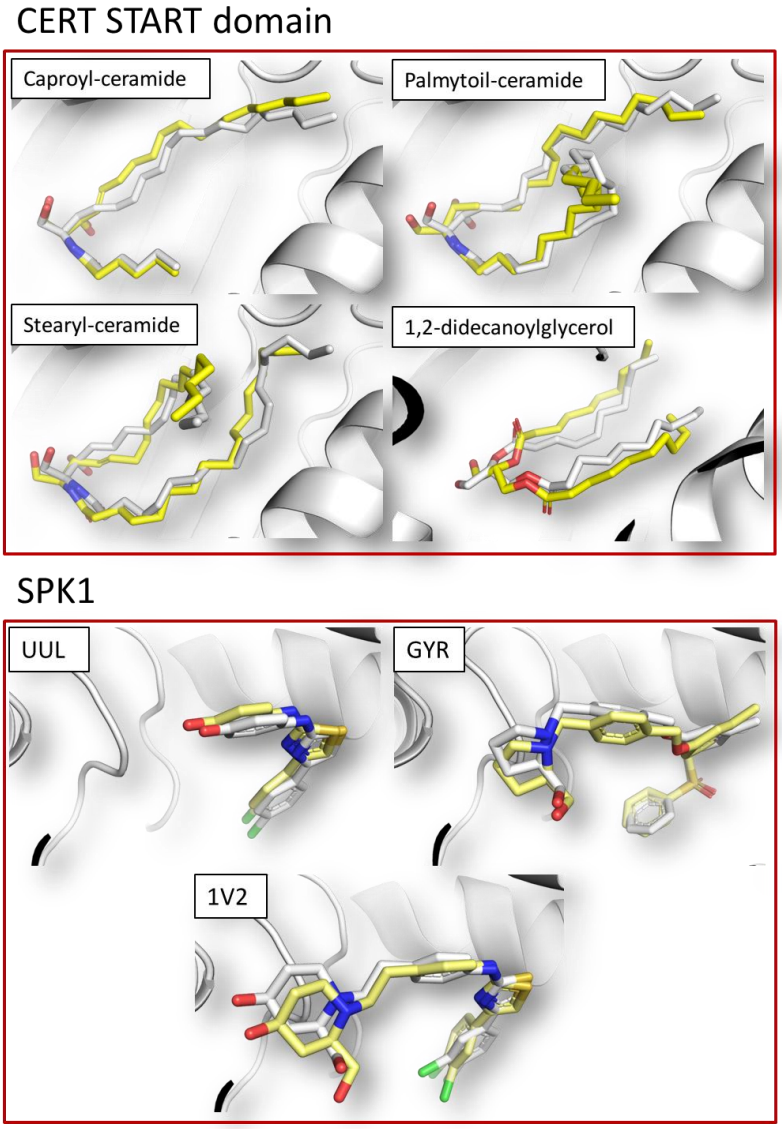

Figure S3. Comparison between crystallographic architectures of binding (white) and calculated poses (yellow) of reference compounds within CERT START domain [1] and SPK1 [2-4].

Statistical analysis

Each run was performed in triplicate and data are expressed as the mean ± standard deviation (SD). Data were statistically compared by one-way ANOVA ($\alpha = 0.05$), using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY).

References

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(3) Wang, Z., Min, X., Xiao, S. H., Johnstone, S., Romanow, W., Meininger, D., Xu, H., Liu, J., Dai, J., An, S., Thibault, S., and Walker, N. (2013) Molecular basis of sphingosine kinase 1 substrate recognition and catalysis. *Structure 21*, 798-809.

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