

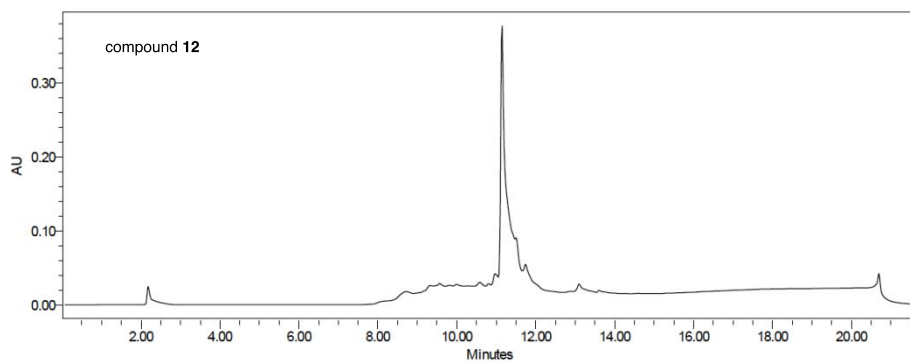
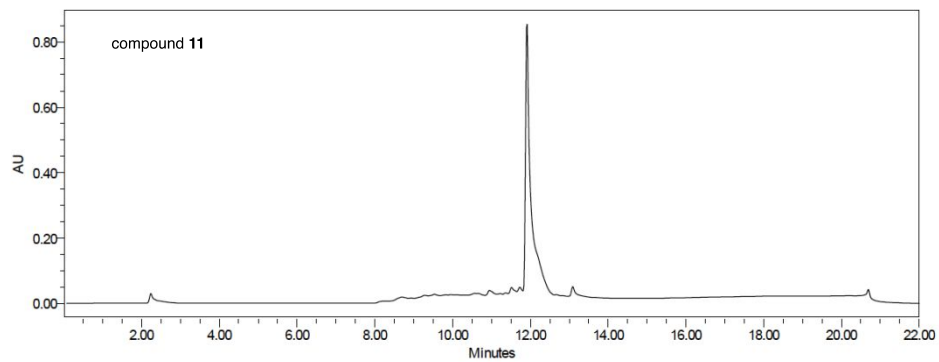
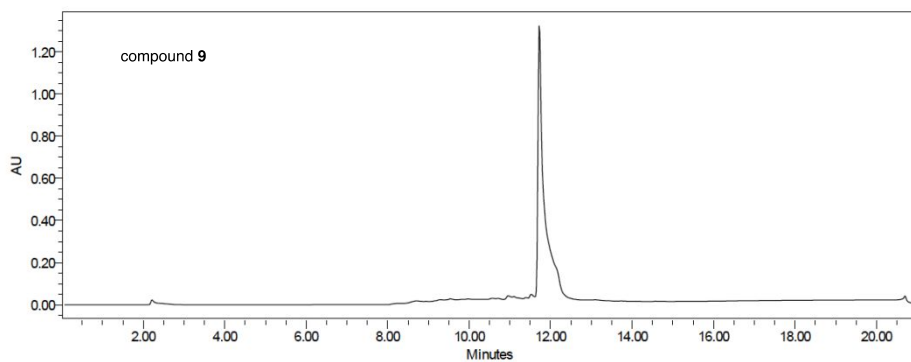
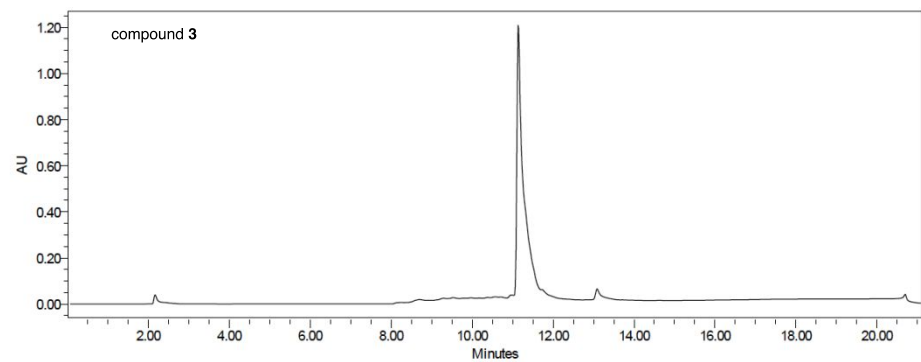
## Supporting Information

### **Discovery of a Synergistic Inhibitor of cAMP-Response Element Binding Protein (CREB)-mediated Gene Transcription with 666-15**

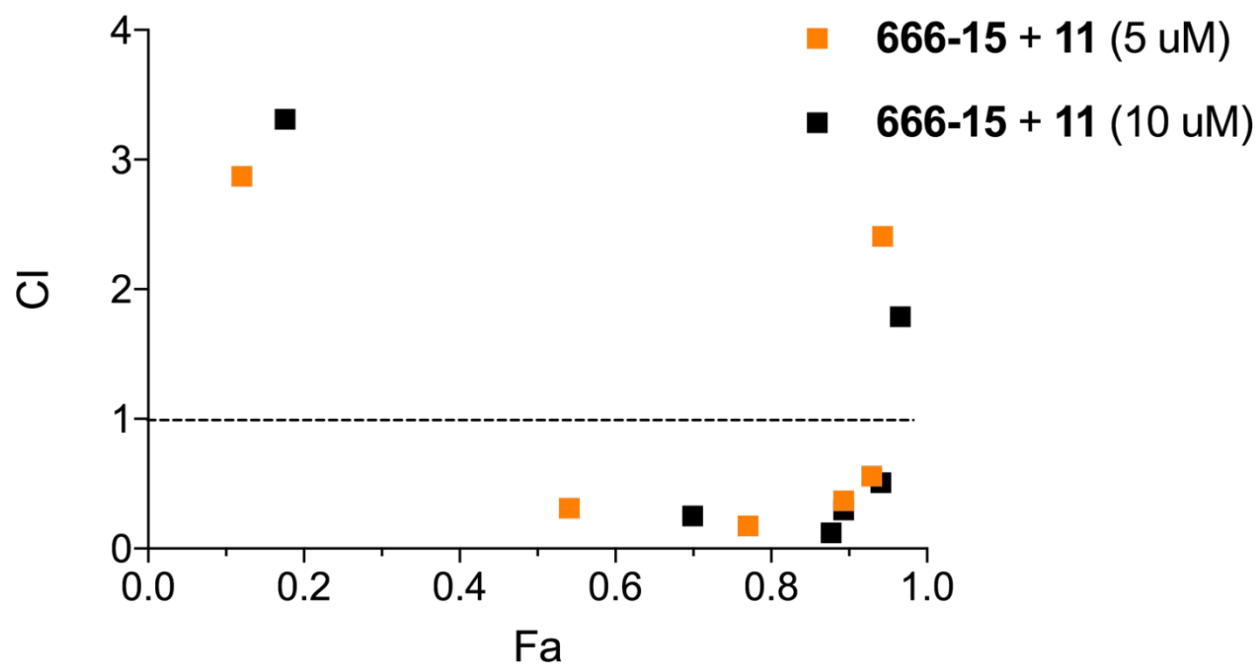
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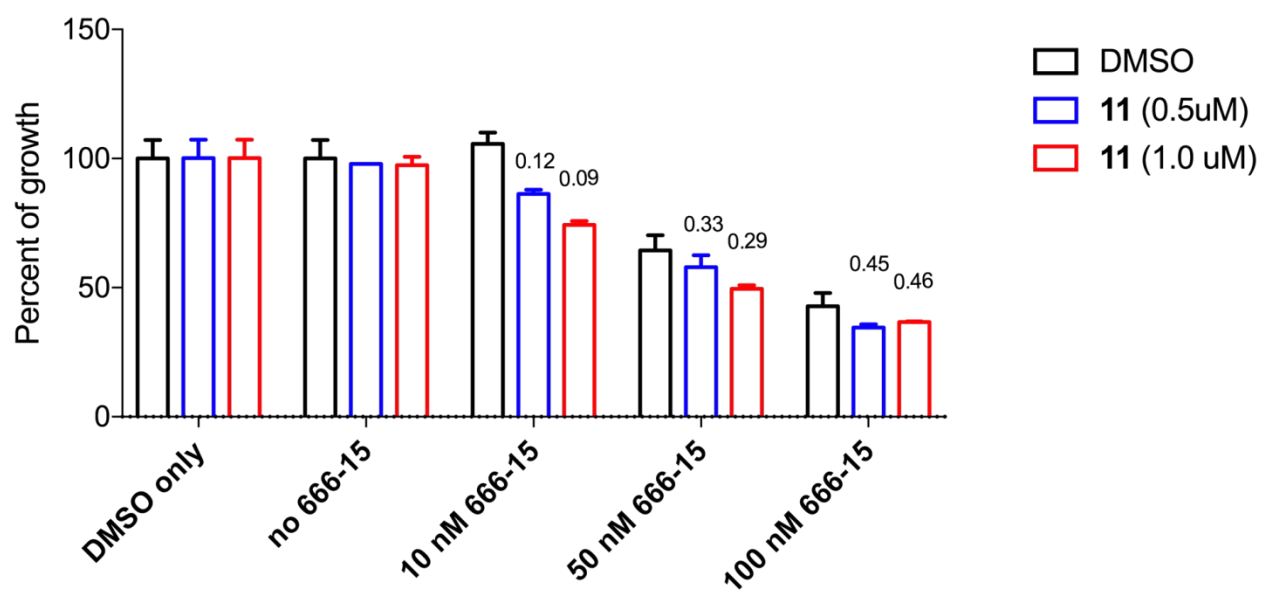
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**Figure S1.** HPLC traces of different compounds. The analyses were performed on reverse phase HPLC.



**Figure S2.** The combination indexes (CI) of **666-15** and compound **11** in inhibiting CREB-mediated gene transcription. The CI values were calculated using Chou-Talalay method from the data in Figure 3 in the main paper. *Fa* represents affected fraction.



**Figure S3.** Synergistic anti-proliferative effect of **666-15** and compound **11** in MDA-MB-231 cells. The cells were incubated with the indicated concentrations of **666-15** along with or without **11** (0.5 or 1.0  $\mu$ M) for 72 h. Then the viable cells were quantified by the MTT reagent. The numbers above each bar indicated the CI values for each combination. The data are presented as mean + SEM. The SEM was from one representative experiment performed in duplicates.

**Table S1.** The combination indexes (CI) of **666-15** and compounds **11** in inhibiting CREB-mediated gene transcription. The CI values were calculated using Chou-Talalay method.

Compounds	<b>666-15</b> ( $\mu\text{M}$ )					
	0.01	0.05	0.1	0.5	1.0	5.0
<b>11</b> (5 $\mu\text{M}$ )	2.87	0.31	0.17	0.37	0.56	2.41
<b>11</b> (10 $\mu\text{M}$ )	3.31	0.25	0.12	0.3	0.51	1.79