Supplementary **Materials**

Small Molecules as Toll-like Receptor 4 Modulators. Drug and *in-house* Computational Repurposing

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Compound 152

Compound 568

Compound 383

Compound 368

Compound 492

Compound 42

Compound 138

Compound 575

Compound 548

Compound 46

Compound 40

Compound 35

Compound 187
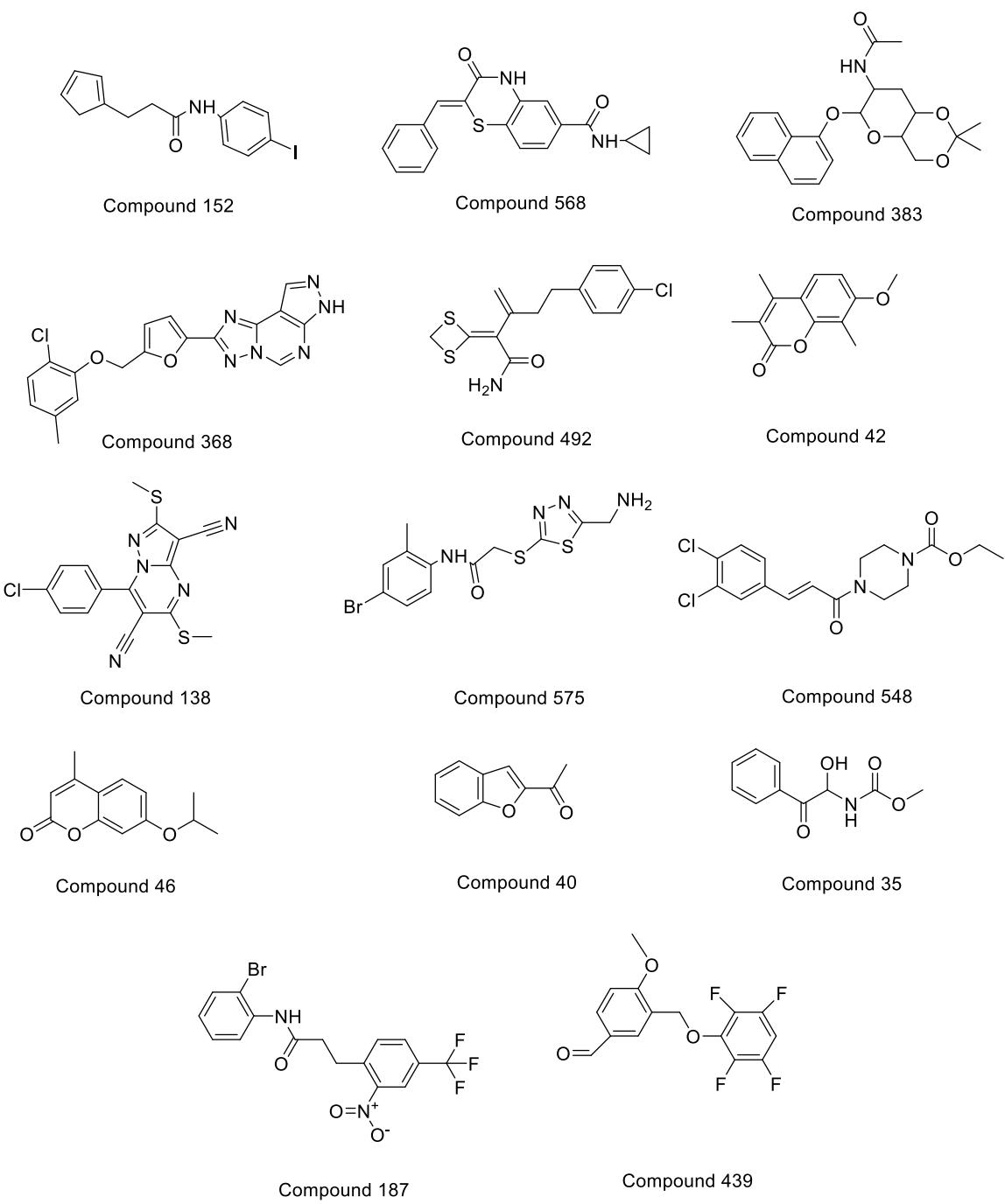
Compound 439

**Figure S1.** Top scoring compounds obtained by SBVS and LBVS on the Log P 1000 database.
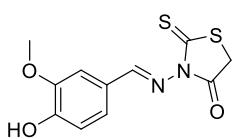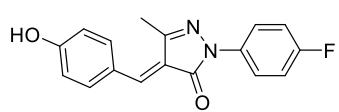
Compound 481   Compound 19907   Compound 20513
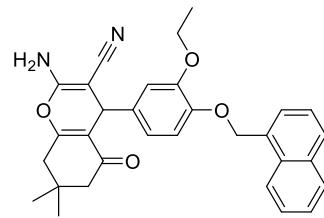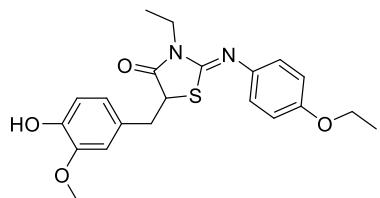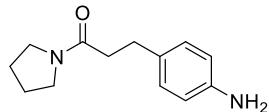
Compound 20700   Compound 21315   Compound 120
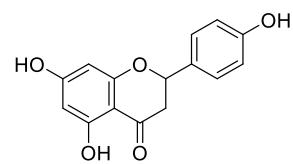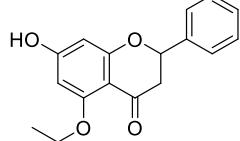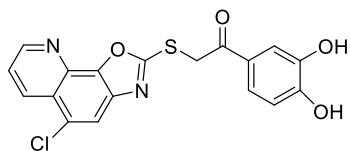
Compound 28   Compound 22298   Compound 23010
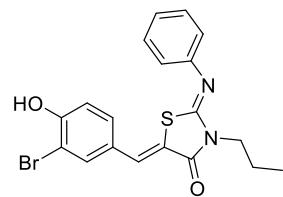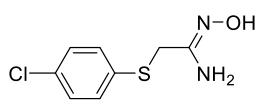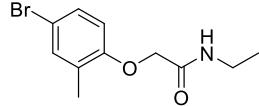
Compound 3203   Compound 23599   Compound 1171
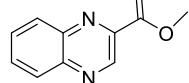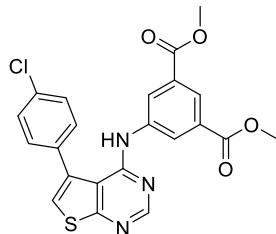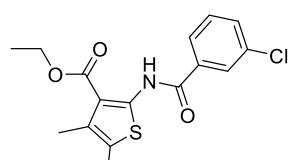
Compound 10959   Compound 14650

**Figure S2**. Top scoring compounds obtained by SBVS and LBVS on the SPECS database.
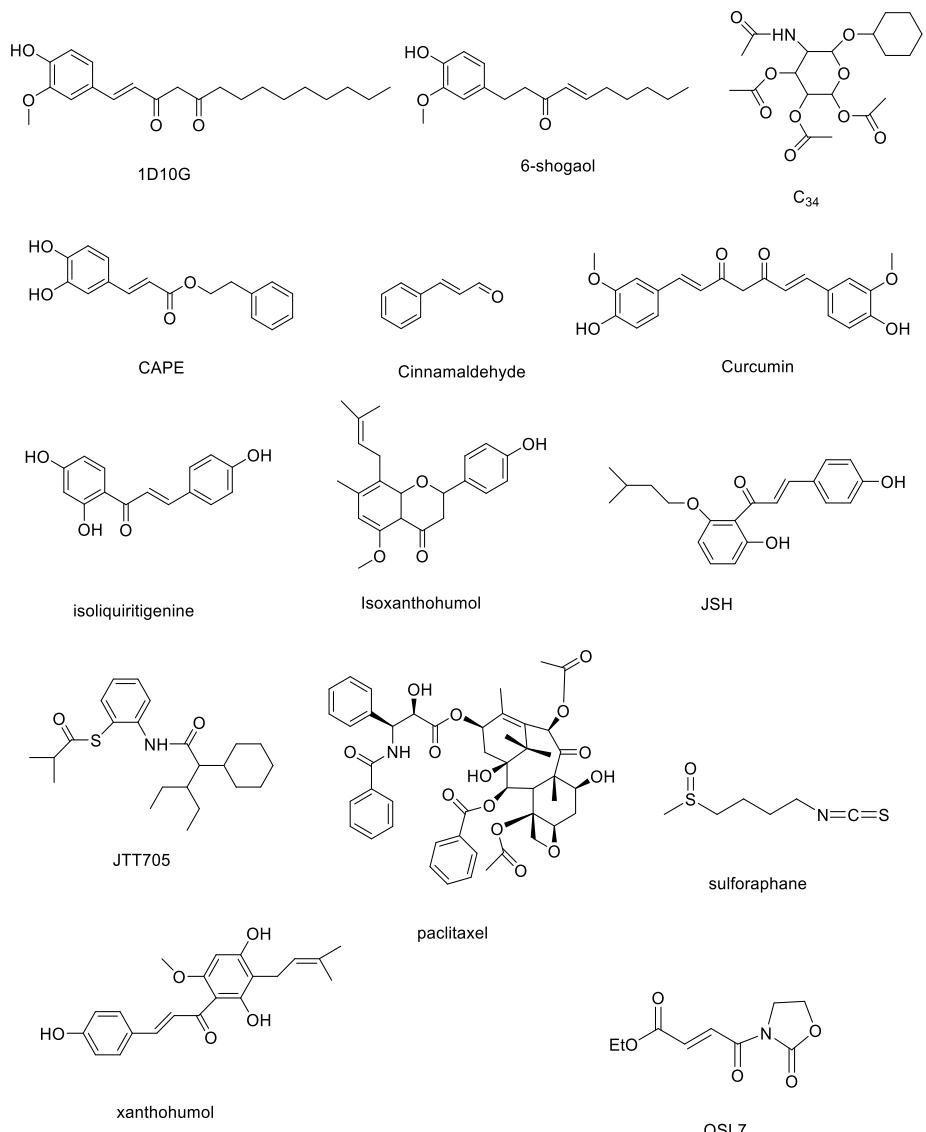
**Figure S3**. Known antagonists of the MD-2 reported in the literature.
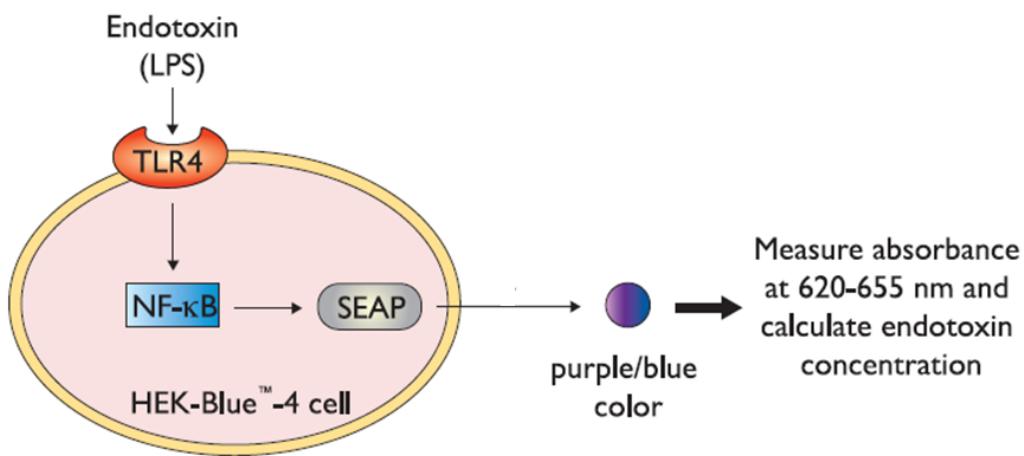
**Figure S4.** Cell-based colorimetric assay for the detection of biological active endotoxin (figure extracted from https://www.invivogen.com/hek-blue-lps-detection-kit).
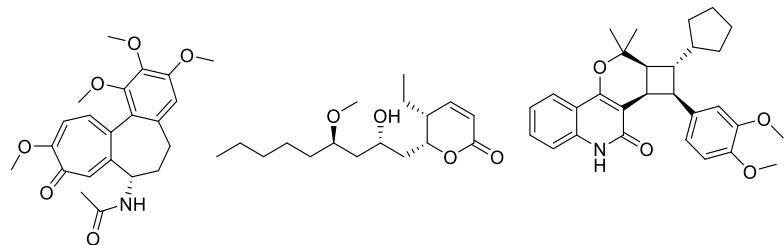
Figure S5. Colchicine (left), pironetin (center) and euodenine A (right) chemical structures.

| Compound	Database	S-score	Structure
ID-5382	Log P 1000	1.231	
AG-690/11203225	SPECS	1.114	
AF-399/15128553	SPECS	1.074	
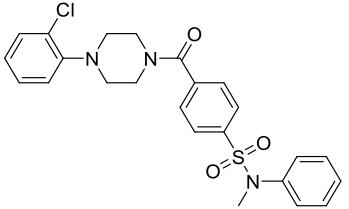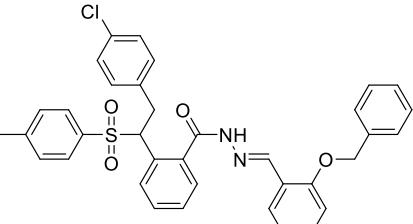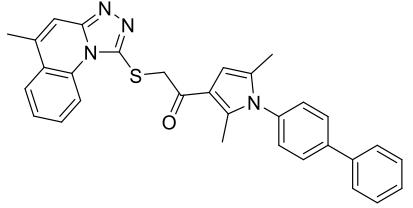
Table S1. 2D description and the respective scores from **ID-5382**, **AG-690/11203225** and **AF-399/15128553**.

Compound number	ZINC ID	Usual/Commercial name	2D structure
146	3830716	Diphenoxylate	
157	1493878	Sorafenib	
177	15919406	Ono-Rs 411	
179	52509366	Zelboraf	
208	53073961	Antrafenine	
212	19685790	Lercanidipine	

Table S2. 2D Chemical structure of predicted TLR4 modulators identified by computational drug repurposing, and kept for future structure similarity search.

Number	Compound	Structure
1	PM1097_p_R/1097	
2	PM1811	
3	PM1779	
4	PM567S ó R	
5	PM1090	
6	PM810	
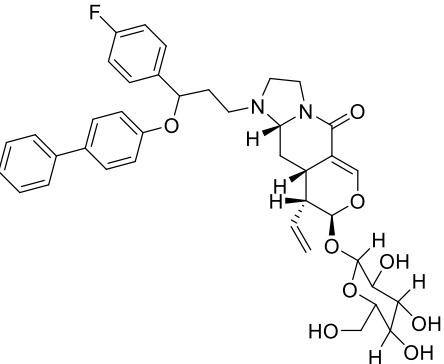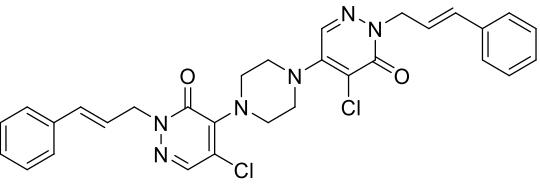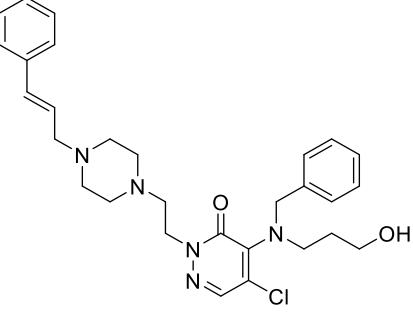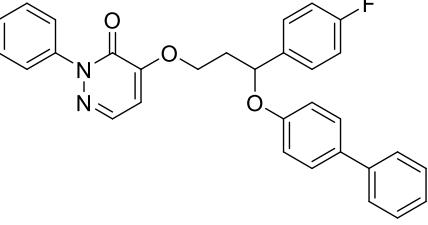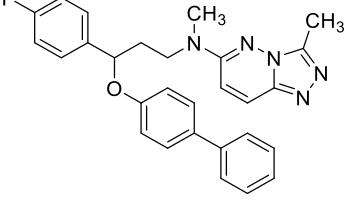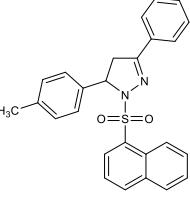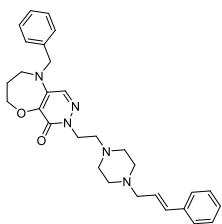
7	PM1758	
8	PM1200	
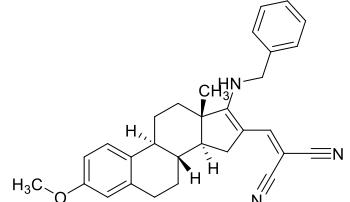
Table S3. 2D Chemical structure from PM databases obtained from SBVS.

| Number	Compound	Structure
1	MS_35/35p	
2	MS_29	
3	MS_40	
4	MS_34	
5	MS_31	
6	MS_22	
7	MS_45	
8	MS_21	
9	MS_32	
10	MS_26	
11	MS_14	
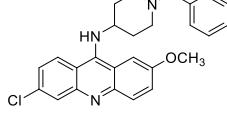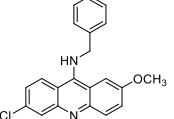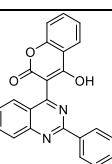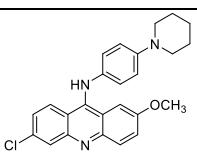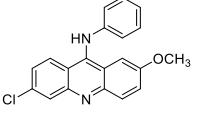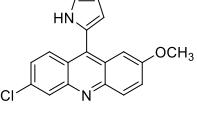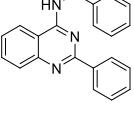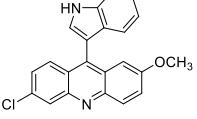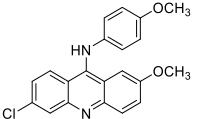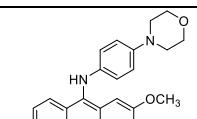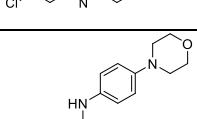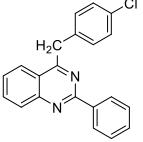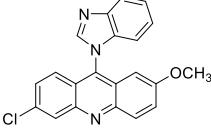
12	MS_49	
13	MS_37	
14	MS_46	
15	MS_20	
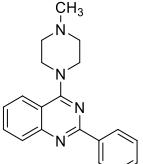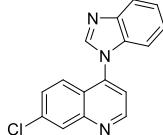
Table S4. 2D Chemical structure from JCM databases obtained from SBVS. Quinoline family: MS-**14**, MS-**20**. Quinazoline family: MS-**40**, MS-**45**, MS-**49.** Acridine family: MS-**32,** MS-**21,** MS-**35**, MS-**29,** MS-**22**, MS-**26**, MS-**31**, MS-**34**, MS-**37**

Name	Structure	Name	Structure
JRP07		**AM15**	
JRP10		**AM18**	
JRP18		**AM19**	
AM20 momo		**AM54**	
AM21		**AM57**	
AM20		**AM58**	
		AM59	
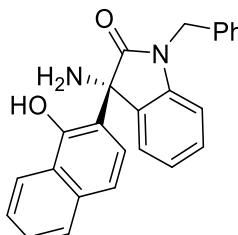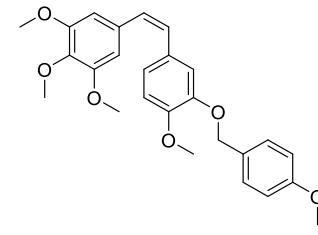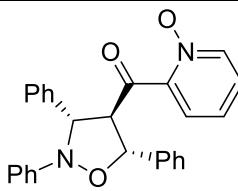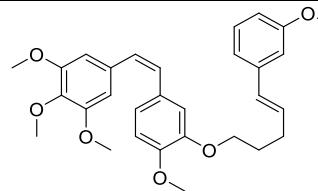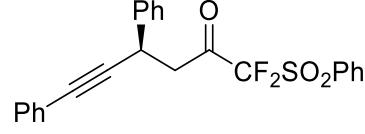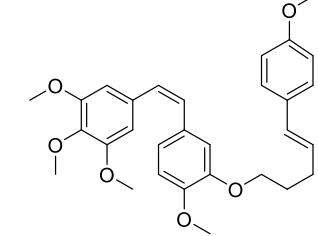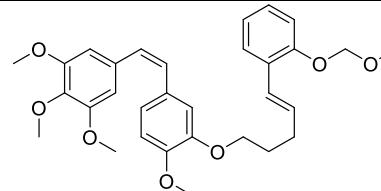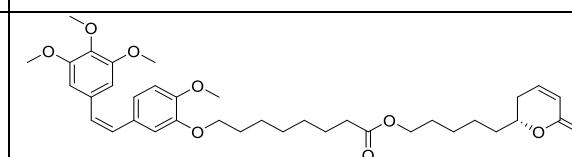
AM22		**AM62**	
AM23		**AM65**	
AM24		**AM66**	
AM25		**AM72**	
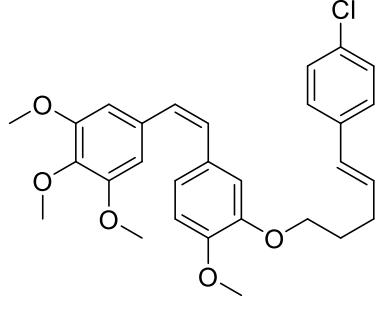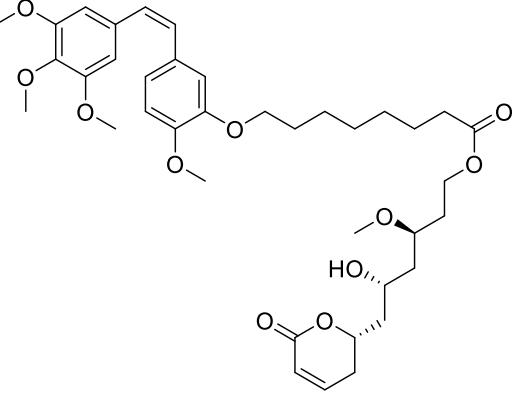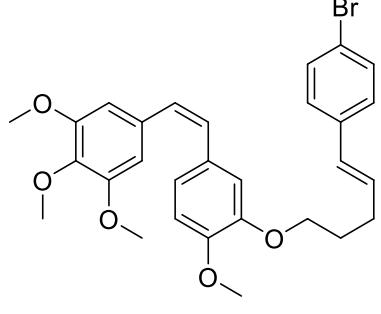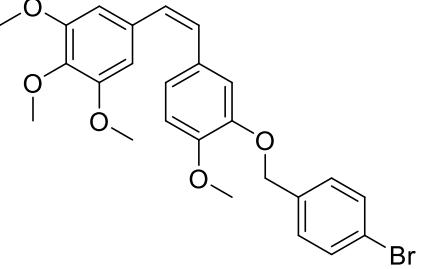
AM40		**AM16**	
AM41		**JRP01**	
AM42		**AM08**	
AM48		**AM14**	
AM53		**AM71**	

Table S5. 2D Chemical structure from JRP and AM databases obtained from SBVS.