Supporting Information

On the mechanism of action underlying the anti-inflammatory activity of hypericin: an *in silico* study pointing to the relevance of janus kinases inhibition

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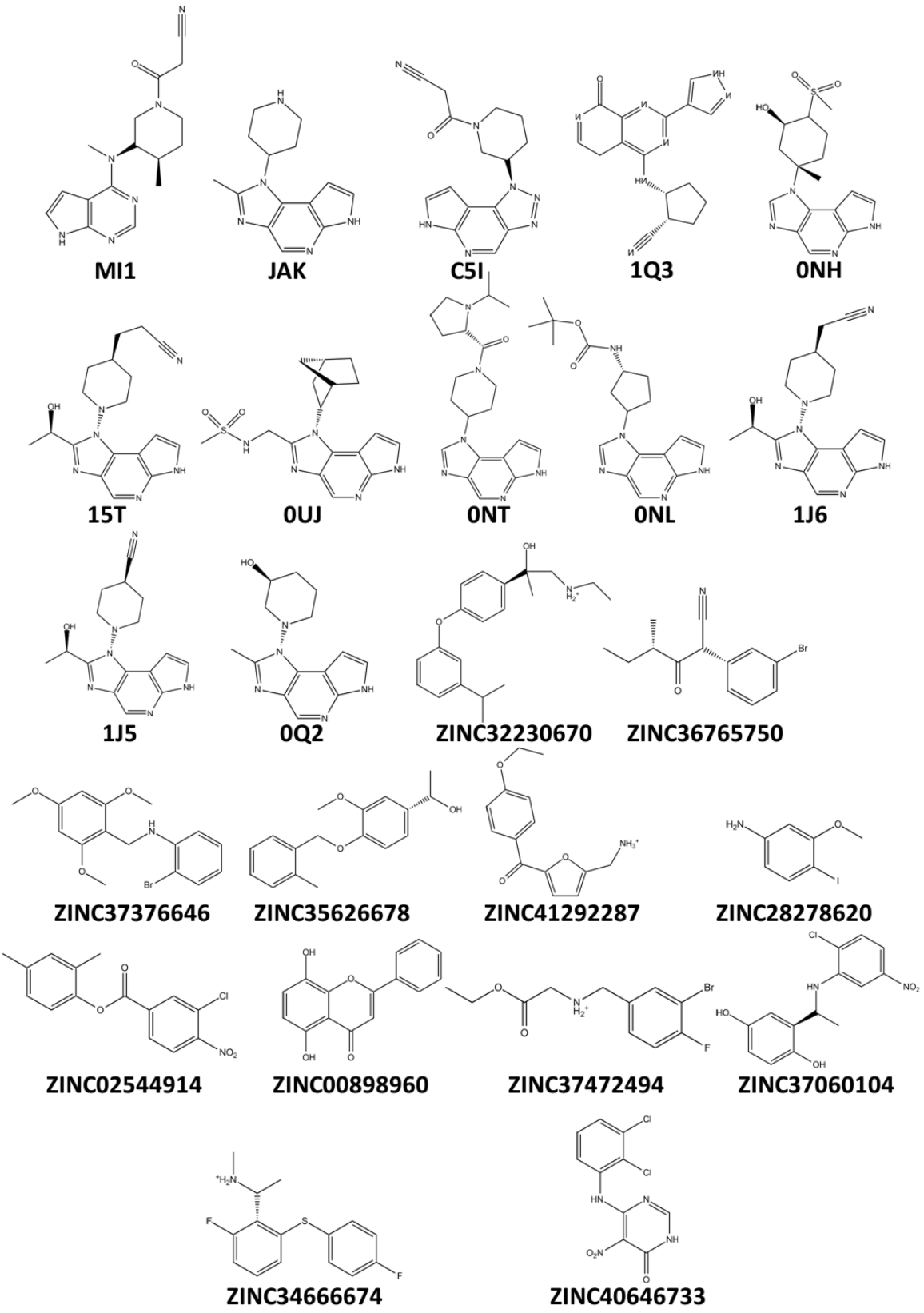

Figure S1. Chemical structures of compounds included in the training set.

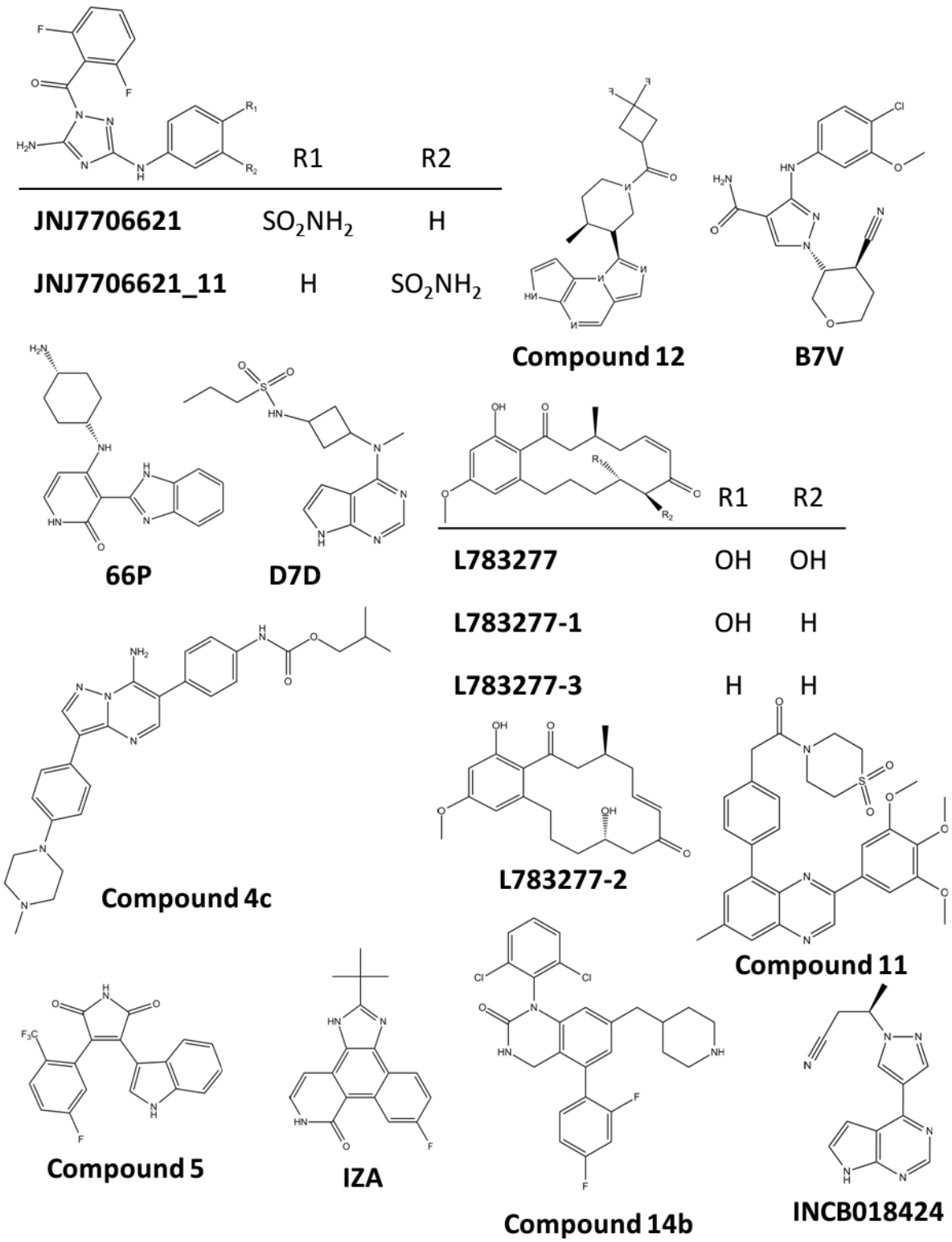

Figure S2. Chemical structures of compounds included in the validation set.

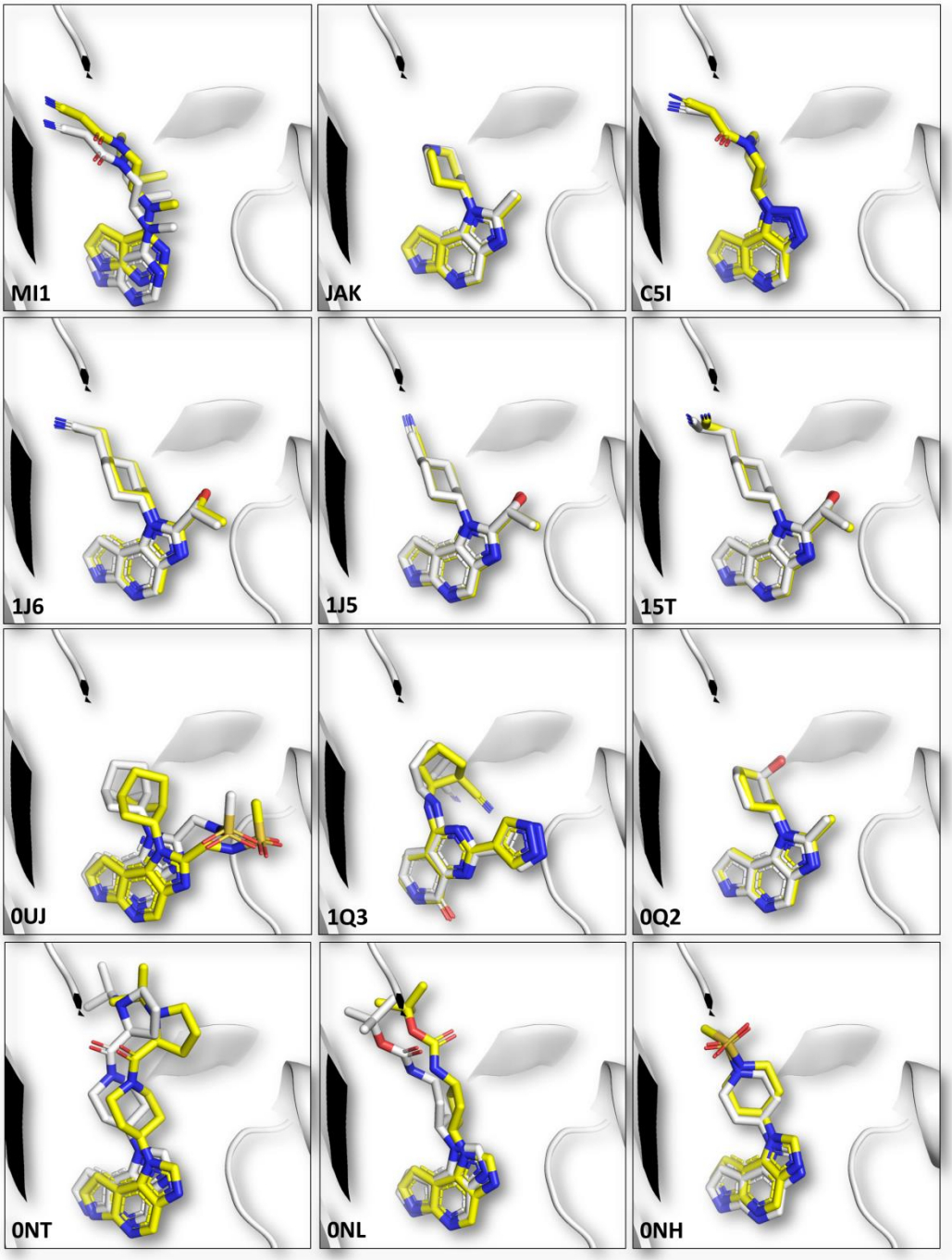

Figure S3. Comparison between calculated (yellow) and crystallographic (white) pose of true inhibitors included in the training set.

The subset of true inhibitors belonging to the training set was retrieved from the RCSB PDB databank (https://www.rcsb.org/). Experimental activities and computed scores are reported below (Table S1).

Table S1. Experimental and calculated values of true inhibitors included in the training set

Compound (PDB ID)	**Experimental K_i (nM) [a]**	**Computational Scores**
MI1	0.7	78.8 ± 1.0
JAK	10	65.6 ± 0.0
C5I	1.5	74.5 ± 0.4
1Q3	2	61.7 ± 0.8
1J6	0.1	72.9 ± 1.0
1J5	1.9	71.1 ± 0.2
15T	0.3	79.3 ± 0.1
0Q2	1.8	62.1 ± 0.1
0NH	1.7	64.1 ± 0.1
0UJ	0.2	80.2 ± 0.2
0NT	22	66.5 ± 1.8
0NL	0.9	73.6 ± 0.7

[a] according to the external ligands annotation reported in the RCSB PDB databank (https://www.rcsb.org/; last database access 27th March 2018)

Table S2. Experimental and calculated values of molecules included in the validation set

Compound	Experimental activity	Computational Scores	Computed activity [a]
66P	Active [b]	69.4 ± 0.5	Yes
B7V	Active [b]	72.5 ± 0.7	Yes
D7D	Active [b]	74.7 ± 2.4	Yes
IZA	Active [b]	64.8 ± 0.2	Yes
JNJ7706621_11	Active [c]	81.0 ± 1.6	Yes
Compound 12	Active [d]	74.5 ± 0.5	Yes
JNJ7706621	Active [c]	68.6 ± 1.1	Yes
INCB018424	Active [c]	63.7 ± 0.9	Yes
L783277	Inactive [e]	9.2 ± 2.7	No
L783277-1	Inactive [e]	0	No
L783277-2	Inactive [e]	21.6 ± 2.3	No
L783277-3	Inactive [e]	0	No
Compound 4c	Inactive [f]	0	No
Compound 5	Inactive [g]	53.4 ± 0.3	No
Compound 14b	Inactive [h]	No poses found	No
Compound 11	Inactive [i]		No

[a] the threshold above which compounds were considered able to positively interact with the pocket was set at 57.5 units
[b] according to the external ligands annotation reported in the RCSB PDB databank (https://www.rcsb.org/; last database access 27th March 2018)
[c] Malerich et al., 2010
[d] Norman, 2012
[e] Liniger et al., 2011
[f] Gommermann et al., 2010
[g] Thoma et al., 2011
[h] Stelmach et al., 2003
[i] Pissot-Soldermann et al., 2010

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