Supplementary Table 1: Hit Profiles

Compound	ID	IC50 (nM)	Maximum Inhibition (%)
1	LDN-0118790	38	80
2	LDN-0118870	74	70
3	LDN-0119629	37	70
4	LDN-0121669	100	80
5	LDN-0124614	306	85
6	LDN-0125734	15	75
7	LDN-0125735	139	75
8	LDN-0130436	174	80
9	LDN-0196125	No fit	50
10	LDN-0015257	152	100
11	LDN-0057218	290	100
12	LDN-0057325	1920	100
13	LDN-0066337	No fit	50
14	LDN-0076437	1293	70
15	LDN-0202779	11	75
16	LDN-0209285	180	70
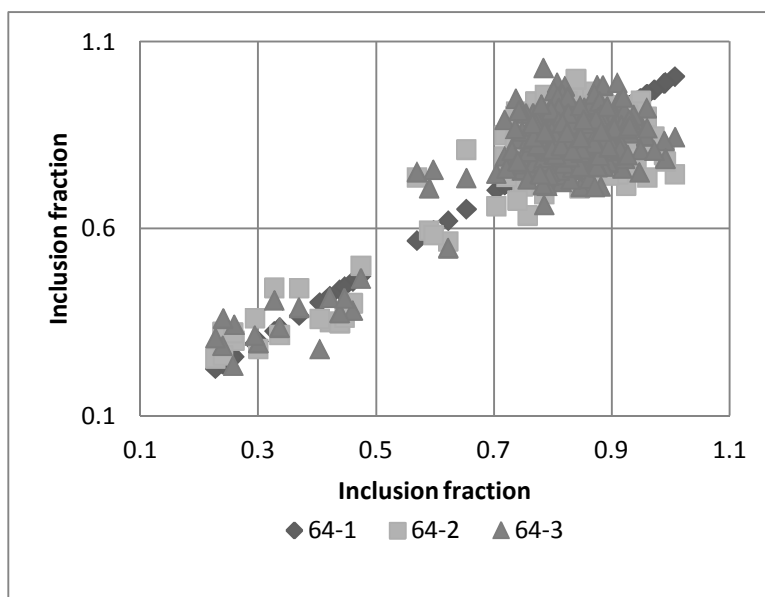
Supplementary Figure 1: Plotted inclusion fraction against 64-1 in triplicate. The inclusion fraction was examined in test Plate 64. Values above 0.6 exhibits significant variability, with little correlation among the replicates. In contrast, inclusion fractions below 0.6, values in which we are selecting putative hits, display robust correlation and reproducibility
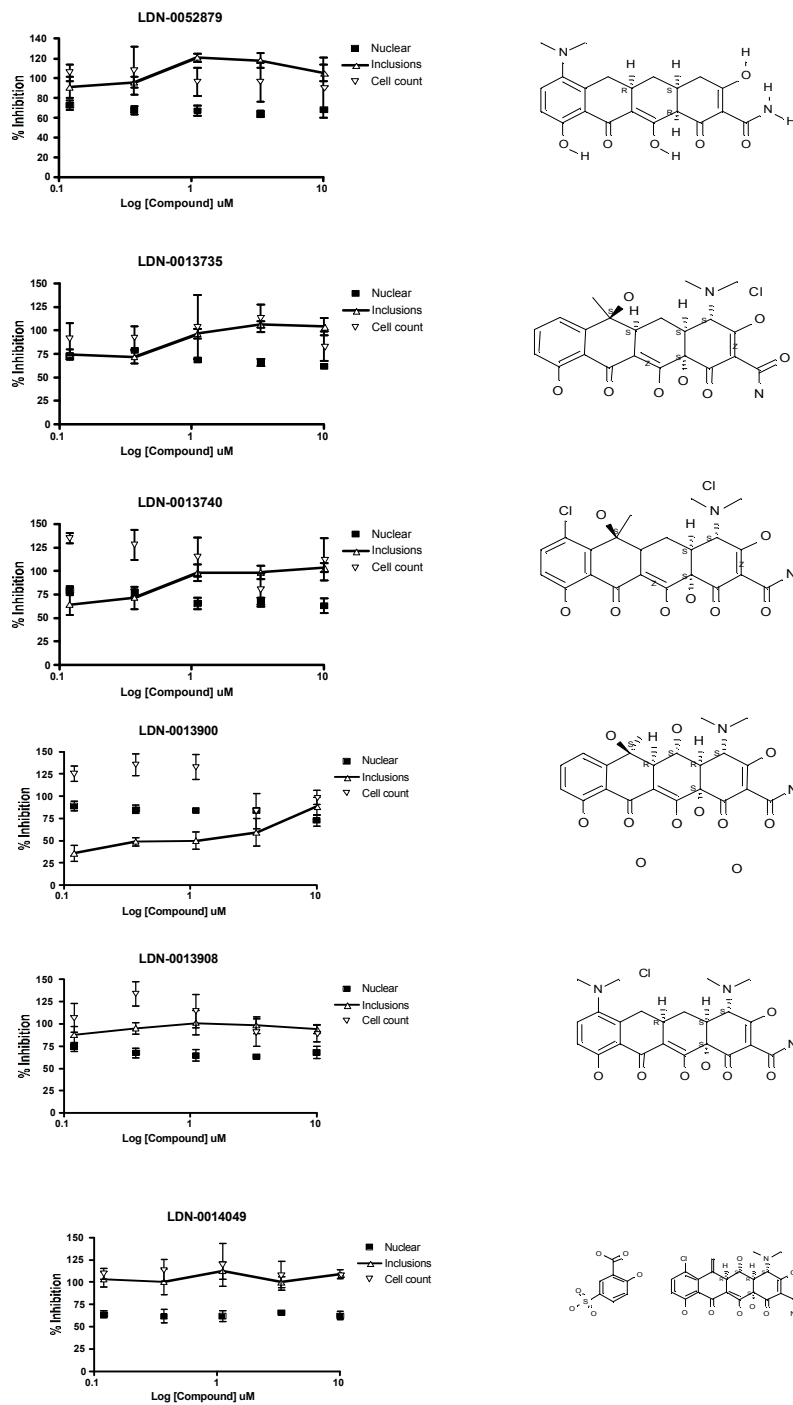
Supplementary Figure 2: Doxycycline analogues hit in screen. 5 point dose response confirmation identified doxycycline analogues. Note structural similarity among the analogues. Each structure exhibited dose-dependent increased percent inhibition of the aggregation fraction and reduced total TDP-43::GFP expression. Data represent mean ± standard deviation, n = 4.