

Expanded View Figures

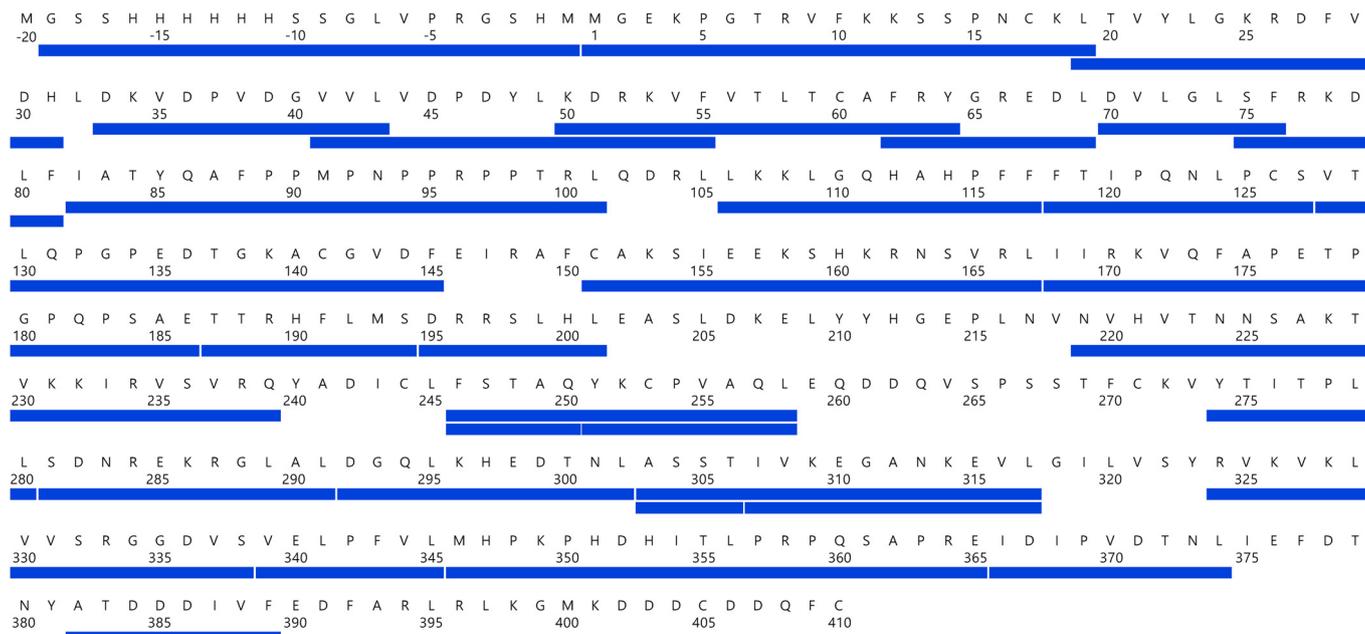


Figure EV1. Sequence coverage map of wild-type β -arrestin-2 (β arr2).

The blue bars indicate analyzed peptic peptides.

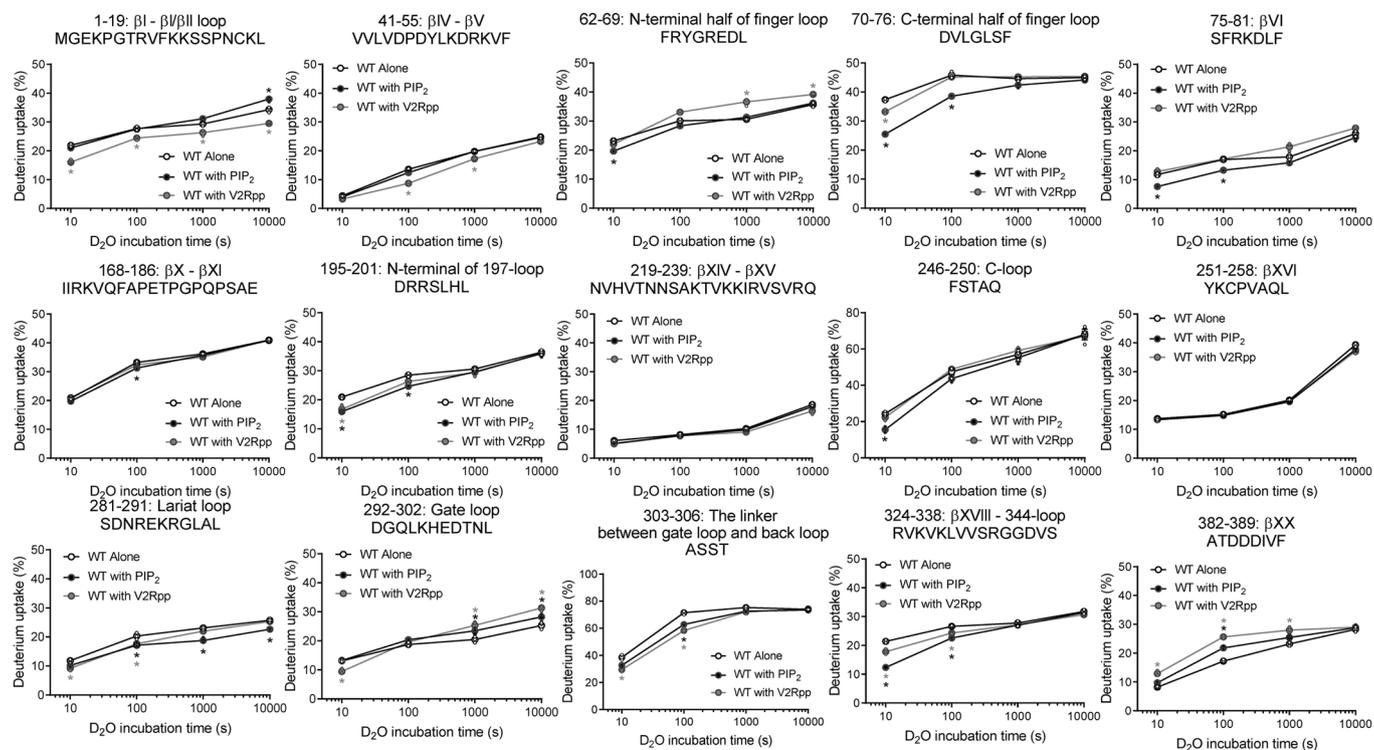


Figure EV2. Deuterium uptake plots of selective peptides of WT β arr2 with or without V2Rpp or PIP₂ co-incubation.

Results were derived from three independent experiments. The statistical significance of the differences was determined using Student's t test (* $P < 0.05$). Exact p -values are provided in Dataset EV1. Data are presented as mean \pm standard error of the mean. Black or grey * indicates statistically significant difference between apo WT β arr2 and PIP₂-bound WT β arr2 or V2Rpp-bound WT β arr2, respectively. Smaller symbols indicate each data point.

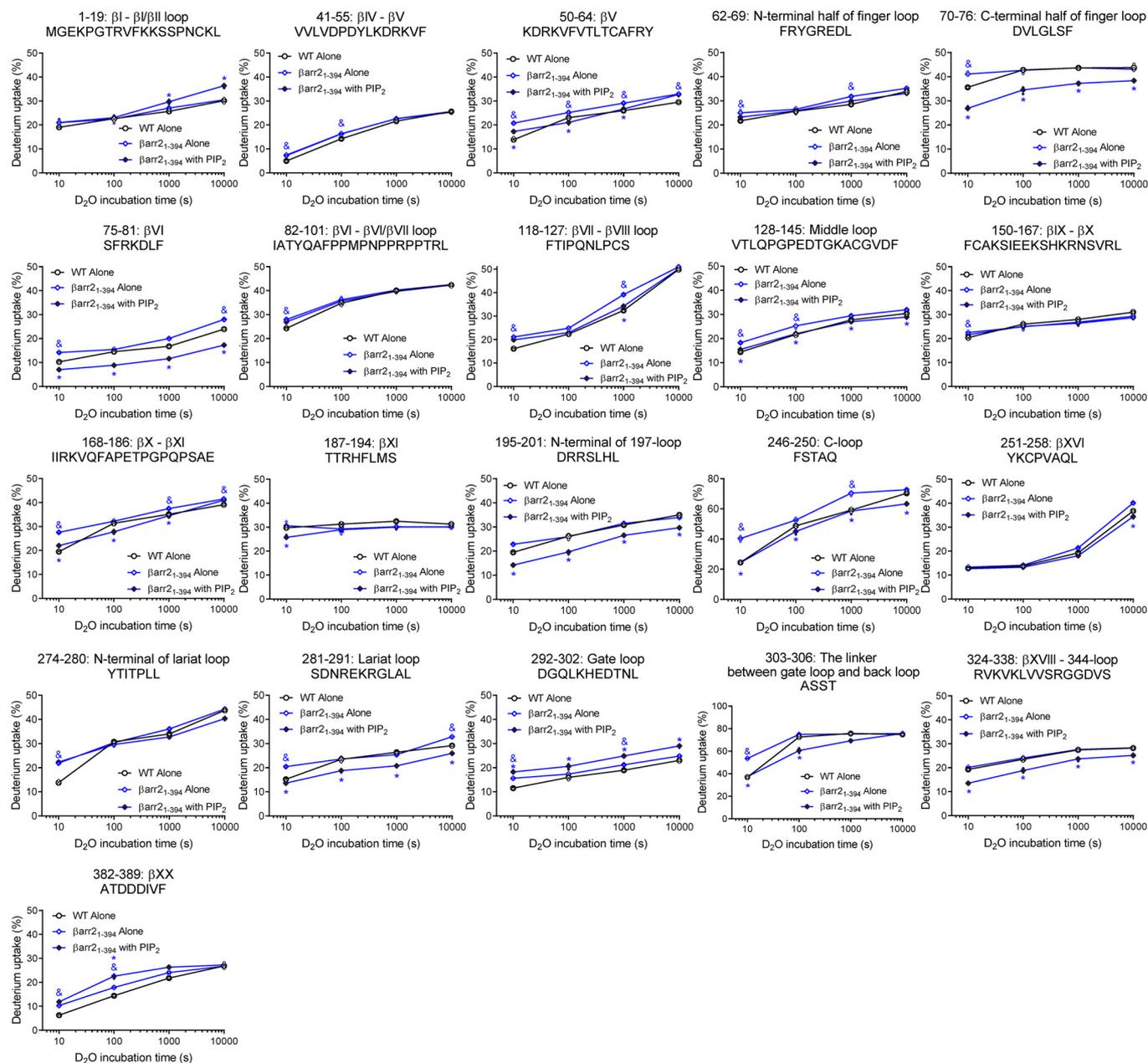


Figure EV3. Deuterium uptake plots of selective peptides of apo WT β arr2 and β arr2_1-394 with or without PIP₂ co-incubation.

Results were derived from three independent experiments. The statistical significance of the differences was determined using Student's *t* test (&**P* < 0.05). Exact *p*-values are provided in Dataset EV1. & indicates statistically significant difference between apo WT β arr2 and apo β arr2_1-394. * indicates statistically significant difference between apo and PIP₂-bound β arr2_1-394. Data are presented as mean \pm standard error of the mean. Smaller symbols indicate each data point.

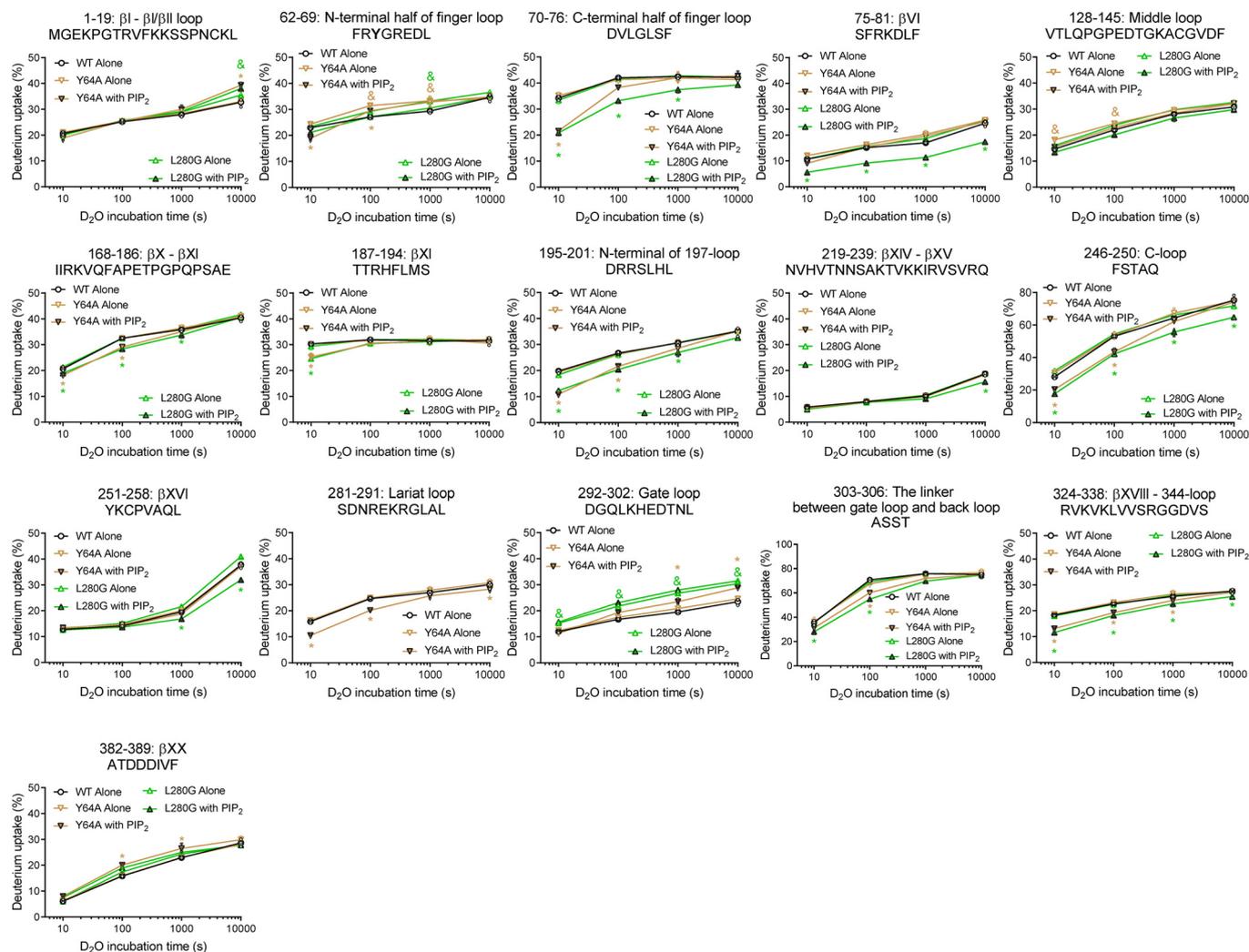


Figure E4. Deuterium uptake plots of selective peptides of apo WT β arr2 and Y64A and L280G with or without PIP₂ co-incubation.

Results were derived from three independent experiments. The statistical significance of the differences was determined using Student's *t* test ($^{*}P < 0.05$). Exact *p*-values are provided in Dataset EV1. Yellow green & indicates statistically significant difference between apo WT β arr2 and apo Y64A or L280G, respectively. Yellow or green * indicates statistically significant difference between apo and PIP₂-bound Y64A or L280G, respectively. Data are presented as mean \pm standard error of the mean. Smaller symbols indicate each data point.

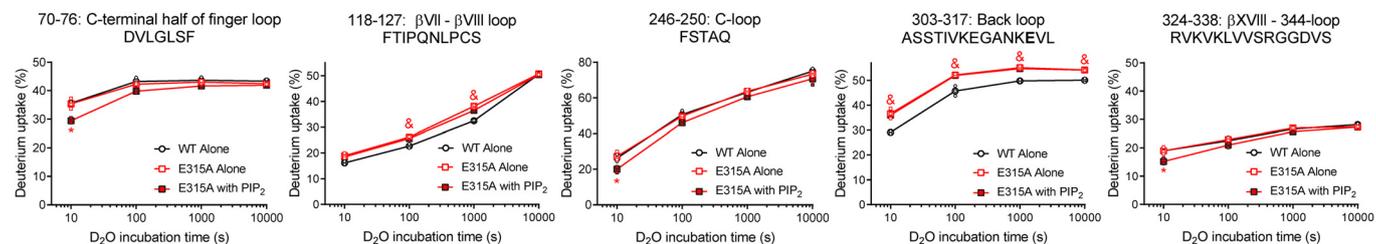


Figure EV5. Deuterium uptake plots of selective peptides of apo WT βarr2 and E315A with or without PIP₂ co-incubation.

Results were derived from three independent experiments. The statistical significance of the differences was determined using Student's *t* test (&**P* < 0.05). Exact *p*-values are provided in Dataset EV1. & indicates statistically significant difference between apo WT βarr2 and apo E315A. * indicates statistically significant difference between apo and PIP₂-bound E315A. Data are presented as mean ± standard error of the mean. Smaller symbols indicate each data point.