**Supplementary Information Table S1**. Summary of TR-FRET assay (IC50) and Biacore data for active and inactive ERK2 proteins with SCH772984.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | ***Active*** | | | | | ***Inactive*** | | | |
|  | **IC50**  (nM) | ***K*D** (nM) | ***k*on**  (M-1s-1) 106 | ***k*off**  (s-1) 10-3 | ***t*½** (min) | ***K*D** (nM) | ***k*on**  (M-1s-1) 106 | ***k*off**  (s-1) 10-4 | ***t*½** (min) |
| **ERK2 WT** | 0.03 ± 0.01 | 0.51 | 3.52 ± 0.01 | 1.79 ± 0.01 | 6.5 | 0.026 | 1.34 ± 0.01 | 0.352 ± 0.001 | 330 |
| **ERK2 G169D** | 4.9 ± 0.9 | 138*a* | rapid | rapid | <0.01*b* | 7.8 | 1.78 ± 0.01 | 139 ± 1 | 0.8 |
| *a* – See Supplementary Information Figure S5. *b* – Upper limit estimate based on detection limit of Biacore instrument. | | | | | | | | | |

SCH772984 binding to both active/inactive wildtype ERK2 and active/inactive ERK2G169D mutant, showing weaker binding for ERK2G169D. The active ERK2G169D mutant also exhibits weaker binding to SCH772984and a rapid on /off rate.