SUPPLEMENTARY INFORMATION

Supplementary Table 1. Upadacitinib Kinome Selectivity

Of the kinases in the panel, 14 kinases have an IC50 below 10 μM, but only 2 non-JAK kinases have IC50 values below 1 μM (Rock1 at 0.92 μM and Rock2 at 0.43 μM).

JAK activity assays using isolated kinase domains in the presence of 0.1 mM ATP and trFRET kinome profiling were conducted as described previously ([17](#_ENREF_17)).

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| **Kinase** | **Assay** | **[ATP] (mM)** | **Average IC50 (μM)** |
| JAK1 | HTRF activity | 0.1, 0.001 | 0.043, <0.0032 |
| JAK2 | HTRF activity | 0.1, 0.001 | 0.12, <0.0032 |
| JAK2 | trFRET binding | - | 0.008 |
| JAK3 | HTRF activity | 0.1, 0.001 | 2.1, 0.054 |
| JAK3 | trFRET binding | - | 0.068 |
| TYK2 | HTRF activity | 0.1, 0.001 | 0.055, 4.7 |
| ABL | trFRET binding | - | >10 |
| ACVR1 | trFRET binding | - | >10 |
| Akt1 | trFRET binding | - | >10 |
| ALK | trFRET binding | - | >5.5 |
| AMPK | trFRET binding | - | >4.5 |
| Aurora 1 | trFRET binding | - | >5.5 |
| Aurora 2 | trFRET binding | - | 4.5 |
| BRAF | trFRET binding | - | >10 |
| BTK | trFRET binding | - | >10 |
| CAMK1D | trFRET binding | - | 2.3 |
| CAMK2A | trFRET binding | - | >10 |
| CAMKK2 | trFRET binding | - | >10 |
| CDK11 | trFRET binding | - | >10 |
| CDK2 | trFRET binding | - | >10 |
| CDK7/Cyclin H/Mat1 | trFRET binding | - | >10 |
| CDK8/Cyclin C | trFRET binding | - | >10 |
| CDK9/Cyclin K | trFRET binding | - | >10 |
| CLK2 | trFRET binding | - | >10 |
| Ck1alpha1 | trFRET binding | - | >10 |
| cMET | trFRET binding | - | >10 |
| CSF1R | trFRET binding | - | >10 |
| DDR1 | trFRET binding | - | >10 |
| DYRK1A | trFRET binding | - | >10 |
| DYRK1B | trFRET binding | - | >10 |
| EGFR | trFRET binding | - | >10 |
| Erk2 | trFRET binding | - | >10 |
| FAK | trFRET binding | - | >10 |
| FGFR1 | trFRET binding | - | 4.8 |
| Flt1 | trFRET binding | - | >10 |
| Fyn | trFRET binding | - | >10 |
| GRK5 | trFRET binding | - | >7.9 |
| Gsk3a | trFRET binding | - | >10 |
| Gsk3b | trFRET binding | - | >10 |
| IGF1R | trFRET binding | - | >10 |
| IKKE | trFRET binding | - | >10 |
| InsR | trFRET binding | - | >10 |
| JNK1 | trFRET binding | - | >10 |
| JNK2 | trFRET binding | - | >10 |
| KDR | trFRET binding | - | >1.5 |
| LCK | trFRET binding | - | >10 |
| LTK | trFRET binding | - | 2.7 |
| MAP2K3 | trFRET binding | - | >10 |
| MAP3K10 | trFRET binding | - | >10 |
| MAP4K2 | trFRET binding | - | >10 |
| MAP4K4 | trFRET binding | - | >10 |
| MEK1 | trFRET binding | - | >10 |
| MEK2 | trFRET binding | - | >10 |
| MST1 | trFRET binding | - | >10 |
| Nek2 | trFRET binding | - | >10 |
| PAK4KD | trFRET binding | - | >10 |
| PDGFRA V561D | trFRET binding | - | >10 |
| PDGFRB | trFRET binding | - | >10 |
| Pim1 | trFRET binding | - | >10 |
| Pim2 | trFRET binding | - | >10 |
| PKA | trFRET binding | - | >10 |
| PKCtheta | trFRET binding | - | 5.1 |
| PKCzeta | trFRET binding | - | >10 |
| PKG1A | trFRET binding | - | >10 |
| Plk3 | trFRET binding | - | >10 |
| Prkcn | trFRET binding | - | >10 |
| p38 alpha | trFRET binding | - | >10 |
| RET | trFRET binding | - | 2.4 |
| Rock1 | trFRET binding | - | 0.92 |
| Rock2 | trFRET binding | - | 0.42 |
| Rsk2 | trFRET binding | - | >9.6 |
| SGK1 | trFRET binding | - | >10 |
| Src | trFRET binding | - | >10 |
| STK16 | trFRET binding | - | 9.7 |
| STK33 | trFRET binding | - | >10 |
| Syk | trFRET binding | - | >10 |
| TAOK2 | trFRET binding | - | >10 |
| TBK1 | trFRET binding | - | >10 |
| TNK2 | trFRET binding | - | 5.1 |
| TrkA | trFRET binding | - | >10 |
| TrkB | trFRET binding | - | >10 |
| TrkC | trFRET binding | - | >10 |
| TTK | trFRET binding | - | >10 |
| TYRO3 | trFRET binding | - | >10 |
| Wee1 | trFRET binding | - | >10 |
| Zipk | trFRET binding | - | >10 |

ATP, adenosine triphosphate; HTRF, homogenous trFRET; IC50, concentration producing 50% inhibition; JAK, Janus kinase; trFRET, time-resolved fluorescence energy transfer.