**Figure 1 –** **Source Data 1:** Reactions and rates constant involved in signaling pathway leading to Ras and Rap1 activation

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Reaction equation | Kf (nM-1 Sec-1) | | Kb (Sec-1) | Kcat (Sec-1) | Reference |
| *Gby + Src Src\_Gby* | | 2.00E-04 | 1.00E-01 |  | Estimated |
| *Grb2 + Sos Grb2\_Sos* | | 2.50E-04 | 1.68E-02 |  | Chook et al., 1996; Jain and Bhalla, 2014 |
| *Src\_Gby +Shc pShc +Src\_Gbg* | | 8.00E-03 | 1.28E-01 | 3.20E-02 | Estimated |
| *pShc + Src\_Grb2\_Sos pShc\_Grb2\_Sos* | | 5.00E+00 | 1.00E-01 |  | Bhalla and Iyengar, 1999; Jain and Bhalla, 2014; Sasagawa et al., 2005 |
| *pShc\_Grb2\_Sos + RasGDP pShc\_Grb2\_Sos + RasGTP* | | 1.98E-02 | 8.00E-01 | 2.00E-01 | Bhalla and Iyengar, 1999; Jain and Bhalla, 2014; Sasagawa et al., 2005 |
| *pShc Shc* | | 2.00E-01 | 0.00E+00 |  | Jain and Bhalla, 2014 |
| *ppERK +pShc\_Grb2\_SosppERK +pShc\_Grb2 + pSos* | | 1.95E-02 | 4.00E+01 | 1.00E+01 | Jain and Bhalla, 2014; Sasagawa et al., 2005 |
| *pSosos* | | 1.00E+00 |  |  | Jain and Bhalla, 2014 |
| *CaMCa4 + Ras-GRF2 Ras-GRF2\_CaMCa4* | | 6.00E-02 | 9.24E-01 |  | Jin et al., 2014 |
| *Ras-GRF2\_CaMCa4 + RasGDP Ras-GRF2\_CaMCa4 + RasGTP* | | 1.98E-02 | 8.00E-01 | 2.00E-01 | Farnsworth et al., 1995; Jin et al., 2014, |
| *PKAc + Src pSrc + PKAc* | | 2.04E+00 | 8.00E+01 | 2.00E+01 | Jain and Bhalla, 2014 |
| *pSrc + Cbl pCbl + Src* | | 4.00E-01 | 1.60E+02 | 4.00E+01 | Jain and Bhalla, 2014 |
| *Crk\_C3G + pCbl Crk\_C3G\_pCbl* | | 1.00E-03 | 2.00E-01 |  | Jain and Bhalla, 2014; Knudsen et al., 1994; Sasagawa et al., 2005 |
| *pCbl Cbl* | | 1.00E+02 |  |  | Jain and Bhalla, 2014 |
| *pSrc Src* | | 1.00E+02 |  |  | Jain and Bhalla, 2014 |
| *Crk\_C3G\_pCbl + Rap1GDP Crk\_C3G\_pCbl + Rap1GTP* | | 1.01E-02 | 8.00E-02 | 2.00E-02 | Gotoh et al., 1995; Jain and Bhalla, 2014; Sasagawa et al., 2005 |
| *Epac + cAMP Epac\_cAMP* | | 1.21E-04 | 1.45E-01 |  | de Rooij et al., 2000; Luczak et al., 2017 |
| *Epac\_cAMP + Rap1GDP Epac\_cAMP + Rap1GTP* | | 1.20E-03 | 9.60E-01 | 2.40E-01 | Estimated |
| *Rap1GTP+Rap1Gap Rap1GDP* | | 2.00E-01 | 2.00E+02 |  | Daumke et al., 2004; Jain and Bhalla, 2014; Sasagawa et al., 2005 |
| *RasGTP+ RasGap RasGDP* | | 4.95E-02 | 4.00E+01 |  | Bhalla and Iyengar, 1999; Jain and Bhalla, 2014 |

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