

S4 Table. Values of the literature parameters for the PBPK model of IFN- α used in this study.

Parameter	Fitted Values	Reference Value	Unit	Reference
Molecular Weight	19500(fixed)	19500	g/mol	[1]
CLplasma (Kidney)	0.003	0.0027	l/min/kg organ	[2–5]
IFNAR1 Concentration	0.26	-	$\mu\text{mol/l}$	[6–9]
IFNAR2 Concentration	0.5	-	$\mu\text{mol/l}$	[6–9]
K(IFNAR1)	0.1	-	1/nmol*s	-
K(IFNAR2)	0.00022	-	1/nmol*s	-
K_{eq} IFNAR1	0.00077	0.0001-0.01	1/nmol	[10, 11]
K_{eq} IFNAR2	1.5	0.002-0.1	1/nmol	[12, 13]
$K_{\text{endocytosis}}$	8.93226	-	1/min	-
K_t _IFNAR1	0.02298	-	1/min	-
K_t _IFNAR2	0.074999	-	1/min	-

References

- Wishart DS, Knox C, Guo AC, Shrivastava S, Hassanali M, Stothard P, et al. DrugBank: a comprehensive resource for in silico drug discovery and exploration. Nucleic acids research. 2006;34(Database issue):D668–72. doi:10.1093/nar/gkj067.
- Wills RJ, Dennis S, Spiegel HE, Gibson DM, Nadler PI. Interferon kinetics and adverse reactions after intravenous, intramuscular, and subcutaneous injection. Clinical Pharmacology & Therapeutics. 1984;35:722–727.
- Bocci V, Pacini A, Muscettola M, Paulesu L, Pessina GP, Santiano M, et al. Renal filtration, absorption and catabolism of human alpha interferon. Journal of interferon research. 1981;1:347–352. doi:10.1089/jir.1981.1.347.
- Tamar Bino AG Zacharai Madar, Rosenberg H. The Kidney is the Main Site of Interferon Degradation. Journal of Interferon Research. 1982;2:301–308. doi:10.1089/jir.1982.2.301.
- Bino T GA Edery H, H R. Involvement of the kidney in catabolism of human leukocyte interferon. The Journal of general virology. Mar 1982;59(Pt 1):39–45. doi:10.1099/0022-1317-59-1-39.
- François-Newton V, de Freitas Almeida GM, Payelle-Brogard B, Monneron D, Pichard-Garcia L, Piehler J, et al. USP18-based negative feedback control is induced by type I and type III interferons and specifically inactivates interferon α response. PLoS ONE. 2011;6(7). doi:10.1371/journal.pone.0022200.
- Wilmes S, Beutel O, Li Z, Francois-Newton V, Richter CP, Janning D, et al. Receptor dimerization dynamics as a regulatory valve for plasticity of type I interferon signaling. Journal of Cell Biology. 2015;209(4):579–593. doi:10.1083/jcb.201412049.
- Moraga I, Harari D, Schreiber G, Uzé G, Pellegrini S. Receptor density is key to the alpha2/beta interferon differential activities. Molecular and cellular biology. 2009;29(17):4778–87. doi:10.1128/MCB.01808-08.

9. Schreiber G, Piehler J. The molecular basis for functional plasticity in type I interferon signaling. *Trends in Immunology*. 2015;36(3):139–149. doi:10.1016/j.it.2015.01.002.
10. Gavutis M, Jaks E, Lamken P, Piehler J. Determination of the Two-Dimensional Interaction Rate Constants of a Cytokine Receptor Complex. *Biophysical Journal*. 2006;90(9):3345 – 3355. doi:<http://dx.doi.org/10.1529/biophysj.105.072546>.
11. Lavoie TB, Kalie E, Crisafulli-Cabatu S, Abramovich R, DiGioia G, Moolchan K, et al. Binding and activity of all human alpha interferon subtypes. *Cytokine*. 2011;56(2):282–289. doi:10.1016/j.cyto.2011.07.019.
12. Cutrone EC, Langer JA. Contributions of cloned type I interferon receptor subunits to differential ligand binding. *FEBS Letters*. 1997;404(2-3):197–202. doi:10.1016/S0014-5793(97)00129-4.
13. Rengachari S, Groiss S, Devos J, Caron E, Grandvaux N, Panne D. Structural Basis Of STAT2 Recognition By IRF9 Reveals Molecular Insights Into ISGF3 Function. *bioRxiv*. 2017;doi:10.1101/131714.