

# Case Study: Dose Feasibility of LNP-delivered mRNA Therapeutics

*LNP-delivered mRNA for UGT1A1 replacement in Crigler-Najjar syndrome type 1 patients*

## Supplementary Information

Information on the default parameters used in the LNP-delivered mRNA Therapeutics models can be found at [doc.appliedbiomath.com](http://doc.appliedbiomath.com). For this case study, the default values were used for all parameters aside from those described in Table 1 below which are specific to the drug and target.

**Table 1.** Summary of parameter values used in the LNP-delivered mRNA case study that differ from the default values.

Parameter	Case Study Value	Parameter Unit	Description	References
Molecular weight of drug	534,700	Da	Calculated based on molecular weight of human UGT1A1 protein	Assumed average molecular weight of an amino acid is 110 Da and average molecular weight of a nucleotide is 329 Da
Molecular weight of target protein	59,591	Da	Molecular weight of human UDP-glucuronosyltransferase 1A1 (UGT1A1) protein	<a href="https://www.uniprot.org/uniprotkb/P22309/entry">https://www.uniprot.org/uniprotkb/P22309/entry</a>
Molecular weight of substrate	584	Da	Molecular weight of bilirubin	<a href="https://pubchem.ncbi.nlm.nih.gov/compound/Bilirubin">https://pubchem.ncbi.nlm.nih.gov/compound/Bilirubin</a>
Half-life of target protein	10	hr	Half-life of wild-type UGT1A1 protein in rat and assumed the same in human	Emi et al. 2002
Half-life of	157	hr	Half-life of bilirubin	Apgar et. al 2018

substrate				
Half-life of product	15.7	hr	Half-life of monoglucuronide bilirubin	Apgar et. al 2018
Catalytic constant ( $k_{cat}$ )	0.0354	1/s	Enzymatic rate for glucuronidation of bilirubin	Median value calculated from $V_{max}$ and UGT1A1 concentration data in Sridar et al. 2013
Michaelis constant ( $K_M$ )	200	nM	The bilirubin concentration at which the enzymatic reaction rate is half of its maximum value.	Apgar et. al 2018
Substrate concentration	342,000	nM	200 mg/L based on Crigler-Najjar syndrome type 1 patients	Apgar et. al 2018; <a href="https://www.ncbi.nlm.nih.gov/books/NBK562171/">https://www.ncbi.nlm.nih.gov/books/NBK562171/</a>

## References

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