Supplementary Information

Transport of nucleosides in vcCNT facilitated by sodium gradients from Molecular Dynamics Simulations

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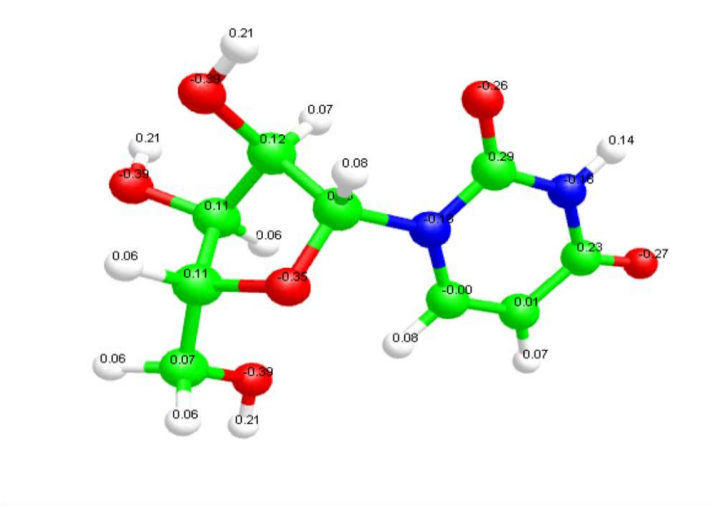
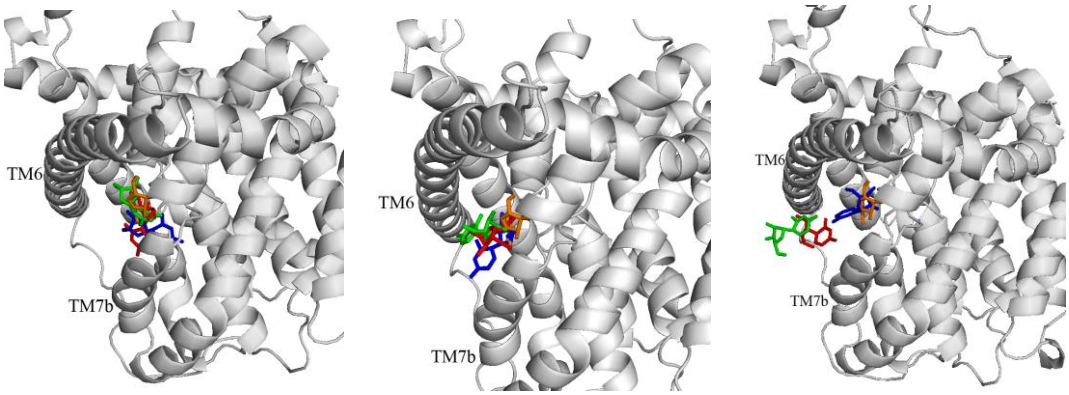


Figure S0. Partial charges of the ligand.



(a) **(b)** **(c)**

Figure S1. Comparison of three independent simulation trajectories with the crystal

structure. Uridine highlighted in orange is the ligand in the crystal structure. Uridines highlighted in red, green, and blue color represent the ligands from three independent trajectories. (a) Our results show that uridine is trapped in the binding pocket with no sodium bound. (b) Our results show that uridine moves from the binding pocket toward the central pore of the trimer in the presence of 20 mM NaCl. (c) Our results show that uridine is transported into the central pore of the trimer in the presence of 100 mM NaCl.

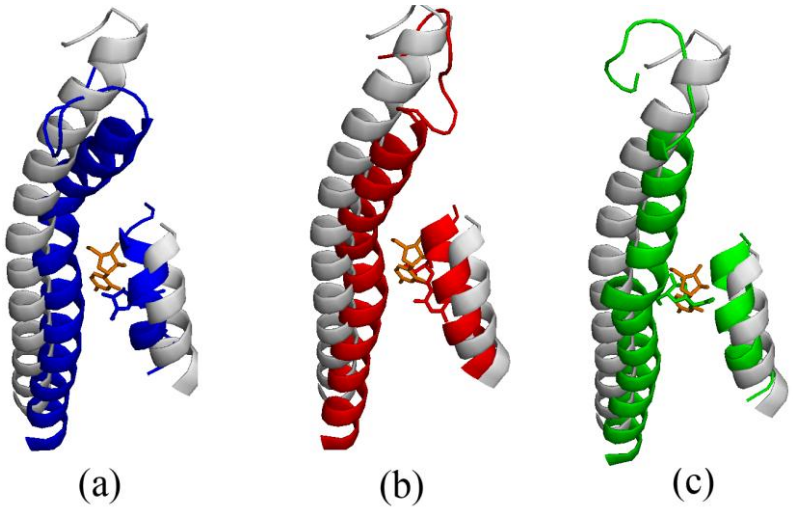


Figure S2. (a), (b), (c) represent results from three independent molecular dynamics simulation trajectories. All of them show that, without Na^+ bound, the distance between TM6 and TM7b becomes small, preventing the uridines from transporting into the central pore of trimer of vcCNT.

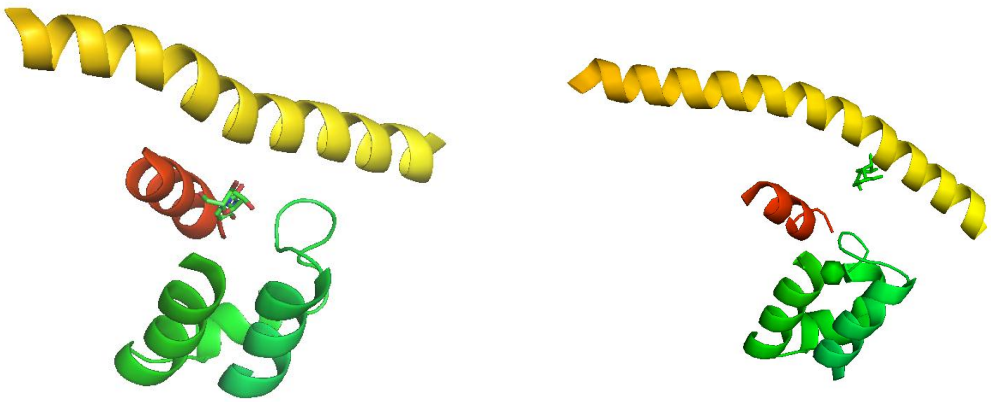


Figure S3. Cartoon representation of VcCNT-mediated nucleoside transport is Na^+-dependent. (a) Without Na^+ bound, our results show that uridine is trapped in the

binding pocket. With Na^+ bound, our results show that uridine is transported into the central pore of the trimer.

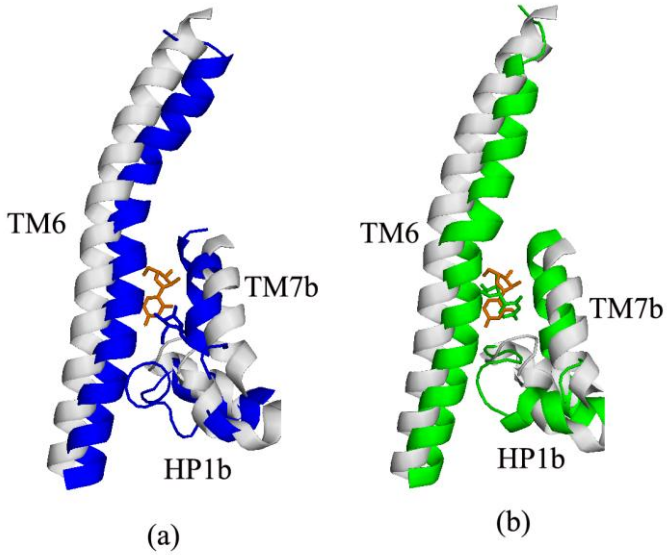


Figure S4. (a), (b) represent results from two independent molecular dynamics simulation trajectories. Both of them show that, without Na^+ bound, loop between HP1a and HP1b shows large flexibility. And HP1b breaks into coil, making uridine trapped in the binding pocket.

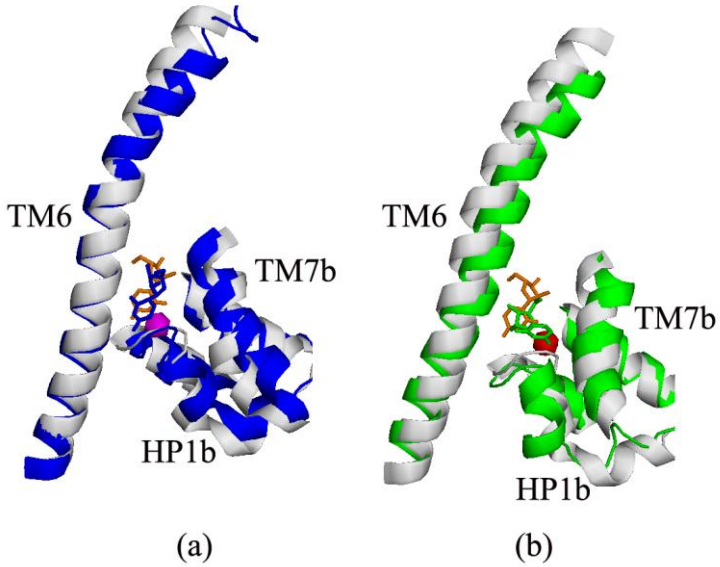


Figure S5. (a), (b) represent results from two independent molecular dynamics simulation trajectories. Both of them show that, in the presence of 20 mM NaCl, loop of HP1 becomes less flexible, and the outward-movement of HP1b makes uridine leave from the binding pocket.

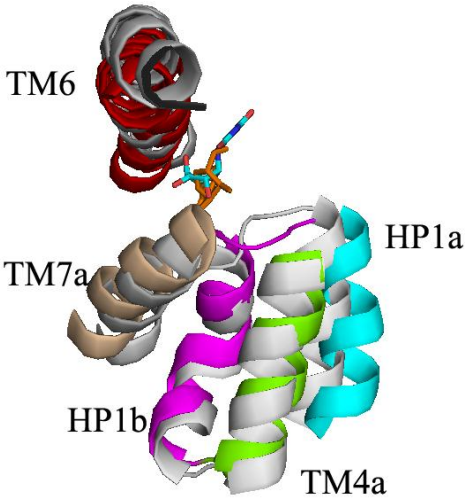


Figure S6. In the presence of 20 mM NaCl without Na^+-coupled in the protein, uridine is trapped in the binding pocket as in the presence of no NaCl.

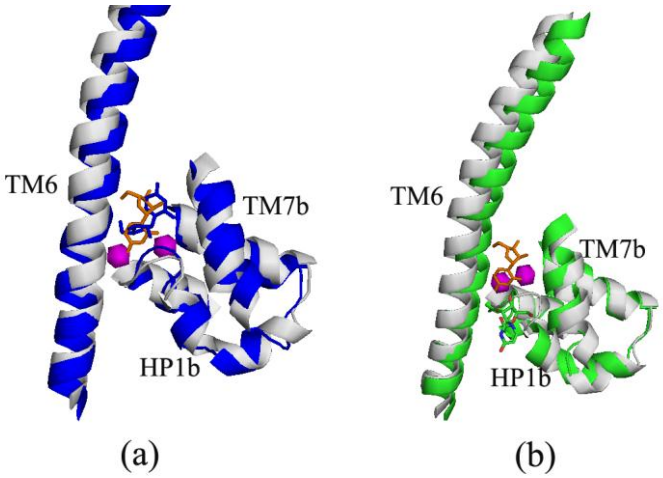


Figure S7. (a), (b) represent results from two independent molecular dynamics simulation trajectories. Both of them show that, in the presence of 100 mM NaCl, uridine is transported into the intracellular side.

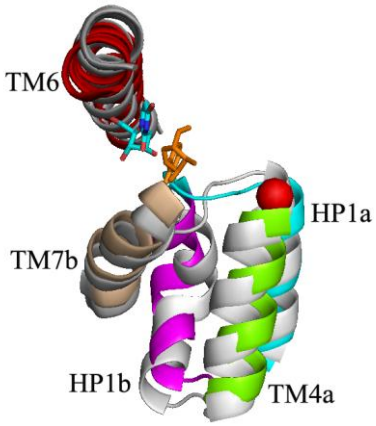


Figure S8. In the presence of 100 mM NaCl with one Na^+-coupled, uridine leaves from the binding pocket to the intracellular side of vcCNT as in the presence of 20 mM NaCl.

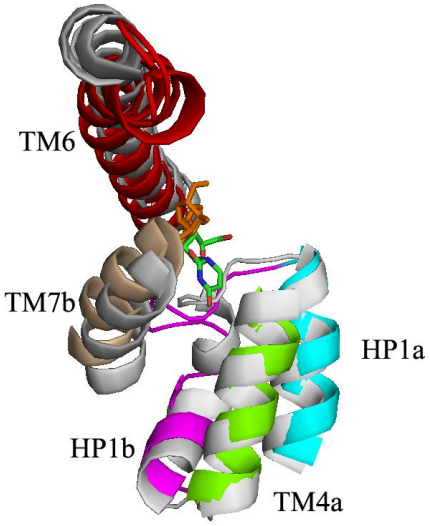


Figure S9. In the presence of 100 mM NaCl without Na^+-coupled, uridine is trapped in the binding pocket as in the presence of no NaCl.