Effect of Palmitoylation on Claudin-14 Tight Junction Proteins

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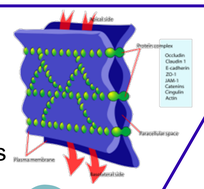
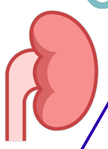
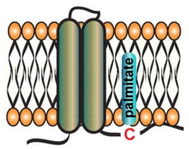
Introduction

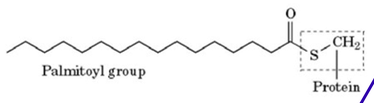
Claudins are membrane proteins that form paracellular barriers and pores that determine tight junction permeability. The claudin family has 27 known claudin proteins in humans. The expression levels of the claudins are tissue specific. Claudin-14 is found in the inner ear and the kidneys. Defects in claudin-14 expression can lead to: deafness, kidney stones, and reduced bone density





Previous study showed that specific mutations of palmitoylation sites in claudin-14 affect its ability to create tight junctions





Methods

Coarse Grain models of claudin-14 were generated with and without palmitoylation chains

The atomistic structures used to create the coarse grain models using Martini v2.2 force field

The systems were solvated with standard Martini CG water with 0.15 M NaCl

All CG MD simulations were performed in GROMACS

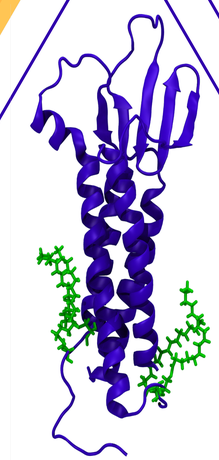
Simulations were run in triplicates

Each run was performed for 10 μs

Palmitoylation of claudin-14 protein impacts its interactions with the surrounding lipids

SCAN ME

Claudin-14



Palmitoylated Claudin-14

Conclusions

The simulations showed that when palmitoylated, claudin 14's interactions with the DPPC increased. This was also observed in six other claudins. These results can lead to further studies to see how two claudins interact with each other when they are in the same membrane.

Acknowledgements

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References

Palmitoylation of Claudin-5 Proteins Influences Their Lipid Domain Affinity and Tight Junction Assembly at the Blood-Brain Barrier Interface. N. Rajagopal, F. J. Irudayanathan, S. Nangia, Journal of Physical Chemistry B. 123, 983-993 (2019).

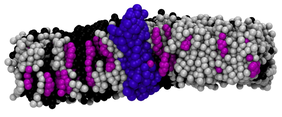
CLDN14 claudin 14 [Homo sapiens (human)] - Gene - NCBI. (2019, June 3). Retrieved from https://www.ncbi.nlm.nih.gov/gene/23562

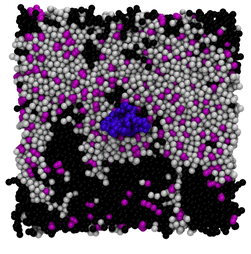
Genetics Home Reference. (2019, June 11). What are proteins and what do they do?. Retrieved from https://ghr.nlm.nih.gov/primer/howgeneswork/protein

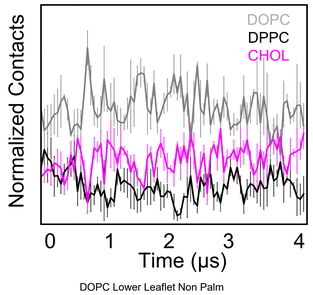
Voet, D., Voet, J. G., & Pratt, C. W. (2011). Lipids and Biological Membranes. In Fundamentals of Biochemistry: Life at the Molecular Level, 4th Edition: Life at the Molecular Level(4th ed., pp. 241-290).

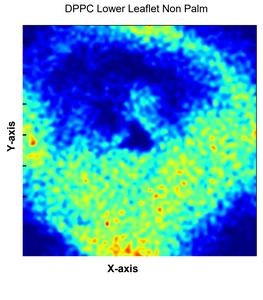
Results

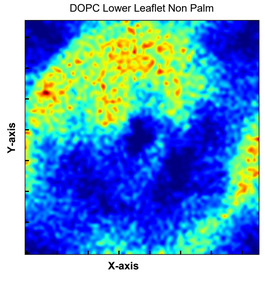
Non Palmitoylated

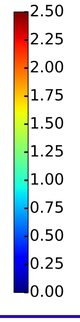












Palmitoylated