Project Title:

Studies on the aminolysis reaction and sterospecificity of papain for the generation of new peptides

Name: ○Joan Gimenez Dejoz (1), Taichi Kurita (2) Keiji Numata (1,2)
Laboratory at RIKEN:
(1) Laboratory at RIKEN: (1) Center for Sustainable Research Science, Biomacromolecules Research Team
(2) Lab for Biomaterial Chemistry, Department of Material Chemistry, Graduate School of Engineering, Kyoto University

1. Background and purpose of the project, relationship of the project with other projects

Natural rubber is a biomaterial with unique physical and chemical features. The α-terminal groups of its molecules play a critical role in its exceptional characteristics. The second most common compound in natural rubber particles is l-quebrachitol, but its interaction with rubber and molecular mechanism are still unknown. We studied how these components interact increasing the knowledge of the molecular rubber structure.

Another project studies cell-penetrating peptides (CPPs), which have the remarkable ability to penetrate biological membranes. The molecular internalization mechanism and structure–function relationships of CPPs are not clear. Moreover, the incorporation of unnatural amino acids such α-aminoisobutyric acid (Aib) into their structure affects their internalization abilities and biostability.

2. Specific usage status of the system and calculation method

We use molecular dynamics simulations with AMBER in implicit solvent to study the interaction of rubber molecules with different alpha-terminal groups and the molecules of L-quebrachitol. To study the CPPs, we used advance molecular dynamics simulations in AMBER, simulating 5 distinct peptides together with 2 cell membranes with different lipid composition. To simulate the systems, we used enhanced sampling techniques: adaptably steered molecular dynamics and adaptably biased molecular dynamics

3. Result

The simulations showed that rubber and l-quebrachitol can interact in the highly hydrophobic environment of rubber particles. L-quebrachitol clearly shows a higher number of contacts with rubber molecules with α-termini having an alcohol group in their structure.

The CCPs incorporating Aib showed the lowest energies for internalization on both model membranes, with distinct internalization mechanisms depending on the lipid composition of the model membranes. The presence of Aib residues allows these CPPs to adopt amphipathic folding to efficiently penetrate through the membranes. The different internalization of them in membranes, suggests that the lipid composition of the membrane is important fot the efficient internalization of CPPs.

4. Conclusion

Specific α-terminal groups on rubber on its α-terminal groups could impact its unique physical and chemical properties of rubber molecules. The results provide significant insights into the internalization of the studied peptides and help to better understand how peptides can internalize into membranes.

5. Schedule and prospect for the future

We would like to extend the use of the supercomputer of the Quick User account to fiscal year 2022 to perform more molecular dynamics simulations with peptides.

Fiscal Year 2021 List of Publications Resulting from the Use of the supercomputer

[Paper accepted by a journal]

Joan Gimenez-Dejoz, Katsuhiko Tsunoda, Yasuo Fukushima, Keiji Numata. Computational study of the interaction between natural rubber α-terminal groups and L-quebrachitol, one of the major components of natural rubber. Polymer Journal, 54, pages 229–233 (2022)

Joan Gimenez-Dejoz, Keiji Numata. Molecular dynamics study of the internalization of cell-penetrating peptides containing unnatural amino acids across membranes. *Nanoscale Advances,* 4, 397-407 (2021)

[Conference Proceedings]

[Oral presentation]

T. Kurita, T. Terabayashi, K. Numata, S. Kimura, H. Uji.
"Nano-scale piezoelectric and mechanical properties of cyclic peptides"
3584988 (Oral presentation), Pacifichem2021, Online, December 16-21, 2021.

[Poster presentation]

T. Kurita, Joan Gimenez-Dejoz, S. Fujita, H. Uji. K. Numata.,
"Synthesis of novel cyclic peptides for inclusion of polymer chains and evaluation of their inclusion ability"
P3-086 (Poster presentation), The 11st CSJ Chemistry Festa, Online, October 19-21, 2021.

T. Kurita, Joan Gimenez-Dejoz, S. Fujita, H. Uji. K. Numata.,
"Synthesis of novel cyclic peptides for inclusion of polypeptides and characterization of their inclusion ability"
P-067 (Poster presentation), The 58th Japanese Peptide Symposium, Online, October 20-22, 2021.

[Others (Book, Press release, etc.)]