Laboratory of Biofunctional Materials Design

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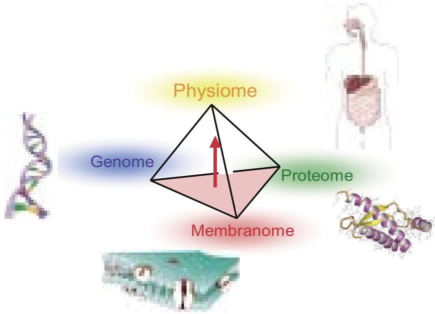
Membrane Stress Biotechnology based on the Life-Environment Minimum Unit (LEM-Unit) for the Bio-Sphere Membrane

The "Membranome" is defined as the sum total of all the information obtained from the study of "membranomics", which is the systematic and extensive accumulation of knowledge regarding the potential functions of the biomembrane, dynamically induced by environmental stresses. It has previously been reported that a model biomembrane, vesicle or liposome (closed phospholipid bilayer membrane with a boundary water layer) could induce a range of potential functions under stress conditions, including the molecular chaperone-like function, the protein translocation function and the aggregation/fusion functions. The study of membranome has, therefore, now become an important issue to elucidate the deeper understanding of biological systems and to help solve global environmental problems.



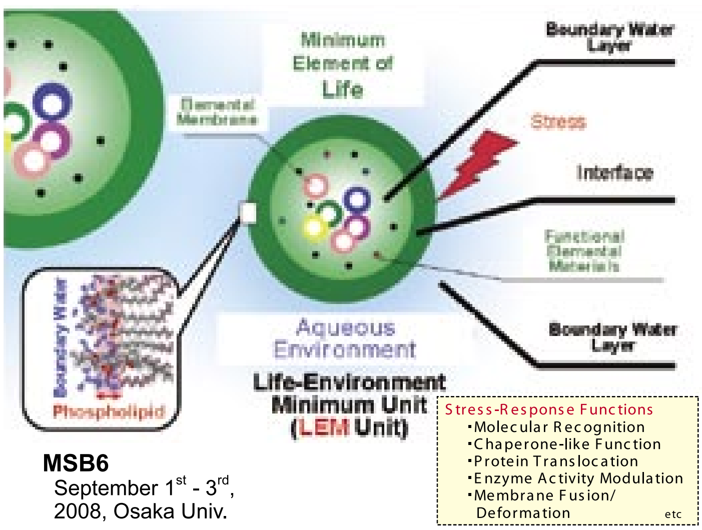
Here, we define the liposome as the "Life-Environment Minimum Unit (LEM-Unit)", which is the minimum unit required for elucidating preliminary biological functions under certain stressed environmental conditions and for harmonizing with other units and the "Bio-Sphere Membrane (BSM)", i.e. the global environment.

<u>Membrane-Based Understanding of Alzheimer's Disease (AD)</u>

(i) A key pathological peptide of AD, amyloid β-peptide (Aβ), has been reported to act as a metalloenzyme-like catalyst via the formation of complexes with copper ions. The activity of Aβ/Cu complexes involved in the oxidation of cholesterol or catecholamines was highly modulated by the membrane properties of the liposomes. (ii) The fibril formation, aggregation and polymerization could all be effectively controlled, especially on the surface of the oxidatively-damaged or fatty acid-modified liposome. (iii) The microdomain, formed by the fatty acids, cholesterol, oxidized lipids and so on, could play a key role in regulating the above membrane-related phenomena because of the control of the stabilization of hydrogen bonds along the main chain of the peptide. The above results may highlight potential problems with conventional drug design.

<u>Membrane-Based Sensing Systems</u>

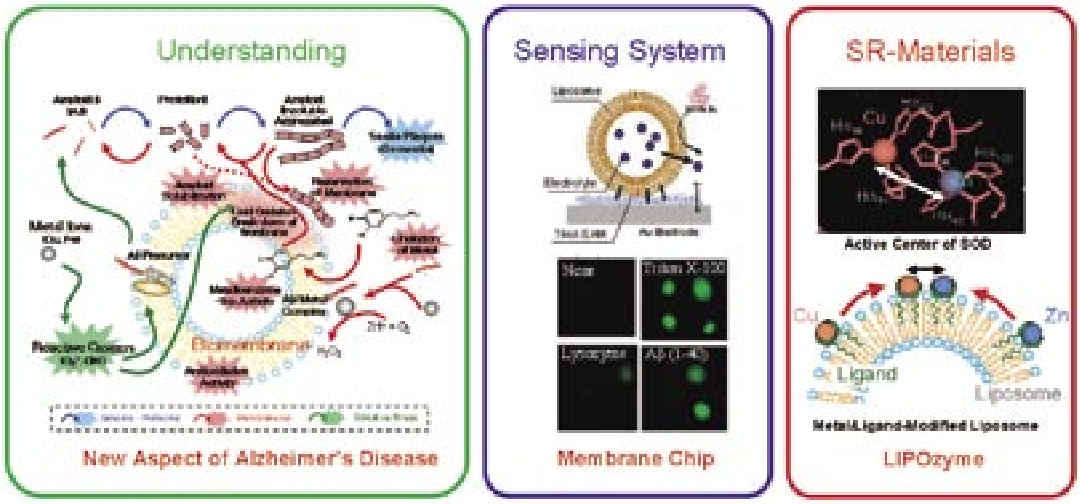
(i) Good progress is being made in the design and development of a "membrane chip" that is able to dynamically assess the stressed state of the liposome. (ii) A metal affinity immobilized liposome chromatography for the measurement of the metal-peptide complex has also been developed. (iii) Methods based on the dielectric dispersion phenomena have also been upgraded in order to characterize the dynamic properties of the membrane surface. The above methodologies could help resolve the quantitative properties of the membrane.



<u>Membrane-Based Stress Responsive Materials</u>

(i) LIPOzyme has been designed to elucidate the enzymatic function on the liposome and, as a case study, the antioxidative LIPOzyme elucidating dual activities of SOD and catalase has been developed. (ii) A membrane-based artificial organ which can support biological functions has also been developed.

It is considered that the above findings regarding the membranome could help lead the way to a new future for membrane stress biotechnology through the combined use of membrane-based sensing systems and membrane-based stress responsive materials.



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