Towards Structure Determination of Human Membrane Receptors

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The results of various genome projects have shown that up to 30% of human proteins occur in cell membranes. Membrane proteins play crucial roles in many biological functions and are of key importance for medicine. Over 50% of commercially available drugs target membrane proteins, GPCRs (G-protein coupled receptors). Kobayashi et al. have reported that by use of two lines of GPCRs (thromboxane A_2 (TXA_2) receptor and prostacyclin (PGI_2) receptor) knockout mice, TXA_2 receptor promotes and PGI_2 receptor prevents the initiation and progression of atherogenesis through control of platelet activation and leukocyte-endothelial cell interaction[1)].

In spite of the abundance and importance of membrane proteins, there are only 100 unique membrane protein structures in the Protein Data Bank. To address the technical bottlenecks preventing the structure determination of membrane proteins, we have recently started “ERATO human receptor crystallography project” supported by the Japanese Science and Technology Agency. We have also obtained a support from the Wellcome trust to establish an outstation of Imperial College London at the new UK synchrotron Diamond. I will discuss our strategy how to establish the structure determination method of human membrane proteins using these new facilities and its impact on biological sciences, pharmacology and medicine[2), 3), 4)].

[1] T. Kobayashi, Y. Tahara, M. Matsumoto, M. Iguchi, H. Sano, T. Murayama, H. Arai, H. Oida, T. Yurugi-Kobayashi, J.K. Yamashita, H. Katagiri, M. Majima, M. Yokode, T. Kita, and S. Narumiya. Roles of thromboxane A_2 and prostacyclin in the development of atherosclerosis in apoE-deficient mice. (2004) *J Clin Invest*, **114**, 784-794.

[2] http://www.hrc.jst.go.jp/jis_e_main.html

[3] http://www3.imperial.ac.uk/lifesciences/research/molecularbiosciences/membraneproteincrysta

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