

【Grant-in-Aid for Specially Promoted Research】

Science and Engineering (Engineering)



Title of Project : Bio-design for interface molecules in nano scale

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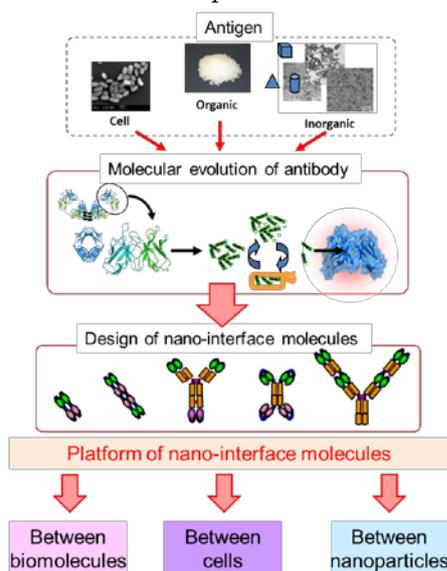
Research Area : Biofunction / Bioprocess

Keyword : Biofunction engineering

【Purpose and Background of the Research】

An attainment of molecular and nano-scale manipulations are expected to open the way for making an effective linkage among biomolecules and cells, and for fabricating bottom-up structures from nanomaterials. Recently, we focus on antibodies which have high-binding affinity for a specific antigen in immune system, and we have identified the antibodies with high affinity for low organic molecules, receptors on cells, and inorganic surfaces by using molecular evolution techniques.

In this study, we construct a new method by which antibodies against various materials in organic, inorganic, and biological fields can be generated. The generated antibody fragments are built up to multispecific molecules which can make an effective linkage between target materials (proteins, cells, and nanomaterials). We, further, physicochemically and biologically analyze the structure and function of the interface molecules in detail to optimize the function from the viewpoint of structural biology.



【Research Methods】

In this study, we focus the generation of interface molecules on the application to cancer immune therapy and nanotechnology. The antibody fragments with high affinity for the surfaces of

cancer cells, lymphocyte cells, and nanomaterials are generated by using molecular evolutionary methods, and multispecific molecules are designed from the fragments to construct interface molecules which can make an effective linkage between target materials. The designed molecules are carefully analyzed by X-ray structural and thermodynamic measurements to improve the function of interface molecules.

【Expected Research Achievements and Scientific Significance】

The interface molecules for proteins, cells, and nanomaterials are generated because the molecules play important roles in the fields of medicine, regenerative therapy, and nanotechnology; however, the methodologies are independently studied. The demonstration that antibodies can be almighty interface molecules would open the way for the construction of important and convenient operation unit for medicine, regenerative therapy, and nanotechnology.

【Publications Relevant to the Project】

- 1) R. Asano, M. Umetsu, I. Kumagai et al., Cytotoxic enhancement of a bispecific diabody by format conversion to tandem single-chain variable fragment (taFv), *J. Biol. Chem.*, **286**, 1812 (2011).
- 2) T. Hattori, M. Umetsu, Izumi Kumagai et al., High affinity anti-inorganic material antibody generation by integrating graft and evolution technologies, *J. Biol. Chem.*, **285**, 7784 (2010)

【Term of Project】 FY2012-2016

【Budget Allocation】 400, 000 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.che.tohoku.ac.jp/~kuma/index.htm>