

【Grant-in-Aid for Scientific Research(S)】
Science and Engineering (Engineering II)



Title of Project : Protein engineering design for biointerface molecules in nano world

Izumi Kumagai
(Tohoku University, Graduate School of Engineering,
Professor)

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.

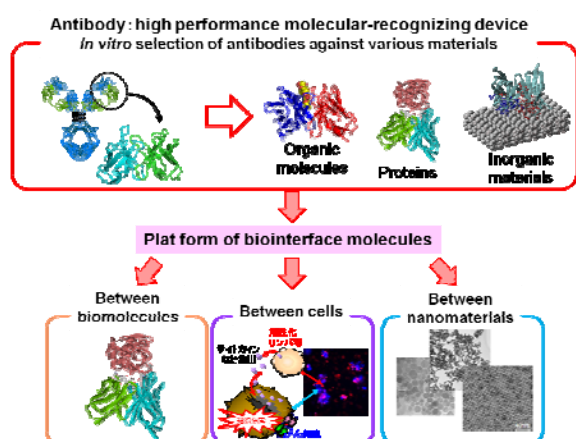


Fig.1 Almighty biointerface molecules from antibody fragment

【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) H. Watanabe, M. Umetsu, I. Kumagai *et al.*, Human anti-gold antibodies: Biofunctionalization of gold nanoparticles and surfaces with anti-gold antibodies, *The Journal of Biological Chemistry*, **283**, 36031-38 (2008)
- 2) R. Asano, M. Umetsu, I. Kumagai *et al.*, Highly effective recombinant format of a humanized IgG-like bispecific antibody for cancer immunotherapy with retargeting of lymphocytes to tumor cells *The Journal of Biological Chemistry*, **282**, 27659-27665 (2007)

【Term of Project】 FY2010-2014

【Budget Allocation】 167, 500 Thousand Yen

【Homepage Address and Other Contact Information】

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