

PEG-MODIFIED NANOPARTICLES FOR NEW MOLECULAR RECOGNITIONY.Nagasaki¹, T.Ishii¹, K.Uchida¹, H.Otsuka² & K.Kataoka²¹Department of Materials Science, Tokyo University of Science, Noda 278-8510, Japan.²Department of Materials Science, Graduate School of Engineering, The University of Tokyo, Tokyo 113-8656, Japan.

INTRODUCTION: In the case of microanalysis in a crude sample such as serum, nonspecific adsorption of various proteins and lipids to the surface is an important consideration to achieve specific biosensing with high S/N ratio. In order to avoid the nonspecific adsorption, many types of modification on the sensor surface have been considered. Modification by poly(ethylene glycol) (PEG) tethered chains leads to reduce the nonspecific interaction of biomolecules such as proteins and cells with biomedical devices because PEG is a nontoxic and hydrophilic polymer with low interfacial free energy in water and high-chain mobility inducing excluded volume effects.

In this paper, we are focusing on preparation of complete non-fouling surface by mixed PEG tethered chain, which denotes the introduction of short under-brushed PEG layer to the surface pre-modified with comparatively long PEG chain resulted. By using our original heterotelechelic PEG, which means PEG having a functional group at one end and another functional group at the other chain end quantitatively, ligand-installed non-fouling surface was constructed.

EXPERIMENTS: CHO-PEG-SH and CHO-PEG-b-poly(2-N,N-dimethylaminoethyl methacrylate) (CHP-PEG/PAMA) were synthesized by our original method^{1,2}. Protein adsorption measurements were carried out using surface plasmon resonance analyzer (BIAcore 3,000) after the bare gold surface was modified by the prepared PEG samples. Gold and semiconductor nanoparticles were modified in the same manner as the gold sensor surface and used for high sensitive molecular recognition.

RESULTS and DISCUSSION: Figure 1 shows performances of protein adsorption character of SPR sensor chip coated by PEG tethered chains as a function of protein sizes. In the case of dextran gel as a control, non-specific adsorption was avoided to some extent in the case of high molecular weight protein. With decreasing the size of the protein, the non-specific adsorption increased significantly. The conventional PEG tethered chain surface suppressed the non-specific adsorption of the proteins possessing the molecular weight higher than 10kD. However, it is not enough performance for the

protein lower than 10kD. In the case of the mixed PEG tethered chain surface, complete non-fouling character was observed. Especially, the mixed PEG tethered chain avoided tetrapeptide (RGDS, MW=450), which is anticipated as ideal biomaterials surface.

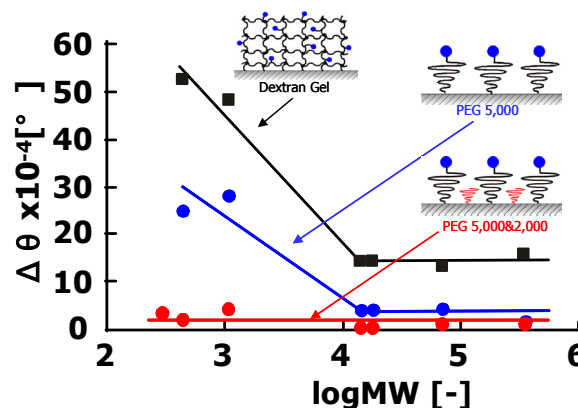


Fig. 1: Protein adsorption on SPR sensor chip modified by heteroPEG as a function of protein size.

By using the same technique, nano-sized gold and semiconductor particles were modified by the heteroPEG in order to improve both non-fouling character and high dispersion stability even in high salt concentration conditions. In this case, CHO-PEG/PAMA was also used as a surface modification agent. For example, stabilized CdS semiconductor nanoparticle was prepared by a simple coprecipitation method of Cd²⁺ with S²⁻ in the presence of CHO-PEG/PAMA block copolymer to form nano-sized crystal. The block copolymer coordinated on the growing CdS crystal to control the size of the particle. At the same time, the block copolymer stabilized the formed CdS particle. The installation of biotin moiety at the PEG chain end made feasible to recognize specific affinity with streptavidin. By the labeling streptavidin with fluorescent probe, TexasRed in this study, an effective FRET was observed, which can be utilized for a high sensitive detection of the protein.

REFERENCES: ¹Y.Akiyama, et al., Bioconj.Chem., 11, 947(2000). ²Kataoka, et al. Macromolecules, 32, 6892(1999).