

Rapid Generation of Monoclonal Antibodies by the ADLib System

○Kunihiro Ohta¹, and Hidetaka Seo^{1,2}

(¹ Genetic Dynamics Research Unit, RIKEN Discovery Res. Inst.; ² Chiome Bioscience Inc.)

Tel: +81-48-467-9277, Fax: +81-48-462-4671, e-mail: kohta@riken.jp

In chicken immune systems, gene conversion is primarily involved in the diversification of immunoglobulin (Ig) gene. Chromatin structure and its local changes mediated by histone acetylation play crucial roles in the regulation of homologous DNA recombination such as the gene conversion and meiotic recombination in immune and meiotic cells. To study roles of histone modification in gene conversion at Ig locus, we treated chicken B cell-derived DT40 cells with histone deacetylase inhibitor trichostatin A (TSA). After the TSA treatment for 6-8 weeks, more than 90% of the cell population underwent diversification of Ig locus mainly due to induced gene conversion events. This result indicates that the TSA-treatment induces the autonomous diversification of the surface IgM (sIgM).

Using these effects, we have newly developed a B-cell based rapid *in vitro* system to generate specific antibodies against antigens (Seo et al., *Nature Biotech.* 23:731, 2005). Magnetic beads conjugated with various antigens were applied to perform panning of DT40 cells producing specific antibody. We have succeeded to isolate many clones that produce monoclonal antibodies specifically reactive with antigens within one week. ELISA (and SPR in some cases) experiments revealed that those monoclonal antibodies exhibit high specificity to the antigens. It should be noted that antibodies against self-antigens and small molecules could be easily isolated in this method. This system (ADLib: Autonomously Diversifying Library) has a remarkable advantage in establishment of the antibody specificity, and has possibility of future applications for rapid and flexible design of specific monoclonal antibodies applicable to various biological sciences.