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Transgenic bovine system to produce fully human IgG polyclonal antibodies to fight infectious diseases

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Antigen-specific human polyclonal antibodies (hpAbs), produced by hyper-immunization, could be useful for treating a wide variety of human diseases, including infectious diseases. Here, we report on a transchromosomic (Tc) bovine system capable of producing a large volume of hyperimmune hpAbs. Tc cattle were generated by transferring a human artificial chromosome (HAC) vector carrying the entire unrearranged, human immunoglobulin heavy (hIGH) and κ light (hIGK) chain loci and by inactivating the two endogenous bovine heavy chain loci (bIGH). The oldest animal produced >2 g/l of hIgG, paired with either (hIgκ, ~500 μg/ml, fully human) or bovine (chimeric) light chain in plasma with a normal hIgG subclass distribution. Hyper-immunization with anthrax protective antigen resulted in a hIgG-mediated humoral immune response and a high proportion of antigen-specific hIgG. Purified, fully and chimeric hIgGs were both shown to be highly active in an in vitro toxin neutralization assay and protective in an in vivo mouse challenge assay. These results demonstrate that Tc cattle could be useful as a source of antigen-specific hyper-immune hpAbs that could fight human infectious diseases (Kuroiwa, Y. et al. Nature biotechnology 27, 173-181, 2009). Recently, we have developed a system to also generate recombinant, fully hIgG antibodies from Tc bovine.

Biography

Kuroiwa acquired his Ph.D. in molecular genetics from Tokyo Institute of Technology, Japan, studying genomic imprinting in mammals. Right after his Ph.D. work, he joined KIRIN Brewery, CO. LTD., to develop its original chromosome engineering technology and contributed to generation of transgenic mice producing human antibodies for human therapy. This achievement was highly recognized and he moved to US to join Hematech Inc to lead a project of transgenic cattle producing human polyclonal antibodies to treat a wide variety of human diseases, as a Research Director of Molecular Genetics department. He established an efficient genetic modification system in cattle and produced the world's first transchromosomic and knockout cattle. As of July 1st in 2009, he became a Chief Scientific Officer (CSO) of Research division in Hematech.

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