ABSTRACT OF THE DISCLOSURE

Generation of Xenogeneic Antibodies

The subject invention provides non-human mammalian hosts characterized by inactivated endogenous Ig loci and functional human Ig loci for response to an immunogen to produce human antibodies or analogs thereof. The hosts are produced by multiple genetic modifications of embryonic cells in conjunction with breeding. Different strategies are employed for recombination of the human loci randomly or at analogous host loci. Chimeric and transgenic mammals, particularly mice, are provided, having stably integrated large, xenogeneic DNA segments. The segments are introduced by fusion with yeast spheroplasts comprising yeast artificial chromosomes (YACs) which include the xenogeneic DNA segments and a selective marker such as HPRT, and embryonic stem cells.

Fig. 1.