Development of human Fab antibodies against human death receptors and death decoy receptors from a phage display library

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Tumor necrosis factor (TNF) family cytokine, Apo2L, and its death receptors (DRs) is a unique system which exhibits cancer-specific apoptosis-inducing activity without significant cytotoxicity on normal cells due to the overexpression of death decoy receptors (DcRs) which compete with DRs for the binding of Apo2L in normal cells. Thus selective, bispecific targeting for DRs and DcRs with proapoptotic antibodies is an attractive strategy for the efficient cancer therapy. Phage display is a technique used to establish antibody libraries in vitro without immunization and select antigen-specific antibodies, usually singe chain variable fragment (scFv) or antigen binding fragment (Fab)[(1,2)]. Here we constructed a phage-displayed nonimmune human Fab library using pComb3X system. From this library, a panel of DR5 and DcR1-specific human Fab antibodies were isolated by several rounds of panning. The selected Fab antibodies showed high specific affinity (~ 1 nM) and no cross reactivity with DR5 and DcR1, measured by ELISA and Biacore. Cancer-cell specific apoptosis activity will be presented using several model cancer and normal cell lines.

References

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