Combination of phage and Gram-positive bacterial display of human antibody repertoires enables isolation of functional high affinity binders - DTU Orbit (29/03/2019)

Combination of phage and Gram-positive bacterial display of human antibody repertoires enables isolation of functional high affinity binders

Surface display couples genotype with a surface exposed phenotype and thereby allows screening of gene-encoded protein libraries for desired characteristics. Of the various display systems available, phage display is by far the most popular, mainly thanks to its ability to harbour large size libraries. Here, we describe the first use of a Gram-positive bacterial host for display of a library of human antibody genes which, when combined with phage display, provides ease of use for screening, sorting and ranking by flow cytometry. We demonstrate the utility of this method by identifying low nanomolar affinity scFv fragments towards human epidermal growth factor receptor 2 (HER2). The ranking and performance of the scFv isolated by flow sorting in surface-immobilised form was retained when expressed as soluble scFv and analysed by biolayer interferometry, as well as after expression as full-length antibodies in mammalian cells. We also demonstrate the possibility of using Gram-positive bacterial display to directly improve the affinity of the identified binders via an affinity maturation step using random mutagenesis and flow sorting. This combined approach has the potential for a more complete scan of the antibody repertoire and for affinity maturation of human antibody formats.

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