Immunome Res 2016, 12:2(Suppl)
http://dx.doi.org/10.4172/1745-7580.C1.006

Preferential germline usage and VH/VL pairing observed in human antibodies selected by mRNA display

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Since the invention of phage display, *in vitro* antibody display technologies have revolutionized the field of antibody discovery. In combination with antibody libraries constructed with sequences of human origin, such technologies enable accelerated therapeutic antibody discovery while bypassing the laborious animal immunization and hybridoma generation processes. Many *in vitro* display technologies developed since aim to differentiate from phage display by displaying full-length IgG proteins utilizing eukaryotic translation system and codons increasing library size or real-time kinetic selection by fluorescent activated cell sorting. We report here the development of mRNA display technology and an accompanying HCDR3 size spectratyping monitor for human antibody discovery. Importantly, the mRNA display technology maintains a monovalent linkage between the mRNA (genotype) and display binding protein (phenotype), which minimizes avidity effect common in other display systems and allows for a stringent affinity and off-rate selection. The mRNA display technology successfully identified 100 human antibodies in fifteen different selections against various targets from naive human antibody libraries. These antibodies in general have high affinity and diversity. By analyzing the germline usage and combination of antibodies selected by the mRNA display technology, we identified trends and determined the productivity of each germline subgroup in the libraries that could serve as the knowledge base for constructing fully synthetic, next generation antibody libraries.

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Local antibody as a correlate of protection against influenza infection

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In spite of there being a vaccine, influenza is still a major cause of disease and we still do not fully understand how influenza vaccines protect against infection (correlates of protection). Antibody is a key candidate, but the optimum subtype, location and specificity are not known. The need for greater understanding about protection from influenza is timely because of the recent introduction of live attenuated influenza vaccine (LAIV) into the childhood vaccination schedule (2013/14 season). It has been suggested that LAIV induces broader protection than inactivated vaccine, however, for unknown reasons LAIV is not fully protective against the circulating H1N1 virus, possibly because it fails to induce antibody. We use mouse models and clinical studies to measure the relative roles of antibody compared to other components of the immune response.

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