High throughput screening of phage display libraries for production of fully human antibodies challenged to cells expressing native claudin-1

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Monoclonal antibodies (mAbs) represent valuable tools in many biological fields. Screening of antibody libraries by phage display allows for rapid selection of single-chain variable fragments (scFvs). In the paradigm of viral hepatitis the availability of mAbs preventing hepatitis C virus (HCV) infection of hepatocytes is an active field of investigation within medical biotechnologies. We describe a complete pipeline for high-throughput screening of libraries by next-generation sequencing (NGS) approach, to select human scFv against native Claudin-1, a tight-junction protein involved in hepatitis C virus infection. Our strategy allows to rapidly identify the potential binders of a given antigen, based on the counts of the corresponding scFv fragments, within a cycle, and on the kinetic of their enrichments, within consecutive cycles. After their identification, the clones of interest need to be recovered from the DNA sub-library of the relevant selection cycle, for validation of binding. Thus, we also implemented a rapid and effective method, for one-step recovery of scFv. The checked clones were successfully converted to active IgG4 antibodies and produced in a scale-down process, thus demonstrating the effectiveness of the whole procedure. This novel approach provides rapid and cheap isolation of antibodies for virtually any native antigen involved in human diseases, for therapeutic and/or diagnostic applications.