Recombinant approach to develop ScFv antibodies and vaccines against viral diseases as Ebola, flu (AH1N1) and cancer (polyomavirus)

Luis Mario Rodriguez-Martinez

Instituto Tecnologico y de Estudios Superiores de Monterrey,

Mexico, Vaccine tech Inc., USA

Abstract

Currently, production of vaccines and diagnostic systems for infectious diseases has failed to provide a systematic vision that merges state-of-the-art technologies with industry to provide an effective commercial solution. Infectious and rapidly transmitted diseases, such as cancer, Ebola and influenza, should be a focus of interest for these prospects. While technological advances of recent years have been revolutionizing the life sciences industry, specifically in the biopharma field, these advances have been disproportional in terms of their applications towards infectious diseases. Working on the development, recombinant technology is needed for the production of chimeric proteins using mammalian, yeast, and bacterial cells modified for those purposes. Proteins developed through a process of molecular engineering, which begins with in silico bioinformatic processes, using validations and algorithms, subsequently through synthetic biology, molecular biology, genetic engineering, and Bioprocess development. The aim being, the scaling efforts towards pilot plant levels. The primary goal of these proteins is the development of integrated solutions that can be used as antigens or antibodies in diagnostic systems, as well treatments and vaccines. The main challenge is in the final application that results in the free exposure of epitopes for recognition between the antibody and the antigen of interest, which implies their effectiveness in terms of use. A secondary challenge is productivity rates in bio-production systems, which vary greatly depending on the platform used and the quality of the bioprocess developed. The recombinant proteins HA-RBD, tAg, scFv-13F6, scFv-13C6 and Fab-KZ52 were designed, developed, expressed and characterized by the integral use of molecular engineering and bioprocess engineering. The expressed proteins showed biological antibodies (HA-RBD and tAg) and antigen (scFv-13F6 and scFv-13C6) recognition, recognizing specific epitopes. Significantly tAg production occurred with a yield of 50 mg L-1 and HA-RBD protein was produced in 120 mg L-1Antibodies are essential molecules for diagnosis and treatment of diseases caused by pathogens and their toxins. Antibodies were integrated in our medical repertoire against infectious diseases more than hundred years ago by using animal sera to treat tetanus and diphtheria. In these days, most developed therapeutic antibodies target cancer or autoimmune diseases. The COVID-19 pandemic was a reminder about the importance of antibodies for therapy against infectious diseases. While monoclonal antibodies could be generated by hybridoma technology since the 70ies of the former century, nowadays antibody phage display, among other display technologies, is robustly established to discover new human monoclonal antibodies. Phage display is an in vitro technology which confers the potential for generating antibodies from universal libraries against any conceivable molecule of sufficient size and omits the limitations of the immune systems. If convalescent patients or immunized/infected animals are available, it is possible to construct immune phage display libraries to select in vivo affinity-matured antibodies. A further advantage is the availability of the DNA sequence encoding the phage displayed antibody fragment, which is packaged in the phage particles. Therefore, the selected antibody fragments can be rapidly further engineered in any needed antibody format according to the requirements of the final application. In this review, we present an overview of phage display derived recombinant antibodies against bacterial, viral and eukaryotic pathogens, as well as microbial toxins, intended for diagnostic and therapeutic applications. Virus-like particles (VLPs) are virus-derived structures made up of one or more different molecules with the ability to self-assemble, mimicking the form and size of a virus particle but lacking the genetic material so they are not capable of infecting the host cell. Expression and self-assembly of the viral structural proteins can take place in various living or cell-free expression systems after which the viral structures can be assembled and reconstructed. VLPs are gaining in popularity in the field of preventive medicine and to date, a wide range of VLP-based candidate vaccines have been developed for immunization against various infectious agents, the latest of which is the vaccine against SARS-CoV-2, the efficacy of which is being evaluated. VLPs are highly immunogenic and are able to elicit both the antibody- and cell-mediated immune responses by pathways different from those elicited by conventional inactivated viral vaccines. However, there are still many

challenges to this surface display system that need to be addressed in the future. VLPs that are classified as subunit vaccines are subdivided into enveloped and non- enveloped subtypes both of which are discussed in this review article. VLPs have also recently received attention for their successful applications in targeted drug delivery and for use in gene therapy. The development of more effective and targeted forms of VLP by modification of the surface of the particles in such a way that they can be introduced into specific cells or tissues or increase their half-life in the host is likely to expand their use in the future. Recent advances in the production and fabrication of VLPs including the exploration of different types of expression systems for their development, as well as their applications as vaccines in the prevention of infectious diseases and cancers resulting from their interaction with, and mechanism of activation of, the humoral and cellular immune systems are discussed in this review.

Biography:

Luis Mario Rodriguez-Martinez has his expertise in Virology and Bioprocess Development. He is working with recombinants and their applications against viral diseases as Influenza, Ebola and Members of the Polyomaviride family like the newly discovered MCPyV. He is a Scientist and Innovation Manager with expertise in Prototype Technology projects those results in commercial technology (i.e. High fidelity DNA polymerase under commercialization, vaccines and Monoclonal antibodies, licensed). He is an Advisor of technological companies in USA and Mexico. He is part in Mexico from SNI (National Researchers System) from CONACYT.

E-mail: luisrm@yahoo.com