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Immunoglobulin Light-Chain Partners: Key to high yields of recombinant monoclonal antibodies in transient transfection systems?

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In the 1990s, the first monoclonal antibodies (mAbs) were Food and Drug Administration (FDA) approved as cancer therapies. Since then, this field has expanded rapidly. The initially approved mAbs are IgGs. Clinical trials have been performed with IgM mAbs. Recombinant mAb technology cannot only generate IgG mAbs, but also mAbs of other immunoglobulins (Ig) classes, including recombinant IgM and dimeric IgAs (dIgAs). Our group has systematically examined the potential of recombinant mAbs of different Ig classes to block mucosal transmission of simian-immunodeficiency virus (SHIV) in nonhuman primates and used it as a model system for blocking mucosal human immunodeficiency (HIV-1) transmission in humans.

Generation of polymeric recombinant mAbs can present technical challenges. When constructing isogenic recombinant IgM/IgG pairs, we discovered that mu (μ) heavy chains strongly prefer partnering with lambda (λ) light chains for optimal IgM expression in a transient cotransfection system. When μ chains were paired with kappa (κ) light chains, IgM yields were low but increased by logs – up to 20,000 X – by using λ chains instead. Switching light chains did not alter epitope specificity. For dIgA2, optimal expression involved pairing with λ chains, whereas light chain preference varied for other Ig classes. In summary, the production of recombinant IgM can be markedly increased by using λ chains, an important aspect of clinical studies.

Recent Publications

1. Ruth M Ruprecht, et.al, (2022). Antibody light chains: key to increased monoclonal antibody yields in Expi293 cells?. Antibodies; 11(2):37.

2. Ruth M Ruprecht, et.al, (2021). Cooperation between systemic IgG1 and mucosal dimeric IgA2 monoclonal anti-HIV Env antibodies: passive immunization protects Indian rhesus macaques against mucosal SHIV challenges. Frontiers Immunology; 12:705592.

3. Ruth M Ruprecht, Siqi Gong, (2020). Immunoglobulin M: an ancient antiviral weapon – rediscovered. Front Immunol; 11:1943

Biography

Ruth Ruprecht completed her PhD at Columbia University, USA, and her MD at the University of Miami School of Medicine, USA; she is board-certified in Internal Medicine and Medical Oncology. She served as a tenured Professor of Medicine at the Dana-Farber Cancer Institute and Harvard Medical School and is currently a Senior Professor of Research at the University of Louisiana at Lafayette, USA. She has published more than 200 peer-reviewed papers (cited more than 13,000 times); her publication H-index is 57. She is the inventor of several patents, including a cancer vaccine approach. She has been serving as a Member of Scientific Advisory Boards, as an Associate Editor/Editorial Board Member of highly regarded Journals, and as a Consultant for WHO and pharmaceutical companies. She has received a number of honors, including being named Honorary Professor of the Institute of Medical Biology at the Chinese Academy of Medical Science at Peking Union Medical College, Kunming, PRC

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