IGg rheumatoid factors isolated by the surface-displaying phage library technique

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摘要

Abstract

Our analysis of IgG rheumatoid factors (RFs) from three patients with rheumatoid arthritis (RA) revealed that most contained significant numbers of skewed mutations per V region, suggesting that these RFs arose from antigen-driven responses. To further study IgG RFs in RA, we used pComb3 vector to construct an IgG1, λ combinatorial antibody library from a synovial fluid sample. After panning against human IgG, Fab fragments from 71/96 phage clones bound to Fc-coated wells. Sequence analysis of 20 randomly chosen Fc-binders showed that 17 (85%) clones had identical heavy (H) and light (L) chain V regions, represented by Humha311 and Humla211, respectively. Of the remaining three clones, two had the same Humla211 L chain, but each with a different H chain V region. All the putative germline V genes for these RFs also encode RF in RA patients. However, none of these RF V regions are similar to those of the two IgG RFs derived by the hybridoma technique from the same synovial fluid. The Humha311 H chain has two frameshifts: a one-base insertion upstream of the JH region and a four-base deletion near the end of the CH1 region, resulting in a mainly unconventional amino acid sequence in the CH1 region. In the future, it will be important to study the presence of IgG molecules with such unconventional CH1 amino acid sequences, and the effects of these amino acid sequences on the structures and immunological properties of the IgG molecules