

Biological effects in vitro of monoclonal antibodies to human epidermal growth factor receptors.

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Abstract

Four mouse hybridomas secreting monoclonal immunoglobulin G (IgG) antibodies to epidermal growth factor (EGF) receptors of A431 cells were obtained independently from four fusion experiments. Three of the antibodies, 528 IgG, 225 IgG, and 579 IgG, inhibited the binding of [¹²⁵I]EGF to A431 cells by at least 95%, and they competed with each other for binding to A431 cells. These antibodies bound to A431 cells, HeLa-S cells and human foreskin fibroblasts with dissociation constants in the range of $K_d = 0.6 \times 10^{-9}$ to 2.5×10^{-9} M. The fourth monoclonal antibody, 455 IgG, bound to A431 cells with lower affinity ($K_d = 2.0 \times 10^{-8}$ M), and it had no effect on the binding of either EGF or the other antibodies to A431 cells. All four antibodies immunoprecipitated EGF receptors from Triton X-100 extracts of A431 membranes, but they were unable to bind to three rodent cell lines. In biological assays, none of the antibodies was able to mimic EGF. The antibodies which inhibited the binding of EGF blocked EGF-enhanced phosphorylation of A431 membrane proteins and inhibited EGF induced human fibroblast proliferation. These three antagonistic antibodies also partially reversed the inhibition of A431 growth by EGF. In contrast, 455 IgG had no effect on the early or delayed cellular responses to EGF.

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