

25a Egf Receptor Signaling Affects Retroviral Gene Transfer to Primary Epidermal Cells

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Although a lot of progress has been made in the molecular biology of retroviral vector design, the interactions of recombinant retrovirus with the host cells remains largely elusive. Here we report our findings on the role of EGF signaling in retrovirus mediated gene transfer to human epithelial cells. Surprisingly, growth factors such as EGF and HGF decreased retroviral gene transfer to epidermal cells and this effect could be reversed by an EGF receptor antibody, an EGFR phosphorylation inhibitor and an inhibitor of novel and atypical PKC isoforms. In contrast, inhibitors of classical PKCs had no effect. Abolishing PKC activity by treatment with the phorbol ester, PMA also abolished the effect of EGF, further supporting a possible PKC involvement in retroviral gene transfer. Multiple PKC isoforms have been shown to affect EGF signaling either directly or through downstream effectors of the MAPK pathway such as Ras and Raf-1. We are currently employing a siRNA based strategy to block several PKC isoforms in a specific manner in order to explore the mechanism of EGFR signaling in retrovirus-cell interactions. Knowledge of these interactions may inspire novel strategies to promote gene transfer as well as to reduce unwanted effects of recombinant retrovirus, especially when administered in vivo.