Expression of epidermal growth factor receptor in neoplastic pituitary cells: evidence for a role in corticotropinoma cells.

Abstract:
The oncogenic effects of epidermal growth factor (EGF) have long been established. EGF receptor (EGFr) is overexpressed in many types of tumors and constitutes a target for cancer treatment. The pituitary gland is a target of EGF action and it is very likely that EGFr plays a role in pituitary tumor formation and progression. However, there is a controversy in the literature concerning EGFr expression in the different types of pituitary adenomas. In the present study we investigated the expression pattern of the wild type EGFr (EGFrWT) and the constitutively active variant III (EGFrIII) at the mRNA and protein levels in a large series of pituitary tumors. EGFrWT was found in a high percentage of hormone-secreting tumors, but only in a small fraction of non-functioning pituitary adenomas, while no expression of the EGFrIII could be detected by nested RT-PCR in any tumor. Among the hormone-secreting adenomas, the highest incidence of EGFr expression was found in Cushing’s pituitary adenomas. Furthermore, immunohistochemistry for the phosphorylated EGFr revealed the presence of activated EGFr in most Cushing’s adenomas, compared with most pituitary adenomas. Taking into account that downregulation of p27/Kip1 plays a significant role in corticotrope tumorigenesis and that EGFr mitogenic signaling results in
decreased p27/Kip1, we searched for a correlation between EGFr expression and p27/Kip1 levels in corticotropinomas. Low p27/Kip1 immunoreactivity was observed in corticotropinomas expressing EGFr. On the other hand, somatotropinomas expressing EGFr had high p27/Kip1 immunoreactivity. These data suggest a corticotrope-specific phenomenon and indicate that EGFr may have a role in the unbalanced growth of corticotrope tumoral cells.