Mol Cell Biochem. 1994 Jan 12;130(1):1-9.

In vitro inhibition of the actions of basic FGF by a novel 16 amino acid peptide.

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Abstract

A composite procedure involving molecular modelling and a property-pattern algorithm, the Resonant Recognition Model (RRM), has been applied to structure-function studies with basic fibroblast growth factor (bFGF). Property-pattern characteristics for biological activity and receptor recognition for a group of FGF-related proteins were defined and then used to aid the design of a set of peptides which can act as bFGF antagonists. Molecular modelling techniques were then employed to identify the peptide within this set with the greatest conformational similarity to the putative receptor domain of bFGF. This 16 amino acid residue peptide (16mer), which exhibits no sequence homology to bFGF, antagonised the stimulatory effect of bFGF on fibroblast [3H]thymidine incorporation and cell proliferation, but exerted no effect itself in these in vitro bioassays.

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Y-box binding protein, YB-1, as a marker of tumor aggressiveness and response to adjuvant chemotherapy in breast cancer.

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Abstract

The Y-box binding protein 1 (YB-1) regulates gene expression through transcription and translation. YB-1 has been shown to be associated with up-regulation of P-glycoprotein (Pgp), an ATP-binding transporter involved in multi-drug resistance. In this study, we determined the prognostic significance of YB-1 and its relationship with Pgp in patients with breast cancer. YB-1 and Pgp expression were evaluated by immunohistochemistry in resected specimens of infiltrative ductal breast cancers from 99 patients and 57 patients respectively and correlated with clinicopathological parameters and adjuvant chemotherapy regimes. The antibody for the YB-1 protein was prepared by injecting a rabbit with a purified recombinant chicken YB1 protein. The relationship between YB-1 and Pgp was also evaluated by a computational approach using the Resonant Recognition Model (RRM). We found that breast tumors which were both estrogen receptor-negative and lymph node positive were associated with high YB-1 expression (P=0.017). In patients who did not receive adjuvant chemotherapy, recurrence risk was reduced in breast cancers having lower YB-1 expression (P=0.034), suggesting that high levels of YB-1 expression in breast cancer is associated with tumor aggressiveness. We were able to demonstrate a direct interaction between YB-1 and Pgp using the computer-based RRM. Interestingly, we found that patients who were on a chemotherapy regime which contained an anthracycline (a Pgp substrate) and subsequently developed recurrence, had a higher YB-1 score compared to patients on the Cyclophosphamide/Methotrexate/5-Fluorouracil regime (P=0.024). YB-1 expression in breast cancer may be a potential marker of chemoresistance and could possibly aid in selection of the appropriate adjuvant chemotherapy regime for breast cancers.