Lack of C-erbB-2 protein expression in pulmonary carcinoid tumours

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Abstract

To determine if amplification of the *C-erbB-2* proto-oncogene could be correlated with prognosis in carcinoid tumours, 49 pulmonary carcinoid tumours (26 typical, 23 atypical) were examined using a polyclonal antibody to the C-terminal peptide of the *C-erbB-2* protein sequence. No *C-erbB-2* gene product could be shown: the demonstration of *C-erbB-2* does not seem to help, therefore, in determining diagnosis or prognosis in pulmonary carcinoid tumours.

C-erbB-2 is a proto-oncogene present on chromosome 17¹ which encodes a 18.5 kilodalton transmembrane glycoprotein with tyrosine kinase activity.² Amplification of the *C-erbB-2* gene has been seen in gastric³ and breast carcinomas. In the latter, amplification has been correlated with relapse and survival.⁴ Gene amplification has been shown to be closely associated with immunohistochemical assessment of the gene product in both frozen and paraffin wax embedded material.⁵ We were interested to see if immunohistochemical assessment of the *C-erbB-2* gene product would be of value as a prognostic indicator in carcinoid tumours of the lung.

We therefore looked at 49 formalin fixed, paraffin wax embedded carcinoid tumours of the lung, of which 26 were typical and 23 were atypical, using a polyclonal antibody to the C-terminal peptide of the *C-erbB-2* protein sequence.⁶ The antibody was kindly provided by Dr B Gullick, Imperial Cancer Research Fund, London. A breast carcinoma known to be positive for the *C-erbB-2* oncoprotein was used as the positive control and primary antibody was omitted as the negative control. The primary antibody was used at a concentration of 5.2 µg/ml and sections were kept at 4°C overnight. The sections were washed in

phosphate buffered saline (PBS) the next day and then incubated for an hour with secondary antiserum (biotinylated swine anti-rabbit immunoglobulin) (Dakopatts) at a dilution of 1 in 100 in PBS. After further washing in TRIS-buffered saline (TBS) the sections were treated for 60 minutes with swine antirabbit (1 in 100 dilution). A further wash for 30 minutes in TBS was followed by peroxidase antiperoxidase (1 in 100) for 60 minutes, then a further wash in TRIS buffered saline for 30 minutes. Peroxidase activity was shown using diaminobenzidine solution. Nuclei were counterstained with haematoxylin.

The breast carcinoma showed focal strong membrane staining of the malignant cells with some diffuse, granular, cytoplasmic staining. All the 49 carcinoid tumours, however, were negative. Diffuse cytoplasmic staining of bronchial chondrocytes was noted in some sections, but no membrane staining was observed.

This study shows that *C-erbB-2* oncoprotein is not expressed by carcinoid tumours of the lung and therefore immunohistochemical assessment of the *C-erbB-2* gene product is of no value in determining diagnosis or prognosis.

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