

Anti-Epidermal Growth Factor Receptor (EGFR) Antibodies

ICR Licensing Opportunity November 2012

- Several rat monoclonal antibodies against human EGF receptor are available
- High affinity binding to EGFR
- Inhibit growth in vitro and in vivo of a number of human tumours that over-express EGFR
- Block the binding of EGF, TGF α and HB-EGF to the EGFR
- Induce terminal differentiation in tumour cells
- One antibody has been in Phase I trial in H&N / lung cancer

Background

Epidermal growth factor and its receptor are involved not only in the regulation of normal cell proliferation and differentiation but also when over-expressed, are linked to a number of human malignancies including cancer of the breast, brain, bladder, head and neck, pancreas and lung.

Over-expression of the receptor is often accompanied by the production of one or two of its ligands (EGF and/or TGF α) by the same tumour suggesting that an autocrine loop may be responsible for the growth of these tumours.

Thus EGFR receptor is an excellent target due to:

- The high level of expression of the EGFR by squamous cell carcinomas compared to normal tissues
- The ligand induced activation of tumour cells acts primarily via receptors on the cell surface
- The important role of the receptor in signal transduction

EGFR Antibodies and Cancer

A panel of antibodies has been raised against four epitopes on the external domain of the EGFR.

Results in vitro show that eight of the antibodies completely inhibit the growth of head and neck carcinoma cell lines and restrict the growth of breast and vulval carcinoma cell lines over-expressing the EGFR.

Result in vivo show that three of the antibodies cause complete regression of established head and neck tumour xenografts. One antibody induced complete regression of xenografts of a breast carcinoma.

Receptor blockade by these antibodies has also been shown to induce terminal differentiation (ie the cellular reversion to normal phenotype) of squamous cell carcinomas which over-express the EGF receptor.

The panel of antibodies includes high affinity binders which have diagnostic and therapeutic potential.

Phase I Clinical Trial

The purpose of this study was to determine the effect of one anti-EGFR rat monoclonal antibody to the EGFR in a phase I clinical trial in patients with unresectable squamous cell carcinomas. Eleven patients with squamous cell carcinoma of the head and neck and nine patients with squamous cell carcinoma of the lung, whose tumours expressed EGFR, were recruited.

Results showed that:

- antibodies could be detected in the sera of the patients.
- localisation of the antibodies to the membranes of the tumour cells was detected.
- Only 4/20 patients showed HARA responses

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Therefore it was shown that EGFR antibodies can be administered safely to patients with squamous cell carcinomas and that it can localise efficiently to metastases even at relatively low doses.

Inventors

Dr Suzanne Eccles and Dr Helmut Modjtahedi are the two principal scientists involved in this project. Dr Eccles is based at ICR, Sutton, Surrey.

Key Publications

O-Charoenrat et al
Int. J. Cancer (2000), 86 (3), 307-17

O-Charoenrat et al
Cancer Research (2000) 60, 1121-1128

O-Charoenrat et al
Int. J. Cancer (1998) 75, 310-316

Modjtahedi et al
Int. J. Oncol. (1998) 13(2), 335-42.

Modjtahedi et al,
Br. J. Cancer. (1996) 73(2), 228-235.

Modjtahedi et al,
Cancer Research (1994) 54, 1695-1701.

Modjtahedi et al,
Br. J. Cancer. (1993) 67(2), 247-253.

Intellectual Property

Intellectual property rights include: EGFR Antibody Sequence. The sequences of some antibodies are now in the public domain whilst others remain confidential.

EGFR Antibody Hybridomas. Ownership of all hybridomas vests with ICR.

Know-How

ICR and principal scientists have considerable experience and expertise with these antibodies and considerable expertise in the fields of growth factor signalling, monoclonal antibody technology and the development of novel therapeutics.

ICR holds no patent protection in the Anti-EGFR area. A patent which claimed terminal differentiation using a selection of antibodies was abandoned in all territories.

Commercial Opportunity

ICR is currently seeking an industrial partner interested in licensing one or a selection of these antibodies for further development of EGFR targeted therapeutic or diagnostic applications.

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