Monoclonal Antibodies against Cerb-B2

ICR Licensing Opportunity November 2012

- A panel of 7 rat monoclonal antibodies available, directed against the external domain of the erbB2 tyrosine kinase receptor.
- Stable high affinity cell surface binding to erbB2 protein core.
- Therapeutic efficacy demonstrated pre-clinically in both a targeted pro-drug and targeted radiotherapy setting.
- Tumour localisation demonstrated in pilot clinical imaging studies.
- Provides for selective delivery of erbB2 targeted therapeutics and / or diagnostic agents.

Background

The epidermal growth factor receptor (EGFR) family of structurally related transmembrane tyrosine kinases are known as the ErbB receptors. Under normal conditions EGF receptor signalling plays a fundamental role in the regulation of key cellular processes including survival, proliferation and differentiation. Dysregulation of ErbB signalling has been associated with several types of cancer, for example resulting from gene amplification, or mutations leading to increased receptor transcription, translation or stability.

To date four members of the erbB receptor family have been characterised: erbB1 (also known as HER1 or EGFR), erbB2 (HER2 or Neu), erbB3 (HER3) and erbB4 (HER4). Amplification of the c-erbB2 proto-oncogene and high levels of erbB2 overexpression are found in approximately 20-30% of metastatic breast cancers, and it is in this setting that much drug discovery effort has been focused.

CerbB2 as a target

The very low levels of receptor associated with normal adult tissues makes erbB2 an attractive tumour target for therapeutic intervention. Importantly, the receptor is an accessible extracellular target compatible with antibody based therapeutics and delivery systems.

Inhibition of tyrosine kinase activity and proliferation of erbB2 positive cells has now been demonstrated both for monoclonal antibody and small molecule constructs, thus demonstrating the therapeutic potential of erbB2 targeting.

Institute antibodies

A panel of 7 rat IgG2 monoclonal antibodies has been raised, which recognise epitopes on the external domain of erbB2. The antibodies have been characterised extensively in-vitro and therapeutic potential has been demonstrated in-vivo using breast cancer xenografts. Strategies explored to date include erbB2 targeted enzyme for pro-drug activation, and targeted radionuclide therapy. Pilot clinical studies have been carried out, which demonstrate tumour localisation of radiolabelled antibody in patients with breast cancer.

Lead scientists

Dr Sue Eccles and Dr Steve Hobbs are the two principal scientists involved in this project. They are based at ICR, Sutton, Surrey, UK.

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Contact

Contact: Jonathan Beech, Business Development Manager
e-mail: jonathan.beech@icr.ac.uk
Telephone: +44 (0) 20 7153 5427

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Bibliography and Key Publications

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The ErbB receptor family: a therapeutic target for cancer. Trends in Molecular Medicine, 8(4) Suppl. S19-S26.

Dean CJ, Eccles SA, Valeri M et al. (1993)
Rat MAbs to the product of the c-erbB-2 proto-oncogene for diagnosis and therapy in breast cancer.
Cell Biophys. 22(1-3):111-27.

Eccles SA, Court WJ, Box GA et al. (1994)
Regression of established breast carcinoma xenografts with antibody-directed enzyme prodrug therapy against c-erbB2
p185. Cancer Res. 54(19):5171-7.

Intellectual property

Intellectual property rights include the following:

- Antibody sequences
- Sequence data concerning all Institute CerbB2 antibodies remain undisclosed.
- Antibody hybridomas
- Ownership of all hybridomas vests with the Institute.

Know how

ICR and principal scientists have longstanding research experience and considerable expertise in the fields of growth factor signalling, monoclonal antibody technology and the development of novel therapeutics.
A chimaeric version of one member of this panel (ICR12) has been created in which the rat light and heavy chain constant regions have been replaced with human C kappa and gamma 1 counterparts.

Commercial opportunity

ICR is currently seeking an industrial partner interested in licensing one or a selection of these antibodies for further development of erbB2 targeted therapeutic or diagnostic applications.

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The ROYAL MARSDEN NHS Foundation Trust

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Contact: Jonathan Beech, Business Development Manager
e-mail: jonathan.beech@icr.ac.uk
Telephone: +44 (0) 20 7153 5427

The Institute of Cancer Research: Royal Cancer Hospital,
123 Old Brompton Road, London, SW7 3RP, UK
www.icr.ac.uk/enterprise