OVERVIEW

- Novel tumour endothelial marker: antibody target for anti-angiogenesis approaches
- Expression is highly restricted to tumour endothelial cells
- Evidence of role in endothelial migration and tube formation
- CLEC14A KO mice and in-house generated murine monoclonal antibodies demonstrate in vivo tumor burden reduction and inhibition of invasion
- Potential in antibody-drug conjugate therapies
- Intellectual property protected with two patent applications

BACKGROUND

Angiogenesis, the formation of new blood vessels from existing vasculature, is recognised as a critical requirement for initiation and development of many diseases including cancer. As a result, inhibition of angiogenesis is one of the most intensely investigated areas of cancer research at present.

Tumor endothelial markers (TEMs) that are highly expressed in human tumor vasculature compared with vasculature in normal tissue hold clear therapeutic potential. C-type lectin CLEC14A is a novel TEM, a transmembrane protein that is specifically expressed on the surface of tumour endothelial cells.

Extensive immunohistochemical data demonstrated that CLEC14A is strongly and specifically overexpressed on the tumour vasculature in a wide range of tumours tested, in contrast to vessels of the corresponding normal tissue (Figure 1 and Table 1[1]). The endothelium-specific expression has also been demonstrated by an independent laboratory [2].

Figure 1: CLEC14A is specifically overexpressed on tumour endothelial cells in different tumour indications. Immunofluorescence analysis of CLEC14A in normal and tumour tissue.
COMMERCIAL OPPORTUNITY

CRT is seeking to exclusively license the patent application and related know how / materials for development of anti-CLEC14A antibody based therapy.

LEAD SCIENTIST

Prof. Roy Bicknell, Cancer Research UK Molecular Angiogenesis Group, University of Birmingham.

INTELLECTUAL PROPERTY

CRT has filed a patent application (WO2011/027132; priority date: September 2009) describing the potential of CLEC14A as a suitable target for vascular targeting and anti-angiogenesis approaches and a second patent application (priority date: January 2015) claiming differential mechanism of action and therapeutic potential between specific Abs based on unique epitope recognition.

FURTHER READING

2. Rho SS et al; Clec14a is specifically expressed in endothelial cells and mediates cell to cell adhesion. Biochem Biophys Res Commun. 2011 Jan 7

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**Table 1**: CLEC14A expression is present on the vessels of all tumour tissues tested

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Breast</th>
<th>Prostate</th>
<th>Colon</th>
<th>Rectum</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Pancreas</td>
<td>Ovarian</td>
<td>Liver</td>
<td>Kidney</td>
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<td></td>
<td>Oesophagus</td>
<td>Bladder</td>
<td>Lung</td>
<td>Stomach</td>
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Interfering with CLEC14A function in vitro using CLEC14A-specific siRNAs or antisera impaired HUVEC cell migration and tube formation. Equally, in vivo knockdown of CLEC14A in zebrafish embryos resulted in defects of the developing zebrafish vasculature further confirming a role of CLEC14A in angiogenesis.

**APPLICATION**

Novel tumour endothelial marker. Antibody target for tumour angiogenesis inhibition; naked Ab and/or delivery of toxic payload to target.

**CURRENT STATUS**

CLEC14A KO mice as well as murine monoclonal antibodies recognising both human and mouse CLEC14A have been generated and are currently being characterised. These novel models have demonstrated the ability of CLEC14A inhibition to substantially reduce the tumour burden (Figure 2) as well as inhibit cell migration and invasion. These results further validate the therapeutic potential of such an approach as demonstrated by previously published data [1,3].

![Figure 2](image1.png)

Fig 2. (A) Mice injected with Lewis Lung Carcinoma cells were treated twice per week with 100 μg of mIgG1 (con) or C4 antibody (C4); (B) Representative images of LLC tumours

The current research programme in Prof. Roy Bicknell's laboratory is directed to further validate CLEC14A as a tumour endothelial marker and its role in angiogenesis via functional inhibition with the proprietary monoclonal antibodies. In addition, preliminary in vivo experiments successfully demonstrate the potential of using the CLEC14A antibodies in antibody-drug conjugate therapeutic approaches.

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