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 role as cancer biomarker
- Intellectual property protected with two patent applications

BACKGROUND

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.

Read more overleaf
CURRENT STATUS

CLEC14A is a novel target of high interest for anti-angiogenesis therapies. This is mainly due to its specific expression in tumour endothelial cells versus normal tissue. 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 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).

Furthermore, a range of other reagents have been developed as part of this project that would aid in pre-clinical and clinical development of CLEC14A targeted therapeutics.

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, the potential of using CLEC14A as a cancer biomarker is being investigated.

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


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