Characterisation of novel CD73 antibodies as a therapeutic method of adenosine regulation

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INTRODUCTION

CD73 is a membrane-bound nucleotidase receptor which is frequently overexpressed in the tumour microenvironment and can be found on both tumour and infiltrating immune cells. Its function is to catalyse the conversion of adenosine monophosphate (AMP) to adenosine and phosphate and it has been proposed as a therapeutic target in cancer due to the role of adenosine in tumour immune suppression.

Here using multiple in vitro approaches we have characterised a panel of novel anti-CD73 antibodies to evaluate their therapeutic potential.

1. Antibodies bind to CD73 protein with differing affinities

2. CD73 antibodies show direct inhibition of enzyme activity

3. CD73 antibodies induce receptor internalisation

4. CD73 antibodies show inhibition of membrane-bound CD73-mediated hydrolysis of AMP

5. CD73 antibodies show inhibition of soluble CD73-mediated hydrolysis of AMP

CONCLUSIONS

We demonstrate, that amongst our panel of antibodies, candidates which inhibit CD73 function by two different mechanisms, direct inhibition of enzyme activity and modulation of cell surface expression; both of which have therapeutic potential to disrupt CD73-mediated adenosine production and therefore reduce anti-tumour immune responses.

Several antibodies from this panel will be advanced into late-stage preclinical development to identify a clinical candidate.