Oral Presentations
Plenary symposium 3: B cells in immunooncology

03.05 TOWARDS A B CELL VACCINE FOR TUMOUR EXPRESSED SELF-ANTIGENS
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Background Monoclonal antibodies have huge potential in cancer therapy, but are expensive in production, storage, and delivery and have limited retention in the patient. To overcome this, active vaccination is a well-established procedure to induce long term production of antibodies. It also activates the response to multiple epitopes, which may confer additive effects on the target antigen. We try to use vaccination to induce antibodies targeting self-antigens expressed on tumours.

We have shown that a conjugate vaccine can induce high titres of autoantibody specific to the tumour endothelial cell antigen Robo4, which is selectively expressed on tumour vascular endothelium, but not healthy vasculature. By covalently linking the extracellular domain of Robo4 to a common vaccine carrier protein, autoreactive B cells could recruit T cell help specific for the carrier. This protocol could efficiently induce specific anti-tumour vessel antibodies and suppress tumour growth in a Lewis Lung carcinoma (LLC1) mouse model. This project aims to optimise the vaccine-induced antibody response to Robo4 in LLC1 tumours and understand how the vaccine breaches immune tolerance in cancer.

Materials and Methods As most patients have pre-existing T cell memory to tetanus, we decided to use the non-toxic fragment C of tetanus toxin (FrC) as the carrier protein. Our data show that vaccination of mice with Robo4 genetically linked to FrC in adjuvant can efficiently induce the production of Robo4-specific antibodies.

Results The injection of Robo4-conjugate vaccine in adjuvant in a Lung Lewis carcinoma model did elicit Robo4-specific antibodies and retarded tumour growth. Further we discovered an increase in NK cell, CD4+ and CD8+ T cell and dendritic cell populations in tumours after Robo4 vaccination. LLC1 is ICT-resistant having potential to improve the results of cancer therapy for immunosuppressive factors present in LLC1 tumours, therefore we try to use vaccination to induce antibodies targeting self-antigens expressed on tumours.

Conclusions Our data indicate that this vaccination strategy may promote immunogenic pathway activation and inhibit immunosuppressive factors present in LLC1 tumours, therefore having potential to improve the results of cancer therapy for ICT-resistant ‘cold’ tumours.

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