

P011 The Role of Cathepsin S in Astrocytoma Invasion
**Caroline McGoohan, Wei Chen, Tianbao Chen,
Chris Shaw & Brian Walker**

School of Pharmacy, Queen's University of Belfast

Astrocytomas are the most common primary brain tumours. The prognosis for patients with these tumours is poor, due to their invasiveness. Proteolytic enzymes are known to play a major role in facilitating tumour invasion. Cathepsin S (Cat S) is a lysosomal cysteine protease which previous work from our laboratory has demonstrated is expressed and secreted by astrocytoma cells. In addition, our group has illustrated that Cat S expression in astrocytomas is associated with tumour progression and poor outcome in glioblastomas.

This current study focuses on establishing the functional role of Cat S in these invasive brain tumours using synthetic Cat S inhibitors to modulate the activity of this protease. Two synthetic inhibitors, BipChaLeuCOCHO and BipChaLeuDMK were synthesised in-house and evaluated as putative inhibitors of Cat S. The efficacy and specificity of these inhibitors was assessed against purified Cat S employing steady-state fluorimetric assays. The effect of Cat S inhibition on astrocytoma invasion *in vitro* was also determined in the astrocytoma cell line (U251 mg) using a modified Boyden chamber. These inhibitors displayed significant anti-invasive effects on the astrocytoma cell line. These results demonstrate that Cat S plays a functional role in astrocytoma invasion and highlight it as a putative target for novel anti-invasive therapies.