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Use of Cell Penetrating Peptides to Treat Inflammatory Responses in Human Uterine Cells.

Leo RI Gurney,¹ Stephen C Robson,¹ Arwyn T Jones,² Michael Taggart.¹ *1Newcastle University, Newcastle Upon Tyne, United Kingdom; 2Cardiff University, Cardiff, United Kingdom.*

INTRODUCTION: A lack of effective therapies continues to impair attempts to prevent preterm birth associated with inflammation. With the aim of broadening the scope of candidate agents available to be tested to address this clinical problem we investigated the ability of a novel class of peptide vectors, termed Cell Penetrating Peptides (CPPs) attached to a peptide cargo, the Nemo Binding Domain (NBD) peptide directed at the inhibition of inflammatory Nuclear Factor Kappa B (NFκB)-related signalling in uterine cells.

METHODS: The ability of three CPP derived vectors (Pen, TAT and R8) to deliver fluorescent cargo to human primary myometrial cells was tested using live cell confocal microscopy. Western blotting and quantitative polymerase chain reaction gene array techniques examined the efficacy of the CPP linked peptide cargo NBD peptide to dampen cytokine stimulated inflammatory responses in these cells.

RESULTS: Pen, TAT and R8 were able to deliver fluorescent cargo to uterine myometrial cells within one hour over a concentration range of 1-10μM. The NBD peptide, conjugated to Pen CPP (Pen-NBD), significantly inhibited cytokine stimulated cyclo-oxygenase 2 (COX2) protein induction at four hours.

Representative Western blots indicating COX2 protein expression in myometrial cells over a four hour time frame following IL1B exposure alone (Control) or with 1 hour pre-incubation of increasing concentrations of Pen-NBD.

This effect was not seen with other CPP-NBD conjugations, nor with mutant or un-conjugated peptide controls. Data derived from both Western blot and gene array indicated that the anti-inflammatory effects of Pen-NBD were comparable with a series of non-peptidic small molecule inhibitors of NFκB.

CONCLUSIONS: This research demonstrates that CPPs can enter human uterine cells and deliver cargo to exert an anti-inflammatory effect, opening new avenues for the development of treatments aimed at preventing preterm birth associated with inflammation.