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Anti-human CD59 conjugated gold nanoparticles for targeted induction of photo-hyperthermia *in vitro*

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Cancer is a leading cause of death globally. Whilst current approaches to treatment are effective, they are accompanied by significant side effects. Gold Nanoparticles (AuNP) have been explored for their potential use as chemotherapeutics. AuNPs induce hyperthermia in response to excitation by Near Infrared Light (NIR), which then can induce apoptosis in a controlled manner. CD59 an 18-22 kDa membrane protein responsible for the inhibition of complement, is over expressed in multiple cancer sites, is associated with poor prognosis and is a potential target molecule for cancer treatment. Here research is presented relating to the ability to achieve controlled cell viability reduction using anti-human CD59 targeted gold nanoparticles. AuNPs (1.25-20 µg/ml) were shown to reduce HeLa cell viability in a concentration-dependent manner as assessed using MTT assay. Inclusion of polymer (PEG) coating significantly reduced ($p<0.05$) the impact on cell viability. Interestingly, CD59 expression was reduced significantly following exposure to AuNPs compared to PBS controls when assessed using fluorescent microscopy, this impact being negated by PEGylating the AuNPs. Further modification to conjugate an anti-human CD59 monoclonal antibody (AuNP -MaB) resulted in additional reduction in nanoparticle-induced cytotoxicity. HeLa cells treated with a combination of AuNP-MaBs and NIR light (519/520 nm) led to significant reduction in cell viability compared to untreated PBS controls ($p<0.01$) and untargeted AuNP ($p<0.05$) controls. CD59 knock down HeLa's exhibited increased sensitivity to both unmodified and targeted AuNPs compared to normal HeLa's, suggesting a protective role for CD59. Data presented here suggests that CD59 provides a stable anchor point, allowing for induction of hyperthermia associated cytotoxicity through NIR treatment. Reducing CD59 expression levels in response to AuNP exposure, along with increased sensitivity of CD59 deficient cells, indicates that PEGylation to improve biocompatibility of AuNPs is required before they should be considered for treatment in this manner.

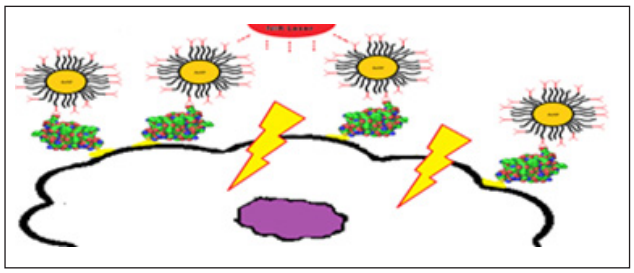

Figure 1: MaB conjugated gold nanoparticles can bind specifically to CD59 found on the cell surface. Anchored to the extracellular side of the plasma membrane these nanoparticles can induce photo hyperthermia associated cytotoxicity in a targeted manner following exposure NIR. This results in a decrease in cellular viability compared to non-NIR treated controls.

Biography

Thomas A Illingworth is currently a PhD student based at Leeds Beckett University, UK and has been working within the School of Clinical and Applied Sciences since 2014. He has received BSc in Biology from the University of Derby in 2011 and MSc in Molecular and Cellular biology from Sheffield Hallam University in 2013. His research interests include nanotechnology and nanobiotechnology, with a focus on how these technologies can be used to improve the treatment of cancer.

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