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Anti CD59 aptamer for Targeted Delivery of Gold Nanoparticles in cancer Therapeutics: An *in vitro* study

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Targeting nanoparticles to specific sites/cell types is seen as a way of preventing non-specific toxicity associated with their use. CD59, a cancer biomarker, is a membrane complement regulatory protein. Upregulation of complement inhibitory factors, such as CD59, is associated with tumour growth and progression as it allows cancer cells to evade complement surveillance (2). Targeting strategies have focused predominantly on monoclonal antibody's (Mab's) due to their high specificity and relative ease of conjugation (3). Batch to batch variations and high cost of Mab's incentivizes development of alternatives. Aptamers are short oligonucleotides capable of targeting agents via Systematic Evolution of Ligands by Exponential enrichment (SELEX). Interestingly gold nanoparticle (AuNP) use as a delivery vehicle for therapeutics have shown promise due to their unique properties(1). Within this work we raised an anti CD59 DNA aptamer and conjugated it to an AuNP surface through a bi-functional Poly(ethylene) glycol linker (AptAuNP). Replacing Mab's with aptamers has shown promise in recent years when combined with AuNP's for delivery of drugs to cells (4) as well as potentially as aptasensors (5). Data suggests that following exposure to AptAuNP HeLa cells exhibited significantly increased toxicity compared to Mab conjugated nanoparticle (Mab-AuNP) at 10µg/ml and 20µg/ml, but no significant difference in toxicity was observed at 5µg/ml and 2.5µg/ml. 3D immunofluorescence microscopy analysis suggested that AptAuNP's accumulate within the intracellular space at higher concentrations whereas MaB-AuNP's remained outside the cells. AptAuNP's may be binding to CD59 contained within the Golgi disrupting it resulting in cell death (see figure 1). Our work suggests that an anti CD59 aptamer conjugated AuNP could be useful in targeting CD59 overexpressing cells. More work is required to establish the specific mechanism of cell death in this instance but demonstrates promise of an anti CD59 aptamer's use in alternative applications such as biomarker detection.

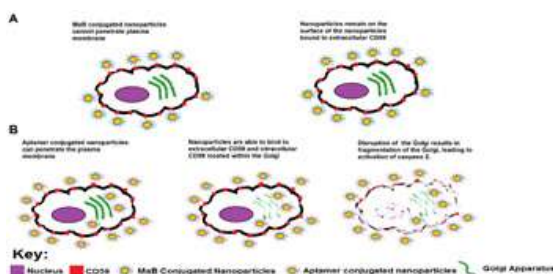


Figure 1: Aptamer conjugated nanoparticles have the potential to penetrate the lipid membrane and bind to intracellular CD59 contained within the Golgi. At a critical concentration, rate of penetration exceeds removal resulting in membrane destabilisation and cell death.