Nanomedicine for siRNA delivery of gene therapies on medulloblastoma

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Medulloblastoma, the most prevalent malignant childhood brain tumour originating from cerebellum, has garnered considerable attention due to the adverse effects associated with conventional treatments such as surgery, chemotherapy and radiotherapy. Hence, newer drugs that specifically target molecules and signalling pathways driving medulloblastoma are of great interest. siRNA therapeutics delivered by nanoparticles offer promising potential to mitigate side effects as highly specific cancer targets can be chosen and nanoparticles can be engineered to create safe and effective passage across the blood-brain barrier (BBB). Iron oxide nanoparticles coated with fluorinated polymers demonstrated reduced cytotoxicity based on AlamarBlue assay results, and exhibited higher delivery efficiency according to gel shift assays, flow cytometry, and immunofluorescence confocal microscopy. The *in vitro* BBB model established for permeability assays and characterized by transendothelial electrical resistance (TEER) values revealed that fluorinated polymer-iron oxide nanoparticles could effectively deliver siRNA across the BBB and into medulloblastoma cells. Furthermore, the effect of PLK1 gene silencing was evaluated using western blotting techniques, indicating that the fluorinated polymer-iron oxide nanoparticles could successfully deliver functionally active siRNA at pH 6.7 (the tumour environment) rather than at pH 7.4 (the normal cellular environment) *in vitro*. Nude mice bearing D425 orthotopic tumours were implanted for *in vivo* research, whose tumour growth monitored by IVIS was inhibited after treated with the nanocomplexes, and the western blot on tumours exhibit 50% PLK1 expression inhibition.