

Project Title

Selective and synergistic treatment of advanced ovarian cancer using DNA nanotechnology

Supervisor(s)

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Project Description

Ovarian cancer is the second most common gynaecological cancer and the deadliest one, with a 5-year survival rate of 10-30%. The standard of care for all women with advanced ovarian cancer is chemotherapy (carboplatin and paclitaxel). However, this is associated with significant toxicity, including myelosuppression, nausea and vomiting. This toxicity arises due to the non-specific activity of chemotherapy and the resultant normal tissue toxicity. Therefore, there is a significant need to develop technologies that can deliver chemotherapy selectively to malignant cells.

This project proposes nanoparticle-enabled delivery of an antisense oligonucleotide (ASO) acting as a switch to deliver potent chemotherapeutic drugs inside metastatic ovarian cancer cells only. This protects healthy cells and reduces the side effects associated with IP chemotherapy. To engineer this switch, ASOs will be redesigned into hairpin structures that enable the loading of chemotherapy through π - π stacking. The selectivity of the switch to metastatic cancer cells will be provided by the ASO target. Previous studies have demonstrated that inhibiting MMP-9 prior to chemotherapy enhances drug toxicity, and that MMP-9 is commonly overexpressed in metastatic cancer cells, but not in healthy cells. By exploiting the differential expression of MMP-9, the DNA switch will release the drug upon hybridisation with the MMP-9 target only in metastatic cancer cells, both inhibiting MMP-9 production and promoting cancer cell toxicity. This will allow the treatment to avoid healthy cells altogether.