FACTSHEET

Validation in vitro and in vivo of nanoparticle treatment to induce anti-tumoral alloreactivity

Abstract

As part of ULISES, project partner IMIB-Arrixaca has carried out in vitro validation. This involved performing cytotoxicity assays using human pancreatic adenocarcinoma cells (PANC-1). These were transformed with the nanoparticles to express allogeneic Human Leucocyte Antigen (HLA) molecules.
For in vivo validation, a tumour-xenotransplant mouse model treated with nanoparticles was used to evaluate anti-tumour alloreactivity. The in vitro results indicate that the transformed cells become vulnerable to the effector mechanisms of the immune system and can be efficiently targeted. The in vivo results are promising, but they will require better therapeutic approaches.

Key points

- Nanoparticles can be used to induce the expression of HLA molecules in pancreatic cancer cells.
- Transformed pancreatic cancer cells can be killed in vitro for natural immune effector mechanisms (anti-HLA antibodies, complement, and NK cells)
- The use of nanoparticles in the in vivo model will require further optimisation to obtain effective therapies

Research on pancreatic cancer cells treated with nanoparticles has shown promising results, offering new avenues for targeted cancer therapy. This factsheet summarizes the key findings from in vitro (lab-based) and in vivo (animal-based) experiments, highlighting the effectiveness and potential of nanoparticle treatments.

In Vitro Experiments

The first task of IMIB-Arrixaca was to conduct the in vitro assays to evaluate the cytotoxic effects of nanoparticles on pancreatic ductal adenocarcinoma cells (PANC-1) through two mechanisms: complement-dependent cytotoxicity (CDC) and natural killer (NK) cell-dependent cytotoxicity. In the CDC assay, transformed PANC-1 cells expressing allogeneic HLA molecules were exposed to anti-HLA antibodies and complement proteins. This resulted in significant cell lysis, indicating the nanoparticles' ability to enhance the immune response. In the Natural Killer (NK) cell-dependent assay, isolated NK cells were co-cultured with nanoparticle-treated PANC-1 cells. The NK cells effectively targeted and killed the cancer cells, demonstrating the nanoparticles' potential to boost immune cell-mediated cytotoxicity. Both assays highlighted the nanoparticles' role in enhancing immune-mediated destruction of cancer cells.

In Vivo Experiments

An in vivo study was conducted to assess the therapeutic potential of nanoparticles on pancreatic cancer cells (PANC-1) implanted in mice. The experiment involved treating these mice with nanoparticle-based therapy targeted to act on the tumour. The presence of nanoparticles in the tumour environment can stimulate the body's immune system to recognise and attack the cancer cells. This immune response enhances the overall effectiveness of the treatment and provides an additional mechanism for combating the tumour. Initial trials have not been shown to be effective in vivo, and further

improvement of the modes of delivery of nanoparticles and effectors mechanisms in animals (nanoparticles, anti-HLA antibodies, complement, and immuno-effectors cells) will be necessary.

In conclusion, the use of nanoparticles has been shown to induce allogeneic responses capable of mediating the elimination of pancreatic cancer cells in vitro. Further research and clinical trials will pave the way for these innovative therapies to become a standard part of cancer care.

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