

Investigation of the effect of novel arsenoliposomes on cancer neural stem cells

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Cancer neural stem cells comprise a small proportion of the heterogeneous population of tumour cells that have been reported to be responsible for tumour recurrence and metastasis. Successful treatment of brain tumours would mean cancer neural stem cell elimination. However, anticancer agents suffer efficacy problems due to either physiological barriers (Blood Brain Barrier) or formulation problems due to their physicochemical properties.

Liposomes are drug delivery carriers composed of phospholipids which improve drug bioavailability due to increase of drug solubility and reduction of drug side effects. They can be actively targeted to particular cell types by attaching specific ligands onto the carrier surface. Arsenoliposomes are a novel class of liposomes made of arsenolipids, where the phosphono-group of the phospholipid has been replaced with the arseno-group. They have exhibited high toxicity to cancer cells and not to normal cells.

Based on this fact, arsenoliposomes were used in the current study to explore the potential of the anticancer activity of the carrier itself on the neural cancer stem cells. The long-term aim is to develop optimized targeted drug-loaded arsenoliposomes for brain tumour treatment. A human tumour medulloblastoma cell line (VC321); an established glioma cell line (C6) and an enriched fraction of cancer neural stem cells were used in this study. 3T3 cell line was used as control. Cell viability (MTT assay), membrane integrity (LDH assay) and uptake profile studies on those cell lines were carried out.

Preliminary MTT results over a period of 4 days show that the arsenoliposomes were much more toxic towards the C6 and VC321 cells in comparison to the conventional liposomes, while 3T3s were not appreciably affected by the arsenoliposomes. Those findings agree with previously reported data using different cell lines. Preliminary qualitative data using nestin/CD133 immuno-reactivity showed that a higher proportion of cancer neural stem cells were found in VC321 with respect to C6 cancer cells. This outcome correlates well with the growth pattern of the VC321 in culture. Also, the same data set showed co-localization of the fluorescently labelled arsenoliposomes with nestin positive stem cells. Quantitative data of the uptake profile will be presented.

Therefore, these preliminary studies form an important basis for the development of a highly specific targeted drug delivery system that focuses on the critical elimination of cancer neural stem cells.