Coating superparamagnetic iron oxide nanoparticles with antisense oligonucleotides for targeting cyclin B1

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Background: Antisense oligonucleotides (ASO) represent an attractive trend in the development of targeted cancer therapies with more than 90 ASO-based drugs targeting cancer in different phases of clinical trials. Coupling of ASO to superparamagnetic iron oxide nanoparticles (SPIONs) overcome many challenges related to ASO delivery including; stabilization in physiological environments, protection from nuclease degradation, enhanced cellular uptake without using auxiliary reagents and prolonged intracellular half-life.

Aim: To functionalize SPIONs with ASO targeting the mRNA of Cyclin B1, a potential cancer target and to explore its anticancer activity.

Methods: Four different SPIONs-ASO conjugates termed S-M (1-4) were designated depending on the sequence of ASO and prepared by crosslinking carboxylated SPIONs to amino labeled ASO. The impact of S-M (1-4) on the level of Cyclin B1, cell cycle, ROS and viability of the cells were assessed by flowcytometry.

Results: S-M3 and S-M4 reduced the level of Cyclin B1 by 35 and 36%, respectively. In addition, MCF7 cells were arrested at G2/M phase (60.7%) as a consequence to downregulation of Cyclin B1. S-M (1-4) led to the induction of ROS formation in comparison to the untreated control cells. Furthermore, S-M (1-4) resulted in an increase in the percentage of dead cells compared to control ones.

Conclusion: Targeting Cyclin B1 with ASO-coated SPIONs may represent a specific biocompatible anticancer strategy.

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