Poster M-2

Downregulation of anti-apoptotic gene expression by antisense oligonucleotides induces apoptosis and sensitizes head and neck squamous cell carcinoma cells to chemotherapy.

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Short Abstract: We addressed the question whether antisense approach towards anti-apoptotic proteins could restore the apoptosis and sensitize the HNSCC cells to chemotherapy. Our results suggest that antisense treatment against these survival factors in combination with lower doses of chemotherapy offers potential as a less toxic chemoadjuvant therapy.

Long Abstract:
We have earlier reported that the inhibition of apoptosis in head and neck squamous cell carcinomas (HNSCC) is because of upregulated expression of Bcl-2, Bcl-XL and Survivin. Hence, we addressed the question whether antisense approach towards these inhibitors of apoptosis could restore the apoptosis in HNSCC. Further, we wanted to see whether chemotherapeutic efficacy of Cisplatin could be enhanced by using this drug in combination with antisense oligonucleotides in human laryngeal carcinoma HeP2 and cells. The effect of these antisense oligonucleotides was examined on the mRNA expression by RT-PCR and on protein expression by Western blotting. Apoptosis was measured by flowcytometry, TUNEL assay and caspase-3 activity assay. Treatment of HeP2 cells with 400nM antisense oligonucleotides against Bcl-2, Bcl-XL and Survivin for 48 hrs decreased their expression both at the mRNA as well as at the protein level, resulting in the induction of apoptosis. Treatment of HeP2 cells with these antisense oligonucleotides augmented Cisplatin induced apoptosis. Our findings emphasize the importance of Bcl-2, Bcl-XL and Survivin as survival factors in HNSCC cells. Antisense treatment against these survival factors in combination with lower doses of chemotherapy offers potential as a less toxic chemoadjuvant therapy.