NT-09. CO-DELIVERY OF siRNA AND CHEMOTHERAPY; A NEW APPROACH FOR GBM TREATMENT USING A NANOCARRIERS SYSTEM
Zvi R. Cohen1, Naama Peshes-Yeloz1, Anton Voll1, Zion Zibly1, and Dan Peer2; 1Sheba Medical Center, Ramat Gan, Israel; 2Tel Aviv University, Tel Aviv, Israel

Over the past decade, progress in genomics and proteomics has paved the way for identifying promising macromolecular therapeutics including small RNAs, peptides and proteins. Still, the vast majority of leading drugs candidates for the treatment of CNS diseases is ineffective, mainly due to restricted passages across the BBB. Nanoparticles packaging of therapy is of particular interest for its potential to treat brain tumors, due to their ability to transport drugs through the BBB, while improving the performance of drugs by decreasing systemic and local toxicity. We chose GBM known for its poor prognosis, as a model for brain tumors. In our model we used a novel cluster-based nanoparticles termed Gagomers (GAGs) as our delivery system. GAGs are coated with the glycosamine glycan hyaluronan and can therefore bind to a specific CD44 variants expressed on tumor cells. We found that GAGs can successfully bind to both cultured cells and neurospheres (stem cells) of GBM patients and to GBM cell lines. In vitro, GAGs loaded with Kif-11 siRNA, dramatically reduced the expression of Kif11 mRNA in GBM cell lines, suggesting it can efficiently target GBM and reduce the expression of specific genes. Additionally, GAGs loaded with Doxorubicin (DXR) induced higher rates of GBM elimination than free DXR. As a next step, we examined GAGs’ ability to bind specifically and efficiently to GBM cell lines in-vivo. U87 cell lines were stereotactically injected into the brains of SCID-NOD mice. Following tumor inoculation and growth mice underwent convection with GAGs loaded with Cy5 siRNA. only U87 cells were labeled with Cy5 suggesting that local treatment with GAGs can efficiently target GBM cells in-vivo. Our future plans are to examine the activity of GAGs co-entrapping siRNA and DXR on human GBM cell lines in-vitro and in-vivo. This strategy may ultimately become a novel therapeutic modality to treat GBM.