Purpose: To locally increase the relative biological effectives (RBE) of proton therapy by introducing phage-targeted-gold-nanoscaffolds into cancer cells.

Methods: Prostate-cancer cells were treated with a ligand-directed nanoscaffold, a non-targeted nanoscaffold, gold nanoparticles or no treatment. After incubating, the cells were irradiated in a clinical 160MeV proton beam to doses of 1, 2, 3, 4 and 6CGE. Two configurations were tested: with the cells at a depth of 2cm and spread-out Bragg peak (SOBP) of 4cm and the other at a depth of 9cm with a 10cm SOBP. The clonogenic assay was performed post-irradiation to determine the effects of the treatments on cell survival. We fit the surviving fraction (SF) data to the linear-quadratic model for analysis. A control irradiation of cells in a Co-60 unit was also performed.

Results: Our analysis showed that all proton treatments resulted in lower SF than the Co-60 treatment over the measured doses. For proton irradiations, the actively targeted nanoscaffold achieved the lowest SF compared to all of the control treatments. In the range of typical clinical fractionation, 1.8-4 CGE/fraction, the nanoscaffold treatment reduced the SF by 22%-42% more than the untreated cells for proton irradiation at 2cm. For the 9cm depth, the reduction in cancer cell SF was 8-33% for the targeted nanoscaffold versus the untreated cells. RBE calculated at 50% and 10% SF showed 27 and 28% enhancement at the 2cm depth and 7 and 18% at 9cm.

Conclusions: The observed decrease in SF of cells treated with the targeted nanoscaffold prior to irradiation confirms that the nanoscaffold enhances the RBE of the radiation. The enhanced RBE is likely due to the specific internalization of the nanoscaffolds into cells. With further investigation, we believe that targeted nanoscaffolds will be a clinically viable platform to enhance the sensitivity of localized tumors to proton radiation.

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Conflict of Interest: Drs. Pasqualini and Arap have shared interest in Alvos Therapeutics.