

Radioactive drugs emitting alpha particles can be used to kill cancer cells, but it is not known how their effectiveness changes when delivered to different locations within cancer cells. Here, we report a model radiobiological system that allows us to directly compare the effect of the same alpha emitter in different subcellular locations. By treating engineered human cancer cells with a novel alpha-emitting antibiotic, astatine-211 trimethoprim, we show that an alpha emitter's proximity to the DNA leads to more effective killing of individual cancer cells and small cancer cell clusters. Importantly, our results can guide future alpha emitter development to improve treatment of microscopic cancer deposits in addition to macroscopic tumors.