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Size-dependent targeted GNPs as CT contrast agents for molecular imaging of cancer

Darya Tsvirkun, Yael Ben Nun, Emmanuelle Merquiol and Galia Blum
The Hebrew University of Jerusalem, Israel

In this study, we generated a new classes of cathepsin targeted probes based on different sizes of GNP (10, 30, and 100 nm) for functional CT imaging of cancer. ABPs are small molecules that have been engineered to covalently modify enzyme targets in an activity dependent manner. These novel probes enable detection of the elevated cathepsin activity within cancerous tissue using a CT instrument, thus creating a direct link between imaging signals and biological process. X-ray CT instruments are among the most available, efficient and cost-effective imaging modalities in hospitals. The field of CT molecular imaging agents is emerging relying mainly on detection of gold and bismuth nanoparticles, iodine and gadolinium labeled compounds. However, the low sensitivity of CT scanners to contrast reagents in comparison to other imaging modalities makes this a challenging task. We have generated chemical scaffolds of GNP-ABPs with combination of different protective layers of PEG studied in terms of length (3 or 5 kDa) and ratio (10, 50, and 100%). Efficiency of targeting moiety, based on different PEG coatings, was evaluated for tumor accumulation and enzyme inhibition effectiveness. Using a combination of analytical methods as TGA, DLS and ZETA, we estimated the average number of PEG units (~0.21 PEG/ nm2) on one particle, conducting the peptide quantity for each derivative. After chemical and biochemical evaluations, we selected the most potent and stable probes to proceed to non-invasive imaging in cancer mice models. CT contrast from the tumor could be detected 5 hours post injection of targeted GNP probes. This specific signal increased over time and was significant at 24-72 hours post injection, compared to non-targeted particles. Contrast agent concentrations and sub-cellular localization within the tumor cells was detected using TEM. In conclusion, we found our GNP-ABPs as promising new tools for functional imaging of specific protease activity in-vivo by CT instrument.

daryatsv@gmail.com

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