

Selective Photothermal Therapy of Glioblastoma with Anti-EGFR-Functionalized Gold Nanorods in a 3D Optical Setup Operating in the First Biological Window

Vincenzo De Mei¹, Paolo Rosa¹, Francesca Petronella², Flaminia Pompeo¹, Marco Iuliano¹, Giorgio Mangino¹, Selenia Miglietta³, Luca Buccini^{4,5}, Anacleto Proietti^{4,5}, Marco Rossi^{4,5}, Luciano De Sio^{1,5}

¹Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

²National Research Council of Italy, Institute of Crystallography, CNR-IC, Rome Division, Area della Ricerca Roma 1 Strada Provinciale 35d, n. 9 - 00010 Montelibretti (RM)

³Department of Human anatomy, Histology, Forensic medicine and Orthopedics, Sapienza University of Rome, Rome, Italy

⁴Department of Basic and Applied Sciences for Engineering (SBAI), Sapienza University of Rome, Rome, Italy

⁵Center for Nanotechnology Applied to Engineering (CNIS), Sapienza University of Rome, Rome, Italy

Photothermal therapy (PTT) is a minimally invasive and precise thermo-ablative treatment that exploits photothermal agents to convert optical energy into heat, inducing localized temperature increases capable of destroying cancer cells¹. Its clinical application against infiltrating malignancies like glioblastoma demands therapeutic selectivity. We addressed this challenge by functionalizing² gold nanorods (AuNRs) with an anti-EGFR antibody (AuNRs/Ab) that specifically targets the overexpressed epidermal growth factor receptors on U87-MG glioblastoma cells. Bioconjugation was confirmed by UV-Vis absorption spectroscopy, photoluminescence, dynamic light scattering (DLS), and transmission electron microscopy (TEM). A customized thermo-optical setup operating in the first biological window (700-900 nm) was employed to evaluate the 3D distribution and localization of PTT heating. Cells targeted with AuNRs/Ab were embedded in a PDMS/polystyrene phantom mimicking a tumor at a depth of approximately 1cm and illuminated from below with a CW 808 nm NIR laser. Three synchronized thermal cameras enabled real-time 4D heat mapping and its relation to therapeutic outcomes. The efficacy of AuNRs/Ab-mediated PTT was quantified by fluorescence-activated cell sorting (FACS). After 10 minutes of PTT illumination, AuNRs/Ab-treated samples showed a mean temperature increase of about 9 °C, inducing a cell death of approximately 40%, while bare AuNRs induced only a 2 °C temperature increase and negligible cell mortality. Cellular uptake of AuNRs/Ab and ultrastructural changes were confirmed using TEM analysis, highlighting a significant enhancement of AuNRs/Ab compared with bare AuNRs. These results demonstrate the robustness of AuNRs/Ab-mediated PTT in treating aggressive brain tumors.

References

- 1) Huang et al., *Lasers Med. Sci.* (2008) | 23, 217
- 2) Petronella et al., *Environ. Sci. Nano* (2022) | 9, 3343