# Green Synthesis of Near-Infrared Plasmonic Gold Nanostructures by Pomegranate Extract and Their Supramolecular Assembling with Chemo- and Photo-Therapeutics

**Francesca Laneri[1]**, Mimimorena Seggio[1], Adriana C.E. Graziano[1], Marta M. Natile[2], Aurore Fraix[1] and Salvatore Sortino[1]

[1]University of Catania, Department of Drug and Health Sciences, Viale A. Doria, 6, *95125*, Catania, Italy
[2]ICMATE-CNR Institute of Condensed Matter Chemistry and Technologies for Energy, National Research Council, Department of Chemical Science, Corso Stati Uniti, 4 *35127*, University of Padova, Padova, Italy

Francesca.laneri@phd.unict.it

In the last few years, gold (Au) nanostructures have collected a tremendous attention thanks to their manifold applications in different fields spanning photonics, catalysis, sensing and medicine [1]. Among the unique properties of Au nanostructures, photothermia is one of the most intriguing in view of its biomedical applications [2]. It is based on a straightforward working mechanism, based on the ability of the noble metal to absorb light in the visible (Vis)/near infrared (NIR) region thanks to its localized surface plasmon resonance (LSPR), and to convert the excitation light into heat with superb efficiency while preserving excellent photostability. This phenomenon is at the basis of the photo-thermal therapy (PTT), which represents one of the emerging unconventional treatments for cancer and bacteria diseases, with great prospects in the burgeoning field of nanomedicine [3]. The ease of manipulation of light in terms of intensity, wavelength, duration and location, combined with the nanodimensions of Au structures offer the great advantage to confine a rapid in increase of temperature in a very small volume with high spatiotemporal precision, inducing cellular death with great efficiency and selectivity [4].
Au nanostructures exhibiting a localized surface obtained in a single, green step by pomegranate extract in the presence of a biocompatible β-cyclodextrin branched polymer, without the need of preformed seeds, external reducing and sacrificial agents, and conventional surfactants [5]. The polymeric component makes the Au nanostructures water dispersible water, stable for weeks and permits their supramolecular assembling with the chemotherapeutic sorafenib (SRB) and a Rhodamine- bond nitric oxide (NO) photodonor (RD-NO), chosen as representative for chemo- and photo-therapeutics [6-7] SRB is a multi-kinase inhibitor, already approved by the U.S. Food and Drug Administration and currently widely employed in hepatocellular and advanced renal cell carcinomas treatment [8]. Irradiation of the plasmonic Au nanostructures in the “therapeutic window” (650-1300 nm), with 808 nm laser light, results in a good photothermal response, which (i) is not affected by the presence of either the chemo- or the phototherapeutic guests and (ii) does not lead to their photoinduced decomposition. Besides, irradiation of the hybrid Au nanoassembly with the highly biocompatible green light results in an efficient release of NO, a well-known anticancer species if produced within a specific concentration range. The suitability of these nanoassemblies in the prospect of multimodal anticancer applica-tions has been demonstrated by preliminary experiments against Hep-G2 hepatocarci-noma cell lines which revealed synergistic action between the cytotoxic species involved.

## References

[1] Schuller, J. A.; Barnard, E. S.; Cai, W.; Jun, Y. C.; White, J. S.; Brongersma, M. L., Nat. Mater., 9 (2010) 193–204.
[2] Jain, P. K.; Huang, X.; El-Sayed, I. H.; El-Sayed, M. A. Acc. Chem. Res., 41 (2008) 1578–1586.
[3] Li, X.; Lovell, J. F.; Yoon, J.; Chen, X., Nat. Rev. Clin. Oncol., 17 (2020) 657.
[4] Kennedy, L.C.; Bickford, L.R.; Lewinski, N.A.; Coughlin, A.J.; Hu, Y.; Day, E.S.; West, J.L.; Drezek, R.A., Small, 7 (2011) 169–183.
[5] Nocito, G., Petralia, S., Malanga, M., Béni, S., Calabrese, G., Parenti, R., Sortino, S. ACS Applied Nano Materials, 2 (2019) 7916-7923.
[6] Seggio, M., Laneri, F., Graziano, A. C., Natile, M. M., Fraix, A., Sortino, S. Nanomaterials, 12 (2022) 4476.
[7] Parisi, C., Failla, M., Fraix, A., Rolando, B., Gianquinto, E., Spyrakis, F., Sortino, S. Chemistry–A European Journal, 25 (2019) 11080-11084.
[8] Kane, R. C.; Farrell, A. T.; Madabushi, R.; Booth, B.; Chattopadhyay, S.; Sridhara, R.; Justice, R.; Pazdur, R. Oncologist, 14 (2009) 95–100.

We thank MIUR (Italy) for the Industrial PhD grant (DOT1308125) to F.L. and AIRC – Italian Association for Cancer Research (IG-198559) for financial support.

## Figure

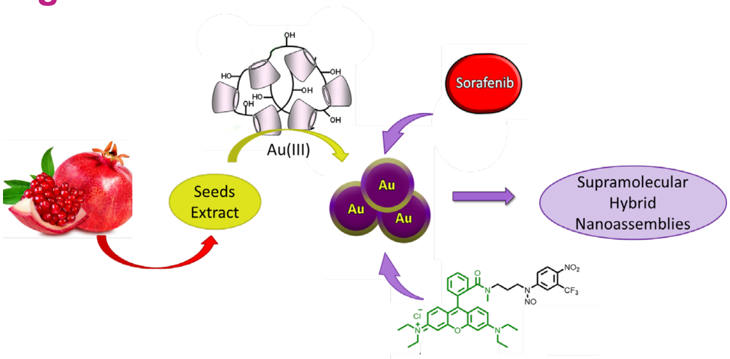


**Figure 1.** Schematic preparation of the NIR plasmonic Au nanostructures and their supramolecular assembling with SRB and RD-NO.