## > The most significant results obtained in the project

Finding the most suitable (Fe-Co)<sub>f</sub> ferrimagnetic nanoparticles in terms of size (13-16 nm) and biocompatibility with the biological environment (nanobioconjugates) ((Fe-Co)<sub>f</sub>-PAA–(HP-γ-CDs)), and establishing optimal parameters (frequency, amplitude) for the alternating magnetic field, using 3D computational simulation and molecular docking, which lead to obtaining the maximum specific loss power (SLP) in magnetic field (Fig. 1), and their efficient heating to ~43°C, in order to be used in superparamagnetic hyperthermia (SPMHT) with increased efficiency and reduced toxicity for the alternative therapy of skin (melanoma, squamous) and breast cancer: P-PAA–(HP-γ-CDs), where P is (Fe-Co)<sub>f</sub> sample of magnetic nanoparticles, PAA is polyacrylic acid and (HP-γ-CDs) is hydroxypropyl gamma-cyclodextrin;

## References:

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- [2] Costica Caizer, Computational study regarding Co<sub>x</sub>Fe<sub>3-x</sub>O<sub>4</sub> ferrite nanoparticles with tunable magnetic properties in superparamagnetic hyperthermia for effective alternative cancer therapy, NANOMATERIALS, 11 (2021) 3294 (IF: 5.076; Q1 - red area).
- [3] Isabela Simona Caizer, Costica Caizer, Superparamagnetic Hyperthermia Study with Cobalt Ferrite Nanoparticles Covered with γ-Cyclodextrins by Computer Simulation for Application in Alternative Cancer Therapy, INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES, 23 (2022) 4350 (IF: 6.208; Q1 - red area).
- [4] Costica Caizer, Isabela Simona Caizer, Roxana Racoviceanu, Claudia Geanina Watz, Mioc Marius, Cristina Adriana Dehelean, Tiberiu Bratu, Codruta Marinela Soica, Fe<sub>3</sub>O<sub>4</sub>-PAA–(HP-γ-CDs) Biocompatible Ferrimagnetic Nanoparticles for Increasing Efficacy in Superparamagnetic Hyperthermia, NANOMATERIALS, 12 (2022) 2577 (IF: 5.719; Q1 - red area).



(a)

(b)

Fig. 1. Specific loss power (SLP) as a function of the nanoparticle diameter (D) and frequency of the magnetic field (f) with amplitude of H=16 kA/m, in the cases: (a)  $Fe_3O_4$ -PAA–(HP- $\gamma$ -CDs) fixed nanoparticles, and (b)  $Fe_3O_4$ -PAA–(HP- $\gamma$ -CDs) mobile nanoparticles.

Successful *in vitro* testing and validation of superparamagnetic hyperthermia (SPMHT) using superparamagnetic (SPM) nanobioconjugates of (Fe-Co)<sub>f</sub>-PAA–(HP-γ-CDs) ((Fe-Co)<sub>f</sub> is Fe3O4 (P1), Co0.05Fe2.95O4 (P2) or CoFe2O4 (P6), and PAA is polyacrylic acid, (HP-γ-CDs) is hydroxypropyl gamma-cyclodextrin) for melanoma (A375) and breast (MCF-7) cancer alternative therapy (Fig. 2), the tumor cells being destroyed up to a very high percentage, of approx. 98 % in the case of melanoma and approx. 95 % in the case of breast cancer, for the nanoparticles concentration of 10 mg/mL (Fig. 3).

## References:

[1] Costica Caizer, Isabela Simona Caizer, Roxana Racoviceanu, Claudia Watz, Mioc Marius, Cristina Adriana Dehelean, Tiberiu Bratu, Codruta Marinela Soica, *Fe*<sub>3</sub>O<sub>4</sub>-*PAA*-(*HP*-γ-*CDs*) *Biocompatible Ferrimagnetic Nanoparticles for Increasing Efficacy in Superparamagnetic Hyperthermia*, NANOMATERIALS, 12 (2022) 2577) (IF: 5.719; Q1 - red area).
[] other references under publication.

Alamar Blue 24h 120 100 80 Viabilitate celulara (%) 60 40 20 0 P1-PAA-yCDs 1 P1-PAA-yCDs 5 P1-PAA-yCDs P2-PAA-yCDs P6-PAA-yCDs mg/mL mg/mL 10 mg/mL 10 mg/mL 10 mg/mL Standard A375 A431 MCF7 Standard

Fig. 3. Viabilities of tumor cells A375 (melanoma cancer), A431 (squamous cancer) and MCF-7 (breast cancer) obtained after the application of superparamagnetic hyperthermia at a temperature of 42.9 °C for 30 min. in the case of using P-PAA–(HP- $\gamma$ -CDs) nanobioconjugates at different concentrations, where P is: P1 (Fe3O4), P2 (Co0.05Fe2.95O4) and P6 (CoFe2O4).



Fig. 2. (a) Coil magnetic hyperthermia generator for *in vitro* studies; CC-S: cell culture with  $Fe_3O_4$ -PAA-(HP- $\gamma$ -CDs) nanobioconjugates; (b) T-t diagram for cell culture with  $Fe_3O_4$ -PAA-(HP--CDs) nanobioconjugates.