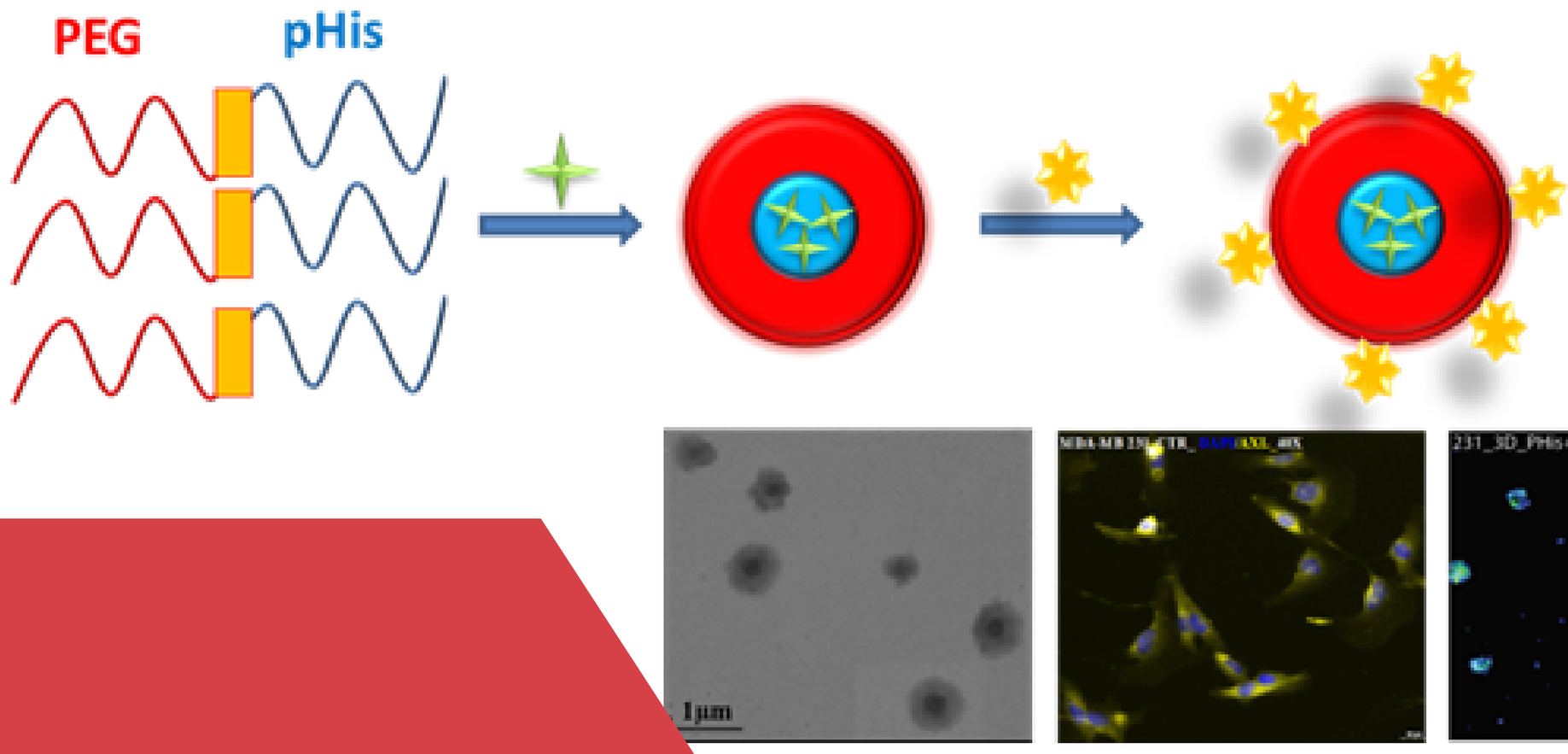

Restore Her2 dependent sensibility using AXL inhibitors packed in pH dependent nanostructures

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This project proposes to apply modular supramolecular system consisting of pH sensitive nano-assemblies, recognition moieties and functional molecules to build up therapeutic entities sensitive to the tumor microenvironment, and to investigate mechanisms for targeted breast cancer treatment in vitro and in vivo. These nanostructures were used to encapsulate therapeutics (HER2 blockers and AXL inhibitor), to protect the therapeutic agent and to improve circulation time, thereby increasing the amount of active drug that reaches the targeted site. This study already provided novel nano-delivery systems with narrowly tuned pH dependent properties which allow targeting of the cancer cells and deliver important cancer drugs. Additionally, it offers insights into synergistic effect of different drugs (trastuzumab and AXL inhibitor) which can potentially result in more effective treatment of cancer. We expect that the proposed nanoparticle system, by inheriting the separate merits, can improve drug pharmacokinetics through modulation by both the EPR effect, low pH of hypoxic tumors and/or small molecules targeting (HER2-ab).

The project results generated up to date have already successfully demonstrated the potential of the designed nan-carrier platforms to perform pH depended targeted drug release in 2D and 3D in vitro systems. The on-going investigations will provide further information on the ability of the proposed strategy to serve as a viable alternative in overcoming the existing mechanisms of drug resistance in cancer treatment.