

Breast cancer is the most prevalent malignancy in women. About 20% of all diagnosed cases are breast tumors overexpressing HER2 receptor on the cell surface and HER2 is currently considered as one of the major oncogenic drivers in breast cancer. Several therapeutic strategies have been developed so far, which unfortunately display limited effectiveness. The large problem is also the high cost of current therapies and the ability of cancer cells to become resistant to drugs. The development of effective therapies against HER2+ breast cancer is still a major challenge in the modern medicine. One of the current therapeutic approaches for the treatment of HER2 overexpressing breast tumors are conjugates of antibodies with a cytotoxic drug. An important feature determining the effectiveness of these therapies is the specific and efficient penetration of cytotoxic conjugates through the HER2 receptor into the cancer cells, where the active drug is released. Unfortunately, HER2 is a receptor with low cell penetration, therefore novel strategies to improve effectiveness of this process are urgently needed. Based on our previous data we hypothesize that cross-linking of HER2 receptor into larger complexes on the cell surface triggered by oligomeric cytotoxic conjugates will boost penetration of the drug into cancer cells through HER2. The ultimate goal of the proposed project is to develop a novel oligomeric cytotoxic conjugate for the effective elimination of cancer cells with HER2 overexpression. An additional advantage of the designed conjugate is its fluorescence, which will allow to monitor distribution and effect of the cytotoxic drug.