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It has been hypothesized that drug delivery by nanoparticles may well circumvent the resistance machinery of cancer stem cells (CSC). To be able to study efficacy of nanomedicines in population of CSC, we first developed an *in vitro* model in which CSC are tagged by a fluorescent reporter gene under the control of a CSC specific promoter. Using this system, we demonstrated that while bulk cancer cells die, CSC population augments after paclitaxel (PTX) treatment. We then investigated the prospects of different targeted and non-targeted delivery systems loaded with PTX and functionalized with specific antibodies against cancer stem cell populations in regular breast cancer cell lines, as well as in our CSC models. Our data shows that reducing tumor resistance of cancer stem cells might be related to specific active targeting of DDS and not attributed to a general mechanism of action of nanomedicines.