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# Pretargeting in nuclear imaging and radionuclide therapy: improving efficacy of theranostics and nanomedicines

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## Abstract

Pretargeted nuclear imaging and radiotherapy have recently attracted increasing attention for diagnosis and treatment of cancer with nanomedicines. This is because it conceptually offers better imaging contrast and therapeutic efficiency while reducing the dose to radiosensitive tissues compared to conventional strategies. In conventional imaging and radiotherapy, a directly radiolabeled nano-sized vector is administered and allowed to accumulate in the tumor, typically on a timescale of several days. In contrast, pretargeting is based on a two-step approach. First, a tumor-accumulating vector carrying a tag is administered followed by injection of a fast clearing radiolabeled agent that rapidly recognizes the tag of the tumor-bound vector in vivo. Thereby, pretargeting circumvents the use of long-lived radionuclides that is a necessity for sufficient tumor accumulation and target-to-background ratios using conventional approaches.

In this review, we give an overview of recent advances in pretargeted imaging strategies. We will critically reflect on the advantages and disadvantages of current state-of-the-art conventional imaging approaches and compare them to pretargeted strategies. Thereby, we will discuss the pretargeted imaging concept and the involved chemistry. Finally, we will discuss the steps forward in respect to clinical translation, and how pretargeted strategies could be applied to improve state-of-the-art radiotherapeutic approaches.

**Key words:** Pretargeted imaging, pretargeted radionuclide therapy, EPR effect, nanomedicines, bispecific antibody and hapten recognition, (strept)avidin–biotin interaction, hybridization of complementary oligonucleotides, SPAAC, tetrazine ligation