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STEM

Polyrotaxanes for Bladder Tumor Targeted MRI Contrast

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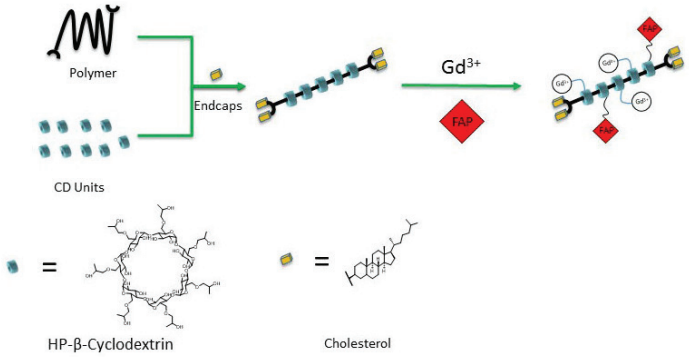
Bladder cancer is the fourth most common cancer in men and the tenth most common in women, and while long-term survival is more predominant compared to other common cancers, more than 47% percent of bladder cancer deaths could have been avoided with an early diagnosis (Verma et al., http://dx.doi.org/10.1148/rg.322115125). Initial diagnosis is generally made via cystoscopy, but magnetic resonance imaging (MRI) can be considered superior due to higher soft-tissue contrast that can detect small tumors and increased accuracy in determining the extent of muscle invasion. The Thompson Group has used fibronectin attachment protein (FAP) to target liposomes to bladder tumor cells.

To expound upon this previous work, we designed a synthetic pathway for a peptide-targeted MRI contrast agent and have made significant progress toward the final construct, which is composed of HP-β-CD threaded onto a polymer core and further modified with Gd-DOTA and a maleimide linker to attach the FAP peptide.

This type of construct is called a polyrotaxane (PR), and we have shown that PRs whose CDs have been modified with Gd-DOTA have a high relaxivity and extended contrast in various organs. New preparation and attachment methods for the maleimide linker are under investigation, as is the most effective coupling method for the FAP peptide. Subsequent studies will include cell culture, relaxivity measurements, and in vivo MR imaging with mice to determine the agent's targeting and contrast enhancement abilities.

Research advisor Bradley Loren writes: "I have been lucky to have had the opportunity to work with Cheyenne for the last two years. She always strives to excel at everything she does, and I know she will continue to do great things as a graduate student at the University of Pennsylvania next year."



A cartoon depiction of polyrotaxane formation. Hydroxypropyl-β-cyclodextrin units are threaded onto the polymer core akin to beads being threaded onto a string, followed by an endcapping reaction to prevent dethreading. The polyrotaxane is further modified with Gd-DOTA and the targeting FAP peptide to produce the MR contrast agent.

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