Single-Hairpin Based Self-Hybridization Chain Reaction

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Abstract

Hybridization chain reaction (HCR), generally composed of two hairpins (H1 and H2) for signal amplification, is a classical DNA circuit first reported by Pierce in 2004 and has become a versatile tool for bioanalysis. In the HCR system, when a single-stranded initiator DNA was introduced, it opened H1, and a new single-stranded region was exposed to open H2. Then, a sequence region identical to the initiator DNA in H2 was exposed. The processes were repeated, and finally, a nicked double helix was formed in the resulting chain reaction. This isothermal and enzyme-free polymerization process has been successfully applied for signal-amplified detection of nucleic acids and various non-nucleic acid targets. However, current HCR systems still meet some limitations (*e.g.*, still complicated), especially, since two hairpins are indispensably required. Engineering simpler yet powerful HCR would decrease the cost and the complexity of sequence design and operation. Here, a facile HCR system based on a single DNA hairpin was reported and rationally designed with a palindromic sequence in the stem, while a self-hybridization chain reaction (SHCR) can be triggered once the initiator DNA strand was introduced. This single-hairpin based SHCR system yielded around 36% increased signal-to-noise ratio and exhibited higher single-base mismatch selectivity compared to the conventional two-hairpins based HCR system. By integrating SHCR with adenosine triphosphate (ATP) aptamer, this system has been applied for ATP detection, as well as monitoring ATP either in living cells or released from dead cancer cells after radiotherapy. The single-hairpin-based SHCR system we proposed here has dramatically simplified the sequence design of HCR and may become a potential alternative to the conventional HCR system.

Keywords

Self-hybridization Chain Reaction, Single Hairpin, ATP Detection, Cancer Cell