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Autonomous DNA walker: probing cell membrane dynamics

Jie Wang & Quan Yuan*

College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, China

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We are all familiar with DNA as the substance that encodes the genomes of all living things. In addition to genetic function, DNA is one of the smartest building blocks for innovative nanostructures. DNA walker is a kind of self-assembled molecular machine that mimics the movement of protein motors in living systems. Usually, DNA walker consists of three parts: a single stranded DNA track, several anchorage sites and a walker strand. The walker strand can move from one anchor site to another along the track [1]. A major problem in DNA walker design is autonomous motion at the expense of controllability, that is, the walker strand cannot be stopped at a desired position or time, or it cannot be easily restarted once stopped. Prof. Weihong Tan and co-workers [1,2] have developed a series of autonomous and highly controllable DNA walkers based on photo-responsive DNA molecules and toehold-mediated strand displacement reaction. The smart DNA walkers can move along the track autonomously under light irradiation, and their movement behavior (stop or restart) can be precisely controlled by off/on switching of the light source [1,2]. In biological systems, autonomous and well-controlled movements of biomolecules are fundamental to life activities. For instance, molecular motors move along protein tracks to delivery cargo or make macroscopic motion. The smart DNA walkers hold good potential to mimic the movement of biomolecules in cellular environment, which can open new possibilities to explore the molecular mechanisms underlying life activities and promote the development of artificial living systems.

*Corresponding author (email: yuanquan@whu.edu.cn)

In a recent work published in *Nature Nanotechnology*, Profs. Weihong Tan and Mingxu You [3] have developed an autonomous DNA walker to decipher the dynamics of molecular movements on live cell membranes. The DNA walker copies the movement of the membrane components, thus it can signal the diffusion dynamics of the components in native contexts. With a toehold-mediated DNA strand displacement reaction initiated by the movement of DNA walker, the diffusion dynamics of the corresponding membrane components is transduced into readable cumulative fluorescence signals.

Dye-labelled walker strand hybridizes with the anchorage-2 strand, and quencher-labelled anchorage-1 strand is blocked with a complementary DNA strand (Figure 1). After adding initiator strand, the blocker on anchorage-1 is removed. As long as the two anchors encounter with each other, the walker strand will translocate from anchorage-2 to anchorage-1 by DNA strand displacement reaction, leading to quenching of the walker strand fluorescence. The rate of anchor encounters linearly correlates with the strand displacement reaction rate, thus the encounter dynamics can be obtained by measuring the time-dependent variation of fluorescence intensity.

The authors demonstrated that the DNA walker is an efficient probe to measure the encounter dynamics of anchors on cell membrane. The encounter dynamics of different lipids were further determined, and results show that the same lipid tend to accumulate in the same type of lipid domain on cell membrane. The authors further developed a sophisticated competition game to study the encounter preference of membrane components. The DNA walker can walk to two po-

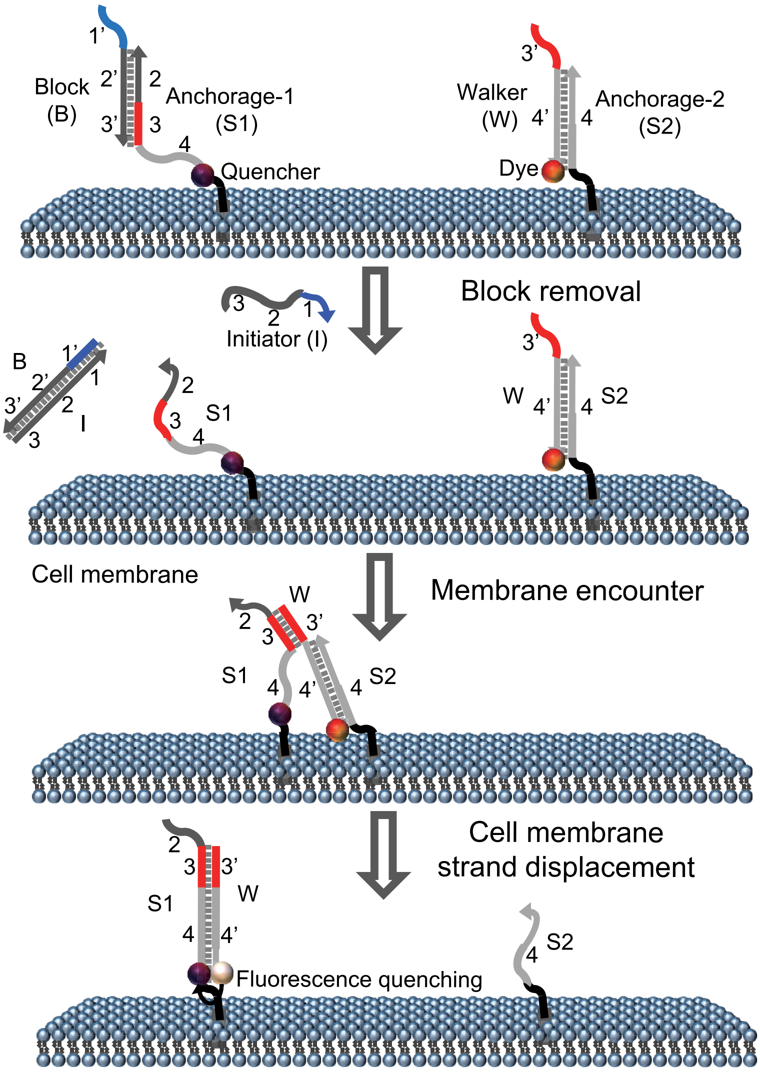

Figure 1 Schematic illustration of probing molecular encounters on cell membranes with the DNA walker [3] (color online).

tential anchorage sites where only one site is labelled with quencher. The drop in fluorescence intensity is correlates with the encounter rates between the initial anchorage site and the two potential anchorage sites. Such competition game offers a highly reliable approach to simultaneously probe two encounter pairs in a single step.

The authors further demonstrated that the DNA walker can be applied to probe various membrane components by tethering the anchorage strands on the target components with the assistance of DNA aptamers. The dynamic encounters of four different membrane proteins were measured with the DNA walker as proof of concept. As aptamers can recognize any target of interest with strong binding affinity and good specificity, the DNA walker can serve as a powerful tool to characterize the interaction of various molecules on cell membrane.

A major goal in DNA nanotechnology is to construct biomimetic or bioinspired nanostructures that can communicate and actuate in living systems. This work shows that artificial DNA walker can be used to read the dynamic and transient molecular encounters on live cell membranes. With this work, it is believed that DNA nanotechnology opens exciting new possibilities to study the signaling networks in cellular world.

Conflict of interest The authors declare that they have no conflict of interest.

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