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A Multivalent Structure-Specific RNA Binder with Extremely Stable Target Binding but Reduced Interaction to Nonspecific RNAs

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Abstract

By greatly enhancing binding affinities against target biomolecules, multivalent interactions provide an attractive strategy for biosensing. However, there is also a major concern for increased binding to nonspecific targets by multivalent binding. A range of charge-engineered probes of a structure-specific RNA binding protein PAZ as well as multivalent forms of these PAZ probes were constructed by using diverse multivalent avidin proteins (2-mer, 4-mer, and 24-mer). Increased valency vastly enhanced the binding stability of PAZ to structured target RNA. Surprisingly, nonspecific RNA binding of multivalent PAZ can be reduced even below that of the PAZ monomer by controlling negative charges on both PAZ and multivalent avidin scaffolds. The optimized 24-meric PAZ showed nearly irreversible binding to target RNA with negligible binding to nonspecific RNA, and this ultra-specific 24-meric PAZ probe allowed SERS detection of intact microRNAs at an attomolar level.

Keywords : biosensors; multivalent interaction; RNA recognition; SERS; specific interaction

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