A Capture-SELEX Strategy for Multiplexed Selection of RNA Aptamers Against Small Molecules

In vitro selection of aptamers that recognize small organic molecules has proven difficult, in part due to the challenge of immobilizing small molecules on solid supports for SELEX (Systematic Evolution of Ligands by Exponential Enrichment). This study describes the implementation of RNA Capture-SELEX, a selection strategy that uses an RNA library to yield ligand-responsive RNA aptamers targeting small organic molecules in solution. To demonstrate the power of this method, we selected several aptamers with specificity towards either the natural sweetener rebaudioside A or the food-coloring agent carminic acid. In addition, Bio-layer interferometry is used to screen clonal libraries of aptamer candidates and is used to interrogate aptamer affinity. The RNA-based Capture-SELEX strategy described here simplifies selection of RNA aptamers against small molecules by avoiding ligand immobilization, while also allowing selection against multiple candidate targets in a single experiment. This makes RNA Capture-SELEX particularly attractive for accelerated development of RNA aptamers targeting small metabolites for incorporation into synthetic riboswitches and for analytical biosensors.