A COUPLED CHLORINASE-FLUORINASE SYSTEM WITH HIGH EFFICIENCY OF TRANS-HALOGENATION AND A SHARED SUBSTRATE TOLERANCE

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Enzymatic trans-halogenation enables radiolabeling under mild and aqueous conditions, but rapid reactions are desired. We discovered two new S-adenosyl-L-methionine (SAM)-dependent chlorinases from soil bacteria and developed a coupled chlorinase-fluorinase system for highly improved trans-halogenation reactions. The chlorinase was for the first time demonstrated to tolerate the modification at the C-2 position of the adenine ring and act cooperatively with the fluorinase to accelerate the trans-halogenation of 5'-chlorodeoxy-2'-ethynyladenosine (5'-CIDEA) to 5'-fluorodeoxy-2'-ethynyladenosine (5'-FDEA). The acetylene group will enable the linkage with an azide tethered peptide via a “click” reaction. The coupled chlorinase-fluorinase system offers the prospect of developing rapid radiolabeling protocols under mild and aqueous conditions.