Washington University in St. Louis
Office of Technology Management

OBLIGATE HETEROTETRAMERIC PAIRS OF CRE RECOMBINASE MUTANTS FOR EFFICIENT RECOMBINATION AT ASYMMETRIC SITES

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Background: The function of enzymes involved in homologous recombination can be exploited in the field of genetic engineering in order to generate mutations of interest. However, this machinery is not functionally efficient in post mitotic or terminally differentiated cells. Viral gene therapy techniques are not site specific, and thus cannot efficiently generate highly specific mutant clones. Researchers at Washington University in St. Louis have developed a technology that allows for highly targeted recombination events at the endogenous gene loci in terminally differentiated cells by generation of heterotetrameric Cre recombinase complexes to eliminate off target recombination events and limit cytotoxicity.

Technology Description: Researchers at Washington University in St. Louis have invented a new system that will be useful for gene conversion at endogenous loci in post-mitotic cells. They have developed pairs of Cre recombinase mutants that only perform their catalytic function when they are both present in a cell. This invention leads to the formation of an ABAB heterotetrameric complex that allows for the cleavage of DNA at non-loxP sites. Furthermore, these engineered Cre mutants could eliminate the limitations currently observed with the wild type Cre-lox system and could therefore lead to increased specificity and decreased cytotoxicity. This technology could be used to target a locus that has a large number of disease-associated polymorphisms that span several kilobases, or to assess binding sites on a promoter that is important in gene regulation.