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(54) Title: METHOD FOR THE PRODUCTION OF A TARGET-SPECIFIC LARGE SERINE RECOMBINASE

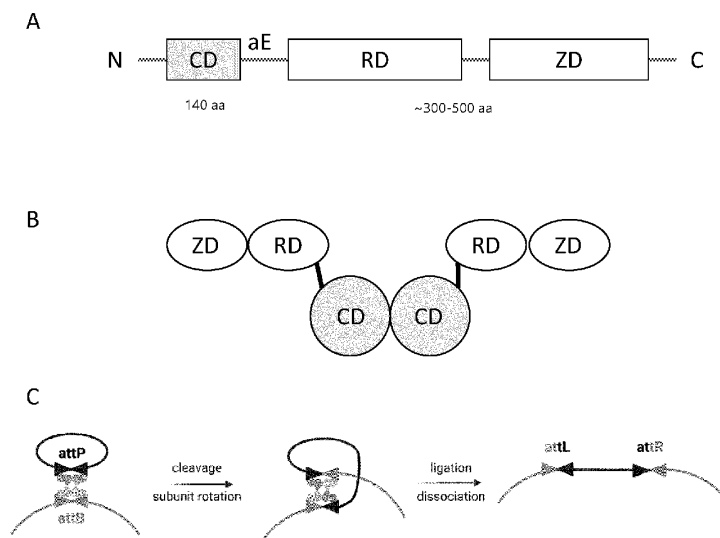


Fig. 2

(57) Abstract: The present invention pertains to a method for generating a target-specific large serine recombinase (LSR), the method comprising the steps of: a) generating a plurality of first variants of an LSR by introducing one or more mutations into a sequence encoding the LSR; b) generating a library of expression vectors, wherein each expression vector comprises a first region encoding one of the first variants of an LSR, and a second region comprising at least two first target sites of the LSR, wherein the two first target sites are different from each other; c) introducing the library of expression vectors into host cells; d) culturing the host cells and expressing the first variant LSR; e) isolating plasmid DNA from the culture of host cells; f) determining whether a portion of the second region of the expression vector between the two first target sites has been excised by the variant LSR; g) generating a plurality of second LSR variants by introducing one or more mutations into the sequence encoding those first LSR variants that excised the portion of the second

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region of the expression vector between the two first target sites; and h) repeating steps b) to f) optionally with at least one second target site, wherein the at least one second target site differs from the first target sites in at least one nucleotide. The present invention further provides variant LSRs obtained by the method, a nucleic acid or group of nucleic acids encoding a variant LSR, a vector comprising said nucleic acid(s); a system for integrating a donor DNA into a target nucleic acid; and uses of the LSRs, the nucleic acid(s) or the vector.