



US006232112B1

(12) **United States Patent**  
**Catcheside**

(10) **Patent No.:** **US 6,232,112 B1**  
(45) **Date of Patent:** **May 15, 2001**

(54) **REAGENTS AND METHODS FOR DIVERSIFICATION OF DNA**

(75) Inventor: **David E. Catcheside**, Bellevue Heights (AU)

(73) Assignee: **Flinders Technologies Pty Ltd of Flinders University** (AU)

(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/977,171**

(22) Filed: **Nov. 24, 1997**

(51) **Int. Cl.**<sup>7</sup> ..... **C12N 1/14**

(52) **U.S. Cl.** ..... **435/254.4**

(58) **Field of Search** ..... 435/6, 7.31, 254.4, 435/254.1, 255.2

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*Primary Examiner*—Scott W. Houtteman

(74) *Attorney, Agent, or Firm*—Merchant & Gould P.C.

(57) **ABSTRACT**

The present invention provides methods and compositions for diversification of heterologous DNA sequences in vivo. The present invention employs a recombination hotspot functionally coupled to the heterologous DNA. The process of recombination generates new versions of the foreign sequences by recombining their differences in new combinations. Errors in recombination generate additional sequence diversity.

**69 Claims, 23 Drawing Sheets**

Map of the *his-3, cog, lpl* region of Linkage Group I of *Neurospora crassa*. Vertical bars, triangles and hairpins show the location of sequence differences that distinguish the St Lawrence and Lindgren wild type strains. The corresponding full DNA sequences are given in Fig. 7 and Fig. 8. Vertical slashes indicate one to seven base substitutions per 10 base pairs. Triangles indicate short sequence insertions and the hairpin a 101 base pair inverted repeat transposon fragment present in St Lawrence.

