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(71) Applicant (for all designated States except US): **EVIA-GENICS S.A.** [FR/FR]; Pépinière Paris Santé Cochin, 29, Rue du Faubourg Saint-Jacques, F-75014 Paris (FR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **PANDJAITAN, Rudy** [AT/FR]; 13, Rue Chabert, F-94700 Maisons Alfort (FR). **SEBAL, Sarra** [FR/FR]; 6, Rue Santerre, F-75012 Paris (FR). **LUQUE, Alejandro** [AR/FR]; 1 Rue Guy Moquet, F-75017 Paris (FR).(74) Agents: **REDL, Gerda** et al.; Donau-City-Str. 1, A-1220 Vienna (AT).

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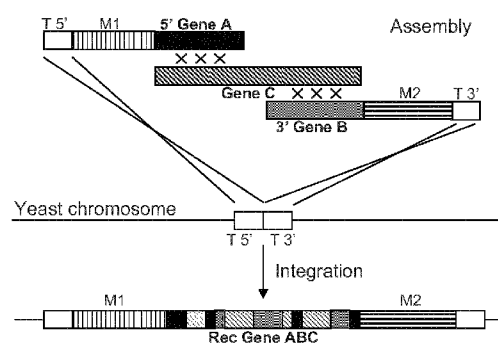
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(54) Title: METHOD OF METABOLIC EVOLUTION

Fig. 3



(57) **Abstract:** The invention relates to a method for metabolic evolution of a variant of a natural small aromatic molecule product of a metabolic pathway, by somatic in vivo assembly and recombination of said metabolic pathway employing a gene mosaic of at least one gene A, which comprises a) in a single step procedure (i) transforming a cell with at least one gene A having a sequence homology of less than 99.5% to another gene to be recombined that is an integral part of the cell genome or presented in the framework of a genetic construct, (ii) recombining said genes, (iii) generating a gene mosaic of the genes at an integration site of a target genome, wherein said at least one gene A has a single flanking target sequence either at the 5' end or 3' end anchoring to the 5' or 3' end of said integration site, (iv) recombining eventual further genes of said metabolic pathway, and b) selecting clones comprising said gene mosaic and said eventual further genes capable of expressing said variant, methods of preparing a library of cells producing variants of natural small aromatic molecule products of a metabolic pathway, the libraries so produced and used to prepare said variants.

