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- [54] **BACTERIOPHAGE RESISTANT RECOMBINANT BACTERIA**
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- [51] Int. Cl.⁶ **C12N 1/20; A23C 9/00; C12P 7/56**
- [52] U.S. Cl. **435/69.1; 426/61; 435/139; 435/235.1; 435/236; 435/243; 435/252.3**
- [58] **Field of Search** **435/69.1, 139, 435/172.1, 172.3, 243, 320.1, 235.1, 252.3, 252.4, 236; 426/42, 61; 536/23.1, 24.1**

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[57] ABSTRACT

Recombinant bacteria containing phage-encoded resistance ("Per") and methods of making and using the same are disclosed. Such bacteria are made by (a) conducting a fermentation of a substrate in a medium containing a defined bacterial culture until bacteriophage are detected in the medium, the bacteriophage being specific to at least one bacteria in the medium; (b) isolating the bacteriophage; (c) digesting DNA of the bacteriophage to produce a library of DNA fragments; (d) transforming the bacteria susceptible to said bacteriophage with the library of DNA fragments to provide transformed bacteria; (e) selecting from among the transformed bacteria, a bacteriophage-resistant transformed bacteria; (f) adding bacteriophage resistant transformed bacteria to the medium; and (g) recommencing step (a). Also disclosed are bacterial cells which contain a first bacteriophage defense mechanism (Per), wherein Per comprises a bacteriophage origin of replication (ori) operatively associated with a DNA sequence incapable of producing live bacteriophage. The bacterial cell is capable of being infected by a bacteriophage, the DNA of which, once injected into the bacterial cell, competes with Per for binding to DNA polymerase.

13 Claims, 5 Drawing Sheets