

**United States Patent** [19]**Chiba et al.**[11] **Patent Number:** **6,004,565**[45] **Date of Patent:** **Dec. 21, 1999**[54] **COMPOSITIONS AND METHODS OF USING COMPOSITIONS WITH ACCELERATED LYMPHOCYTE HOMING IMMUNOSUPPRESSIVE PROPERTIES**[75] Inventors: **Kenji Chiba; Kunitomo Adachi**, both of Fukuoka, Japan[73] Assignee: **Yoshitomi Pharmaceutical Industries, Ltd.**, Osaka, Japan[21] Appl. No.: **08/933,738**[22] Filed: **Sep. 23, 1997**[30] **Foreign Application Priority Data**

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[51] **Int. Cl.<sup>6</sup>** ..... **A61K 31/135**[52] **U.S. Cl.** ..... **424/278.1; 514/487; 514/546; 514/653; 560/29; 560/163; 564/223; 564/355**[58] **Field of Search** ..... **564/223, 355; 560/29, 163; 514/653, 487, 546; 424/278.1**[56] **References Cited**

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The methods and compositions of the invention and the compounds used in the invention involve a novel immunosuppression mechanism, accelerated lymphocyte homing immunosuppression (ALH-immunosuppression). For example, the compound FTY720 specifically directs lymphocytes to the peripheral lymph nodes, mesenteric lymph nodes, and Peyer's patches. By reversibly sequestering lymphocytes in these tissues, the compounds can inhibit an immune response in a mammal. Understanding these mechanisms provides a novel immunosuppression therapy that can synergistically interact with other immunosuppressive compounds. Screening methods for identifying similar ALH-immunosuppression compounds are also described. The invention allows better treatments and therapies whenever an immunosuppression regimen is desired.

**6 Claims, 11 Drawing Sheets**

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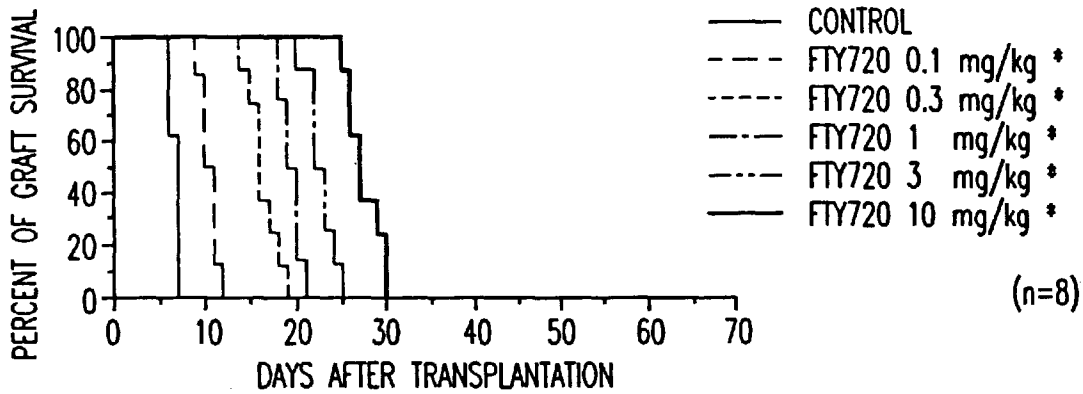


FIG. 1A

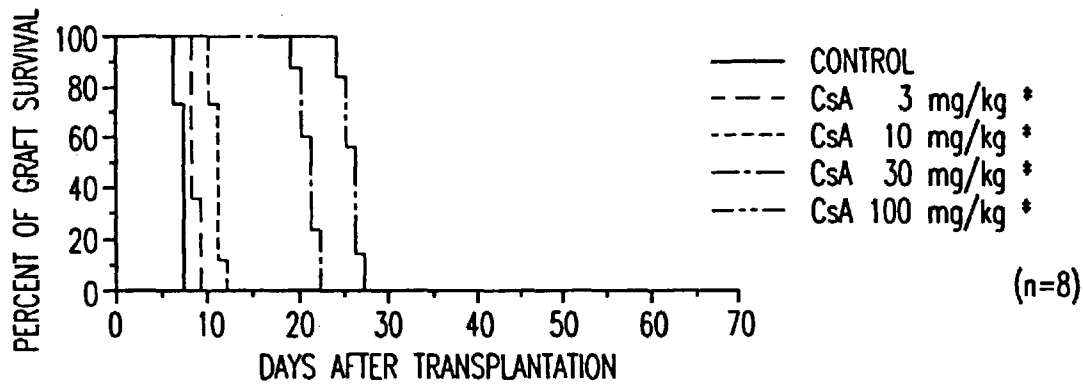


FIG. 1B

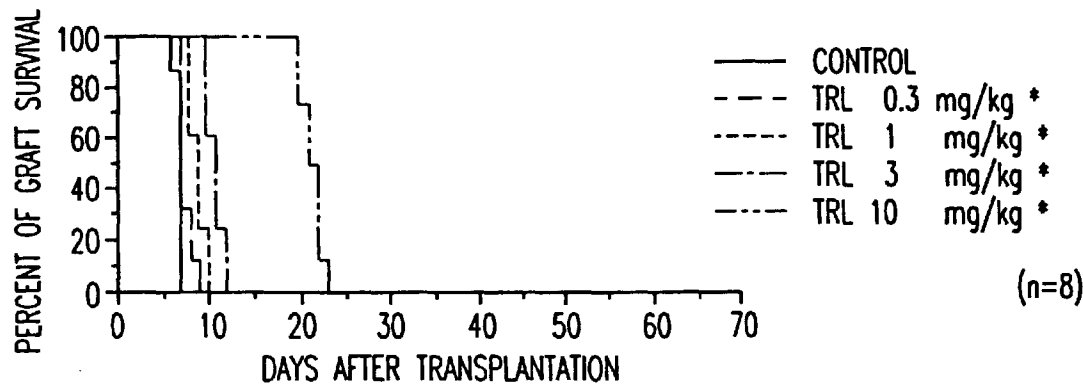


FIG. 1C

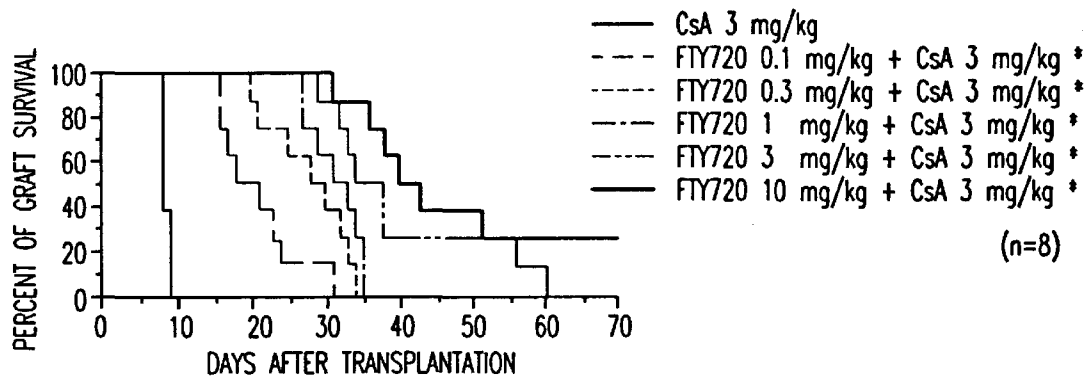


FIG. 2A

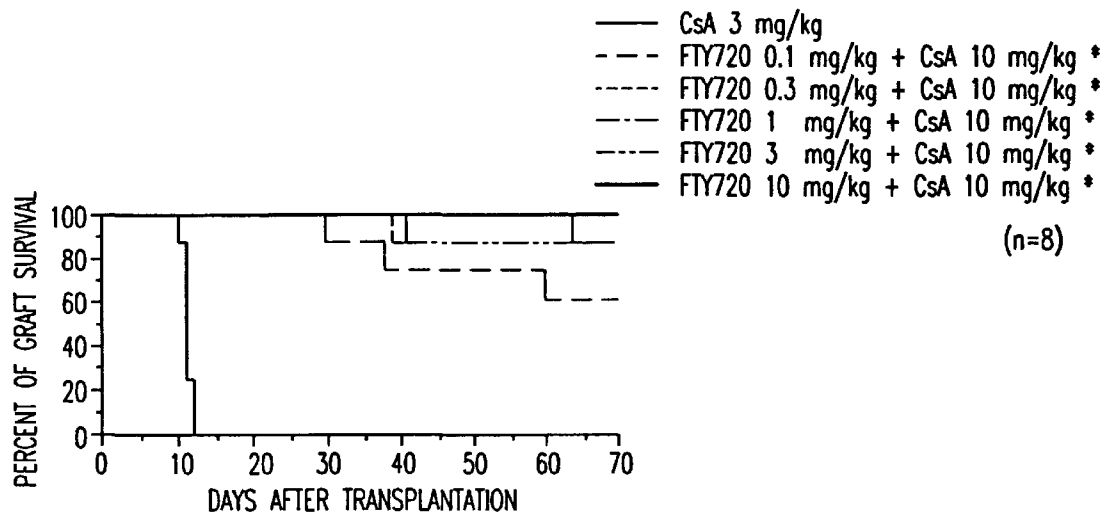


FIG. 2B

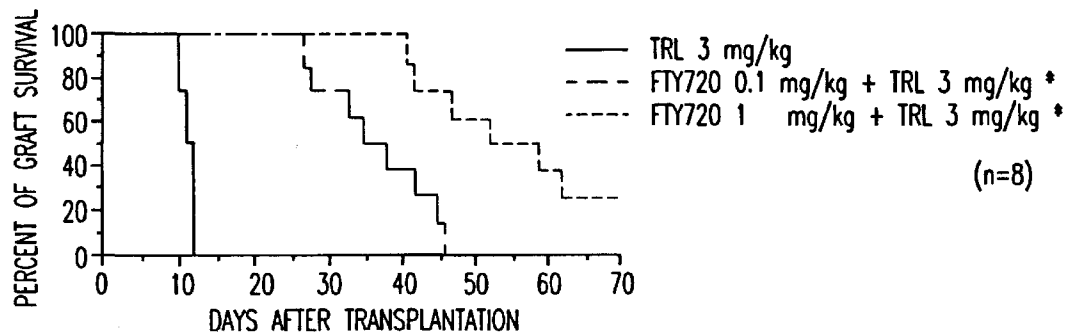


FIG. 2C

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