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(54) Title: GENETIC MODIFICATION OF RATS

(57) Abstract: Compositions and methods are provided for making rat pluripotent and totipotent cells, including rat embryonic stem (ES) cells. Compositions and methods for improving efficiency or frequency of germline transmission of genetic modifications in rats are provided. Such methods and compositions comprise an *in vitro* culture comprising a feeder cell layer and a population of rat ES cells or a rat ES cell line, wherein the *in vitro* culture conditions maintain pluripotency of the ES cell and comprises a media having mouse leukemia inhibitor factor (LIF) or an active variant or fragment thereof. Various methods of establishing such rat ES cell lines are further provided. Methods of selecting genetically modified rat ES cells are also provided, along with various methods to generate a transgenic rat from the genetically modified rat ES cells provided herein. Various kits and articles of manufacture are further provided.