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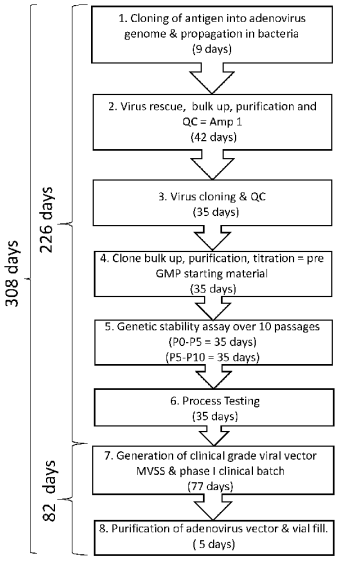
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(54) Title: METHODS AND COMPOSITIONS FOR PRODUCING A VIRUS

Figure 1



(57) Abstract: The invention relates to methods for generating a recombinant adenovirus comprising a nucleotide sequence encoding a heterologous gene of interest for use as a vaccine comprising the steps of inserting the heterologous gene of interest into the adenovirus genome by recombining terminal protein complexed adenovirus genomic DNA (TPC-Ad gDNA) with a polynucleotide comprising a nucleotide sequence encoding the gene of interest and having 5' and 3' ends that are homologous to the insertion site sequence of the adenovirus genomic DNA in an in vitro recombination reaction, transfecting cells growing in individual vessels with a dilution of the in vitro recombination reaction mixture from (i) such that a number of such individual vessels contain a single cell that is infected by a recombinant adenovirus comprising the nucleotide sequence encoding the heterologous gene of interest, and identifying those individual vessels in which a single cell has been infected by the recombinant adenovirus comprising the nucleotide sequence encoding the heterologous gene of interest. Suitably said TPC-Ad gDNA comprises serotype-matched terminal protein and adenovirus genome, and said gene of interest codes for a single epitope, a string of epitopes, a segment of an antigen or a complete antigen protein. The invention also relates to recombinant adenoviruses and compositions made using these methods.

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