immunized with cancer cells of a patient, where after cancer-specific B cells are harvested from the animal and used for *ex vivo* antibody production. Since such antibodies are a tailor-made medicine for the individual patient, they should be produced as fast as possible so that the patient can start his/her Ab therapy as soon as possible. Such antibodies that are specific for an individual's tumor cannot be produced beforehand.

It is one of the objects of the present invention to provide means and methods for producing improved *ex vivo* B cell cultures with a shorter doubling time.

The present invention provides the insight that B cell cultures with a shorter doubling time, as compared to the B cell cultures disclosed in WO 2007/067046, are obtained when rabbit B cells are used. Whereas commonly used B cells such as human B cells, murine B cells and llama B cells typically have a doubling time of 25-36 hours, the present inventors have surprisingly found that rabbit B cell cultures can be obtained with a doubling time of 20 hours or less. This insight allows significant faster production of antibodies of interest, resulting in a higher yield within a given time frame, which is particularly valuable for commercial antibody production and therapeutic applications.

Summary

In one aspect, the present invention refers to use of a rabbit B cell for obtaining an ex vivo B cell culture with a mean doubling time of 20 hours or less. In another aspect, the present invention refers to a method for obtaining an ex vivo B cell culture with a mean doubling time of 20 hours or less, the method comprising inducing, enhancing and/or maintaining expression of Bcl-6, or a rabbit homologue thereof, in a B cell and inducing, enhancing and/or maintaining expression of at least one anti-apoptotic nucleic acid molecule in said B cell, characterized in that said B cell is a rabbit B cell. In yet another aspect, the present invention refers to a method for increasing the replicative life span of a rabbit B cell, the method comprising inducing, enhancing and/or maintaining expression of Bcl-6, or a rabbit homologue thereof, in a rabbit B-cell and inducing, enhancing and/or maintaining expression of at least one anti-apoptotic nucleic acid in said B-cell, characterized in that said rabbit B cell is provided with a nucleic acid molecule encoding Bcl-6, or a rabbit homologue thereof, or a functional part or a functional derivative thereof, and/or with at least one anti-

apoptotic nucleic acid molecule, via transduction with a gene delivery vehicle that comprises at least a functional part of the extracellular domain of a gibbon ape leukemia virus (GALV) envelope protein or a protein that has at least 70% sequence identity with at least a functional part of the extracellular domain of a GALV envelope protein. In a further aspect, the present invention refers to use of at least a functional part of the extracellular domain of a gibbon ape leukemia virus (GALV) envelope protein, or a protein that has at least 70% sequence identity with at least a functional part of the extracellular domain of a GALV envelope protein, for introducing a nucleic acid molecule of interest into a rabbit B cell. In yet another aspect, the present invention refers to a method for obtaining antibodies, comprising inducing, enhancing and/or maintaining expression of Bcl-6, or a rabbit homologue thereof, in a rabbit B-cell; inducing, enhancing and/or maintaining expression of at least one anti-apoptotic nucleic acid molecule in said B-cell; culturing said B cell *ex vivo*; and harvesting antibodies produced by said B cell within 7-14 days, preferably within 9-12 days. In a further aspect, the present invention refers to an isolated or recombinant rabbit B cell bound to at least a functional part of the extracellular domain of a gibbon ape leukemia virus (GALV) envelope protein, or to a protein that has at least 70% sequence identity with at least a functional part of the extracellular domain of a GALV envelope protein. In yet another aspect, the present invention refers to an isolated or recombinant rabbit B cell comprising:

- a non-rabbit anti-apoptotic nucleic acid molecule, preferably encoding Bcl-xL or Mcl-1 or Bcl-2 or A1 or Bcl-w or Bcl2L10 or a functional part or a functional derivative thereof, and a non-rabbit nucleic acid molecule encoding Bcl-6 or a functional part or a functional derivative thereof. In a further aspect, the present invention refers to an *ex vivo* rabbit B cell culture which has a mean doubling time of 20 hours or less. In yet another aspect, the present invention refers to an antibody when obtained by a method as disclosed herein. In a further aspect, the present invention refers to an antibody produced by a rabbit B cell as disclosed herein or by an *ex vivo* rabbit B cell culture as disclosed herein. In one aspect, the present invention refers to use of a gene delivery vehicle comprising at least a functional part of the extracellular domain of a gibbon ape leukemia virus (GALV) envelope protein, or a protein that has at least 70% sequence identity with at least a functional part of the extracellular domain of a GALV envelope protein, and a nucleic acid sequence encoding Bcl-6, or a rabbit homologue thereof, or a

functional part or a functional derivative thereof, and/or at least one anti-apoptotic nucleic acid sequence, for increasing the replicative life span of a rabbit B cell.

Accordingly, the ~~invention provides~~disclosure describes a use of a rabbit B cell for obtaining an *ex vivo* B cell culture with a mean doubling time of 20 hours or less. *Ex vivo* rabbit B cell cultures according to the present invention are typically obtained by expression of Bcl-6, or a rabbit homologue thereof, and an anti-apoptotic nucleic acid molecule in a rabbit B-cell. Further ~~provided~~ described is therefore a method for obtaining an *ex vivo* B cell culture with a mean doubling time of 20 hours or less, the method comprising:

- inducing, enhancing and/or maintaining expression of Bcl-6, or a rabbit homologue thereof, in a B-cell and
- inducing, enhancing and/or maintaining expression of an anti-apoptotic nucleic acid molecule in said B-cell,

characterized in that said B cell is a rabbit B cell.