presence of doxycycline.

It was studied if polyploidization of megakaryocytic progenitor cells derived from an ROCK inhibitor by the presence or absence of expression of a BCL-XL gene (FIG. 7).

The degree of polyploidization was studied (ploidy assay) by suppressing expression of MYC/BMI1 in the presence of 10 μM of Y27632 while inducing suppression of BCL-XL, and culturing the resulting cells for 7 days. It was confirmed that the number of polyploidized cells with 8N or greater significantly increased in the BCL-XL expressed cell line (a shaded bar in FIG. 7B) compared with a cell line (a blank bar in FIG. 7B) in which BCL-XL was not expressed. In addition, it was observed that the number of the cells in which BCL-XL was expressed showed a gradual increase (■ in FIG. 8) while the number of the cells in which BCL-XL was expressed decreases (▲ in FIG. 8).

This suggests that ~~in order to avoid oncogene dependence in~~ the megakaryocytes before polyploidization which acquired high proliferation capacity as a result of forced expression of the oncogene became oncogene-dependent and, once the oncogenes like MYC/BMI1 were removed, became susceptible to apoptosis, and thus, the expression of genes suppressing apoptosis such as BCL-XL gene was necessary in order to prevent such apoptosis~~were effective~~.

[0060] 2-7-4. Influence of ROCK inhibitor + forced expression of BCL-XL gene + suppression of p53 gene

It was studied whether suppression of expression of

p53 promoted polyploidization of megakaryocytes before polyploidization or not.

Expression of the p53 gene was suppressed as in 2-2 by lentivirus infection at MOI=10 by using a lentivirus FG12 vector in which ~~one~~ H1 promoter, shp53 had been introduced.

After suppression of expression of MYC/BMI1, forced expression of BCL-XL, and suppression of expression of p53 in the presence of Y27632, culturing was conducted for 7 days at 39°C. After culturing, the degree of polyploidization was studied. As a result, it was found that compared with control cells (black bar in FIG. 9B) in which p53 was not knocked down, cells (blank bar in FIG. 9B) in which p53 was knocked down showed an increase in the number of the cells with 8N and polyploidization was promoted.

[0061] 2-7-5. Influence of ROCK inhibitor + forced expression of BCL-XL gene + suppression of p53 gene + valproic acid

Influence on polyploidization was studied by further treating the cells, which was subjected to the treatment of 2-7-4, with valproic acid. After suppression of expression of MYC/BMI1, forced expression of BCL-XL, treatment with the ROCK inhibitor (10 μM), and suppression of expression of p53, valproic acid (final concentration: 0.5 mM) was added to the medium and culturing was conducted at 39°C for 7 days. As a result, it was found that cells (blank bar in FIG. 10B) treated with valproic acid showed promoted polyploidization compared with control cells