★★★ ＜第29回知的財産翻訳検定試験【第14回英文和訳】＞ ★★★
≪１級課題 -バイオテクノロジー-≫

【解答にあたっての注意】

１．問題の指示により和訳してください。

２．解答語数に特に制限はありません。適切な箇所で改行してください。

３．課題文に段落番号がある場合、これを訳文に記載してください。

４．課題は４題あります。それぞれの課題の指示に従い、４題すべて解答してください。

問１． 次の英文は欧州特許の従来技術（Background）の記載です。***(Start)***から***(End)***までの部分を日本語に訳して下さい。

Next-generation sequencing enables researchers to obtain large amounts of data at a reduced cost and thus provides a tremendous opportunity to genotype an individual of any species in depth (Lai et al. "Genome-wide patterns of genetic variation among elite maize inbred lines" 2010, Nat Genet 42: 1027-1030). Recently, several genotyping-by-sequencing (GBS) approaches were developed to genotype hundreds of individuals simultaneously (Andolfatto et al. "Multiplexed shotgun genotyping for rapid and efficient genetic mapping" 2011, Genome Res 21: 610-17; Baird et al. "Rapid SNP discovery and genetic mapping using sequenced RAD markers" 2008, PLoS One 3: e3376; Elshire et al. "A Robust, Simple Genotyping-by-Sequencing (GBS) Approach for High Diversity Species" 2011 PLoS One 6: e19379).

(Start)

Conventional genotyping is most often conducted using pre-defined SNP markers that must be discovered and validated in advance; these markers are often population-specific. These SNPs are typically detected via hybridization or by individual SNP-specific PCR-based assays. In contrast, GBS technology enables the detection of a wider range of polymorphisms than PCR-based assays (e.g., SNPs plus small insertions and/or deletions, e.g., "indels"). GBS technology eliminates the need to pre-discover and

validate polymorphisms. Hence, GBS can be used in any polymorphic species and any segregating population.

However, conventional GBS methods share at least two drawbacks. First, conventional methods use double-stranded adaptors and, consequently, associated methods require stringent control of the template:adaptor concentration ratio in the adaptor ligation. As a result, precisely quantified, high quality input DNA is required as a starting material (see, e.g., Elshire et al.). Second, these methods survey hundreds of thousands or more sites and thus require numerous sequencing reads to generate enough coverage for each site in each sample.
(End)

For example, WO 2007/114693 discloses a method for identifying molecular markers using double-stranded adaptors. The method includes digesting nucleic acid with restriction enzymes and ligating each side with a double-stranded adaptor to produce templates that are amplified and sequenced.

問２．***START***から***END***までを和訳してください。

START

The present invention is based, at least in part, on the discovery that inhibiting or blocking Programmed Death 1 (PD-1) or Programmed Death- 1 Ligand (PD-L1) in combination with inhibition of an immune checkpoint inhibitor (e.g., one or more of TEV1-3, LAG-3 or CTLA4) results in a synergistic therapeutic benefit for treating a hematologic cancer, e.g., a myeloma. This finding is unexpected given the lack of such benefit observed for inhibiting or blocking other combinations of immune checkpoint regulators.

Accordingly, in one aspect, the invention features a method of treating a subject afflicted with a hematologic cancer comprising

administering to the subject an inhibitor of PD-1 or PD-L1, and an inhibitor of an immune checkpoint regulator (e.g., an inhibitor of one or more of TEVl-3, LAG-3 or CTLA4). In one embodiment, an inhibitor of PD-1 or PD-L1 is administered in combination with an inhibitor of TEVI-3. In another embodiment, an inhibitor of PD-1 or PD-L1 is administered in combination with an inhibitor of LAG-3. In yet another embodiment, an inhibitor of PD-1 or PD-L1 is administered in combination with an inhibitor of CTLA-4.

END

問３．***(Start)***から***(End)***までの部分を日本語に訳して下さい。

Autophagy-Defective Tumor Cells Accumulate p62 in Response to Stress

To address the potential role of autophagy-dependant protein quality control in tumor suppression, p62 modulation was assessed during metabolic stress and recovery in autophagy-competent (beclin1$^{+/+}$ and atg5$^{+/+}$) and autophagy-defective (beclin1$^{+/-}$ and atg5$^{-/-}$) immortalized baby mouse kidney (iBMK) cells. ***(Start)***Cells were engineered to express Bcl-2, as the assessment of autophagy is facilitated in an apoptosis-defective background. Under normal growth conditions, p62 levels were low in wild-type cells and slightly elevated in autophagy-defective iBMK cells (FIG. 1B). Following 7 days of metabolic stress there was dramatic p62 induction in wild-type cells that was further elevated in autophagy-defective cells in a predominantly punctate pattern suggestive of p62 aggregation. In wild-type cells, most p62 aggregates were eliminated within 24 hr of recovery, whereas p62 remained predominantly in large aggregates in autophagy-defective cells (FIG. 1B). p62 aggregates persisted in mutant cells after 2 days of recovery (FIG. 1B) and remained so for at least a week (data not shown), indicating that autophagy is required to limit the formation and to promote the clearance of p62. Consistent with this, higher p62 levels were observed in

autophagy-deficient ($atg5^{-/-}$), as compared to wild-type ($atg5^{+/+}$) iBMK cells stably expressing myc-tagged p62 (myc-p62) (FIG. 1C). Thus, metabolic stress induced p62 accumulation and aggregate formation, requiring autophagy for elimination. ***(End)***

問４．reference は明細書の一部を抜粋したものです。この内容を参考にして、以下の請求項を訳してください。

1. A small inhibitory nucleic acid (siRNA) molecule comprising between about 15 base-pairs and about 40 base-pairs and at least one universal-binding nucleotide.

2. The siRNA molecule of claim 1 wherein said universal-binding nucleotide is selected from the group consisting of inosine, 1-ß-D-ribofuranosyl-5-nitroindole, and 1-ß-D-ribofuranosyl-3-nitropyrrole.

4. The siRNA molecule of claim 3 wherein said siRNA molecule comprises a double-stranded region.

14. The siRNA molecule of any one of claims 1- 13 wherein said universal-binding nucleotide increases the binding specificity of said siRNA for a target gene when the siRNA is contacted with a biological sample.

15. The siRNA molecule of any one of claims 1- 13 wherein said universal-binding nucleotide reduces off-target effects of the siRNA molecule when the siRNA is contacted with a biological cell.

16. The siRNA molecule of claim 1 wherein said siRNA is capable of specifically binding to a variant of a target gene expressed in a virus selected from the group consisting of a retrovirus and a respiratory virus.

(reference)
The term “universal-binding nucleotide” as used herein refers to a nucleotide analog that is capable of forming base-pairs with each of the natural DNA/RNA nucleotides with little discrimination between them. Non-limiting examples of universal-binding nucleotides include inosine, 1-β-D-ribofuranosyl-5-nitroindole, and/or 1-β-D-ribofuranosyl-3-nitropyrrole.