

Patent Document 1: Japanese Unexamined Patent
Application, Publication No. 2011-22002

DISCLOSURE OF THE INVENTION

Problems to be Solved by the Invention

However, analysis methods using HPLC, LC-MS/MS, and the like, are complicated in setting analysis conditions, and an analysis method using autoradiography or the like needs to use a radioisotope, hence all of them were not convenient methods.

In view of the above circumstances, an object of the present disclosure is to provide a new molecular kinetics evaluation method for evaluating molecular kinetics of a test material, and a new screening method for selecting a test material showing specific molecular kinetics.

Means for Solving the Problems

In one aspect, there is provided a molecular kinetics evaluation method comprising a step of evaluating molecular kinetics of a specific protein affinity molecule or a protein-degradation inducing molecule by detecting degradation of a specific protein in a specimen, wherein the specimen is collected from a human or a non-human animal which has been administered with the protein-degradation inducing molecule, which is a conjugate of a protein-degradation inducing tag as a molecule which has an affinity with a protease and does not inhibit degradation of a protein by the protease and the specific protein affinity molecule which has

an affinity with the specific protein, and in the living body of which the degradation of the specific protein has been induced.

In another aspect, there is provided a screening method comprising a step of selecting a specific protein affinity molecule or a protein-degradation inducing molecule showing specific molecular kinetics by detecting degradation of a specific protein in a specimen, wherein the specimen is collected from a human or a non-human animal which has been administered with the protein-degradation inducing molecule, which is a conjugate of a protein-degradation inducing tag as a molecule which has an affinity with a protease and does not inhibit degradation of a protein by the protease, and the ~~specific protein affinity molecule~~ which has an affinity with the specific protein, and in the living body of which the degradation of the specific protein has been induced.

Specific means for achieving the above object include the following embodiments.

<1> A molecular kinetics evaluation method including:

a step of administering a protein-degradation inducing molecule to a human or a non-human animal, the protein-degradation inducing molecule being a conjugate of a protein-degradation inducing tag that is a molecule that has an affinity with a protease and does not inhibit degradation of a protein by the protease and a specific protein affinity molecule that has an affinity with a specific protein, and inducing degradation of the specific protein in a living body

CLAIMS

1. A molecular kinetics evaluation method comprising:
a step of evaluating molecular kinetics of a specific protein affinity molecule or a protein-degradation inducing molecule by detecting degradation of a specific protein in a specimen,
wherein the specimen is collected from a human or a non-human animal which has been administered with the protein-degradation inducing molecule, which is a conjugate of a protein-degradation inducing tag as a molecule which has an affinity with a protease and does not inhibit degradation of a protein by the protease and the specific protein affinity molecule which has an affinity with the specific protein, and in the living body of which the degradation of the specific protein has been induced.
2. The molecular kinetics evaluation method according to claim 1, wherein in the living body of a human or a non-human animal which has been administered with the protein-degradation inducing molecule, the degradation of the specific protein is induced in a ubiquitin-independent manner.
3. The molecular kinetics evaluation method according to

claim 1 or 2, wherein the protein-degradation inducing tag has a structure where a protease inhibitory activity of a protease inhibitor is inactivated.

4. The molecular kinetics evaluation method according to any one of claims 1 to 3, wherein the protease is proteasome.

5. The molecular kinetics evaluation method according to claim 4, wherein the protein-degradation inducing tag has a structure where a proteasome inhibitory activity of a proteasome inhibitor is inactivated.

6. The molecular kinetics evaluation method according to claim 5, wherein the proteasome inhibitory activity is an inhibitory activity against at least one selected from a caspase-like activity, a trypsin-like activity, and a chymotrypsin-like activity.

7. The molecular kinetics evaluation method according to any one of claims 1 to 6, wherein the protein-degradation inducing molecule is a drug candidate molecule, the method further comprising a step of evaluating a pharmacological action due to induction of degradation of the specific protein in the

living body of a human or non-human animal.

8. The molecular kinetics evaluation method according to any one of claims 1 to 7, wherein the molecular kinetics is specificity to a tissue, an organ, a cell, or a molecule.

9. A screening method comprising:

a step of selecting a specific protein affinity molecule or a protein-degradation inducing molecule showing specific molecular kinetics by detecting degradation of a specific protein in a specimen,

wherein the specimen is collected from a human or a non-human animal which has been administered with the protein-degradation inducing molecule, which is a conjugate of a protein-degradation inducing tag as a molecule which has an affinity with a protease and does not inhibit degradation of a protein by the protease, and the specific protein affinity molecule which has an affinity with the specific protein, and in the living body of which the degradation of the specific protein has been induced.

10. The screening method according to claim 9, wherein in the living body of a human or a non-human animal which has been administered with the protein degradation inducing molecule,

the degradation of the specific protein is induced in a ubiquitin-independent manner.

11. The screening method according to claim 9 or 10, wherein the molecular kinetics is specificity to a tissue, an organ, a cell, or a molecule.
