

process, or biological property of a cancer cell in the tissue piece; and

- (5) identifying the formation of the hierarchical organization, cancer progression process, or biological property of a cancer cell, which is inhibited by the test substance;

[17] the method of [15] for assessing a pharmaceutical agent for treating or preventing a human cancer, which comprises the steps of:

- (1) culturing *in vitro* an NOG-established cancer cell line to mimic a structure characteristic of each cancer progression process or a biological property thereof;
- (2) treating the cultured cell of (1) with a test substance;
- (3) monitoring a time-dependent change of the hierarchical organization, cancer progression process, or biological property of a cancer cell among the cultured cells; and
- (4) identifying the formation of the hierarchical organization, cancer progression process, or biological property of a cancer cell, which is inhibited by the test substance; and

[18] a method of using a non-human animal transplanted with an NOG-established cancer cell line or an NOG-established cancer cell line as a cancer model animal or cell line which mimics hierarchical organization, cancer progression process, or biological property of a cancer cell.

[Effects of the Invention]

The present invention provides non-human animal models of cancer pathology more similar to human cancer and *in vitro* cell culture systems whose cell morphologies are more similar to those in the human cancer pathology. A result closer to human clinical data is expected be obtained by screening for anti-cancer agents or assessing the pharmacological effects of test substances using an animal model of cancer pathology or a cancer cell culture system that more closely reflects human cancer.

Brief Description of the Drawings

Fig. 1 is a photograph showing an epithelium-like proliferation area in colon cancer. The glandular structure is observed, and E-cadherin is expressed on the whole cell surface.

Fig. 2 shows photographs depicting an epithelium-like proliferation under *in vitro* culture conditions. Left panel: three-dimensional suspension culture; right panel: three-dimensional Matrigel culture. Formation of epithelium-like glandular structures is observed with the three-dimensional Matrigel culture. NOG-established colon cancer cell line was used.

Fig. 3 shows photographs depicting an invasive area in colon cancer. E-cadherin expression has disappeared where each invasive area comes into contact with tumor stroma.

out by the following procedure:

control non-human model animals or NOG-established cancer cell line are prepared without administering the test substance, and in the same manner, the transplanted tissues or cancer cells in a culture system are observed for the biological properties of cancer stem cells and checked for the presence of a property unique to human cancer cells; and the property unique to cancer stem cells is compared between the control animals and non-human model animals or NOG-established cancer cell lines administered with the test substance. In this case, when the property unique to human cancer cells is not present in the non-human animal model or NOG-established cancer cell line administered with the test substance as compared to the control animals, the test substance administered to the test animal or with which the culture system is treated can be judged to have a preventive or therapeutic effect against the human cancer, and the level of the preventive or therapeutic effect can be evaluated based on the incidence of the properties.

The present invention relates to methods of using a non-human animal transplanted with an NOG-established cancer cell line or an NOG-established cancer cell line as a cancer model animal or cell line which mimics the hierarchical organization, cancer progression process, or biological property of cancer cells.

The hierarchical organization, cancer progression process, or biological property of cancer cells can be artificially or artifactually mimicked *in vivo* by transplanting an NOG-established cancer cell line into non-human animals. Thus, such non-human animals transplanted with the NOG-established cancer cell line can serve as very useful cancer model animals, for example, when assessing pharmaceutical agents, searching for candidate target molecules as pharmaceuticals or diagnostic agents, or assessing compounds or biological preparations that act on the candidate molecules using the hierarchical organization, cancer progression process, or biological property of cancer cells.

Furthermore, the hierarchical organization, cancer progression process, or biological property of cancer cells can be artificially or artifactually mimicked *in vivo* or *in vitro* by an NOG-established cancer cell line alone. Thus, the NOG-established cancer cell lines can serve as very useful cancer model animals, for example, when assessing pharmaceutical agents, searching for candidate target molecules as pharmaceutical agents or diagnostic agents, or assessing compounds or biological preparations that act on the candidate molecules using the hierarchical organization, cancer progression process, or biological property of cancer cells.

“Mimic” or “reproduce” means that the model mimics/reproduces to a level enough to achieve the objective depending on the model’s purpose of use. Thus, it is not necessary to mimic/reproduce the *in vivo* events perfectly.

All prior art documents cited herein are incorporated herein by reference.