Carbohydrate Sulfotransferase 15 In Vitro and in a Xenograft Model. PLoS One 10:e0142981, 2015.

SUMMARY

PROBLEMS TO BE SOLVED BY THE DISCLOSURE

[0006] An object of the present disclosure is to provide a pharmaceutical composition (hereinafter also referred to as an invasion suppressing agent of cancer) which inhibits invasion of cancer cells and retains them from progressing in the solid cancers and blood cancers.

MEANS TO SOLVE THE PROBLEMS

[0007] The present inventors investigated the effect of siRNA, which suppresses the expression of the CHST15 gene, using various human cancer cell lines, and found that it has an effect of suppressing the progress of cancer cells and retaining them localized, which is completely different from the effect of suppressing the proliferation of cancer cells predicted from conventional techniques. Also, they found that the effect thereof was also effective not only against solid cancer cells but also blood cancer cells. By retaining cancer cells localized through a mechanism different from proliferation control, it may be used in combination therapy to reduce the side effects of anticancer drugs and molecular-targeted drugs based on the conventional proliferation and division suppressing mechanism, in combination therapy with immune checkpoint inhibitors based on the anti-tumor immune mechanism, and further in the suppression of invasion and metastasis to enhance the efficacy of surgical operation and radiotherapy, etc., whereby the application to multidisciplinary cancer treatment and recurrence prevention was expected.

[0008] More specifically, the present disclosure is to provide the following [1] to [8].

[1] A pharmaceutical composition for suppressing invasion of cancer which comprises siRNA that suppresses expression of CHST15 gene.

[2] The pharmaceutical composition described in [1] for suppressing metastasis of cancer.

[3] The pharmaceutical composition described in [1] or [2], wherein the cancer is a solid cancer or a blood cancer.

[4] The pharmaceutical composition described in any of [1] to [3], characterized in that the progress of the cancer is suppressed by retaining the cancer.

[5] A method for suppressing invasion of cancer, which comprises a step of administering siRNA that suppresses expression of CHST15 gene.

[6] An siRNA that suppresses expression of CHST15 gene for use in a method for suppressing invasion of cancer.
[7] Use of an siRNA that suppresses expression of CHST15 gene in the production of an invasion suppressing agent of cancer.
[8] A method for producing an invasion suppressing agent of cancer, which comprises a step of using siRNA that suppresses expression of CHST15 gene.
[0008a] In one aspect, the present disclosure refers to a pharmaceutical composition for suppressing invasion of cancer which comprises siRNA that suppresses expression of CHST15 gene.
[0008b] In one aspect, the present disclosure refers to use of siRNA that suppresses expression of CHST15 gene in the manufacture of a medicament for inhibiting invasion of cancer.
[0008c] In one aspect, the present disclosure refers to an siRNA that suppresses expression of CHST15 gene for use in production of an invasion suppressing agent of cancer.
[0008d] In one aspect, the present disclosure refers to use of an siRNA that suppresses expression of CHST15 gene in the production of an invasion suppressing agent of cancer.
[0008e] In one aspect, the present disclosure refers to a method for producing an invasion suppressing agent of cancer, which comprises a step of using siRNA that suppresses expression of CHST15 gene.
[0008f] In one aspect, the present disclosure refers to a pharmaceutical composition for use in suppressing invasion of cancer, wherein the pharmaceutical composition comprises siRNA that suppresses expression of CHST15 gene.
[0008g] In one aspect, the present disclosure refers to use of a pharmaceutical composition in the manufacture of a medicament for suppressing invasion of cancer, wherein the pharmaceutical composition comprises siRNA that suppresses expression of CHST15 gene.

EFFECTS OF THE DISCLOSURE

[0009] In the progression of cancer cells, there are processes of proliferation at the primary lesion, invasion, metastasis, and angiogenesis at metastatic lesion, each of which is regulated by different mechanisms. Most of the existing anticancer agents and molecular targeted drugs mainly suppress proliferation, but there is a problem of side effects due to their effects on normal cells as well. In addition, due to the Dichotomy (choice of either proliferation or migration) of cell proliferation and migration, proliferation is suppressed and migration can be inversely activated, which is said to be a factor against anticancer agents and radiotherapy, in particular, in cancer cells with high migration capacity. Therefore, in the CHST15 siRNA, there was a concern about a possibility that it activates migration inversely, considering the previously reported suppressing effect on proliferation.

Thus, when *in vitro* test was carried out using BxPC-3 cells, which are pancreatic cancer similar to the previously reported Panc-1 cells but are a different cell line, almost no proliferation suppressing effect was admitted by suppressing expression of CHST15 by adding CHST15 siRNA, but an unexpected result that invasion was suppressed was obtained. Furthermore, surprisingly, it was revealed for the first time that this invasion suppressing effect is present not only against solid cancers but also against blood cancers.

According to the present disclosure, it can be applied to multidisciplinary cancer treatment and recurrence prevention, such as combination therapy that can reduce the side effects of conventional anticancer agents and molecular-targeted drugs based on the conventional proliferation and mitogenic inhibitory mechanisms, combination therapy with immune checkpoint inhibitors based on anti-tumor immune mechanisms, and further to enhance the effect of surgical operation and radiotherapy by suppressing invasion and metastasis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Fig. 1 shows a knockdown effect by CHST15 siRNA (A) , proliferation