**Title**

Suppression of tumoral metastasis and invasiveness via the control of cell-to-cell adhesion networks

**Background**

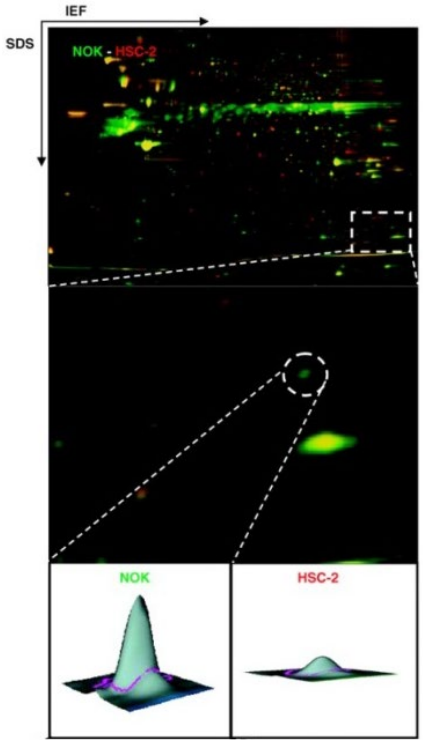
Controlling the metastasis and invasiveness of cancer is a key element of cancer therapy, and is a task that all medical researchers working in cancer therapy must resolve as swiftly as possible. If a new metastasis suppression drug treatment could be established and quickly made clinically applicable, it would provide an unquestionable and unparalleled benefit to patients. Our research focused on Lin7C and Lin7C-Cask-βcatenin network, and we implemented a research protocol that aimed towards the application of metastasis suppression methods.

**Outline**

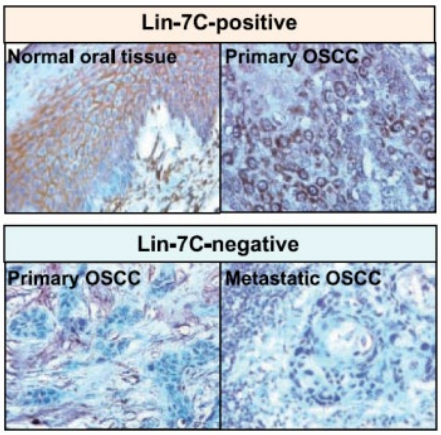
In this research, we have identified Mirtazapine as the most effective pharmaceutical reagent out of six reagents characterized as ligands for, thus agonists to, the gene HTR2C that is an upstream molecule of the Lin7C-Cask-βcatenin network, and through the use of the reagent we have made possible the suppression of invasiveness and migration. We have also identified the optimal Mirtazapine concentration and researched it's possibility as a metastasis and invasiveness suppressant in mouse cancer models. Mirtazapine is already being sold as an antidepressant, and because the clinical application would be incredibly simple, we are planning further research into proving its viability.

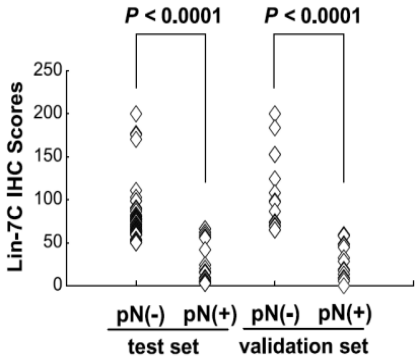
**Molecular Biological Analysis of Lin7C**

Through exhaustive analysis of protein expression, we have compared cancerous mouth cells and normally functioning mouth cells and discovered that the expression of Lin7C is reduced in oral tumors.

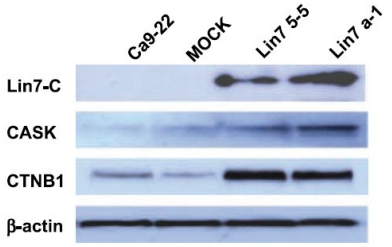


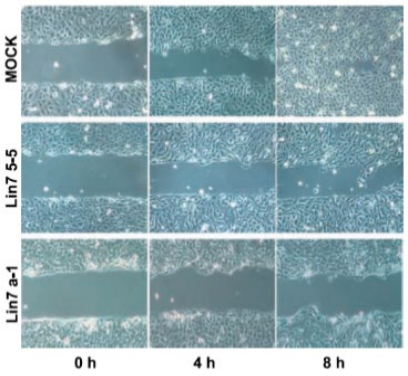
In the clinical oral cancer test result statistics, Lin7C was significantly lower in lymph node metastasis patients.

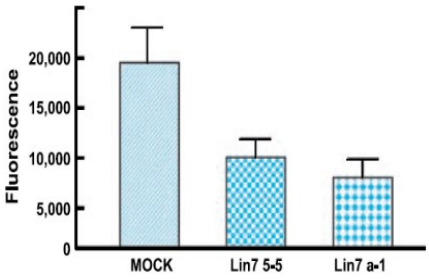



Furthermore, it was clear that when an excessive expression of Lin7C was introduced, the Lin7C-Cask-βcatenin network was activated and metastasisation was suppressed.

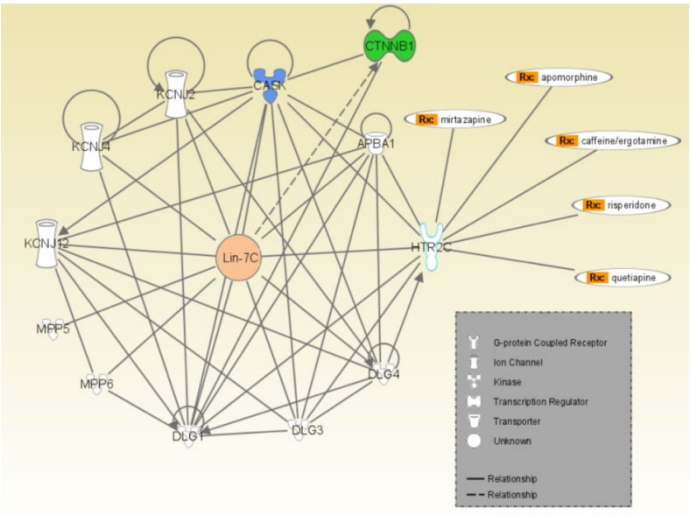



**Network Analysis**

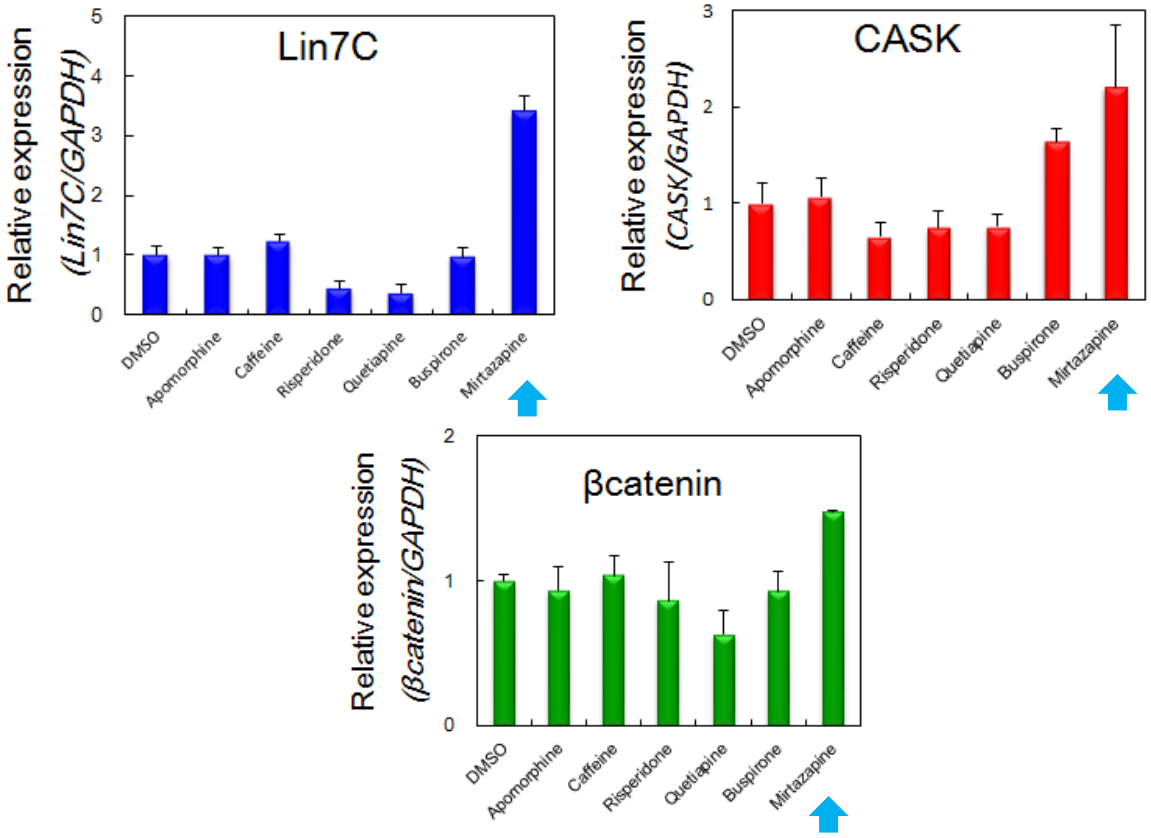
Ingenuity System's Ingenuity Pathway Analysis (IPA) software was used. IPA uses molecular biological, genetic, gene product, and low molecular information gathered from over 300 journals being published around the world and creates a database from unique ontologies (categories). Using IPA, the HTR2C that is an upstream molecule of the Lin7C-Cask-βcatenin network and its agonists were identified.



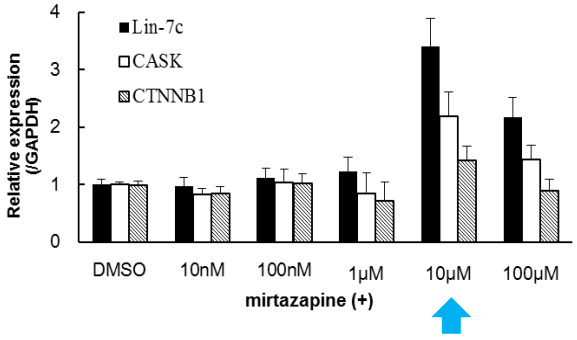
**HTR2C Agonists**

① Apomorphine
② Caffeine
③ Risperidone
④ Quetiapine
⑤ Buspirone
⑥ Mirtazapine

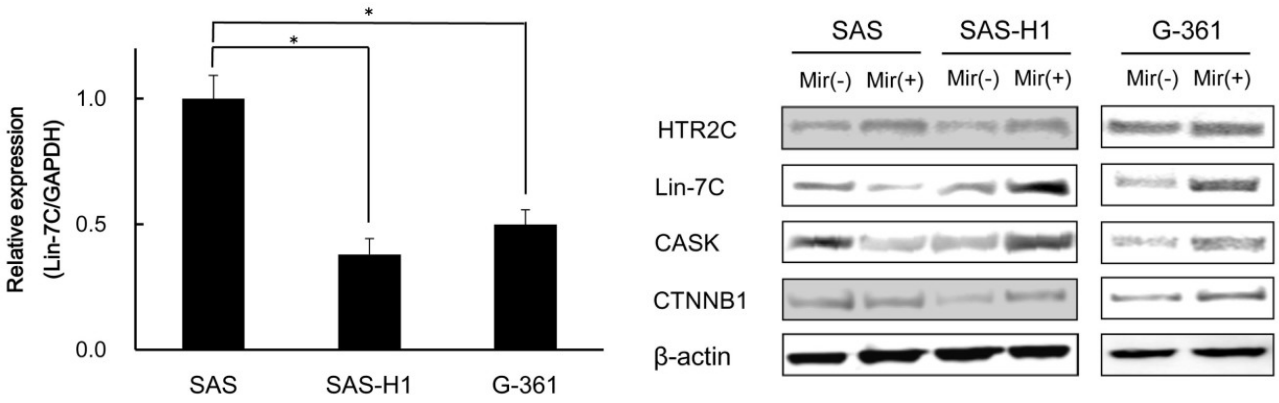
**Analysis of Lin7C expression when 6 agonists to HTR2C were applied to cancerous mouth cells**



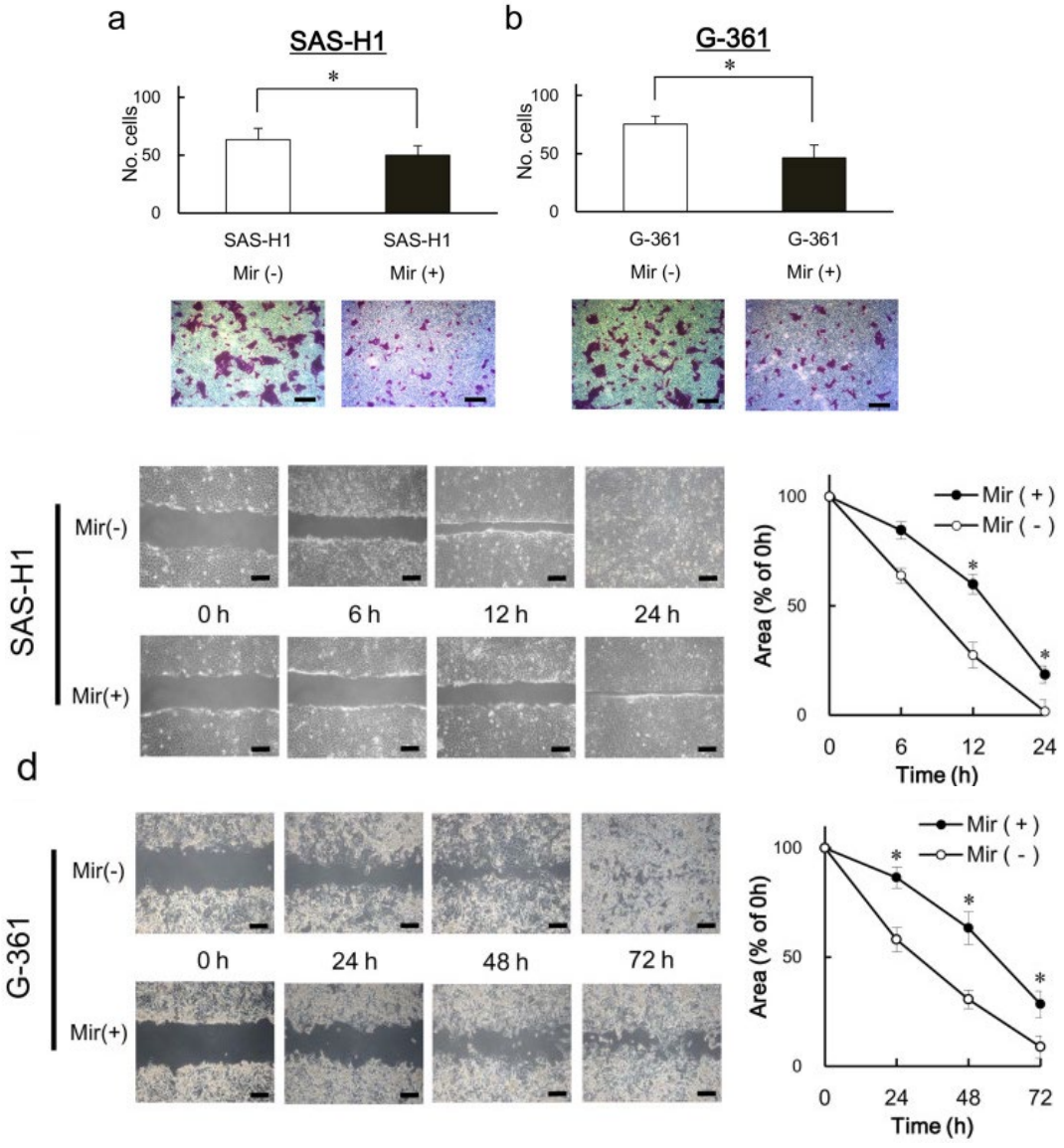

**Optimal Mirtazapine concentration identification analysis**



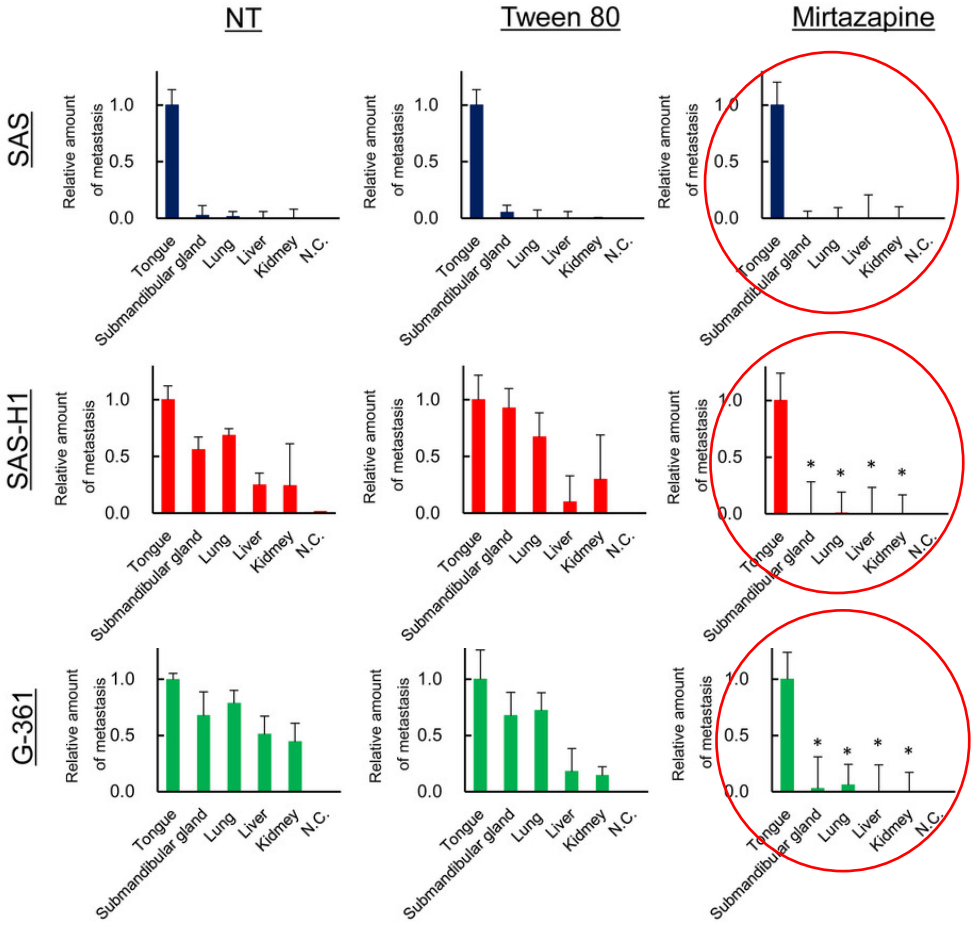
**Analysis of Lin7C-Cask-βcatenin network expression when optimally concentrated Mirtazapine was applied**




**Analysis of cell invasiveness and migration when Mirtazapine was applied**



**Analysis of metastasis when Mirtazapine was applied to cancerous mouse**




**Patent and status**

JP2014-102285 (JP6452954)

**Advantages**

--Because the drug intended is already being used for therapy of another disease, tests for toxicity are unneeded, and actual clinical usage can be expected sooner than usual.

--This therapy is not restricted to specialized facilities, but can be used affordably around the world as a tumoral metastasis and invasiveness suppressant.

--Because supplementary chemical therapy is becoming the standard therapy, can expect domestic and international sales of 100 million to 1 billion yen a year even only considering administration to metastasized patients

**Applications**

--Preventative and restorative treatment for lymph node metastasis.

--Metastasis and invasiveness suppressant

--Can effectively preserve the patient's functions in surgery.

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**Licensing Contact**

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