***Brief Report***

**Novel aminopeptidase N (APN/CD13) inhibitor 24F can suppress invasion of hepatocellular carcinoma cells as well as angiogenesis**

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**Conflict of Interest:** xxxxxx

**Abstract**

Aminopeptidase N (APN)/CD13 is a widely expressed transmembrane protein and its altered expression has been detected in various cancer cells. Several APN inhibitors have been developed and some of them have been found to ……

***Keywords*:** APN, CD13, HCC, cancer growth, invasion, angiogenesis

**1. Introduction**

Aminopeptidase N (APN), which is also known as CD13, is a membranous glycoprotein expressed in a variety of cells and tissues (*1,2*). Several studies have suggested……

Various natural or artificially-synthesized compounds with an ability to work as an inhibitor of APN have been developed (*8*). One well investigated APN inhibitor ……

Hepatocellular carcinoma (HCC) is a common malignant disease, especially in eastern Asia. Various therapeutic strategies of HCC treatment including……

**2. Materials and Methods**

2.1. *Compound*

The hydroxamic acid derivative 24F was synthesized as one of a series of cyclic-imide peptidomimetics with a free amino group using a 3D-QSAR model (*11*). In the present study, this compound was ……

2.2. *Cell lines*

HCC cell line HuH-7 and human promyelocytic leukemia cell line HL-60 were obtained from Health Science Research Resources Bank (HSRRB; Osaka, Japan).….

2.3. *Cell growth assay*

Continuously-cultivated HuH-7 cells were harvested in tubes and resuspended in DMEM containing 10% FBS after washing with……

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**3. Results and Discussion**

The enzyme reaction assay was performed to confirm whether newly-synthesized compound 24F can inhibit the activity of aminopeptidase that is expressed on the surface of cell membranes. HL-60 cells are positive for ……

 Next, the effect of 24F on HCC cell growth was analyzed using HuH-7 cells that were confirmed to have positive expression of APN by flowcytometric analysis (data not shown). HuH-7 cell growth was inhibited by ……

 Cell invasion is the essential event for cancer progression and metastasis (*15*). Therefore, for cancer therapy, inhibition of cancer cell invasion is an important strategy, along with inhibition of cancer cell growth. This study analyzed the effect of 24F on HuH-7 cell invasion by means of……

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 In conclusion, our newly-developed compound 24F can inhibit the activity of the targeted enzyme APN and suppress the invasive capacity of HCC cells. Furthermore, it was also suggested that ……

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……**Figure legends**

**Figure 1.** **Chemical structure of 24F.**

**Figure 2.** ***In vitro* analyses of 24F.** (**A**) Effect of 24F on the inhibition of APN enzyme activity. The absorbance, the level of enzyme reaction of APN, was decreased in samples with 24F in a dose-dependent manner. (**B**) Staining of HuH-7 cells that invaded Matrigel. The number of cells stained was decreased when incubating cells with 100 g/ml of 24F (*right*) compared with ……