Poster session 5: New drugs/targets: signaling pathways

**ISOLATION OF NOVEL CELL MIGRATION INHIBITOR MIGRACINS FROM STREPTOMYCES AND INHIBITION OF CELLULAR INVASION IN OVARIAN CARCINOMA CELLS**

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**Background:** Bioactive metabolites that inhibit cellular migration are considered to be useful for the suppression of cancer metastasis. Then, we have looked for cancer cell migration inhibitors from microorganisms. In one hand, ovarian carcinoma is highly invasive and often metastasizes into liver, lung, and peritoneal cavity.

**Materials and methods:** Cellular migration was assessed by wound healing assay with breast carcinoma MDA-MB-231 cells. We employed about 1500 microbial broths for random screening. From the culture filtrate with positive activity, active principle was isolated by chromatography. The structure was determined mainly by NMR and mass spectroscopy after the purification.

**Results:** After testing the thousands of microbial culture filtrates, we have isolated novel compounds migracin A and B from Streptomyces. Migracin A and B showed similar inhibitory activity on the migration of MDA-MB-231 cells and fibrosarcoma HT-1080 cells. They also inhibited TNF-alpha and TGF-beta-induced migration of lung adenocarcinoma A549 cells. Migracin A inhibited the Matrigel invasion of clear cell ovarian carcinoma ES-2 cells without any toxicity. Since the structure of migracin is related to that of luminacin that inhibits tube formation, we have studied the effect on lumina formation. As a result, migracin A inhibited VEGF-induced lumina formation in HUVEC. The mechanism of inhibition is being studied.

**Conclusions:** We have discovered migracins as novel inhibitors of cellular migration and invasion. Migracin inhibited invasion of ovarian carcinoma cells, and is considered to be a candidate of new metastasis inhibitor.