
Downloaded from: http://e-space.mmu.ac.uk/621162/

Version: Accepted Version

Publisher: Elsevier

DOI: https://doi.org/10.1016/S0959-8049(16)61378-3

Please cite the published version

http://e-space.mmu.ac.uk
Material and Methods: In this study we have identified two human breast cancer cell lines which either in a spontaneous metastasis setting or when injected directly into the circulation, give rise to distant macrometastases in immunocompromised mice. In addition to this we have established an in vitro dormancy assay and an ex vivo lung slice approach in order to interrogate the stromal factors identified from the in vitro and in vivo models, that are required for establishing a dormant state of a proliferative one.

Results and Discussion: In both the in vitro and in vivo models we have demonstrated that these dormant cancer cells can be stimulated to develop productive macro-metastases. Using an ex vivo lung slice approach, we were able to maintain viability of the lung slices for up to 21 days with the breast cancer cells remaining dormant as seen in vivo. This provides a platform to strictly manipulate stromal factors and monitor the emergence from dormancy in live tissue.

Conclusion: Using these models we can interrogate the contribution of the microenvironment to the emergence from dormancy with a view to aim to identify and develop clinically relevant novel strategies to suppress or prevent the development of metastatic disease.

No conflict of interest.

Anticancer effects of lipid encapsulated Bilberry

1Cancer Research Institute of West TN, Cancer Therapeutics, Henderson, USA, 2Union University, Chemistry, Jackson, USA, 3University of Tennessee, Biochemistry, Knoxville, USA, 4Freed Hardeman University, Nursing, Henderson, USA

Rapidly accumulating laboratory and clinical research evidence indicates that anthocyanins have anticancer activity and more intriguing, the evaluation of bilberry anthocyanins as chemo-preventive agents is progressing. These applications are collectively due to the anthocyanins up-regulating tumor suppressor genes, inducing apoptosis in cancer cells, repairing and protecting genomic DNA integrity, which is important in reducing age-associated oxidative stress, as well as improving neuronal and cognitive brain function. Bilberry anthocyanins have pronounced health effects, even though they have a low bioavailability. To increase the bioavailability, Bilberry was encapsulated in 8 nm diameter liposomal nanospheres, called NutraNanoSpheres (NNS), at a concentration of 2.5 mg/ml. These Bilberry NNS were used to study the apoptotic/cytotoxic effects on K562 cancer cells. Flow cytometric fluorescent quantification of the uptake of Propidium Iodide in a special cell viability formulation into dead K562 cells was used to determine the effects of Bilberry on the viability of K562 cells. The concentrations of Bilberry that showed the highest levels of percentage inhibition, relative to the control populations, were biphasic, showing 60–70% inhibition between 0.018–1.14 mg/ml (n = 6) and 60% inhibition at 80 mg/ml. The lowest % inhibition (30%) occurred at 40 mg/ml. The LD50 was determined to be 0.01–0.04 mg/ml of Bilberry per 10^7 cells of cell culture exposure. At 48 hr. incubation, the highest % inhibition was only 27%, suggesting a long-term apoptotic event rather than a dormant state of a proliferative one.

Results and Discussion: In both the in vitro and in vivo models we have demonstrated that these dormant cancer cells can be stimulated to develop productive macro-metastases. Using an ex vivo lung slice approach, we were able to maintain viability of the lung slices for up to 21 days with the breast cancer cells remaining dormant as seen in vivo. This provides a platform to strictly manipulate stromal factors and monitor the emergence from dormancy in live tissue.

Conclusion: Using these models we can interrogate the contribution of the microenvironment to the emergence from dormancy with a view to aim to identify and develop clinically relevant novel strategies to suppress or prevent the development of metastatic disease.

No conflict of interest.


title}

Anticancer effects of lipid encapsulated Bilberry

1Cancer Research Institute of West TN, Cancer Therapeutics, Henderson, USA, 2Union University, Chemistry, Jackson, USA, 3University of Tennessee, Biochemistry, Knoxville, USA, 4Freed Hardeman University, Nursing, Henderson, USA

Rapidly accumulating laboratory and clinical research evidence indicates that anthocyanins have anticancer activity and more intriguing, the evaluation of bilberry anthocyanins as chemo-preventive agents is progressing. These applications are collectively due to the anthocyanins up-regulating tumor suppressor genes, inducing apoptosis in cancer cells, repairing and protecting genomic DNA integrity, which is important in reducing age-associated oxidative stress, as well as improving neuronal and cognitive brain function. Bilberry anthocyanins have pronounced health effects, even though they have a low bioavailability. To increase the bioavailability, Bilberry was encapsulated in 8 nm diameter liposomal nanospheres, called NutraNanoSpheres (NNS), at a concentration of 2.5 mg/ml. These Bilberry NNS were used to study the apoptotic/cytotoxic effects on K562 cancer cells. Flow cytometric fluorescent quantification of the uptake of Propidium Iodide in a special cell viability formulation into dead K562 cells was used to determine the effects of Bilberry on the viability of K562 cells. The concentrations of Bilberry that showed the highest levels of percentage inhibition, relative to the control populations, were biphasic, showing 60–70% inhibition between 0.018–1.14 mg/ml (n = 6) and 60% inhibition at 80 mg/ml. The lowest % inhibition (30%) occurred at 40 mg/ml. The LD50 was determined to be 0.01–0.04 mg/ml of Bilberry per 10^7 cells of cell culture exposure. At 48 hr. incubation, the highest % inhibition was only 27%, suggesting a long-term apoptotic event rather than a dormant state of a proliferative one.

Results and Discussion: In both the in vitro and in vivo models we have demonstrated that these dormant cancer cells can be stimulated to develop productive macro-metastases. Using an ex vivo lung slice approach, we were able to maintain viability of the lung slices for up to 21 days with the breast cancer cells remaining dormant as seen in vivo. This provides a platform to strictly manipulate stromal factors and monitor the emergence from dormancy in live tissue.

Conclusion: Using these models we can interrogate the contribution of the microenvironment to the emergence from dormancy with a view to aim to identify and develop clinically relevant novel strategies to suppress or prevent the development of metastatic disease.

No conflict of interest.


title}

Lysyl oxidase (LOX), an extracellular matrix remodelling enzyme, has a role in both normal embryonic development and connective tissue function. However, LOX promotes tumour progression and metastases although it may also have tumour-inhibitory effects, which depend on the location and the transformation status of the tumour, and the cell type involved. Our previous studies found higher expressions of LOX in clear cell renal cell carcinoma (ccRCC) compared to adjacent normal renal tissues. Clear cell renal cell carcinoma (ccRCC) is an adenocarcinoma of the renal proximal convoluted tubules of the nephron and account for approximately 80% of all renal malignancies. Unfortunately, the link between LOX activity and ccRCC cell adhesion and metastasis remains unclear.

Material and Methods: ccRCC cell line, Caki-2 cells were cultured in McCoy's 5A complete growth medium supplemented with 10% FBS in a humidified 5% CO2 atmosphere at 37 °C. Various concentrations (50 to 200 μM) of beta-aminopropionitrile (BAPN), an irreversible inhibitor of LOX, were used to inhibit LOX activity in ccRCC cells for 24 to 48 hours in vitro. Untreated cells cultured under the same condition were used as control. The activities of LOX were tested using a fluorometric method. BAPN treated and untreated cells adhesion to fibronectin were analyzed. The expression of genes involved in tumour metastatic signalling pathways were assessed by quantitative RT-PCR. Western blotting analyses were performed to evaluate the expressions of matrix metalloproteinases, MMP2 and MMP9, following LOX inhibition in Caki-2 cells.

Results and Discussion: Our results showed that BAPN inhibited LOX activity in ccRCC cells in a dose-dependent manner in vitro. LOX inhibition was associated with a significant increase in ccRCC cell adhesion to fibronectin in vitro. The inhibition of LOX enzyme elevated the expression of metastatic regulatory genes, MTSS1 and NME in ccRCC cells. In contrast, expressions of MMP2 and MMP9 proteins in ccRCC were reduced following LOX inhibition. These results indicate that LOX may promote ccRCC cell progression and metastasis by modulating metastatic gene expressions. Thus, targeting LOX by inhibiting its activity may be a new strategy in preventing ccRCC metastasis.

Conclusions: LOX activity affects ccRCC cell adhesion to extracellular matrix, and is associated with cancer cell metastasis. This study suggests LOX may be a potential therapeutic target in ccRCC patients.

No conflict of interest.