HBB peptide for the treatment of neuroblastoma (NB) lung metastases and microemetastases (Ramot)

code: 10-2013-451

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Technology

A novel cytotoxic peptide against neuroblastoma (NB) lung metastases and micrometastases, has been developed. The peptide is derived from the beta-2 subunit of mouse hemoglobin (HBB2), a factor present in the lung microenvironment which inhibits the propagation of micrometastatic NB cells, the key cause of deaths in NB residual disease. The peptide inhibits the viability of micrometastatic and metastatic NB cells via ERK and FAK signaling, leading to cell cycle arrest.

There is a large body of evidence demonstrating that tumor progression is largely influenced by factors present in the tumor microenvironment. These factors control the progression of dormant micrometastasis to an actively growing macrometastatic lesion that causes a late metastatic relapse. As the critical role of the microenvironment in tumor growth and progression is increasingly appreciated, it has become clear that in order to eliminate metastasis, the full impact of interactions between tumor cells and the microenvironment has to be elucidated.

NB is the most common extracranial solid tumor in children accounting for approximately 15% of all childhood cancer deaths. Despite intensive treatment regimens, 60% to 70% of children with high-risk disease will ultimately experience relapse due to the presence of NB micrometastases.

To date, there are no effective treatment regimens that eliminate micrometastasis in NB. The micrometastatic NB inhibitory peptide and elucidation of its mechanism of action may lead to the development of a novel anticancer drug. Such a drug may eradicate micrometastasis and/or prevent its progression to metastasis.

The peptide:

- Reduces the viability of lung-metastasizing NB cells, specifically that of micrometastatic NB cells.
- Reduces the viability of other lung-metastasizing cancer cells such as MCF-7.
- Reduces cell survival signaling, decreasing ERK and FAK phosphorylation
- Induces cell-cycle arrest in G0-G1 phase
- alters the expression of genes involved in cell proliferation, survival, apoptosis, adhesion, migration and invasion and regulation of actin cytoskeleton
- leads to higher stem-cell marker expression on the surviving micrometastatic NB cells

Patent Status

61/683,863

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