Use of miR-122* for Treating Cancer (Hadasit)

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Need:

Cervical cancer is the 4th most common and 5th deadliest cancer in women worldwide, with half a million new cases and >250,000 deaths per year. There is no available drug therapy. The licensed HPV vaccines have no effect on the progression of pre-existing HPV infection into cervical carcinoma. Pre-malignant lesions are excised in a surgical procedure with complications and consequences for fertility.

Hepatocellular carcinoma (HCC) is the 5th most common cancer in both sexes and 2nd leading cause of cancer mortality worldwide. Surgical resection and liver transplantation are the only cures for HCC, but benefit only ~10-20% of patients – without one of these cures, average survival time is only ~4-6 months. Thus, there is a very large unmet worldwide need for the development of any novel targeted therapy for HCC that can significantly extend this very limited survival period.

Therapies for cervical and liver cancers are major unmet medical needs. Given the millions of subjects with HCC and cervical cancers and >1 million new cases per year, a targeted therapeutic for cervical carcinoma and HCC would command a multi-$billion market.

Innovation:

Intra-cervical treatment with miR-122*, the second strand of the duplex microRNA, a family of ~2500 short RNAs that play major roles in modulating gene expression.

Findings:

miR-122 is the most abundant liver-specific microRNA tumor suppressor miRNA. We have shown that miR-122* (the active RNA for this study rather than miR-122) directly targets and inhibits Mdm2 expression, thus resulting in increased levels of p53 tumor suppressor protein and pro-apoptotic activity in cervical carcinoma and HCC cells. miR-122* also induces IFN-β and its associated signal pathway, which is tumor-suppressive. Thus, the molecular tumor-suppressive mechanism of action of miR-122* is well understood.

Incubation of cervical carcinoma and HCC lines in vitro with miR-122* leads to cell death. miR-122* significant inhibits the growth of cervical and HCC tumors in nude mice, and targets Mdm2 and is pro-apoptotic in tumor cells in vivo.

These data provide strong mechanistic and preclinical proof of principle for this miRNA in the treatment of cervical cancer and HCC.

Indications/applications:

- Local delivery by injection or application.
- Use of agents capable of inducing miR-122* activating transcription factors or

promoters/enhancers.

Competitive advantage:

For the great majority of subjects that are not eligible for surgical resection and liver transplantation, available treatments for HCC are of very limited benefit. Surgical removal of pre-malignant cervical lesions entails risks and negative consequences for fertility. There are few therapies in development that are target-specific for cervical cancer or HCC. Thus, miR-122* would be a novel targeted therapy for cervical cancer and HCC that should be more specific, thus having a wider therapeutic window than non-targeted therapies.

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