Liposome-encapsidated bioactive hexapeptides for targeted pancreatic cancer

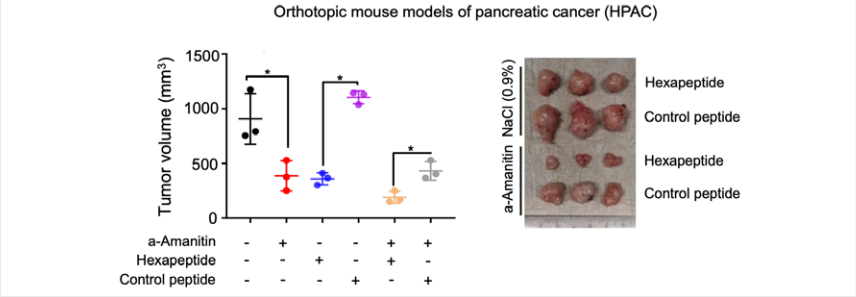
Reference No: B80078

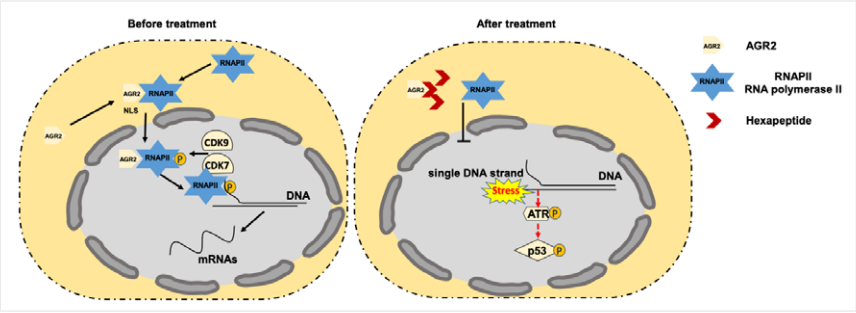
CHALLENGE

Pancreatic cancer is one of the most aggressive malignancies worldwide, with around 459,000 new cases each year and a 5-year survival rate of only 9%. At the time of diagnosis, surgical removal of the malignant tissue is no longer possible in 80-90% of patients, due to the size of the tumor. The treatment consists of a combination of chemotherapy and targeted therapy but this approach can only extend the patient's life for a few months and the side effects are considerable. There is a pressing need for new therapeutic options for this highly malignant tumor entity.

INNOVATION

In tumor cells, but not in normal tissue, the protein Agr2 is needed to transport RNA polymerase II into the nucleus. Our innovation describes a liposome-encapsulated hexapeptide, which prevents the binding of RNA polymerase II to Agr2, which in turn causes a general inhibition of transcription specifically in tumor cells and a resulting upregulation of the tumor suppressor gene TP53.
While TP53 is frequently found mutated in tumors, one third of pancreatic carcinomas show the gene in wild-type form. In these tumors, expression of TP53 is inhibited during the transition from acinar ductal metaplasia (ADM) to intraepithelial neoplasia (PanIN) lesions.
In a mouse model, the inventor has been able to show that the formation of PanIN lesions can effectively be inhibited by injecting the liposome-encapsulated hexapeptide. In addition, when combined with another RNA polymerase II inhibitor, - an α-amanitin-conjugated anti-EpCAM antibody - a clear tumor regression could be shown in a xenograft mouse model. Initial cell culture experiments also suggest that the synergistic effect of hexapeptide and α-amanitin could also be used for the treatment of TP53 wild-type colon, lung and breast carcinomas.





COMMERCIAL OPPORTUNITIES

- Targeted tumor therapy for highly aggressive pancreatic cancers
- Excellently suited for combinational therapy
- Targeted therapies for human solid tumors bearing wild-type TP53

DEVELOPMENT STATUS

Currently seeking partners for further development and licensing options

REFERENCES:

Zhang Z, Li H, Deng Y, Schuck K, Raulefs S, Maeritz N, Yu Y, Hechler T, Pahl A, Fernández-Sáiz V, Wan Y, Wang G, Engleitner T, Öllinger R, Rad R, Reichert M, Diakopoulos KN, Weber V, Li J, Shen S, Zou X, Kleeff J, Mihaljevic A, Michalski CW, Algül H, Friess H, Kong B. *AGR2-Dependent Nuclear Import of RNA Polymerase II Constitutes a Specific Target of Pancreatic Ductal Adenocarcinoma in the Context of Wild-Type p53*. Gastroenterology. 2021 Jul 23:S0016-5085(21)03281-9. doi: 10.1053/j.gastro.2021.07.030. Epub ahead of print. PMID: 34303658.

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