New anti-CKAP4 antibodies deliver hope for pancreatic cancer treatment

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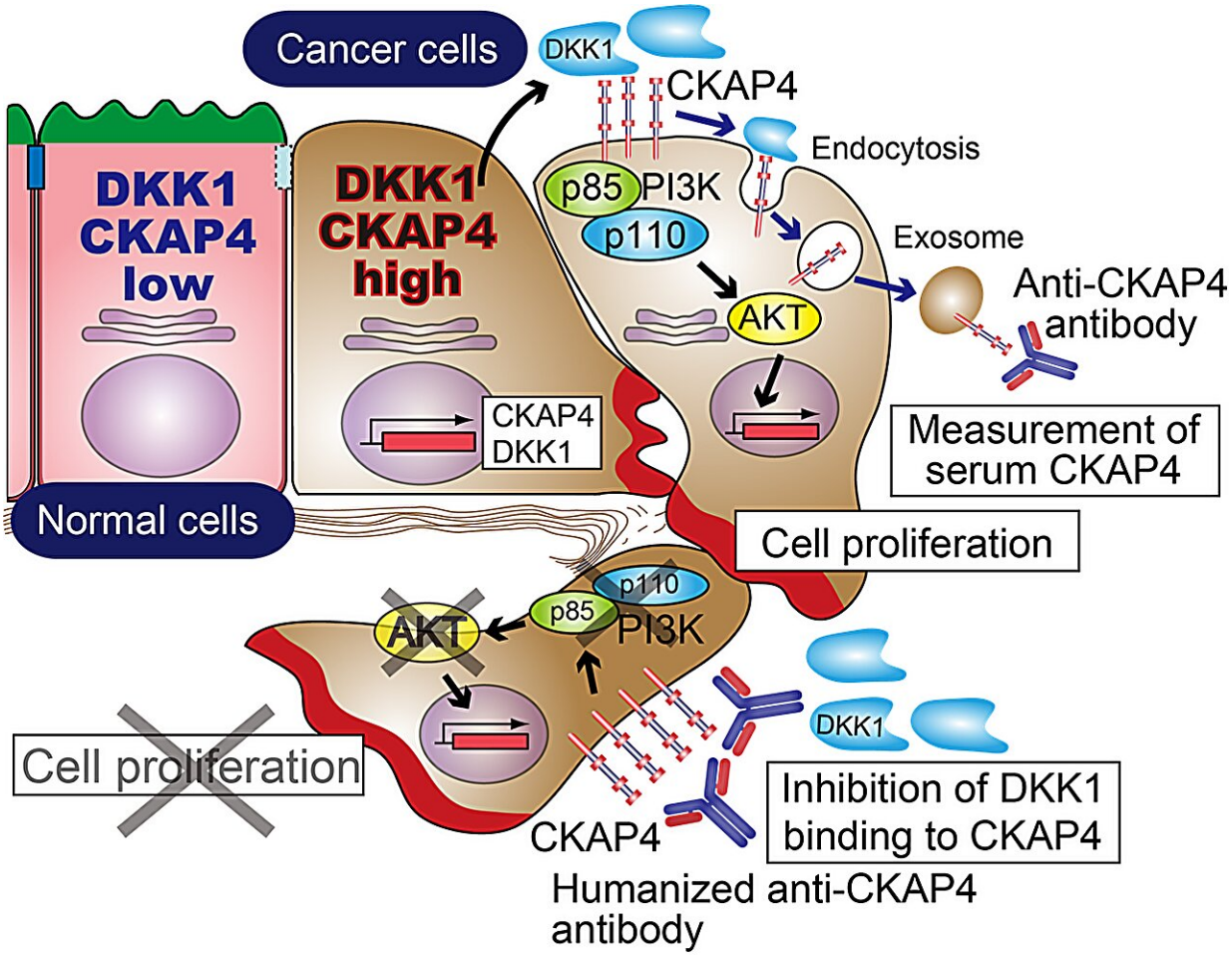


Overview of the DKK1-CKAP4 cancer signaling pathway. Credit: *Cancer Science* (2024). DOI: 10.1111/cas.16278

Pancreatic cancer is an aggressive disease with few available treatments. Thankfully, researchers are hard at work to improve treatment options, and researchers from Japan have now unveiled something promising.

In a study published this month in *Cancer Science*, researchers from Osaka University have developed an "anti-cytoskeleton-associated protein 4 (anti-CKAP4) antibody." This antibody blocks another protein, Dickkopf 1(DKK1), from activating the DKK1–CKAP4, an important pathway that stimulates cancer cell growth and proliferation.

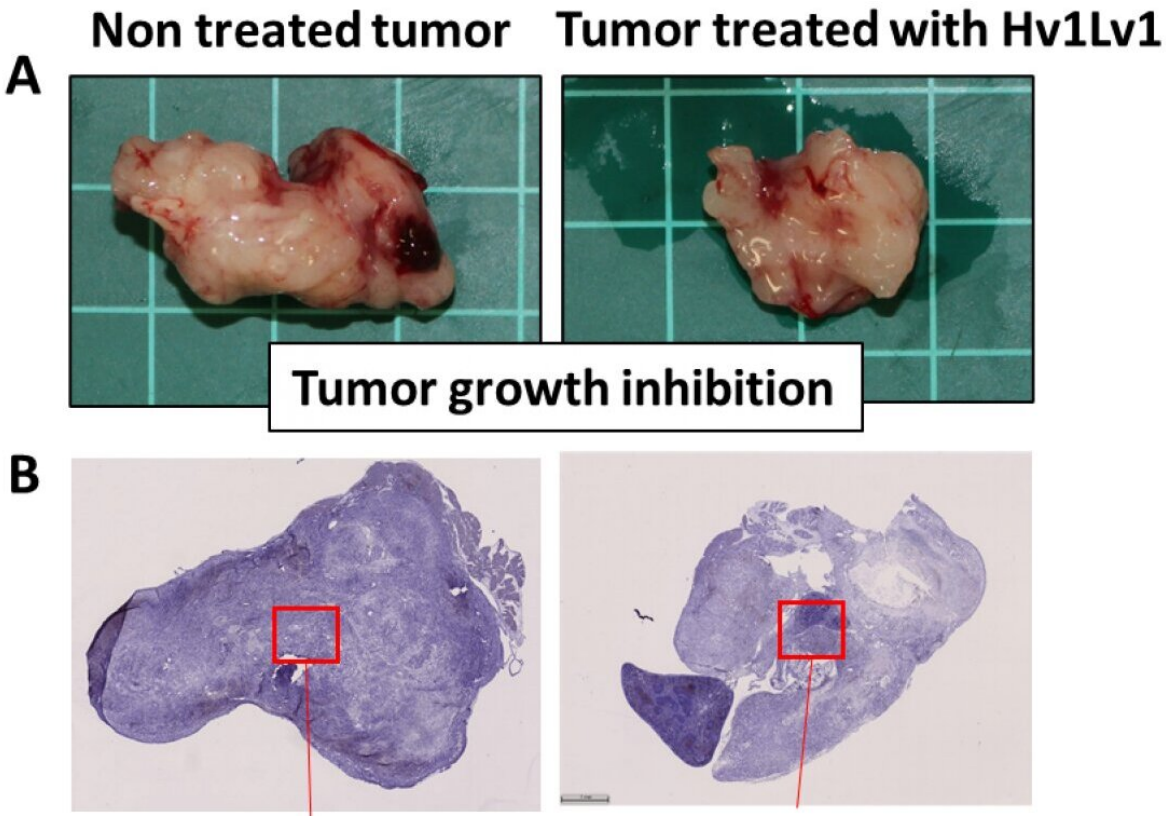
First, some context: CKAP4 is a cell receptor, a structure in the outer part of cells that can be activated by a specific protein. In this case, CKAP4 is activated by DKK1 to promote tumor growth. Elevated DKK1 and CKAP4 levels in patients usually signal malignant transformation and a poor outlook. The research team thus identified the DKK1–CKAP4 pathway as a target for new therapeutic agents.

"We started with a recombinant mouse antibody. Our challenge was to develop a humanized form of this antibody that could achieve the same effect as that achieved in mice models and be safely used in humans," explains lead author of the study, Ryota Sada.

To do this, the researchers first confirmed that the recombinant anti-CKAP4 antibody inhibited DKK1–CKAP4 signaling and tumor formation in lab mice that had received human tumor-cell transplants. Next, they used the recombinant antibody as a base to develop the humanized antibody: Hv1Lt1.

They found that Hv1Lt1 was able to bind to CKAP4 even more effectively than the original antibody; what's more, Hv1Lt1 inhibited sphere formation, which is a measure of the ability of cancer stem cells to multiply into sphere-shaped colonies.

"After we developed the humanized antibody, we tested it on several pancreatic mouse models, and the results were very promising," says Akira Kikuchi, senior author of the study.



Therapeutic effects of humanized anti-CKAP4 antibody on murine pancreatic cancer model. Credit: *Cancer Science* (2024). DOI: 10.1111/cas.16278

The researchers found that Hv1Lt1 suppressed tumor formation in mice that received pancreatic cancer transplants of both mouse and human origin. Hv1Lt1 also helped modulate anti-tumor immune reactions. Moreover, the researchers tested the response of mouse models receiving a combination of Hv1Lt1 and chemotherapy drugs and found that the combination treatment worked better than drugs alone.

Another benefit of antibody-drug combinations is that they may help overcome the problem of chemoresistance by inhibiting the AKT (Protein kinase B) pathway, which is usually activated by chemotherapy drugs. Using Hv1Lt1 together with chemotherapy could also reduce chemotherapy doses and resulting toxicity.

Overall, the researchers' exciting findings open the door to further research on humanized antibodies, with real hopes of improving patient prognosis for one of the deadliest cancers.

More information: Ryota Sada et al, Newly developed humanized anti-CKAP4 antibody suppresses pancreatic cancer growth by inhibiting DKK1-CKAP4 signaling, *Cancer Science* (2024). DOI: 10.1111/cas.16278

Provided by Osaka University