Development of anti-cancer drug targetting CKAP4

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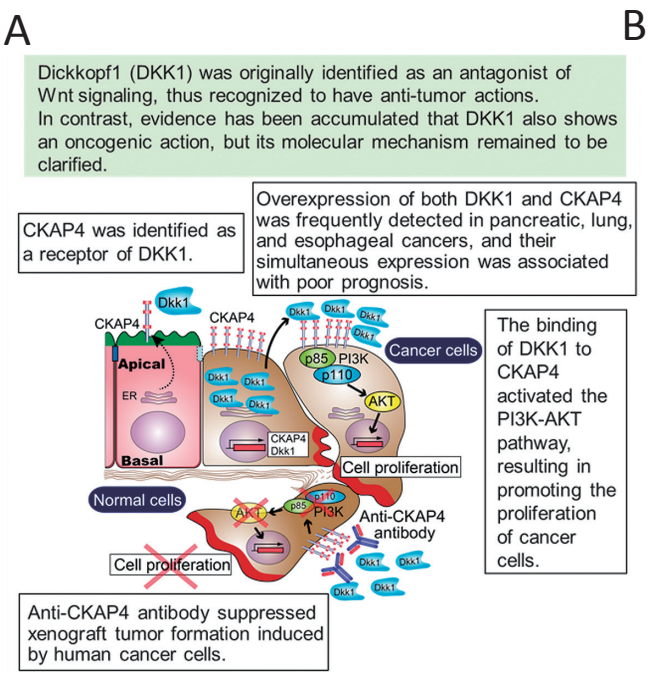
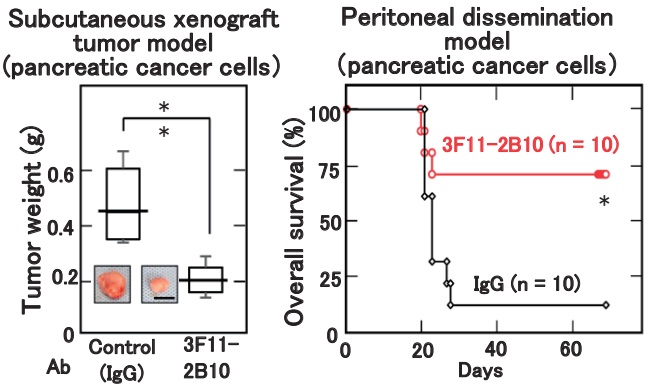
Project Outline

Since elder populations are increasing in Japan, numbers of cancer patients and cancer deaths are predicted to increase more in future. Therefore, novel anti-cancer drugs are required for curing various types of cancers, especially for intractable cancers, such as pancreatic, lung, and esophageal cancers. A secretory protein DKK1 functions as a Wnt antagonist and is essential for embryonic morphogenesis. DKK1 is little expressed in the adult normal tissues, whereas DKK1 has been reported to be expressed in the tumor lesions and to show oncogenic actions. However, the mechanism by which DKK1 is involved in tumorigenesis has been remained to be clarified for a long time. In 2016 we identified CKAP4 as a novel DKK1 receptor and showed that the binding of DKK1 to CKAP4 activates the PI3K-AKT pathway, followed by cancer cell proliferation and that DKK1 and CKAP4 are highly expressed in the tumor lesions of pancreatic, lung, and esophageal cancers, and their simultaneous expression is correlated with poor prognosis. In 2019 we succeeded in generating mouse anti-human CKAP4 monoclonal antibody and confirmed that the antibody suppresses xenograft tumor formation induced by human cancer cells expressing DKK1 and CKAP4. In this project we will develop humanized or human anti-CKAP4 antibody and test its pharmacological effects and safety as the non-clinical trials.





A. Outline of DKK1–CKAP4 cancer signal axis
B. Anti–tumor effects of anti–CKAP4 antibody (3F11–2B10). Left, human pancreatic cancer cells S2–CP8 were subcutaneously implanted into nude mice. When tumor was proliferated to 100 mm^3, control Ig or anti–CKAP4 antibody was injected into the intraperitoneal cavity. Anti–CKAP4 antibody inhibited xenograft tumor formation. Right, S2–CP8 cells were injected intraperitoneally into nude mice and control Ig or anti–CKAP4 antibody was injected into the intraperitoneal cavity. Anti–CKAP4 antibody improved survival of the mice.

Target Diseases：Intractable cancer, especially pancreatic cancer.
Patent Information：Patent registration in Japan, Us. Europe, and Canada.
Technical Features & Marketability：CKAP4 is a novel molecular target for cancer.
Issues in Development：transferability of anti-CKAP4 antibody in pancreatic cancer cells surrounded by thick mesenchymal tissues.
Possible Cooperate Collaboration：Joint development of humanized or human anti-CKAP4 antibody and licensing business.