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**What are the unique aspects of pancreas cancer that lead to the development of novel therapeutics?**

Hi, my name is Dr. Eileen O'Reilly and I am going to cover the topic of, "What are the unique aspects of pancreas cancer that lead to the development of novel therapeutics?" I have a couple of comments on this. Pancreas cancer has a unique microenvironment. It is characterized by a number of issues, one that there is a marked desmoplastic component, meaning that there are relatively few epithelial malignant cells but a lot of other stuff that is present. In addition, the pancreas microenvironment is characterized by a lack of effect or immune cells. It is a relatively immune-suppressed environment, and these days, this is obviously a very important consideration. That, in part explains why there has not been a robust signal as yet with the immune-directed therapies in this disease. Nonetheless, there are some early hints. The microenvironment is also relatively hypoxic, so not well oxygenated. It provides a physical barrier that may, to some degree, protect tumor cells against getting effective doses of cytotoxic and other agents to the environment. This is putated again as one of the mechanisms for why pancreas cancer is a particularly challenging malignancy from the therapeutic perspective. Other points to note is that there are a number of critical genomic mutations (KRAS, P53, CDKN2), and these as yet are not effectively targetable from a drug perspective. Pancreas cancer has also got a marked inflammatory microenvironment with a lot of myeloid suppressive cells, M2 macrophages, and all of the above contributes to the somewhat hostile setting in which pancreas cancer cells are nurtured. These collectively provide challenges from both cytotoxic therapy and from immune-targeted approaches.