Insights into the epigenetic mechanisms controlling pancreatic carcinogenesis.

During the last couple decades, we have significantly advanced our understanding of mechanisms underlying the development of pancreatic ductal adenocarcinoma (PDAC). In the late 1990s into the early 2000s, a model of PDAC development and progression was developed as a multi-step process associated with the accumulation of somatic mutations. The correlation and association of these particular genetic aberrations with the establishment and progression of PDAC has revolutionized our understanding of this process.

However, this model leaves out other molecular events involved in PDAC pathogenesis that contribute to its development and maintenance, specifically those being epigenetic events. Thus, a new model considering the new scientific paradigms of epigenetics will provide a more comprehensive and useful framework for understanding the pathophysiological mechanisms underlying this disease. Epigenetics is defined as the type of inheritance not based on a particular DNA sequence but rather traits that are passed to the next generation via DNA and histone modifications as well as microRNA-dependent mechanisms. Key tumor suppressors that are well established to play a role in PDAC
may be altered through hypermethylation, and oncogenes can be upregulated secondary to permissive histone modifications. Factors involved in tumor invasiveness can be aberrantly expressed through dysregulated microRNAs. A noteworthy characteristic of epigenetic-based inheritance is its reversibility, which is in contrast to the stable nature of DNA sequence-based alterations. Given this nature of epigenetic alterations, it becomes imperative that our understanding of epigenetic-based events promoting and maintaining PDAC continues to grow.