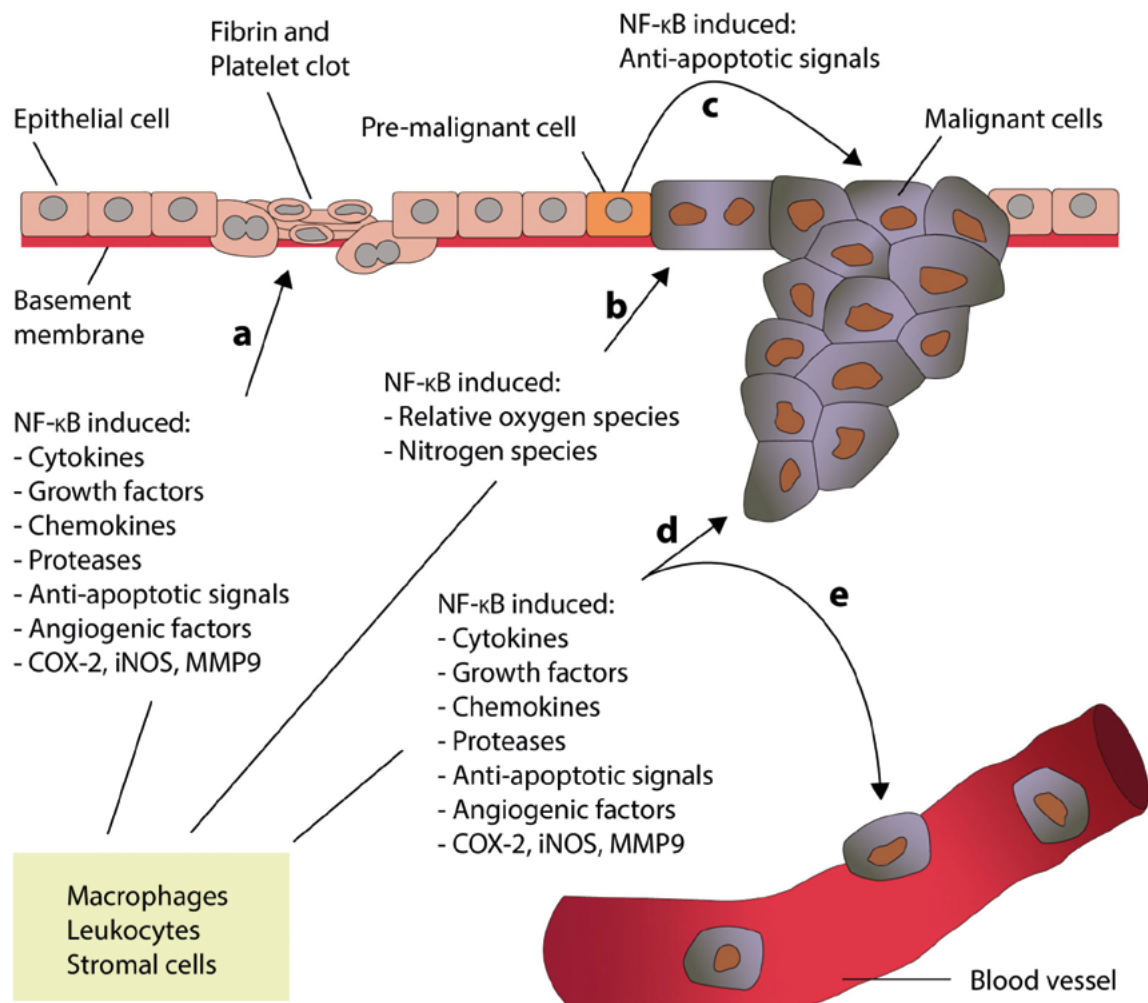


**Fig. 1.** The role of NF-kappaB in the inflammatory process and in the case of inflammation associated with carcinoma (modified according to Zhang et al. (24) – created in collaboration with Service Center for E-Learning at Masaryk University, Faculty of Informatics). A – Leukocytes and stromal cells secrete an abundance of proinflammatory proteins during inflammation. B – Proinflammatory factors in the microenvironment of latent pre-malignant cells lead to the accumulation of DNA damage, which, in turn, causes these cells to become malignant. C – Activation of NF-kappaB in pre-malignant cells induces anti-apoptotic signals, which prevents apoptosis and enhances their proliferation. D and E – Leukocytes and stromal cells secrete proinflammatory proteins in their chronically inflamed microenvironment, which stimulates tumor progression and metastasis



nucleus, which in turn activates transcription of pro-inflammatory cytokines, adhesion molecules, chemokines, growth factors, anti-apoptotic genes, and cyclin D1 (26,27). It should be noted that NF-kappaB induces the production of other proteins, such as COX-2 and nitric oxide synthetase. Thus, it can be deduced that NF-kappaB forms the molecular link between the activation of inflammation and the simultaneous loss of the physiological cell cycle in carcinomas, which is referred to as a dualistic effect.

The three findings that indicate that NF-kappaB is an essential factor in pancreatic cancer are:

- 1) NF-kappaB is activated in 70% of pancreatic cancers and in human pancreatic cell lines such as PANC-1 and BxPC-3 (28,29).
- 2) Supporting arguments from experimental studies – e.g. suppression of NF-kappaB leads to re-initiation of apoptosis in pancreatic tumor cells (30).
- 3) NF-kappaB appears to be involved in the early stages of pancreatic carcinogenesis, which is related to its relationship to the K-ras oncogene and apoptotic resistance (31).

K-ras mutations play a prominent role in the induction of pancreatic carcinogenesis. In 2009, Kamisawa et al. published a paper demonstrating high positive rates of K-ras mutation in pancreatic tissue of individuals with AIP (32). He found positive rates in the tissue of all persons examined with an autoimmune form of pancreatitis. However, K-ras mutation can be detected in 90% of cases of sporadic pancreatic cancer (33).

## Conclusion

AIP, like sporadic chronic pancreatitis, is a risk factor for pancreatic cancer. Chronic inflammation is a precursor of tumor growth. Whereas in the case of chronic pancreatitis, the inflammation-tumor sequence is only connected with pancreatic tissue, in the form of chronic AIP, which is one of the clinical manifestations of a group of diseases referred to as IgG4-RD, malignancy may occur in an organ other than the pancreas. It seems that the appearance of such cancers occurs soon after the diagnosis of AIP.