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Functional and acquired characteristics of the early *pre-cancer* phenotype are intrinsically different from those of a more advanced anaplastic or invasive malignancy. The biologic conversion of pre-malignancy to invasive disease is complex and is likely to influence delivery of nanoparticles (grey circles) to tumors. Intraepithelial neoplasia (IEN) are early pre-cancerous lesions (pink cells) that proliferate until the normal basement membrane is breached by cancerous cells (brown cells). Switching on angiogenesis and chronic inflammation involving the accumulation of proinflammatory, stromal, and blood factors can dilate blood vessels and alter pericyte (green cells) behavior. Elevated hypoxia and apoptosis (condensed yellow cells) further increase vessel leakiness. Angiogenic sprouting and tip cell (elongated yellow cells) driven angiogenesis leads to further recruitment of additional cells during the angiogenic switch. See article by Menter and colleagues (beginning on page 973) for more information.



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