A Review on malignant mesothelioma, a Mini-Review on abnormal histogenesis during the development of pancreatic cancer, and a research article on the overexpression of interleukin-1β (IL-1β) in lymphangiogenesis with related Commentary on lymphangiogenesis and angiogenesis were selected for the April 2013 AJP CME Program in Pathogenesis. The authors of the referenced articles and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose.


Upon completion of this month’s journal-based CME activity you will be able to:

- Discuss the characteristics of malignant mesothelioma, including its molecular defects and detection.
- Describe the characteristics of pancreatic ductal adenocarcinoma.
- Understand the development of pancreatic intraepithelial neoplasias.
- Discuss the effect of hypoxia on pancreatic cancer cells.
- Understand and describe the role of IL-1β.
- Describe angiogenesis and lymphangiogenesis.

1. Malignant mesothelioma (MM) is a relatively rare but devastating tumor. Based on the referenced Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1065-1077.]
   a. The incidence of MM is increasing worldwide.
   b. MM is among the most aggressive tumors.
   c. MMs arise from the mesothelial cells that line the pleura and peritoneum, but never the pericardium.
   d. MMs are most commonly attributed to occupational exposures to asbestos.

2. Asbestos is a regulatory term for a group of fibrous silicates. Based on the referenced Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1065-1077.]
   a. These silicates occur as needle-like amphiboles or curly serpentine fibers.
   b. The needle-like amphiboles include crocidolite, amosite tremolite, anthophyllite, and antigorite.
   c. Chrysotile fibers are in the curly serpentine group of silicates.
   d. Crocidolites are the most commonly used type of asbestos historically.
3. Most MM patients have a poor prognosis. Based on the referenced Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1065-1077.]

   a. The detection of MMs often occurs at an early stage.
   b. A panel of staining approaches is necessary to ascertain MMs and to discriminate pleural MMs from lung carcinomas or peritoneal MMs from ovarian and peritoneal adenocarcinomas.
   c. Several major histologic types and more than a dozen subtypes of MMs exist.
   d. No specific associations between exposure to different fiber types and the pathogenesis of distinct MM tumor subtypes have been reported.

4. MMs display a wide array of defects in mitogenic signaling pathways and disruption of cell cycle control. Based on the referenced Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1065-1077.]

   a. MMs are associated with persistent activation of the canonical receptor tyrosine kinase (RTK)/Ras/ERK1/2 pathway.
   b. The persistent activation of the phosphatidylinositol 3-kinase/Akt pathway is not a common feature of MM cells.
   c. Mesothelial cells respond to an unusually broad array of growth factors.
   d. MM cell lines commonly display phosphorylation of multiple RTKs with phosphorylation of epidermal growth factor receptor (EGFR) and MET being the most prominent among 42 RTKs studied.

5. Pancreatic ductal adenocarcinoma (PDAC) is one of the most feared lethal and painful diseases. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1078-1086.]

   a. The incidence of PDAC is increasing with approximately 4,000 predicted new cases in the United States and 6,000 in Europe.
   b. PDAC arises from epithelial cells through an accumulation of genetic and epigenetic alterations in oncogenes and tumor suppressors.
   c. PDAC genetic and epigenetic alterations contribute to form precursor lesions known as pancreatic intraepithelial neoplasias (PanINs).
   d. PDAC may progress from two types of cystic lesions: mucinous cystic neoplasms and intraductal papillary mucinous neoplasms.

6. The stroma co-evolving with tumor cells during PDAC progression is composed of several cell types. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1078-1086.]

   a. These cell types include fibroblasts, pancreatic stellate cells (PSCs), endothelial cells, bone marrow-derived cells, as well as inflammatory and immunoregulatory populations.
   b. PSCs contribute to pancreatic fibrosis by secreting fibrillar collagens and fibronectin.
   c. PSCs are located between acini and epithelial cells.
   d. PSCs represent less than 5% of cells within the normal gland but in tumors they proliferate to outnumber malignant epithelial cells.

7. PSCs are found within PanINs. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1078-1086.]

   a. PanINs are stimulated by signals from other cells, including epithelial populations.
   b. Transforming growth factor-β (TGF-β) stimulates fibronectin biosynthesis in PSCs but has no influence on collagen synthesis.
   c. Fibroblast growth factor and platelet-derived growth factor induce PSC proliferation.
   d. Expression of Sonic hedgehog in mice using the pdx1 promoter leads to PanIN formation.

8. The effect of hypoxia on pancreatic cancer cells has been modeled extensively in vitro. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1078-1086.]

   a. Cell lines surviving hypoxia show enhanced invasive and migratory propensities.
   b. Mechanistically, oxygen deprivation destabilizes hypoxia-inducible factor 1α (HIF-1α).
   c. HIF-1α dimerizes with HIF-1β to undergo nuclear translocation.
   d. HIF-1α is overexpressed in PDAC.
9. Interleukin-1β (IL-1β) is a key inflammatory cytokine. Based on the referenced article and related Commentary, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1434-1447 and Am J Pathol 2013, 182:1087-1091.]

a. IL-1β is found in many pathologic conditions.
b. IL-1β is responsible for triggering multiple downstream inflammatory pathways.
c. Inhibiting IL-1 signaling by neutralizing antibodies or by blocking IL1R1 receptors is effective in treating inflammation in numerous pathologic conditions.
d. Induction of IL-1β in a conditional expression system in mice was followed by an influx of neutrophils and macrophages, resulting in the transient formation of lymphatic vessels; however, lymphangiogenesis did not persist after cessation of IL-1β expression.

10. IL-1β has a main role in the remodeling of many tissues, including the airways and lungs. Based on the referenced article and related Commentary, select the ONE statement that is NOT TRUE: [See Am J Pathol 2013, 182:1434-1447 and Am J Pathol 2013, 182:1087-1091.]

a. Overexpression of IL-1β in adult mouse airways and lungs results in pulmonary inflammation.
b. In adult mouse airways and lungs, IL-1β overexpression results in the recruitment of inflammatory cells.
c. In neonatal mice, overexpression of IL-1β disrupts lung development, an effect mediated by vascular endothelial growth factor receptor (VEGFR)-3 signaling.
d. IL-1β has been reported to induce angiogenesis in several experimental models and in human diseases.