Articles on the primary effusion lymphoma secretome, an osteoporotic rat model of estrogen and nutrient deficiency, and an investigation of tau as a new link between Alzheimer disease and diabetes were selected for the March 2014 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:
- Define and characterize primary effusion lymphoma (PEL).
- Describe PEL pathogenesis.
- Understand cell secretomes.
- Define and describe the causes of osteoporosis.
- Understand the classic ovariectomy (OVX) rat model.
- Define diabetes and its relationship to Alzheimer disease (AD).
- Describe microtubule-associated tau and its link to AD and diabetes.

1. **Primary effusion lymphoma (PEL) is a rare B-cell neoplasm. Based on the referenced article, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:618-630.]
   a. PEL is characterized by Kaposi’s sarcoma-associated herpesvirus (KSHV) infection of the tumor clone.
   b. PEL usually grows in body cavities without tumor mass formation.
   c. At autopsy PEL presents as multiple small tumor foci involving the serous membranes, which appear irregularly thickened.
   d. Pathologically the basic features of PEL are a net predilection of diffuse spreading along the serous membranes with infiltrative and destructive growth patterns.

2. **PEL is composed of B cells, which bridge immunoblastic and anaplastic features. Based on the referenced article, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:618-630.]
   a. PEL typically displays a non-B, non-T phenotype consistent with late stages of B-cell differentiation.
   b. PEL pathogenesis is poorly understood, although KSHV is thought to play a major role via expression of several viral latent genes that have the potential to affect B-cell growth.
   c. Infection by Epstein-Barr virus occurs in less than half of PEL cases.
   d. PEL pathogenesis includes deregulation of cytokine and growth factor autocrine loops, molecular alterations of the tumor DNA, cell cycle abnormalities, and stimulation and selection by antigen.
3. A recent strategy for discovery of cancer biomarkers involved in PEL pathogenesis is based on the identification of proteins in cancer tissue-proximal fluids and in the conditioned media of cell lines (secretomes). Based on the referenced article, select the ONE statement that is NOT TRUE: [See Am J Pathol 2014, 184:618-630.]

a. Cell secretomes comprise proteins that are secreted or shed from the cell surface, as well as intracellular proteins released into the supernatant as the result of vesiculation, cell lysis, apoptosis, and necrosis.
b. The secretome can accurately reflect the functional state of secreting cells at specific time points.
c. Proteins secreted by cancer cells play important roles in cell interaction, adhesion, and invasion.
d. Surprisingly, within the group of secreted proteins that were specifically found in PEL secretomes, none were involved in functions that are potentially related to PEL pathogenesis and cell growth.

4. Osteoporosis is a progressive skeletal disorder defined by low bone mass and deteriorated bone microarchitecture. Based on the referenced article, select the ONE statement that is NOT TRUE: [See Am J Pathol 2014, 184:765-777.]

a. Osteoporosis predominantly affects postmenopausal women.
b. Estrogen, vitamin D, and calcium deficiency influence the osteoporotic fractures in elderly women.
c. Postmenopausal osteoporosis is characterized by enhanced activation frequency of bone remodeling along with enhanced algebraic difference between bone formation and resorption phases.
d. The skeletal sites of fibula, ankle, and wrist are more prone to osteoporotic fractures.

5. In estrogen-deficient, postmenopausal women, vitamin D and calcium deficiency increase osteoporotic fracture risk. Based on the referenced article, select the ONE statement that is NOT TRUE: [See Am J Pathol 2014, 184:765-777.]

a. In a recent study 97% of osteoporotic patients exhibited inadequate calcium intake with less than the recommended dosage of 500 mg per day.
b. Phosphorus deficiency is another marker of general nutritional inadequacy in elderly patients.
c. Menopause is associated with a sustained increase in calcium excretion.
d. Vitamin D deficiency causes a decrease in calcium absorption.

6. Osteoporosis has study limitations in humans because of its slow progression. Based on the referenced article, select the ONE statement that is NOT TRUE: [See Am J Pathol 2014, 184:765-777.]

a. The classic ovariectomy (OVX) rat model does not consider the highly prevalent nutritional deficiencies in elderly women.
b. Individual supplementation of either vitamin D or calcium is as effective as combinatorial supplementation.
c. OVX combined with a low-calcium diet exhibits decreased bone mineral density, cortical thinning, and deteriorated trabecular architecture.
d. An additive effect on bone loss was reported by combined OVX-deficient calcium or OVX-deficient vitamin D.

7. The incidence and prevalence of age-related neurodegenerative and metabolic disorders are growing because of the increasing life expectancy in industrialized countries. Based on the referenced article, select the ONE statement that is NOT TRUE: [See Am J Pathol 2014, 184:819-826.]

a. Diabetes is the most common metabolic disorder.
b. Diabetes is largely characterized by hyperglycemia, but it is also associated with vascular disorders and cognitive impairments.
c. There are two forms of diabetes: type 1 (insulin-dependent) and type 2 (non-insulin-dependent).
d. More than 200 million individuals are affected by diabetes in the world, and it is estimated to reach 300 million in 2030.

8. Alzheimer disease (AD) is a neurodegenerative disorder characterized by progressive loss of memory and cognitive skills. Based on the referenced article, select the ONE statement that is NOT TRUE: [See Am J Pathol 2014, 184:819-826.]

a. AD is characterized by neuronal and synaptic loss and the presence of senile plaques of β-amyloid and neurofibrillary tangles composed of hyperphosphorylated tau protein.
b. Microtubule-associated protein tau is a cytoskeleton protein that regulates neuronal development and promotes assembly and stability of microtubules.
c. In the central nervous system, over 40% of tau is phosphorylated under physiological conditions.
d. Insulin has a key role in metabolic signaling and regulates the activity of some kinases that are responsible for tau phosphorylation.