A Mini-Review on targeting CD133 for cancer treatment, and articles on varied genetic profiles of head and neck squamous cell carcinoma and CD146 in colitis and colitis-associated carcinogenesis were selected for the May 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:

- Describe cancer stem cells (CSCs) and their role in carcinogenesis.
- Understand the role of cell-surface marker CD133 and its expression in various cancers.
- Define niche-dependent therapy in cancer.
- Describe the link between CD133 and vasculogenic mimicry (VM).
- Describe head and neck squamous cell carcinoma (HNSCC) and its link to human papilloma virus infection (HPV).
- Understand the relationship between chronic colitis and the development of colorectal cancer.
- Define CD146 and understand its association to inflammatory bowel disease.

1. **Cancer stem cells (CSCs) are primitive cell entities able to self-renew and asymmetrically divide to maintain a stem cell pool. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1256-1262.]
   a. CSCs have been isolated or enriched from only a few select tissue types.
   b. CSCs exhibit increased resistance to conventional cancer treatments, including chemotherapy and radiotherapy.
   c. CSCs may explain cancer relapses and metastases.
   d. Targeting CSCs may yield improved survival and treatment outcomes for patients.

2. **The identification and characterization of CSCs is largely owed to the use of cell-surface markers. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1256-1262.]
   a. CD133 expression has been associated with increased chemoresistance and radioresistance.
   b. CD133 is an approximately 80-kDa pentaspan transmembrane glycoprotein.
   c. CD133’s cell-surface epitope, AC133, has been highly used as a cell-surface marker to isolate and enrich for CSCs from a wide range of tissue types.
   d. CD133 expression has been associated with a poor prognosis in various cancers.
3. **CSCs exist in specialized compartments within the tumor known as niches. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1256-1262.]

   a. Niches provide the essential cues for cell-fate determination by achieving a balance between self-renewal and differentiation.
   b. CD133⁺ brain cancer stem cells are localized to the perivascular microenvironment, the so-called perivascular niche.
   c. Disruption of perivascular niches ablates the CD133⁺ brain tumor stem/initiating cells, resulting in growth arrest.
   d. Vascular niches of CD133⁺ CSCs have recently been identified in breast cancer.

4. **CD133 is linked to tumor vascularization. Based on the referenced Mini-Review, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1256-1262.]

   a. CD133 is required for angiogenesis, such as in brain tumors.
   b. CD133 appears to be required for vasculogenic mimicry (VM) in liver, lung, and stomach cancers.
   c. VM networks constitute an alternative mechanism for nutrient supply and act as a potential access point for metastases.
   d. VM is associated with increased tumor aggressiveness and patient mortality.

5. **Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide. Based on the referenced article, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1323-1330.]

   a. Despite recent advances in chemoradiation therapy, the five-year survival rate for HNSCC is about 50%.
   b. Based on epidemiology and disease outcomes, histologically diagnosed HNSCC has been stratified into two distinct prognostic entities, directly linked to infection with high-risk human papilloma virus (HPV).
   c. Of the high-risk subtypes, HPV16 has been found in about 10% of infected HNSCC and HPV18 in approximately 80%.
   d. Other high-risk HPV types, such as HPV31 and HPV33, have been detected in a few cases of HNSCC.

6. **Dissimilarities in prognosis and molecular profiles have attracted much attention in recent years partially due to the increase of HPV infection in HNSCC. Based on the referenced article, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1323-1330.]

   a. Compared to HPV-negative HNSCC patients, HPV-positive HNSCC patients show poor cell differentiation, better response to chemotherapy and radiotherapy, and better survival.
   b. The three-year survival of HPV-positive HNSCC patients is 83% as opposed to 57% observed in HPV-negative HNSCC.
   c. Increased HPV viral copy number is associated with enhanced response to chemotherapy.
   d. High-risk HPV16 and 18 subtypes account for 30% of cervical cancers with poor outcomes, whereas the virus has beneficial effects in patients with HNSCC.

7. **Evidence is accumulating that chronic inflammation contributes to carcinogenesis, including gastrointestinal cancers, lung cancer, and prostate cancer. Based on the referenced article, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1604-1616.]

   a. Chronic colitis-associated colorectal carcinogenesis is a typical model to study inflammation-associated carcinogenesis.
   b. Ulcerative colitis (UC) is characterized by a long-lasting cycle of remission and exacerbation of ulceration of bowels, abdominal pain, diarrhea, bloody stool, and other systemic symptoms.
   c. It is reported that patients suffering from UC for more than 5 years are 10 to 15 times more susceptible to develop colorectal cancer than the general population.
   d. Both the severity and the duration of the chronic inflammatory bowel disease (IBD) significantly correlate with the risk of colorectal cancer.

8. **CD146 is an adhesion molecule belonging to the immunoglobulin superfamily. Based on the referenced article, select the ONE statement that is NOT TRUE:** [See Am J Pathol 2014, 184:1604-1616.]

   a. CD146 has been reported to be expressed on cancer stem cells and most epithelial cells.
   b. CD146 plays a key role in tumor-associated angiogenesis as well as tumor metastasis.
   c. The CD146 antibody AA98 inhibits tumor angiogenesis.
   d. Increased expression of CD146 has been reported in patients with IBD.