HOXB9 as a potential target gene for overcoming platinum resistance in mucinous ovarian cancer

Dong Hoon Suh  
Seoul National University Bundang Hospital, South Korea

Ovarian cancer refers to any cancerous growth that begins within the ovary, this is often the part of the female body that produces eggs. Cancer develops when abnormal cells during a part of the body (in this case, the ovary) begin to grow uncontrollably. This abnormal cell growth is common among all cancer types. Normally, cells in your body divide and form new cells to exchange exhausted or dying cells, and to repair injuries. Because cancer cells still grow and divide, they’re different from normal cells. Instead of dying, they outlive normal cells and still create new abnormal cells, forming a tumour. Tumours can put pressure on other organs near the ovaries. Cancer cells can sometimes visit other parts of the body, where they begin to grow and replace normal tissue. This process, called metastasis, occurs because the cancer cells enter the bloodstream or lymph system of the body. Cancer cells that spread from other organ sites (such as breast or colon) to the ovary aren’t considered ovarian cancer. Cancer type is set by the primary site of the malignancy.

One would think that removal of the fallopian tubes and ovaries would prevent the disease but this is often not always the case (primary peritoneal cancer can arise within the pelvis even after the ovaries are removed). However, there are ways to significantly reduce your risk. If a woman takes contraception pills for quite 10 years, then her risk of ovarian cancer drops significantly. Ligation has long been known to decrease the danger of ovarian cancer.

Although ovarian cancer is heterogeneous with various histologic types, current treatment guidelines are generally an equivalent for all histologic types. Expression of HOX genes in epithelial ovarian cancer (EOC) was known to be histology-specific. We performed a series of in vitro and in vivo studies to seek out a tailored strategy of inhibiting HOXB9 expression for overcoming platinum resistance in mucinous EOC. HOXA10 and HOXB9 showed exclusively high expression in SKOV-3 and RMUG-S, respectively. HOXA10 siRNA treatment made a big decrease in cell viability of SKOV-3, but not RMUG-S. Against this, HOXB9 siRNA treatment made a big decrease in cell viability of RMUG-S, but not SKOV3. HOXA10 siRNA and HOXB9 siRNA treatments: increased the expression level of cleaved PARP and caspase-3 in SKOV-3 and RMUG-S, respectively; expression of vimentin was decreased while expression of E-cadherin was increased; SOX-2, Nanog, and Oct-4 also decreased in both cell lines after specific siRNA treatment. When injected with RMUG-Sko HOXB9 and SKOV-3oe HOXB9 in mouse models, we clearly showed that the tumours from RMUG-Sko HOXB9 grew significantly slower than those from control. Against this, the tumours from SKOV-3oe HOXB9 grew significantly faster than those from control. After harvesting, the cells from the SKOV-3oe HOXB9 were characterized with resistance to cisplatin and better expression of vimentin than those form the control. Our findings suggest that platinum-resistance of mucinous ovarian cancer could be defeated by inhibiting HOXB9, which might be a target of tailored strategy for overcoming the resistance to platinum in mucinous EOC.