Spotlight

By M.O.

How Ovarian Cancer Cells Keep Their Cool

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Hyperthermic intraperitoneal chemotherapy (HIPEC) has emerged as a promising new treatment strategy for women afflicted with epithelial ovarian cancer. Known as the deadliest gynecological cancer worldwide because of the high rate of peritoneal metastasis at the time of diagnosis, ovarian tumors develop rapid multidrug resistance against common chemotherapeutic interventions. During HIPEC, the chemotherapeutic agents are heated to increase the tumoricidal effects and administered directly into the abdomen. Although the benefit of this approach was documented in other peritoneal cancers such as carcinosis from colon cancer, no real benefit in survival was found in women with ovarian cancer. One possibility is that thermoprotective mechanisms exist that specifically interfere with hyperthermia in this cancer type.

Lis and colleagues focused on mesenchymal stem cells because of their central role in tissue maintenance and repair. These cells were recently found in ovarian neoplastic lesions, where they participate in the formation of the tumor stroma. The authors demonstrate that tumor-associated as well as bone marrow-derived mesenchymal stem cells are protected from heat shock-induced apoptosis and confer heat-shock resistance to cocultured ovarian tumor cell lines (SKOV3 and CaOV3). Notably, this effect was not dependent on direct cell-to-cell contact, and the authors identify the cytokine CXCL12 as a mediator of thermoprotection. Indeed, blockage of CXCL12's interaction with its receptor CXCR4 reversed the thermoprotective phenotype of the stem cells in the coculture experiments. These findings could have direct clinical implications because inhibition of CXCL12 action may sensitize ovarian cancers to hyperthermia.