Role of tumor-released small extracellular vesicles in cancer pain

Christine Evans
Physiology, Poster Presentation
Mentor(s): Geoffroy Laumet

Reported by about 80% of patients, pain is the most common and earliest symptom of head and neck cancer (HNC). The underlying mechanism isn't fully understood and discoveries could aid in analgesic drug developments to better the quality of life for cancer patients. Small extracellular vesicles (sEVs) are membrane particles released by cells for intercellular communication. We hypothesized that cancer-derived sEVs communicate with neurons and contribute to pain. To model HNC in mice, oropharyngeal epithelial cells from C57Bl/6 male mice were isolated and transformed into cancer cells (mEERL cells). Immunocompetent mice implanted with mEERL cells developed tumors and quickly developed cancer pain, characteristics true to those of human HNC. Control mice received saline injection. Pain testing involved von Frey (VF) and the Mouse Grimace Scale (MGS). VF responses were noted after the application of filaments gradually increasing in force to the hind paw. MGS involved observed facial appearances.

To test sEVs' contribution to cancer pain, genetically modified mEERL cells unable to release sEVs (mEERL Rab27a$^{-/+}$ and Rab27b$^{-/-}$ cells) were implanted in mice. These were generated by using CRISPR-cas9 to knock out RAB27a and RAB27b genes involved in sEV release. Injection of these cells resulted in a reduced sensitivity to cancer pain. SEVs themselves injected into healthy mice induced pain hypersensitivity. Our results showed that isolated exosomes induce pain and blocking sEVs release reduces cancer pain. Taken together, our data indicate that cancer-derived sEVs are critical mediators of cancer pain and therefore appear as new therapeutic targets for cancer pain.