Table SI. Studies on CGRP in cancer-associated pain.

First author (year)	Objective	Method and sample size	Source of CGRP	Results	Potential mechanism of CGRP in cancer pain	(Refs.)
Hansen 2016	To determine CGRP levels in a mouse model with metastatic bone cancer.	77 3H/HeN mice, 35 of which were induced with bone cancer. CGRP in DRG and released CGRP were tested. Pain-associated behaviors were tested.	Tissue biopsies (DRG ipsilateral).	The treatment group had higher CGRP and released CGRP level in ipsilateral DRG and showed tactile hyperalgesia	The CGRP evoked may act on astrocytic CGRP receptors in DRG and lead to release of ATP, which leads to tactile hyperalgesia	(38)
Jimenez-Andrade 2010	To prove that sensory nerve fibers that innervate the tumor-bearing tissue undergo pathological sprouting and reorganization.	70 athymic nude mice, induced with prostate cancer in femur bone. CGRP(+) nerve sprouts in femurs were tested. Pain-associated behaviors were tested.	Tissue biopsies (femurs, DRG ipsilateral).	The treatment group had higher CGRP(+) sensory nerve sprouting adjacent to the ectopic cancer and showed hyperalgesia.	The increase of CGRP was a result of cancer. The exact mechanism is not specified.	(40)
Bloom 2011	To prove that sensory nerve fibers that innervate the breast cancer cell-bearing bone undergo pathological sprouting and reorganization.	70 athymic nude mice, 34 of which were injected with human breast cancer MDA-MB-231-BO cells into the femoral intramedullary space (left femur). CGRP(+) nerve sprouts in femurs were tested. Pain-associated behaviors were tested.	Tissue biopsies (femurs, DRG ipsilateral).	The treatment group had higher CGRP(+) sensory nerve sprouting adjacent to the ectopic cancer and showed hyperalgesia.	The increase of CGRP was a result of cancer. The exact mechanism is not specified.	(41)
Nagamine 2006	To prove that inoculation of SCC cells into the lower gingiva produces mechanical allodynia and thermal hyperalgesia.	80 male Fisher rats, half of which were inoculated with SCC cells in the lower gingiva. CGRP(+) nerves were tested. Pain-associated mechanical allodynia and thermal hyperalgesia were tested.	Tissue biopsies (lower gingival and TG ipsilateral).	The treatment group had higher CGRP(+) sensory nerve sprouting adjacent to the ectopic cancer and showed mechanical allodynia and thermal hyperalgesia.	The increase of CGRP was a result of cancer. The exact mechanism is not specified.	(44)
Wakabayashi 2018	To prove that TRPV1-deficient mice have decreased sensory nerve excitation and bone pain associated with mouse LLC.	40 C57BL/6 mice, half of which received intratibial injection of LLC cells. The CGRP positive nerves in the DRG were tested. Assessments for bone pain were performed.	Tissue biopsies (tibia and DRG ipsilateral).	The treatment group showed higher degree of pain and had high CGRP(+) sensory nerve fibers in tibia and DRG.	The increase of CGRP was a result of cancer and was associated with the degree of pain. This effect resulted from the upregulation of TRPV-1.	(42)
Levy 2004	To determine if the differential expression of CGRP in a range of pituitary tumors was	Recognized immunohistochemical techniques were examined in 26 consecutive pituitary adenoma specimens for the presence of CGRP.	Paraffin-embedded tumor tissues.	There was no significant association between the presence of CGRP and headaches. CGRP is not	The increase of CGRP was a result of cancer. The exact mechanism is not specified.	(45)

Table SI. Continued.

First author (year)	Objective	Method and sample size	Source of CGRP	Results	Potential mechanism of CGRP in cancer pain	(Refs.)
	related to the presence or absence of headaches.	Patients were divided into two groups: Headache and non-headache. The association between the presence of CGRP and headaches was observed.		observed in controls.		
Abdelaziz 2015	To investigate the measures of pain at distant non-tumor-bearing sites in animals with localized bone metastasis.	40 BALB/c mice, half of which underwent unilateral tibial injections of 4T1 cells. CGRP immunoreactivity and the sensitivity to mechanical and thermal stimuli in the contralateral paw was examined.	Tissue biopsies (tibia and DRG, both ipsilateral and contralateral).	CGRP expression and pain sensitivity were significantly increased in cancer-bearing mice, both ipsilateral and contralateral to the tibial injection side compared to sham controls.	The increase of CGRP was a result of cancer. The exact mechanism is not specified.	(35)
Niiyama 2007	To examine whether bone cancer can change TRPV1 expression and distribution in primary sensory neurons in a mouse model of bone cancer pain.	163 adult male C3H/HeJ mice and 1 TRPV1-deficient mouse. The treatment group received implantation of osteosarcoma into the femur. Cancer-associated pain behaviors and CGRP(+) nerve among DRG neurons were tested.	Tissue biopsies (femurs, DRG ipsilateral).	The number of TRPV1-positive neurons and the number of CGRP-positive neurons were increased.	This effect came from the upregulation of TRPV-1.	(39)

CGRP, calcitonin gene-related peptide; SCC, squamous cell carcinoma; TRPV1, transient receptor potential vanilloid1; DRG, dorsal root ganglion; LLC, Lewis lung cancer.