PROJECT TITLE:

Systemic Effects of Cancer on Thermal Pain Sensitivity in Mice

SPECIFIC AIMS

The overall goal is to study diffuse, widespread effects of cancer on mechanisms that modulate pain. Malignancies can release or induce a number of chemical mediators, e.g., cytokines that modulate sensitivity to nociceptive stimuli.

Hypothesis 1. Thermal pain sensitivity of SCID mice inoculated with human-derived osteosarcoma cells will progressively change throughout the growth period of the tumor.
Specific Aim 1 is to test hypothesis 1 by inducing an osteosarcoma tumor in the dorsal subcutaneous tissue of mice and measuring thermal pain sensitivity of the paws in an operant escape assay.
Expected result: increase in pain sensitivity most likely; decreased pain sensitivity or no effect possible (some of the cancer-induced cytokines are antinociceptive; some chemical mediators may be depressed in the SCID mouse model).

Hypothesis 2. The analgesic effect of systemic morphine in normal mice and mice with osteosarcoma in the dorsal subcutaneous tissue is different.
Specific Aim 2 is to test hypothesis 2 by comparing analgesic effect of systemic morphine in healthy mice and in mice with osteosarcoma in a thermal operant escape test.
Expected result: decreased analgesic effect of systemic morphine (see background section).

Hypothesis 3. The diffuse effect of a growing osteosarcoma tumor on thermal pain sensitivity and on the analgesic effect of systemic morphine is different in male and female mice.
Specific Aim 3 is to test hypothesis 3 by comparing tumor-related changes in thermal pain sensitivity and the effect of exogenous opioid on thermal nociception of male and female mice.
Expected result: cancer effect on pain sensitivity and opioid analgesia more pronounced in male (see background section).