Role of spinal microglia in the development of morphine-induced hyperalgesia

(continued from page 1)

macrophage-1 antigen (Mac-1, 16–32 µg; Mac-1-SAP rat, Cat #IT-33) to selectively ablate spinal microglia in rats with established morphine-induced hyperalgesia. Injections of Mac-1-SAP or saporin alone as control (SAP, 20 µg; Cat #PR-01) were initiated after seven days of morphine treatment and performed at lumbar level once a day for three days. Mac-1-SAP significantly reduced the level of CD11b expression in the lumbar spinal dorsal horn (see Fig.1) and the treatment reversed mechanical and thermal hypersensitivity induced by morphine. Conversely, the immunotoxin did not affect the development of morphine tolerance in the same animals.

These findings point out the specific role of microglia in the development of pain hypersensitivity following morphine treatment. Thereafter, we dissected the underlying molecular mechanisms and found that morphine induced P2X4 receptor upregulation in spinal microglia, which in turn triggered the synthesis and release of brain-derived neurotrophic factor (BDNF). Microglial BDNF has been shown to induce pain hypersensitivity in spinal neurons by hampering the function of the K^+-Cl^- co-transporter KCC2, the main neuronal chloride extruding transporter in neurons, via trkB signaling.[5] Consistently, we found that such BDNF-trkB-KCC2 signaling cascade is activated by morphine and alters chloride-mediated inhibition on spinal neurons, thus increasing network excitability.

All together, our study indicates that morphine-induced hyperalgesia, as neuropathic pain, is a pathological alteration of pain sensitivity whose expression is gated by spinal microglia. Targeting at any level, this microglia-to-neuron cascade is a valuable strategy to improve the use of morphine in chronic pain.

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Society for Neuroscience
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Amer Assoc Cancer Res
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Booth #TBA

Upcoming Events

Targeting Teaser Solution

Congratulations to the puzzle solvers from last quarter. Each winner received a Knockout Mouse Tote Bag.

WINNERS: Maria Kot, Inst of Pharmacology, PAS, Krakow, Poland; Rene Schweickhardt, EMD Serono, Billerica, MA; Prasanthi Geda, Merck, Boston, MA; Shunsuke Takasuga, Akita University, Akita-shi, Japan; Judene Bliss, Roswell Park Cancer Inst, Buffalo, NY; Terry Beltz, Univ Iowa, Iowa City, IA; Richard Fuerstenberg, R&D Systems, Minneapolis, MN; Jheem Medh, California State Univ, Northridge, CA; Adam Farmer, Triangle Research Labs, Research Triangle Park, NC; Shelle Malkmus, University of California, San Diego, CA; Sherie Ma, Florey Inst of Neuroscience and Mental Health, Parkville, Australia; Clay Archer, University of California, San Diego, CA; Glenn Kageyama, Cal Poly University, Pomona, CA; Bob Speth, Nova Southeastern Univ, Fort Lauderdale, FL

Bob Speth with his prize tote bag.
Photo courtesy of Eduardo Carrera.

The solution to the puzzle was:

Jumbles:
PLURIPOTENT
HEDGEHOG
DORSAL
GANGLIONIC
EMBRYONIC

What the ATS Knockout Mouse did to support himself while earning his PhD in Neuroscience.

Answer:
HE WORKED AS A ... MODEL.

Solve this quarter's teaser at www.ATSbio.com/news/13q4_teaser.html.