Newsfronts

Toxic Gas Protects Rodent Hearts

Inhaling carbon monoxide (CO) can kill you, but it may also help prevent rejection of transplanted hearts and reclogging of arteries after angioplasty, according to the results of a study in rats.

Physical trauma to blood vessels during balloon angioplasty or immune-mediated damage after transplant often leads to dysregulated proliferation of smooth-muscle cells in these vessels. The resulting narrowing of the vessels, or stenosis, can curb or completely block blood flow, limiting the success of these lifesaving procedures.

Now, a group led by Leo E. Otterbein at the University of Pittsburgh School of Medicine (Pittsburgh, PA) reports that exposing rats to low levels of CO substantially reduces this vascular narrowing (*Nature Medicine*, February). The research team found that rats exposed to CO (250 p.p.m.) immediately after aortic transplantation and for the subsequent 56 days, exhibited ~60% less stenosis than did control animals. Similarly, the research team found that stenosis was reduced by ~75% in rats exposed to CO for an hour before undergoing a procedure similar to balloon angioplasty.

If similarly successful results can be obtained in humans, CO therapy could substantially improve the prognosis for patients undergoing transplant or angioplasty. As Otterbein tells *Lab Animal*, "The ease of delivery, the short exposure time, and reversibility of the therapy, combined with the over 100 years of understanding of how this molecule functions, not to mention the low cost to produce it, makes [CO] an ideal candidate for development and use as a potential therapy in not only vascular diseases, but a host of inflammatory disorders."

According to Otterbein, his group is "currently testing the effects [of CO] in a pig model as well as carrying out some dose-ranging studies and time courses in rats to better understand the amount and length of exposure that will be optimal." Based on the results of these tests, in addition to safety studies to determine if inhaling comparable doses of CO has untoward effects in humans, they hope to move to testing this therapy in angioplasty patients.

—Tanja Schub

New Toke on Treating Skin Cancer

The active components in marijuana inhibit the growth of nonmelanoma skin tumors in mice, with no inhalation necessary, suggesting that cannabinoids may be a potential therapy for one of the most common malignancies in humans.

The vast majority of nonmelanoma skin tumors arise in the basal or squamous cells, and these tumors account for ~95% of all skin malignancies. Risk factors for nonmelanoma skin cancers include fair skin and excessive sun exposure.

Having already shown that cannabinoids inhibit the growth of malignant gliomas—a highly fatal form of brain cancer—Manuel Guzmán at Complutense University (Madrid, Spain) and a team of Spanish and American colleagues sought to determine if these compounds would have the same effect on skin tumors (*J. Clin. Invest.*, January). Using western blot analysis and immunohistochemistry, Guzmán's group first determined that normal skin and skin tumors in both mice and humans express cannabinoid receptors (CB_1 and CB_2). They then inoculated nude mice with epidermal tumor cells to induce tumors. Local administration of a CB_1/CB_2 agonist was associated with an inhibition of tumor growth, an increase in the number of apoptotic cells, and impaired tumor vascularization.

Guzmán tells *Lab Animal* that the group's next step in this project is to "elucidate the molecular mechanism involved in cannabinoid anti-tumoral action" to determine whether these effects derive primarily from "direct apoptotic action on tumor cells or inhibition of tumor angiogenesis."

—T.S.

Now Hear This—Scientists Map the Primate Auditory System

Neuroimaging research in humans has led to the identification of an extensive auditory system spread throughout numerous regions of the brain, but similar studies in primates have historically been less comprehensive. However, a recent study in rhesus monkeys may help close the gap in understanding auditory processes for the two species.

Brain metabolic activity can be tracked experimentally by injection of 2-[^{14}C]deoxyglucose (2-DG); this radioactively labeled sugar accumulates in the most active neurons, and particle emissions from the decaying isotopes can be monitored and recorded in the living subject through positron-emission tomography (PET). The resulting map allows for the identification and analysis of brain regions involved in responding to a wide variety of stimuli.

Nearly 20 years ago, researchers at NIH (Bethesda, MD) used this method to map the primate visual system; now, Amy Poremba from the University of Iowa (Iowa City) has collaborated with members of this group to develop a functional map of the auditory system. The study, published in *Science* (24 January), was conducted by unilateral ablation of core components of the auditory complex, resulting in monkeys with one "deaf" and one "hearing" brain hemisphere. This technique, used in conjunction with 2-DG uptake, allowed Poremba's group to make direct observations of differences in the responses to sound stimuli of various