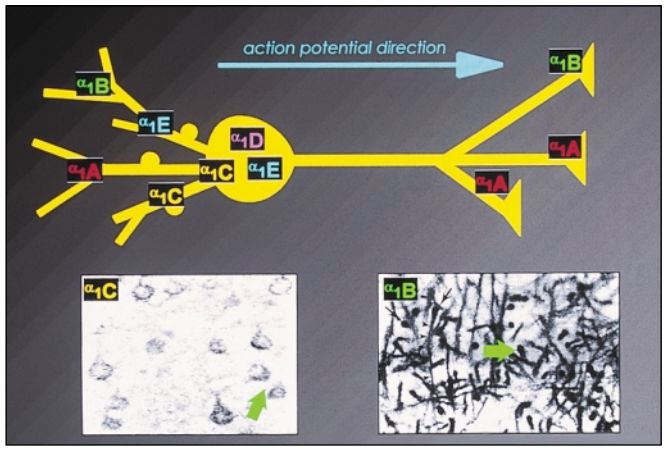
Research Update • Le point sur la recherche

Targeting calcium channels

Calcium-channel research may lead to new treatments for conditions from pain to stroke, and Dr. Terry Snutch, a professor in the University of British Columbia's biotechnology laboratory, is at its cutting edge. Eight years ago Snutch predicted the existence of 12 channels, and to date he and his colleagues have discovered 9 (*Nature* 1997;385:442-6).

Calcium channels, which are present in excitable mammalian cells, are involved in neurotransmitter release, hormone secretion, smooth-muscle contraction, enzyme modulation and gene expression. Snutch has isolated a family of calcium channels — the N-type — and identified their characteristics in nerves, smooth muscle and the heart. Two of the channels are targeted by drugs currently used to treat hypertension, angina and some arrythmias; others are targets for treatment of pain, migraine and epilepsy. These represent "very obvious therapeutic targets," says Snutch, who has cloned 5 genes encoding the channels that regulate calcium entry to brain cells.

No drugs target calcium channels directly, but Snutch's laboratory may soon change that. A toxin from the Micronesian cone snail, which releases more than 100 paralyzing peptides in its natural habitat, is the basis of a drug now being developed by a US company. The snail toxin is 1000 times stronger than morphine, and will have to be injected intrathecally (through the theca of the spinal cord into the subarachnoid space). Orally administered drugs based on small, organic molecules are preferable, says Snutch, and he is working with a British Columbia company, NeuroMed Technologies Inc., to develop this type of drug for disorders such as stroke and neuropathic pain.



(Top) Different types of cloned calcium channels (α1A – E) are located on different parts of nerve cells, where they mediate distinct physiologic functions. (Bottom) Antibody staining shows the localization of 2 types of calcium channels on nerve cells: α1C on cell bodies and α1B on dendrites.

The advantage of calcium-channel-based drugs is that desensitization and addiction are not issues, as they are with narcotic drugs. — © *Heather Kent*

Detecting DNA damage

A new technique to detect genetic mutations has been developed by University of Alberta scientists, and it is up to 100 000 times more sensitive than current procedures used to uncover damaged DNA. Chris Le, a professor of environmental science at the University of Alberta medical school, says the new test holds important implications for the early detection, prevention and treatment of cancer.

Results of experiments by Le and his team (Cross Cancer Institute experimental oncologist Dr. Michael Weinfield, James Xing, Janet Lee and Steven Leadon) were recently published in *Science* (1998;280:1066-9).

The new technique takes advantage of fluorescent antibodies to identify even the smallest mutation in DNA. The researchers find damage by extracting DNA from human cells, then mixing it with 2 types of antibodies: the first binds to a damaged DNA base and the second, which is fluorescent, binds to the first. The researchers then illuminate the mixture to find the damaged DNA base.

The test is so sensitive that it can detect 1 damaged base in a strand of 1 billion bases, says Le. And it can tell researchers what caused the damage, allowing them to differentiate between damage caused by, say, ultraviolet light and by aromatic hydrocarbons.

The result? Researchers can now base estimates of cancer risk not on safe average exposure to carcinogens and best guesses, but on hard data. This is accomplished by measuring an individual's ability to repair damaged DNA. Le said the impact of the research will be felt immediately in the research community, but thinks the technology will spread further. Could the test one day become part of a physician's bag of tricks? "I don't see any reason for it not to," says Le.

His enthusiasm is tempered by his concern about ethical issues. Could the research be used to screen candidates for certain jobs? "I think the area we need to be careful in is with ethical issues, with privacy." — © *Richard Cairney*