Research Update

Inside inflammation: newly discovered receptors are key players in painful conditions

A new mechanism for the excitation of sensory nerves, which play a role in inflammation, has been discovered by researchers at the University of Calgary, in collaboration with colleagues in the US, Italy and the UK (*Nat Med* 2000;6[2]:134-5). The discovery could lead to new treatments for inflammatory conditions.

The researchers discovered that proteases released from sensory cells involved in the inflammatory process activate a newly discovered class of receptors, proteinase activated receptors 2 (PAR2), that are located on sensory neurons. The findings suggest that substances that can block the PAR2 receptors may eventually become new anti-inflammatory drugs. "This direction has yet to be explored; we will now try to study the role of these receptors

in the process of inflammation and pain in models of conditions like colitis," says Morley Hollenberg, professor of pharmacology and therapeutics at the University of Calgary. "The novel thing about our work is the involvement of the nervous system."

An editorial in the *British Medical Journal* (*BMJ* 2000;320:331) describes how the US researchers explored the role of tryptase in the inflammatory process. They looked at the interaction of tryptase with PAR2 receptors when mast cells in the vicinity of sensory nerve endings degranulate. "we wanted to establish whether the mast cells were talking to neurons via tryptase," commented Nigel Bunnett of the University of California. The experiments confirmed "that PAR2 receptors on sensory nerves are criti-

cal to the inflammatory process."

Ultimately, new anti-inflammatory drugs based on these findings could benefit patients with conditions such as arthritis, inflammatory bowel disease and migraine headaches, but Hollenberg says human trials are a long way off. At this stage, he said, "the work has raised the visibility of this receptor as a target for companies to develop drugs. Companies have been interested in developing drugs to target the PAR1 system, but as yet they have not targeted the PAR2 system."

For Hollenberg, who has worked on the project since 1991, a key aspect of the discovery has been "the coming together of people with unique expertise," none of whom could have completed the research alone. — *Heather Kent*, Vancouver

Monitoring measles key to predicting epidemics

The dramatic changes in epidemic patterns that occur in large cities can be predicted using a remarkably simple mathematical model, says David Earn, a professor of applied mathematics at McMaster University, Hamilton, Ont. (*Science* 2000;287:667-70).

After studying 20th-century measles epidemics in London, Liverpool, New York and Baltimore, Earn and collaborators from Cambridge University and the University of Florida concluded that changes in epidemic patterns previously thought to be "chaotic" or "noise-driven," in the mathematical sense, could be predicted using just birth and vaccination data.

"Measles epidemics range from similar outbreaks every year [annual epidemics], to large or small outbreaks in alternate years [biennial epidemics], to very irregu-

lar outbreaks of varying size [irregular epidemics]," Earn says. "In some places there are also records of 3-year cycles."

During the past century, epidemic patterns have changed noticeably. For example, some annual epidemics have shifted to biennial, and biennial epidemics have become irregular.

Earn believes that his paper is the first to indicate the influence of changing birth rates in such transitions.

"The research reported in the current paper allows us to explain transitions in epidemic patterns that have occurred in the past, and to predict transitions in the future. These transitions were not previously thought to be predictable. Since we have revealed a certain type of predictability about the epidemic patterns, we have renewed hope that it may be possible to design

better vaccination strategies — strategies that are more likely to lead to eradication of diseases such as measles," Earn says. The new mathematical model is applicable to other diseases with short latency and infectious periods, he told *CMAJ*. "The approach could be used for diseases such as mumps, rubella, chickenpox and whooping cough. It would not apply to influenza or HIV."

However, Earn's elegant model is by no means the last word on the subject, says Sir Robert May, chief scientific adviser to the UK government, in a commentary in the same issue of *Science*.

"Much relevant work remains to be done in teasing apart the social, genetic, age-related, and other complications that are smoothed out in the usual mass-action assumption," May says. — *David Helwig*, London