



Chat lines and escort services

French researchers reckon they understand a bit more about what keeps cells “chatting” to each other, and it seems an “escort” could be involved. Their findings could lead to a new approach to cancer treatment.

A team at the Laboratory of Signal Transduction and Oncogenesis of the Curie Institute in Paris has investigated the information-conveying mechanisms in cells, in particular the effects of the Ras protein. The gene for Ras is mutated in 30–60% of all cancers and is the central point for cell signaling that leads to proliferation.

All the signals that trigger cell proliferation are modulated in some way by one of three proteins known as Ras, which essentially act as biological switches. When anchored to the inner side of a cell’s plasma membrane, Ras proteins are activated by signals through membrane receptors. Mutant Ras proteins that are constantly active regardless of the presence of a signal are the focus of much cancer research. Improved understanding of what happens when there is no cellular chat has already led to several drugs whose mode of action is based on controlling cell signaling. Anticancer agents such

as Herceptin (trastuzumab) and Glivec (imatinib), are among those on the market. These “anti-signaling” drugs inhibit membrane receptors or proteins involved in signaling and ultimately trigger apoptosis.

Jean de Gunzburg and his colleagues have found that another protein known as PDE_δ acts as an escort for two immature branches of the Ras family tree, the Ras and Rap

proteins, allowing them to enter the intracellular space where they mature into active forms (*J. Biol. Chem.* **2002**, *277* (17), 15076–15084).

It is likely that the PDE_δ escort is intervening in one of the steps necessary to drive Ras to the plasma membrane, its site of action. “We could speculate that preventing PDE_δ’s action on Ras might keep mutated oncogenic Ras proteins from being active, and therefore exert some antitransformation activity,”

Gunzburg explained. “A lack of PDE_δ could prevent Ras from being correctly positioned in the cell, a hypothesis that is being experimentally tested.”

The discovery of the activity of PDE_δ could ultimately provide an alternative target for drug discovery. The team suggests that PDE_δ may be used to deactivate Ras proteins, switching off those that are constantly turned on in human malignancy.

—DAVID BRADLEY

Forgive and be well

The old adage “forgive and forget” has proven beneficial to many personal relationships. However, a new study currently under way will try to determine if forgiveness, in addition to several other psychological and spiritual attitudes, is also beneficial to the immune system of patients infected with HIV.

“Rapidly accumulating research demonstrates a strong correlation between psychosocial and spiritual influences and immunological, biochemical, and disease outcomes, but there have been few scientific studies with empirical data to prove these theories,” says Lydia Temoshok, the study’s principal investigator and professor of psychiatry at the University of Maryland School of Medicine (Baltimore). “This will be one of the first to systematically test these approaches and document their benefit, perhaps not only to HIV/AIDS patients, but to the general public as well.”

Two hundred HIV-positive patients will be enrolled in the two-year study, which will take place at the school’s Institute of Human Virology. Since the status of HIV/AIDS can be screened through routine blood work, the clinical team will explore the development of the infection through frequent blood tests to investigate any parallels with how each patient copes with emotions. Temoshok’s group hypothesizes that letting go of angry thoughts and feelings, or

forgiving, may promote the body’s natural ability to return hyperaroused physiological systems back to more normal levels of homeostasis. This state of homeostasis, they say, is critical in slowing the progression of AIDS and maintaining a higher quality of life.

To determine the patients’ coping styles, each will undergo a 60- to 90-minute structured interview. On the basis of the interview’s results, patients will be placed in three categories, A, B, or C.

Type A people are extremely angry; this personality type has been linked in the past with repeated heart attacks and high blood pressure. Type B individuals typically do not have problems expressing emotions but tend to have immune system problems anyway. Type C individuals do not recognize

their own needs or emotions and put others before themselves; they tend to stay in stressful situations longer because they are not proactive in changing their circumstances.

Once a patient’s coping style is determined, biological markers in the blood might prove that there is a direct connection between coping with emotions and physical health. The study will also try to find whether a connection exists between coping style and the level of homeostasis.

—FELICIA M. WILLIS



