Biomedicine

Rick Weiss reports from New Orleans at the annual meeting of the Society for Neuroscience

The science of cellular suicide

From the earliest days of an organism's development, right up until the bitter end, new cells are born and old ones die. Moreover, cell death can occur in predictable patterns, especially during embryonic development. The fetal hand, for example, looks at first like a paddle. Fingers emerge only after the death of parallel rows of cells.

But what is the actual mechanism of programmed cell death? Do cells simply wither away when their time has come, or do they play an active role in their own demise? Recent research suggests that cells may have suicidal tendencies.

Lawrence M. Schwartz and Brian K. Kay, at the University of North Carolina in Chapel Hill, are exploring mechanisms of cell death in the tobacco hawkmoth. The moth is a popular model of development; it is easily reared in the laboratory, and major anatomical changes can be traced as it undergoes the process of metamorphosis.

The researchers looked at a particular kind of muscle cell that spontaneously degenerates within 36 hours after the emergence of an adult moth from its cocoon. They identified five proteins that are not produced in the cells until just before cell death. To see whether these proteins are crucial to cell death, they treated some moths with a chemical that blocks new protein synthesis. Muscle cells from those moths failed to develop the five proteins, and the cells did not die.

The researchers are currently attempting to inject small quantities of these "cell death" proteins into living, cultured cells, to see if they can stimulate early cell death. They theorize that under certain conditions, hormone levels in the insect (and perhaps in higher animals) "turn on" cell-death genes that code for the production of deadly proteins. They hope that a better understanding of normal cell death may provide insight into diseases in which cells die at inappropriate times, or don't die when they should.

Related research by David Martin and his colleagues at the Washington University School of Medicine in St. Louis suggests that suicide is an inherent tendency in some cells, and that constant intervention is required to prevent it from occurring.

Particularly intriguing are their findings that nerve growth factor (NGF), recognized for years as a critical ingredient for cell growth, may be more properly considered a "death-preventing factor." Like the North Carolina group, the St. Louis researchers found that cell death didn't occur when protein synthesis was blocked. "This result indicates that the neurons took an active role in killing themselves, rather than wasting away passively," the researchers report. They say that those findings, in conjunction with earlier evidence that NGF is needed for cell survival, suggest that "NGF normally suppresses the synthesis of killer proteins' that are designed to kill the cell" when triggered by specific chemical cues.

Are we boring you?

Research into yawning is not very exciting. Scientific studies tend to confirm what most people have known for centuries: that yawning is more common during the hour before bedtime and the hour after waking, that we yawn more when our level of interest drops and that yawning is "contagious."

However, one commonly held belief about yawning – that it can occur as a response to a lack of oxygen or a buildup of carbon dioxide in the body – may not be true. Robert R. Provine and his colleagues at the University of Maryland in Catonsville undertook to test that oft-cited but untested assumption, and found that yawning is neither a response to nor a means of regulating oxygen or carbon dioxide levels.

The researchers gave people different mixtures of oxygen and carbon dioxide to breathe, and found no correlations with yawning behavior. Indeed, their research suggests that yawning and breathing are triggered by entirely different internal states and are probably controlled by separate mechanisms.

As further evidence that yawning does not serve a primary respiratory function, the researchers note that yawning and breathing have different requirements with regard to their routes of inhalation and exhalation. While breathing can be performed satisfactorily through either the nose or mouth, the researchers report that subjects find it "very difficult, if not impossible, to perform a satisfying yawn with their mouth taped shut." Moreover, they say, oral inhalation by itself will not produce a satisfactory yawn unless the jaw is free to move. "Subjects attempting to yawn with clenched teeth often reported the unpleasant sensation of being stuck in mid-yawn."

So much for what the yawn is *not*. As for what it *is*, the researchers must concede that the yawn's true function "remains mysterious."

Worried sick: Hassles and herpes

A growing number of studies are finding links between psychological states – particularly stress – and immune function. The emerging facts have given birth to a new discipline, psychoneuroimmunology, which seeks to understand the links between psychological status, central nervous system activity, endocrine function and immune response.

In trying to understand this complex relationship, neurobiologists and physicians have found it useful to study people with herpesvirus infections. The virus spends most of its time in a latent, or inactive, phase, residing in the cell bodies of certain peripheral nerves. Occasionally it becomes active, reproduces and is transported down the nerve-cell axons to the skin, where it may cause the formation of blisters or "cold sores." Anecdotal evidence has linked herpes reactivation to psychological stress, but only recently have controlled studies confirmed that link.

New research by Susan Kennedy and her colleagues at Ohio State University's College of Medicine in Columbus took psychological and immunological data from married men and compared them to separated or divorced men matched for age and education; all the subjects had herpes. Separated and divorced men were more anxious, depressed and lonely than their married counterparts – and had higher levels of herpesvirus antibodies. Since antibody levels go up during periods of viral reactivation, higher antibody levels are believed to reflect a depressed immune system incapable of keeping the viral infection under control.

Among married men, marital quality had its correlates with immune function as well. Poorer marital quality was related to higher viral antibody levels, and lower ratios of helper T cells to suppressor cells – another measure of immune suppression.

Other researchers are finding that immune function may be linked not only to personal stress, but also to the perception that others nearby are experiencing stress. Jill Irwin at Queen's University in Kingston, Canada, and her colleagues at the University of Rochester (N.Y.) measured the activity of natural killer cells in mice exposed to foot shocks, and compared those measures to unstressed mice. Unstressed mice not in the vicinity of the stressed mice showed no suppression of normal immunity as measured by killer cell activity. But unstressed mice kept in cages close enough to hear and smell their stressed neighbors showed significant drops in killer cell activity.

The researchers suggest that cues associated with a nearby stressful experience may provoke changes in immune function, perhaps as a result of an increase in sympathetic nervous activity. Such activity – the so-called fight or flight response – has been shown to suppress immunity.