

public input; the deadline for submissions was 14 October. Researchers say that bioethics committees are not waiting for new legislation, however: They have already tightened access to human tissues drastically, causing some projects to grind to a halt.

The use of human tissues for research has been a charged issue in the United Kingdom since 1999, when it was revealed that Alder Hey Children's Hospital in Liverpool, as well as hospitals in Bristol and Birmingham, had been removing organs from dead babies for decades without parents' consent. In some cases, the hospitals had allegedly given organs to pharmaceutical research companies in return for financial donations. "What happened at Alder Hey was inexcusable," says Carlos Caldas, a genetic epidemiologist at the University of Cambridge, but he argues that overly cautious regulatory committees have overreacted in a way that is severely hampering legitimate medical research.

The projects hardest hit, according to Caldas, are those that rely on archives of human tissue samples. Such collections consist of tumors and other tissue removed during surgery that are either frozen or embedded in wax. Caldas coordinates an international consortium that hunts for genetic factors in gastric cancer by comparing archived tissue samples from patients going back 20 years. Access to such samples before 1999 was straightforward, but it has now become "very difficult," he says.

Regional bioethics committees now require that consent be obtained from the original owner, or the next of kin if the owner has died, for any new use of an archived tissue. Such requirements are long overdue, says immunologist Herbert Sewell of the University of Nottingham, a member of the Nuffield Council on Bioethics. Although he acknowledges that contacting donors or next of kin for decades-old samples can be difficult, informed consent for all intended uses of donated tissue is a fundamental requirement of ethical research.

But many researchers are not happy. Because of the new requirements, "cancer research has been paralyzed," says Kathy Pritchard-Jones, an oncologist at the Institute of Cancer Research in Sutton. Pritchard-Jones says several of her research projects are on hold because of difficulties in accessing archived tissues. "Legal clarity is needed," she says, because tissue archives are now being treated as equivalent to whole organs from the recently dead.

Caldas is leery of new legislation, however. "Legislating this kind of research could put it in a straitjacket," he says. Caldas would prefer a more flexible set of guidelines that bioethics committees can use to approve research on tissue archives without fear of scandal. In spite of the hardships that have

befallen researchers, Caldas at least hopes that the public debate will help dispel some public misperceptions. "At the end of this," he notes, "[we hope] people will see that researchers are not Frankensteins. We're trying to improve health."

—JOHN BOHANNON

John Bohannon is a writer in Lyon, France.

## CELL PROLIFERATION

### Common Control for Cancer, Stem Cells

**KOBE, JAPAN**—At the very beginning of life, stem cells can develop into all the different tissues of the body; in contrast, cancer cells often end life. Despite these obvious differences, researchers have suspected that similar mechanisms might be at work in both cancer and stem cells. For example, both can multiply indefinitely. Embryonic stem (ES) cells transplanted into mice sometimes develop into tumors. And stem cell lines have been derived from a cancer known as teratocarcinoma.

Now, two researchers have found a new gene that is apparently involved in regulating the proliferation of both stem cells and at least some types of cancer cells. "This could show that stem cell biology and oncology interact," says Ronald McKay, a molecular biologist involved in the experiments at the National Institute of Neurological Disorders and Stroke, part of the U.S. National Institutes of Health (NIH) in Bethesda, Maryland.

Other researchers find the link to cancer cells intriguing, but, as Shin-Ichi Nishikawa, a molecular geneticist at Kyoto University in Japan, says, "we really need more data before saying anything conclusive about the role of this protein in cancer." McKay described the finding briefly on 20 November during a symposium here on Stem Cells and Organogenesis. The full report, by McKay and NIH colleague Robert Tsai, appeared in the 1 December issue of *Genes & Development*.

Stem cells are the focus of intense research interest because of their ability both to self-renew, or proliferate, and to differentiate into a variety of tissues, offering tantalizing possibilities of growing replacement organs in vitro, among other possible therapeutic applications.

McKay and Tsai set out looking for genes with critical roles in the self-renewal mechanism. Working with various rat stem cell lines in culture, they found a new gene expressed in

ES cells, in central nervous system stem cells, and in primitive bone marrow cells. In all cases, the protein encoded by the new gene was abundantly expressed while the cells were proliferating in an early, multipotential state, but it abruptly and almost entirely disappeared at the start of differentiation. The protein was not found in the differentiated cells of adult tissue, suggesting a role in maintaining stem cell self-renewal. The researchers dubbed the new gene *nucleostemin* because its protein product appears to be active almost exclusively within the nucleus of the stem cells.

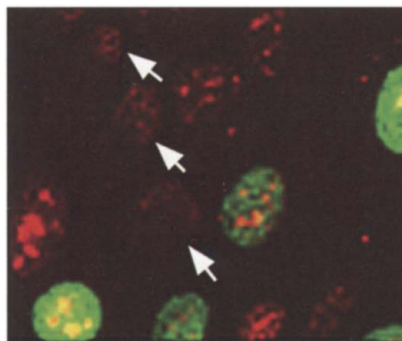
That locus of activity led to "an inspired guess," says McKay. The cell nucleus is also the site of activity of several genes whose proteins are known to regulate the activity of *p53*, a gene with a well-studied role in suppressing tumors. Mutations in *p53* have been implicated in numerous types of cancer. Following the hunch that *nucleostemin* might be involved, McKay and Tsai looked for and found a human homolog active in several human cancer cell lines. They further determined that its protein product binds to the *p53* protein, although just how the two proteins interact is unclear.

To further define the new gene's role, McKay and Tsai interfered with its activity in both rat stem cells and human cancer cells. They shut it off, through a technique known as gene silencing, and overexpressed it, by adding protein to the cells. Both too little and too much of the nucleostemin protein hindered cell proliferation. "There seems to be a critical level involved," McKay says. At that level, they suggest, nucleostemin helps regulate the proliferation of both stem cells and some types of cancer cells, although the precise mechanism is not yet known.

"The method appears to be very sound, and the study suggests the [gene has] some relation to promoting self-renewal," says Nishikawa. But he warns against attributing too big of a role to a single gene. He explains that among different types of stem cells, the evidence indicates that "there may be very diverse ways [of regulating] self-renewal and differentiation." And, he adds, regulation of proliferation in cancer cells is likely to be just as complex.

McKay readily agrees, but he predicts that further studies will find more links between these cells at the opposite ends of life.

—DENNIS NORMILE



**Missing multiplier.** Cells with a minimum of nucleostemin protein (arrows) show no sign of proliferating (green).