light's effects. "When the melatonin hypothesis was first presented," the pair notes, "no putative melatonin receptors [on cells] were known." Since then, three types have been identified.

In the March MOLECULAR CARCINOGENESIS, they lay out the molecular basis for concerns that light at night might prove an endocrine disrupter with the potential to increase cancer risk. They note that recent findings in several laboratories working with cells and with tissues removed from animals indicate that a reduction of melatonin can alter the production of other hormones, may suppress the immune system's ability to recognize and respond to newly emerging cancers, and appears to spur the growth of at least some tumor tissues.

By studying which cells possess melatonin receptors and how cells use them to respond to the hormone—as Barrett's team and others are now doing—science may resolve whether nighttime illumination truly threatens health, and if so, how much and in whom.

Studies now under way are also testing which wavelengths—or colors—are most biologically active. For instance, blue and green light appear especially effective at inhibiting melatonin synthesis in healthy young men, according to studies by Brainard. Indeed, he notes that for some colors, "17 lux was sufficient to produce strong melatonin suppression in these men—and some had full suppression with exposure to as little as 5 lux." The latter "is a little more illumination than what you'd have with full moonlight."

Brainard notes that the payoff for finding out what wavelengths are most hormonally disruptive could be insights on how "to tailor nighttime lighting to provide good vision without interfering with the melatonin rhythm." He says that "it may also help us develop more effective lights for use in treating winter depression and sleep disorders." □

How much light is too much?

At least in rats, a little light throughout the night can have a dramatic impact on cancer, observes David E. Blask of the Mary Imogene Bassett Research Institute in Cooperstown, N.Y.

Tumors can grow especially rapidly in rodents exposed to constant light, he notes—presumably because of a near-total suppression of their melatonin. To test just how much light was necessary to enhance tumor growth, he implanted liver-cancer cells into rats.

His team housed one group of caged animals in a room illuminated around-the-clock with about 850 lux of white light, which is roughly equivalent to an office with medium lighting. A second group of animals spent their days in 850 lux but their nights in total darkness. A third group encountered almost the same light-dark cycle. The only difference: 0.2 lux leaked in at the bottom of the door to their room from a hallway outside—illumination well below that typical of a moonless night, he says.

In the October 1997 LABORATORY ANIMAL SCIENCE, Blask's team reported that tumors in animals exposed to the crack of light coming under the room's door grew almost twice as fast as those in animals getting a night of total darkness. Indeed, he says, "animals exposed to the low-level light contamination had a tumor-growth rate virtually identical to that in the animals exposed to bright, constant light." He has just replicated the findings in an experiment in which the lighting was more rigorously controlled. —*J.R.*

Biology

Diabetes drug stirs cancer confusion

New research has offered hope that troglitazone, a widely prescribed diabetes drug, could become a new colon cancer therapy, but some scientists also express concern that the drug may trigger the cancer in genetically susceptible people.

This seemingly contradictory story emerges from several studies in the September NATURE MEDICINE. In one, Bruce M. Spiegelman of the Dana-Farber Cancer Institute in Boston and his colleagues report that troglitazone and other compounds that activate an intracellular protein called PPAR-gamma can transform colon cancer cells into nonmalignant cells in test-tube experiments. The drug also inhibited growth of tumors formed from human colon cancer cells implanted into mice.

PPAR-gamma normally regulates cell proliferation and specialization. Spiegelman and his colleagues hope soon to test whether troglitazone can help patients with colon cancer. The drug has already shown some promise in people with liposarcoma, a different cancer, says Spiegelman.

Curiously, however, two research groups have found that PPAR-gamma activators increase the incidence of cancer in certain mutant strains of mice. One group, led by Ronald M. Evans, a Howard Hughes Medical Institute investigator at the Salk Institute for Biological Studies in La Jolla, Calif., tested such compounds on mice with mutations in a tumor-suppressor gene called *APC*. These animals are generally predisposed to cancer of the small intestine. People with *APC* mutations almost invariably develop cancer of the colon.

The scientists had hoped that the PPAR-gamma activators might reduce cancer risk, but treated mice developed many more precancerous polyps in the colon than untreated ones. "What we found was exactly opposite what we had expected," says Evans. Yet normal mice receiving the PPAR-gamma activators had no greater incidence of cancer. Similar results have emerged from studies conducted on *APC* mutant mice by a group led by Johan Auwerx of the Pasteur Institute in Lille, France.

Since fats can activate PPAR-gamma, these studies may explain the finding that diets high in fat increase a person's risk of colon cancer. Evans also warns that people with diabetes who take troglitazone, especially those with a family history of colon cancer, should be carefully monitored for any signs of the disease. Spiegelman, however, notes that the mice may not reflect how colon cancer develops in people and that only those with *APC* mutations may face an increased cancer risk. "There's no evidence that [troglitazone] induces polyps in normal people or mice," he says. —*J.T.*

Rats have too much on their minds

Students cramming for an exam sometimes feel as if their brains can't absorb any more information. That overloaded feeling is shared by rodents studied by Edvard I. Moser of the Norwegian University of Science and Technology in Trondheim and his colleagues. The scientists used electrodes to stimulate memory-forming regions of rat brains. The stimulated animals fared poorly on a spatial-learning task that involves swimming for a hidden platform in a water tank, the researchers report in the Sept. 25 SCIENCE.

The overstimulation seems to prevent a strengthening of the connections between brain cells, known as synapses, that occurs after repeated stimulation. Many neuroscientists now believe that this strengthening, called long-term potentiation or LTP, is the primary mechanism by which animals form memories. The overstimulation experiments confirm that LTP can strengthen the synaptic connections between brain cells only so much. Moreover, if a brain reaches maximum stimulation, any learning is difficult if not impossible. "People are now focusing on how such changes in synaptic strength allow memories to form. That's the next issue, and it's a formidable question," says Moser. —*J.T.*