DMS's James Sargent, M.D., recently showed that exposure to smoking in movies is more likely not only to make teens take up smoking but also to make them established smokers.

Celebrating cellular and scientific flexibility

Was it good luck or brilliant insight? That's what Chuck Cole, Ph.D., a professor of biochemistry at Dartmouth Medical School, wonders about a recent discovery in his lab. He and former DMS graduate student Jack Scarcelli, Ph.D., started down one scientific path but ended up making an important, unexpected discovery that brought them onto a very different avenue. They identified a gene that plays a role in allowing the membrane surrounding the cell nucleus to stay flexible. And they showed that this flexibility is very important in the assembly of passageways that allow cellular messages to get in and out of the nucleus.

These passageways, nuclear pore complexes (NPCs), are tunnels made of proteins through the nuclear membrane. NPCs are important because, says Scarcelli, messenger RNA (mRNA), which encodes the proteins that carry out many of the functions of the cell, is made from DNA within the nucleus—but the cellular machinery that makes the proteins is out in the cell's cytoplasm.

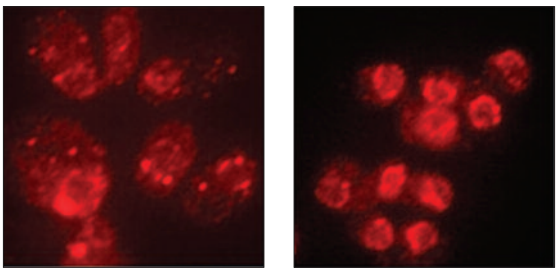
"In science," says Cole, "you have to follow the interesting results."

Studies: The discovery began with studies of how mRNA gets in and out of the cell—something Cole's lab has long been interested in. Scarcelli used robotics to do a large-scale experiment to identify genes in yeast cells that, when missing, cause a defect in the export of mRNA. From this screen, several genes were shown to affect mRNA export, including Apq12. At first the researchers thought Apq12 was directly involved in mRNA export, perhaps as part of the NPC. What they found, however, was quite different.

Hypothesis: When Cole and Scarcelli looked closely at Apq12's role, they saw that, in cells lacking it, NPCs could not be assembled correctly at low temperatures. At lower temperatures, cells adjust the makeup of the nuclear membrane to maintain its fluidity and flexibility. So the researchers hypothesized that yeast cells that lacked Apq12 no longer had the ability to alter the membrane's composition. To test the idea, they treated the cells with benzyl alcohol, a chemical that loosens up the membrane. After the membrane's flexibility had been restored with benzyl alcohol, the NPCs could then be assembled correctly, even in the Apq12 mutants.

So a project that began with mRNA export ended with a discovery in nuclear membrane biophysics—a discovery that has garnered quite a bit of attention. The paper was published in the *Journal of Cell Biology* and featured in *Cell*'s "Leading Edge" section. The researchers still don't know exactly how Apq12 changes the nuclear membrane's flexibility, but that's their next step.

"In science," says Cole, "you have to follow the interesting results that you get." Clearly, his and Scarcelli's ability to switch gears and follow unexpected findings has paid off. Instead of good luck or brilliant insight, maybe this finding is a credit to their ability to remain flexible. KRISTEN GARNER



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Nuclear pore complexes (NPCs) are passageways through which cellular messages move. Researchers stained these NPCs to show that those lacking a protein called Apq12 (on the left) could not assemble the passageways the way normal cells can (on the right).

A hearty endorsement

A DMS team led by cardiologist Michael Simons, M.D., has genetically engineered adult mice to grow new blood vessels around their hearts. Within three weeks, the animals' vasculature had grown 50% percent, and by six weeks their hearts were 50% larger. "This study demonstrates that an increase in the size of the vascular bed in the normal heart leads to increased cardiac mass and myocardial hypertrophy paralleled by increased cardiac performance," the researchers wrote in the *Journal of Clinical Investigation*. The findings may lead to new approaches for treating heart disease.

Looking to stem leukemia

A blood formation gene called mixed lineage leukemia (MLL)—which is essential for the development of embryonic blood stem cells and is involved in a type of childhood leukemia—also plays an unexpected role in the adult blood-forming system, according to a recent study in *Cell Stem Cell*. DMS geneticist Patricia Ernst, Ph.D, and colleagues found that in mice, MLL acts on bone marrow stem cells and controls key aspects of their growth to generate mature blood cells. If it's disrupted, it cannot work properly and leukemia can ensue. The researchers hope that their discovery may one day lead to new anticancer treatments. ■