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New protein booster may lead to better DNA vaccines and gene therapy

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Scientists have discovered a new way to manipulate how cells function, a finding that might help advance an experimental approach to improving public health: DNA vaccines, which could be more efficient, less expensive and easier to store than traditional vaccines.

Their approach, based on research results published this week in the journal *Proceedings of the National Academy of Sciences*, improves upon an existing laboratory technique, transfection, widely used to study how cells and viruses work.

Jaquelin Dudley, a professor of molecular biosciences at The University of Texas at Austin, and her team have developed a method for boosting the amounts of certain proteins a host cell produces when genes are delivered by transfection. Coaxing cells to produce novel proteins, such as those associated with viruses, is a key feature of DNA vaccines. Dudley's method causes cells to produce novel proteins at levels 5 to 20 times as high as with previous methods.

The researchers suggest that their finding might lead to better DNA vaccines, a relatively new method of vaccination that health experts say would increase vaccination rates, especially in the developing world. Whereas traditional vaccines train the body to attack viruses by introducing weakened forms of the virus, a DNA vaccine works differently, using a bit of DNA specified by a virus to prompt the production of proteins that lead to immunity.

By boosting the amount of proteins produced by the hosts' cells, Dudley's new method might invoke a stronger immune response in patients receiving a DNA vaccine. And, by making smaller vaccine doses possible, it might also reduce the risk that the patient's immune system would inadvertently attack healthy host cells.

The scientists' discovery could also help advance another experimental approach: gene therapies, which treat genetic disorders by replacing or disrupting genes that aren't working properly. Gene therapies targeting Parkinson's, hemophilia, leukemia, cystic fibrosis and many other diseases are being developed, but gene therapies have proved difficult, as they sometimes induce a cancer or trigger an immune response against cells with the introduced genes. The new method for boosting novel protein production might prevent these effects by allowing the insertion of smaller amounts of DNA.

The method for boosting production of novel proteins in a host cell was discovered by accident. Dudley and her team were attempting to understand how mouse mammary tumor virus (MMTV), a virus related to HIV that causes breast cancer and leukemia, manipulates an infected host cell to keep the host's immune system from attacking it.

A bit of genetic material that was expected to produce lower levels of a certain protein instead caused cells to produce a lot more of it.

"Everything in the literature would indicate that something abnormal had happened," said Dudley. "But we went back and used several different detection methods to show that what we observed was real."

According to conventional wisdom, when a cell detects the presence of foreign DNA such as the one the researchers introduced, it shuts down production of proteins to prevent the spread of viruses.

"What we've described is that introducing these DNAs leads to a different detection system in the cell that, instead of shutting down protein expression, increases expression," said Dudley.

When the researchers combined this protein-boosting DNA with genes for other novel proteins and introduced them into host cells, those proteins were also produced at a much higher rate than with traditional methods of delivering genes. Dudley suggests that including this extra bit of genetic material could be applied to a wide range of research problems to increase the production of specific proteins within cells.

More information: "Retroviral vectors elevate coexpressed protein levels in trans through cap-dependent translation": www.pnas.org/content/early/201 … 477112.full.pdf+html

Provided by University of Texas at Austin