A method for storing vaccines at room temperature

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Shipping vaccines in an unbroken temperature-controlled supply chain (a "cold chain") all the way to recipients is a major logistical and financial challenge in remote areas and developing countries. According to

Doctors Without Borders, the need to keep vaccines within a temperature range of 2-8°C is one of the main factors behind low immunization-coverage rates.

Researchers at EPFL's Supramolecular Nanomaterials and Interfaces Laboratory (SUNMIL), in collaboration with scientists in Milan, Turin, Leiden, and Oregon, have come up with three simple and inexpensive vaccine additives to get around this obstacle. Using minute quantities of nanoparticles, or FDA-approved polymer (polyethylene glycol), or higher amounts of sucrose, they were able to stabilize vaccines at room temperature for several weeks or, in some cases, months. Their approach, which was successfully tested on a vaccine for rodents, is published in *Nature Communications*.

Nanoparticles, polymers and sugar

The study addressed viral-vector vaccines, the most common type of vaccine, which normally only last for a few days at room temperature. At that point, the viral components of the vaccines lose their structural integrity. "These components fluctuate by their very nature," Stellacci, head of SUNMIL - Constellium Chair. "They are combined in a stable form, and the low temperature maintains that balance. But the thermally induced fluctuations eventually lead to a loss of integrity of the viral vector." The scientists' approach, which consists of stabilizing the vaccines against such fluctuations through simple biocompatible additives, has delivered excellent results.

In their first approach, osmotic pressure is applied on the inactivated viruses (the main component of the vaccine) using a cloud of negatively charged nanoparticles. The virus is already subject to an outward osmotic pressure due to its genetic material (RNA or DNA), which has a high negative charge and is held inside the virus. The nanoparticles form a cloud of negatively charged objects that cannot enter the virus, thus generating counter-osmotic pressure that keeps the virus intact. "With this method, infectivity for a virus reached a half-life of 20 days," says Stellacci.

The second approach consists in stiffening the virus's capsid, which envelops the inactivated virus, by adding polymers. This additive mainly stabilizes the virus by slowing its oscillations by changing the stiffness of the capsid. As a result, the vaccine remained fully intact for 20 days with an estimated half-life of ~70 days.

Finally, adding sucrose, a common sugar, to the vaccine makes the environment more viscous and slows down fluctuations. "It's a little like adding honey, where all motion is slowed down," says Stellacci. With this third approach, 85% of the vaccine's properties were intact after 70 days.

Tests on the Chikungunya virus

Using these results, the researchers applied their methods to a vaccine that is currently in development. They were able to stabilize a vaccine against Chikungunya, a tropical virus, for 10 days, and then successfully inoculated mice with it. "The next step will be to run more extensive tests on specific vaccines, possibly combining the three different approaches."

Cheaper access

This study could really impact the effort to increase immunization coverage. Currently, in areas where electricity and refrigeration are limited, vaccines are moved from one refrigerated space to the next and then delivered to recipients in coolers. This complicated process accounts for nearly 80% of the cost of vaccination programs. And that, up until now, has been a significant impediment.

More information: M. Pelliccia, P. Andreozzi, J. Paulose, M. D'Alicarnasso, V. Cagno, M. Donalisio, A. Civra, R. M. Broeckel, N. Haese, P. Jacob Silva, R P. Carney, V. Marjoma, D. N. Streblow, D. Lembo, F. Stellacci, V. Vitelli & S. Krol. Additives to improve thermal stability of adenoviruses from hours to months: implications for vaccine storage. *Nature Communications*, DOI: 10.1038/ncomms13520

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