Genetically modifying rice to produce HIV-neutralizing proteins

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A team of researchers from Spain, the U.S. and the U.K. has genetically modified a strain of rice to produce HIV-neutralizing proteins. In their paper published in the *Proceedings of the National Academy of Sciences*, the group describes the technique by which they modified the rice and how it might be used to prevent HIV infections.

Medical scientists have made great strides in treating people infected with HIV—death rates from infections have plummeted, especially in the developed parts of the world. Scientists have also put in a lot of time and effort to develop a vaccine against the virus, but thus far, have come up empty. In the meantime, oral medications have been developed that can stave off an infection for a short period of time. But as the researchers with this new effort note, such medications are not generally available in third world countries. To help those at risk, they have been hard at work developing a strain of rice that has the same HIV-neutralizing proteins as the oral medications. Once grown, the rice produces seeds that can be processed on-site to make a topical cream containing the proteins—the cream can then be applied to the skin to allow the proteins to enter the body.

The rice developed by the team produces one type of antibody and two kinds of proteins that bind directly to the HIV virus, preventing them from interacting with human cells. The researchers note that production costs of making the cream are nominal once the rice has been grown—people living in infection areas can grow as much of the rice as they need, then make the paste and apply it themselves. They note that further testing will need to be done to ensure the genetic engineering process does not introduce other unknown chemicals that might be harmful to humans. They also acknowledge that some might be resistant to the idea of using such rice due to the negative press GM crops have been getting in recent years. There will also be regulatory hurdles to overcome in each part of the world where the rice might be grown and used.

More information: Evangelia Vamvaka et al. Unexpected synergistic HIV neutralization by a triple microbicide produced in rice endosperm, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1806022115

Abstract

The transmission of HIV can be prevented by the application of neutralizing monoclonal antibodies and lectins. Traditional recombinant protein manufacturing platforms lack sufficient capacity and are too expensive for developing countries, which suffer the greatest disease burden. Plants offer an inexpensive and scalable alternative manufacturing platform that can produce multiple components in a single plant, which is important because multiple components are required to avoid the rapid emergence of HIV-1 strains resistant to single microbicides. Furthermore, crude extracts can be used directly for prophylaxis to avoid the massive costs of downstream processing and purification. We investigated whether rice could simultaneously

produce three functional HIV-neutralizing proteins (the monoclonal antibody 2G12, and the lectins griffithsin and cyanovirin-N). Preliminary in vitro tests showed that the cocktail of three proteins bound to gp120 and achieved HIV-1 neutralization. Remarkably, when we mixed the components with crude extracts of wild-type rice endosperm, we observed enhanced binding to gp120 in vitro and synergistic neutralization when all three components were present. Extracts of transgenic plants expressing all three proteins also showed enhanced in vitro binding to gp120 and synergistic HIV-1 neutralization. Fractionation of the rice extracts suggested that the enhanced gp120 binding was dependent on rice proteins, primarily the globulin fraction. Therefore, the production of HIV-1 microbicides in rice may not only reduce costs compared to traditional platforms but may also provide functional benefits in terms of microbicidal potency.

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