Self-spreading vaccines: Base policy on evidence

In their Policy Forum "Eroding norms over release of self-spreading viruses" (6 January, p. 31), F. Lentzos *et al*. caution that the risks of introducing viruses to a population to act as vaccines ("self-spreading vaccines") outweigh the benefits and argue for tighter regulation of research in this area. Although we echo the authors' call to modernize regulatory frameworks, their misrepresentations of the risks, benefits, and challenges of developing self-spreading vaccines undermine rational policy and erode public trust in science at a pivotal moment of rising vaccine hesitancy.

To emphasize the dangers of self-spreading vaccines, Lentzos *et al*. reference the unintended escape of rabbit hemorrhagic disease virus (RHDV) and the well-studied reversion of the oral polio vaccine (OPV) to virulence (*1*, *2*). However, neither example portrays relevant risks for developing self-spreading vaccine viruses. RHDV is a natural pathogen of rabbits that was being tested to see if it could selectively kill European rabbits in Australia; it is neither a self-spreading vaccine nor genetically modified. OPV was developed from pathogenic poliovirus through classical attenuation and was not designed to transmit (i.e., spread). Modern self-spreading vaccine development rejects platforms that use attenuated forms of pathogenic viruses; instead, the approach involves inserting a small piece of pathogen genome into intrinsically benign and host-restricted viruses (i.e., vectors) that already circulate in target host populations (*3*). Here, the likely evolutionary outcome is a return to the benign wildtype (*4*).

Lentzos *et al*. also describe a Spanish vaccine created to protect wild rabbits from RHDV and Myxoma virus and suggest that efforts were abandoned due to biosafety concerns. In fact, the vaccine was demonstrated to be safe and effective in field trials in an island population (*5*, *6*). However, poor spread in a mainland rabbit population led to the withdrawal of private funding, and pharmaceutical companies considered the vaccine unprofitable due to its potential to self-spread (*7, 8*). These decisions underscore the scientific challenges that remain to be resolved for self-spreading vaccines to be effective in natural populations and the need for funding of this research through public and non-profit organizations.

Lentzos *et al*. dismiss the benefits of self-spreading vaccines by focusing on the challenges inherent in preventing spillover from animals to humans of zoonoses that have not yet been identified. However, this application is an unlikely first step. Lentzos *et al*. do not mention the potential for managing neglected zoonoses with known animal reservoirs, such as rabies and Lassa fever, or the possibility of combating disease threats to wildlife conservation (*9*–*11*). Self-spreading vaccines could be an inexpensive way to reduce the chronic and predictable burden of such pathogens on human and animal health.

Lentzos *et al*. speculate that self-spreading vaccines can now be made easily and have not been adopted because of widespread concerns. This conclusion is uninformed. Despite substantial technical advances, a vaccine capable of transmitting and immunizing has yet to be developed using a naturally occurring and benign viral vector (*3*). Meeting this challenge requires investment and scientifically informed policy that adopts a balanced view of the risks and benefits.

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