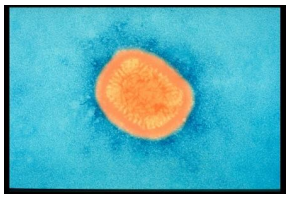
Commentary invited by editors of Scientific American

Fighting Cancer with Poxviruses

By Stephanie Swift | February 15, 2013 |



Just saying, "the pox" out loud sends a microbial shiver down the spine, given the tremendous amount of death and disease the poxviruses have wreaked on mankind. The scourge of perhaps the most notorious member of the poxvirus family, variola virus, which causes smallpox, extended across human history from the ancient Egyptian dynasty to the late 20th century.

This continued until the widespread implementation of an overwhelmingly successful vaccine developed through the efforts of a certain gentleman scientist, Edward Jenner. He famously observed that milkmaids who came into contact with cowpox virus (a close cousin of variola virus) experienced a mild skin infection that protected them against smallpox. After inoculating other people with material scraped from the milkmaids' eruptions, Jenner noted that they, too, became immune to smallpox.

Nowadays, in a pleasant refinement from pustule scrapings, the smallpox vaccine contains a live version of vaccinia virus, a related but much milder poxvirus that looks and behaves enough like variola virus to trick the immune system into developing "smallpox" immunity.

So, poxviruses, like vaccinia virus, can be tamed and moulded from old villains into useful tools to avert or treat human disease. This is particularly true for cancer. Since the mid-1800's, natural virus infections, such as influenza, have been reported to cure cancer patients of their disease. Such testimonials helped to drive the modern development of poxviruses as anti-cancer agents, harnessing their natural preference to search out, infect and kill cancer tissue while shunning normal, healthy areas.

For a poxvirus focused on replicating to produce lots of tiny virus offspring, tumour tissue is a surefire location for success: the mutations that allow cancer cells to grow so quickly also render them defenceless to viral attack. Typically, viral replication in tumour cells pops them open, disgorging their contents and releasing newly-hatched viruses to spread throughout the tumour, before being mopped up, neutralised and contained by the immune system. This approach can have brilliant results for some cancer patients, and poxvirus-based cancer treatments are now into advanced stage clinical trials.

Recently, poxviruses have also been applied to address a long-standing problem affecting cancer patients undergoing tumour removal surgery. Particularly after long and complicated procedures, cancer patients naturally enter a bodywide state of repair, where most energy is diverted into the healing process. Perversely, this temporary disturbance in the natural biological balance actually encourages any missed bits of tumour to spread, causing new patches of disease to spring up. While the reason for this is not entirely understood,

suppression of the normal immune response, in particular a specific population of immune cells known as, 'natural killer' cells, is at least part of the problem.

A team at the University of Ottawa, led by surgical oncologist Dr. Rebecca Auer, reasoned that applying an engineered poxvirus an hour before surgery, which would home to the tumour and deploy immune-stimulating payloads, could restore the balance of the immune system. As they report in the journal, *Cancer Research*, this happily proved to be true: the virus kicked the apathetic natural killer cells into upping their game, reinvigorated the surgically-stunned immune system and, in mice at least, prevented the surgery-induced spread of tumour material. Poxviruses were therefore blended seamlessly into a normal surgical regime with excellent results.

Since poxviruses have been so widely applied to humans in the smallpox vaccine, there is a huge amount of safety data to recommend their use in the clinic, and in the treatment of over 500 cancer patients, there have been no serious complications. Incorporating a naturally-adapted cancer-loving microorganism like poxvirus into the available arsenal of anti-cancer treatments is plainly a splendidly progressive choice.