The Ebola viruses are well-known as dangerous pathogens, capable of causing hemorrhagic fever in humans and animals with varying but generally high rates of mortality in those infected. Although outbreaks of Ebola viruses have been relatively small and well-contained to date, fears of a large-scale outbreak have encouraged research into methods for treatment and prevention. While there has been a great deal of interest in an Ebola vaccine, progress has been slow. Although ongoing tests in primates have shown encouraging results, there is currently no licensed Ebola virus vaccine in humans. Therefore, the recent discovery from a group led by Duncan Wardrop and Lijun Rong (University of Illinois, IL, USA) of a family of small molecules that may “selectively inhibit the Ebola and Marburg glycoprotein (GP)-mediated infection of human cells” could prove to be a great help in the search for an Ebola therapy.

While there has been a great deal of interest in an Ebola vaccine, progress has been slow. Although ongoing tests in primates have shown encouraging results, there is currently no licensed Ebola virus vaccine in humans. Therefore, the recent discovery from a group led by Duncan Wardrop and Lijun Rong (University of Illinois, IL, USA) of a family of small molecules that may “selectively inhibit the Ebola and Marburg glycoprotein (GP)-mediated infection of human cells” could prove to be a great help in the search for an Ebola therapy. Although various potential small-molecule therapies for Ebola have been examined previously, they mostly targeted the virus after cell entry, with limited success. These most recent candidate compounds, however, seem to bind to the protein coat of the virus and inhibit cell entry.

The surface glycoproteins of the Ebola Zaire virus were fused with HIV particles containing a luciferase gene, a process known as pseudotyping, in order to provide a safe and easily-analyzed method to screen a set of 237 small molecules thought to be potential anti-Ebola agents. From this set, two compounds were found to have specific anti-Ebola activity, one of which was also effective against Marburg (a related virus). A total of 56 variants of this lead candidate were then examined in order to determine the functional group requirements for its antiviral properties, a process which uncovered three alternative compounds.

Given the relatively frequent appearance of new Ebola strains, a successful therapy would ideally possess broad effectiveness rather than being strain-specific, which makes the ability of this latest discovery to also inhibit infection by the related Marburg virus particularly encouraging.

In terms of future development, funding for Ebola therapies has demonstrated some unusual contrasts. Although there is limited interest in many areas due to the low number of annual cases worldwide, study of the disease has generated interest from military and defense sources. This latest discovery has broader eventual aims, however, as Wardrop explains that, “From a wider perspective, we’re searching for compounds to use as probes to study biological processes”.


Nipped in the bud: small molecules may inhibit Ebola cell entry

Highlighting the latest news and research in virology

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New CDC guidelines on HIV pre-exposure prophylaxis

Following recent positive trial results, USA CDC recommends tenofovir for HIV pre-exposure prophylaxis in high-risk MSM.

Pre-exposure prophylaxis (PrEP) for HIV is an idea that has been considered for some time. Concerns have been raised regarding cost–effectiveness, target populations and the development of drug-resistant HIV strains, but recent guidance from the USA Center for Disease Control (CDC) has come out in favor of this method for controlling the spread of HIV in high-risk populations, specifically men who have sex with men (MSM). Noting that an effective vaccine is ‘years away’, a recent report noted “mounting evidence that antiretroviral drugs may be able to play an important role in reducing the risk of HIV infection”.

The drugs concerned are tenofovir and emtricitabine in combination, or tenofovir alone, which have been examined in PrEP trials taking place in a variety of locations worldwide. At this stage, no major safety problems have arisen, and the indications are that this therapy is safe and effective in reducing HIV infection.

“...an effective vaccine is ‘years away’.”

At present the recommendations only indicate PrEP for MSM who do not consistently use other methods to control HIV transmission (i.e., condoms), and who experience “frequent partner change or concurrent partners in a geographic setting with high HIV prevalence”, acknowledging the potential for side effects and the high cost of the medication. Given the often low adherence to medication observed in the trial that led to these guidelines being issued, adherence counseling was encouraged, along with a specific warning against “‘intermittent’ dosing just before and/or after sex”.

Although concerns and queries such as those mentioned previously are acknowledged in the CDC report, its timing – very shortly after the first results of a related trial – may indicate an overall policy shift towards PrEP. Citing its use in such situations as the prevention of HIV transmission from mother to newborn during delivery, and in healthcare workers with accidental exposure, CDC information releases seem to signal its support for the eventual use of PrEP in a broader range of high-risk populations than just MSM.

“... (there is) mounting evidence that antiretroviral drugs may be able to play an important role in reducing the risk of HIV infection.”

Correctly handled, it appears that PrEP does have the potential to have a great impact on the current HIV situation worldwide. One of the most important aspects of this form of HIV prevention – oral self-administration of antiretroviral drugs – is that it is fully under the control of the individual concerned, a significant factor in its favor. While condom usage is an effective method of infection prevention when used, it is not female-controlled and it is not always possible for women to insist on this method, which can lead to unwanted exposure risk. PrEP, on the other hand, is a potentially female-controlled infection prevention method, something that could change the course of the HIV epidemic.


Priority Paper Alerts


Generating resistance to HIV has been the subject of intensive research for many years now. This study reports ‘the modification of T cells’ so that infection with HIV-1 and the expression of the viral Tat gene causes the expression of an mRNA interferase protein, MazF, that destroys mRNA transcripts, providing effective HIV-1 resistance in vitro. Although MazF can cause apoptosis when continuously expressed, in this case, the MazF gene was introduced to the T-cells under the control of the HIV-1 long terminal repeat via an adenoviral vector. Resistance was tested by infecting the T-cells with HIV-1 IIIB, which was determined to have been resisted by the lack of p24 protein in the culture medium. This resistance and the survival of the T-cells, indicates that MazF expression is triggered by HIV infection to destroy viral mRNA but not sufficient to cause apoptosis.


An aging HIV-infected population brings with it additional problems in terms of progression to AIDS. This study examines the rapid aging of naive CD4+ T-cells in HIV-infected individuals, and its implications for the faster progression to AIDS in those aged over 50 years. In order to assess CD4+ T-cell ‘age’, T-cells were sampled from groups of ART-naive, HIV-1-seropositive individuals aged 20–32 and 39–58 years, respectively, and their telomere lengths were compared with those of cells taken from age-matched controls. The results showed that HIV-infected individuals showed the same signs of CD4+ T-cell aging as non-infected individuals who were decades older, indicating that this cell population is under considerable stress. Additional analysis showed reconstitution of some CD4+ T-cell populations, but not others. These factors could explain the increased progression to AIDS in older HIV-infected patients, and the increased incidence of diseases associated with older adults in younger HIV patients.
Minor effect, mass appeal? Novel therapeutic vaccine for HIV reported

In the long pursuit of a viable HIV vaccine, there have been numerous minor successes and failures, but a major problem for vaccine candidates has been achieving significant effects in the majority of the population they are tested on. A recent announcement from a group led by Josep Maria Gatell (University of Barcelona, Spain) seems to indicate that this particular challenge has been overcome, albeit with limited applicability at present.

Although prophylactic vaccination (in which prior exposure to an incomplete or attenuated form of an infective agent increases resistance to subsequent exposure) is more familiar to the general public, therapeutic vaccination (in which the immune system of an infected individual is stimulated to control or destroy an infection) is an area of great research interest for many diseases.

This is certainly the case with HIVACAT, the Catalan program for the development of preventive and therapeutic vaccines against HIV, the organization for which Gatell’s group designed this latest vaccine. The end goal is to minimize or even remove the necessity for antiretroviral treatment for those infected with HIV.

...a significant downside is the relatively limited effect of the vaccine on viral load.

As mentioned above, the therapeutic vaccine produced by Gatell’s group appears to be effective for a distinctly greater proportion of the population than previous efforts, although a significant downside is the relatively limited effect of the vaccine on viral load.

While the discovery of a vaccination method that has the potential for a therapeutic effect on such a large proportion of the population, unless this limitation can be overcome the vaccine cannot be considered to be a solution. It does appear to be a candidate for further development, however, with a new clinical trial already underway to test the vaccine in combination with antiretroviral drugs.


Inhalable measles vaccine may improve vaccine delivery in resource-limited areas

While measles is a controllable disease thanks to the availability of highly effective vaccines, in areas where these vaccines are more difficult to obtain or administer, it is still a significant cause of death in children. A recent report from a research group led by Diane Griffin (Johns Hopkins Bloomberg School of Public Health, MD, USA), however, describes a novel measles vaccine that may help to improve this situation.

The report from Griffin’s group describes the successful test of a dry-powder, inhalable measles vaccine in rhesus macaques that provided full protection from measles challenge after a single vaccine dose. The next step will be to seek permission for tests in human volunteers, which is being negotiated in India. Should this be successful, it may lead to the production of this significantly easier-to-use vaccine, and hopefully an overall reduction in child mortality due to measles.

“This novel vaccine can be shipped as powder and does not require reconstitution or special training to administer...”

At present, vaccination against measles requires two separate injections performed several years apart, administered by specially trained staff using reconstituted and subsequently refrigerated vaccine. These requirements can make vaccination a difficult process in resource-limited areas, often meaning that children go without.

Contrasting with this, Griffin explained that “This novel vaccine can be shipped as powder and does not require reconstitution or special training to administer, which could greatly increase the ease and safety of measles vaccination worldwide”.


About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of virology. If you have newsworthy information, please contact:

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