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Submission to the Standing Committee on Health regarding its study on federally funded research (M-132).

Presented by Dr. Keith Fowke, University of Manitoba

Synopsis:
As a university-based researcher funded by the Canadian Institutes for Health Research (CIHR) since 2001, I would like to make the point that federally funded investigator-initiated research has benefits for reducing health care costs, including drug costs. I will provide one small example of this potential. There are thousands of such examples across Canada.

I will try to demonstrate that our research suggests that we may prevent new HIV infections using safe, affordable and globally accessible anti-inflammatory drugs, like acetylsalicylic acid (ASA) also known as aspirin. Yes, that is right, our data suggests that it may be possible to prevent HIV infections using ASA.

Scale of the problem:
Each year 1.8 million people are infected with HIV each year, the majority of whom are in sub-Saharan Africa (http://www.unaids.org/). Globally, the number of new infections has not declined enough over the past 10 years. In the Canadian prairies there is a growing epidemic of new HIV infections among Indigenous communities. HIV prevention methods such a condom use are not possible for everyone, especially where gender-based power differentials exist. Access to HIV medications that can be used to prevent infections in high risk individuals, are not generally available and where available are often not accepted by the community. Therefore, new prevention approaches are needed that would add additional tools to the HIV prevention toolbox.

Reducing HIV target cells:
My CIHR-funded research has focused on understanding the mechanism why some Kenyan women who are intensely exposed to HIV, fail to become infected. We have determined that these women naturally have lower numbers in the genital tract of the type of cells that HIV infects. Our goal has been how to induce this reduction in genital tract HIV target cells in other women who are at risk of acquiring HIV.

At its most basic level HIV infection requires a fit virus and a susceptible cell. Once that cell is infected it quickly spreads the virus throughout the body in a matter of a few days. Most HIV prevention efforts focus on trying to keep the virus away, such as condom use, or crippling the virus using anti-HIV drugs. However, we've taken the approach of trying to prevent the HIV target cell from being present in the genital tract at the time of HIV exposure. Without a susceptible target, the HIV viruses are destroyed and cleared from the body without establishing an infection.

Anti-inflammatory drugs tested:
How do we prevent HIV target cells from being in the genital tract in the first place? The process of immune cells moving from the blood to a tissue is called inflammation. We rationalized that perhaps using an anti-inflammatory drug would help reduce the number of these inflammatory HIV target cells from migrating to the genital tract. When deciding which drugs to test, we chose to test anti-inflammatory drugs that were globally available and affordable with a strong safety tract record. ASA was a leading choice because it is an anti-inflammatory drug, hundreds of thousands of people safely use it daily for the prevention of cardiovascular disease. Most importantly it is already sitting in every small kiosk throughout the developing world and when

asked, Kenya women said it highly desirable as it known in the community and was not stigmatizing like other anti-HIV medications are.

To test our theory that treating with ASA would reduce HIV target cells, we conducted a small CIHR and Grand Challenges Canada-funded pilot study in Nairobi. We gave 38 women low dose ASA daily for 6 weeks and observed a 35% reduction in the number of HIV target cells in their genital tract. While this preliminary data does not prove that ASA will actually reduce HIV infections, we feel that it is logical that if there are fewer targets in the genital tract then should HIV be introduced, the probability of infection will be reduced. (Complete results are published in Lajoie et al Journal International AIDS Society, 2018).
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6060422/pdf/JIA2-21-e25150.pdf

Next Steps:
Our current CIHR-funded study is to assess the optimal dose of ASA and determine how long the effect lasts. This will pave the way for large clinical trials required to assess if an anti-inflammatory drug, like ASA, really does reduce HIV infection rates.

Studies of the use of anti-HIV drugs in HIV prevention, have demonstrated that in the presence of genital inflammation the effectiveness of these drugs drops from 75% to 10% (McKinnon et al Nature Medicine 2018). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5893390/pdf/nihms938866.pdf
Much like a cocktail of drugs are used to fight off cancer, we envision that people will be provided with a range of HIV prevention approaches from which they will choose those that are best for them. Combining an anti-HIV medication with an anti-inflammatory drug may create an additive benefit. Our goal is that using a safe, affordable and globally available drug, like ASA, will be proven to reduce the number HIV infections and will be included as one of the options in the HIV prevention tool box.

Points for the committee to consider
Investigator-initiated federally funded (CIHR and GCC) research has led us to consider a brand new approach to HIV prevention by focusing on the HIV target cell rather than the virus itself.

The choice of drugs tested in this study was a conscious decision based on strong safety records, global availability and low cost. Generic versions of drugs are often more affordable and therefore more accessible globally.

The re-purposing of existing drugs to fight different diseases in new ways has the potential to save long-term on drug spending but requires short-term investment in highly innovative fundamental research.