



University of Cambridge Collaborates with GSK to Fight Against HIV

Human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) devastate millions of lives around the world every year. Despite the availability of medicines, resistance continues to develop. However, recent advances in understanding the HIV lifecycle are revealing weak spots that hold interesting opportunities for new therapeutics.

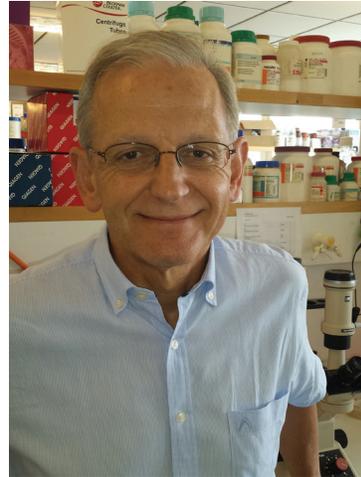
Researchers led by Professor Andrew Lever at the University of Cambridge's Department of Medicine in the UK have been making valuable contributions to our knowledge of the HIV infection process for many years. Professor Lever initially began his research on HIV as a Research Fellow at Dana Farber Cancer Institute in Boston before moving to the University of Cambridge, where he was awarded a Personal Chair in Infectious Diseases in 2000.

Since then, Professor Lever and his research team have been focusing on specific stages of the lifecycle that remain untargeted by the existing repertoire of HIV drugs. They noticed that most drugs exerted their effects upon the early stages of the lifecycle, such as entry inhibitors, reverse transcriptase inhibitors and integrase inhibitors, while later stages remained relatively unexplored. Professor Lever and his group have thus far devoted significant efforts to deciphering the mechanism behind the later stages of the HIV lifecycle.

Early investigations by Professor Lever's team revealed a component of the viral life cycle that was both sensitive to disruption and highly conserved between different strains meaning it was less likely to successfully mutate in response to the selective pressures imposed by new therapeutics targeting the process. Capitalizing on this finding, Professor Lever and his team used an elegant fluorescence-based assay to screen for compounds capable of disrupting this important part of the viral replication process. They then turned to public screening libraries, which held between 2,000 to 3,000 compounds, and identified a small group of compounds that were initially effective at reducing HIV's ability to proliferate and generate additional infectious virus particles.

Looking to larger libraries

As exciting as these findings were, it quickly became apparent that they were going to have to expand their search beyond the limited size of public screening libraries if they hoped to find viable compounds for further study. It was at this point that Professor Lever learned of GSK's Discovery Fast Track Challenge, which would allow his research efforts to be combined with GSK's library of nearly two million chemical compounds, high-throughput screening technology, experience



Prof. Andrew Lever
University of Cambridge

and expertise. According to Professor Lever, "We knew that to do this seriously and properly – and with some speed – this partnership (with GSK) was the logical next stage."

With much of the primary research already complete, Professor Lever and the Discovery Fast Track team worked together to flesh out the scientific strategy using this novel method of targeting HIV. This culminated in his lab being selected as one of 15 winning teams of the 2014 Challenge.

The advantages of collaboration

According to Professor Lever, the collaboration with GSK as part of the Discovery Fast Track Challenge will provide a number of benefits: "While access to such a huge screening library is a powerful asset, we'll also be able to utilize the advanced technologies that GSK can offer. This will allow us to harness the ability to perform studies at a scale that is way beyond the capabilities of an academic department." The partnership will also provide the research team with sound advice on some of the complex regulatory aspects they will need to navigate further down the road, should the collaboration's initial screen prove successful.

"Partnering with GSK has thus far been an interesting, involving and rewarding experience," said Professor Lever. "It's exciting to me that a company such as GSK is approaching HIV treatment in such an imaginative and innovative way, targeting unexplored areas of the virus life cycle in the search for new therapies."

To learn more about GSK's Discovery Fast Track Challenge, please visit gsk.com/discoveryfasttrack