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tRNA retrograde transport in nuclear import of HIV-1

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Lentiviruses and gammaretroviruses are two subdivisions of retroviruses that exhibit cell cycle independence and dependence respectively in their ability to infect cells. Nuclear import of HIV-1, a process that we lack explicit knowledge of, has been speculated to be mediated by several host and viral factors known as nuclear localisation signals. No such signal currently identified however has been determined essential for nuclear import. Recently it has been found that nuclear import of HIV-1 is mediated by retrograde transport of tRNA. We sought to identify whether there is a relationship between the cell cycle dependence of these retroviral subtypes, the tRNA they incorporate, and nuclear import of HIV-1. To investigate this, we studied wild type HIV-1 and MLV and produced two chimeric viruses containing different MLV gag components within a HIV vector. Using these, we identified the infectivity of the viruses, extracted and analysed their tRNA and attempted to assay their effect on nuclear import of reverse transcription complexes. We showed that the viruses encoding MLV CA were less able to infect dividing cells than those encoding HIV CA and were also unable to infect non-dividing cells. We also demonstrated quantitative differences between the tRNAs incorporated by the different viruses, most notably the chimera encoding MLV CA. This suggests that MLV CA may somehow affect interaction with or incorporation of tRNAs that mediate HIV-1 nuclear import. We were unable to assimilate the role of such differences in nuclear import however, we have evidence now to suggest that the capsid protein and its interaction with tRNA in some way could hold the key to nuclear import of HIV-1. This creates great prospects for future investigations into the nature of such a relationship and how it may possibly be manipulated in HIV-1 therapy.

Biography

George Adigbli completed his Bachelor of Sciences degree in Medical Sciences, with Immunology and Cell Pathology, as well as his Bachelor of Medicine and Bachelor of Surgery degrees. He has since completed a Master of Sciences degree at University College London and has been granted a postgraduate scholarship from the University of Oxford to complete a DPhil in Immunology.

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