**UNIVERSITY OF CAPE TOWN COMPUTATIONAL BIOLOGY DIVISION**

**Bioinformatics Support Request**

Please provide us with more information on your request for support. Complete the form as comprehensively as possible, and please indicate where there is still uncertainty.

**Please note, the earlier we are involved the better – for example, it would be better for us to be involved during the study design and even grant application stage**.

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| **CONTACT DETAILS** | |
| Date of request | **2018/07/04** |
| Name | **Walter Nevondo** |
| Email address | **Walter.nevondo@uct.ac.za** |
| Research Group/Department | **Carolyn Williamson/Pathology** |
| Faculty | **Health Science** |
| IF student, name & email of supervisor |  |

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| **PROJECT DETAILS** |
| 1. What is the scientific question? |
| Despite the significant advances in HIV research, HIV infection remains incurable. While therapy can control viral replication to a level below detection in the blood plasma, the virus persists in a latent form of replication‐competent genome in anatomical and cellular reservoirs. The development of HIV-cure strategies is hindered by the fact that there is currently no accurate method to quantify latently infected cells, there is no definite marker to distinguish these cells from uninfected cells, and these cells are extremely low in individuals receiving antiretroviral therapy.  Reports suggest that both activated and resting CD4+ T cells can facilitate the integration of HIV-1 genome in the chromosome. However, the cellular environment that promotes either productive integration (virus production) or latent integration (no virus production) is still elusive. While multiple epigenetic and regulatory factors have been reported to prevent transcription of integrated HIV genome both in vivo and in vitro experimental settings, it is unclear whether these factors control latency individually or combined. Furthermore, factors associated with latency have been studied in cell populations. The general assumption in these experiments is that cell populations are truly homogeneous. The consequent of this assumption is that rare cell populations which may be playing a role in latency maintenance and persistence are masked by the larger cell populations, and the biological mechanisms of latency in this rare cell populations remains unknown. Indeed, given the rarity of latently infected cells in individuals receiving therapy, and that the current latency reversing strategies does not activate all infected cells, it is conceivable that there might be novel cellular factors responsible for latency maintenance and persistence.  This study aims at analysing HIV-1 latency mechanisms at single-cell level through transcriptomic profiling of in vitro and ex vivo latency models of dual reporter virus. Differentially expressed genes between productively and non-productively HIV-1 infected CD4+T cells (Resting and activated) will be analysed to identify molecular pathways leading to HIV-1 latency. Moreover, differentially expressed surface proteins will be analysed to identify possible latency markers. The finding of this study could guide the development of eradication strategies.  The following are some of the specific questions of the study:   1. What is the permissive cellular environment that facilitates HIV-1 productive and latent infection? 2. What are the cellular regulatory mechanisms of HIV-1 latency maintenance and persistence?  * Is latency maintained through global or cell-specific mechanisms? * Are there other novel mechanisms responsible for HIV-latency maintenance?  1. Does HIV-1 infected resting CD4+ T cells show specific transcriptional signature and is there any surface marker unique to these cells? |
| 2. Who are the partners on the project? |
| The NRF and Caprisa |
| 3. What type of collaboration with CBIO is expected? For a project that is done as collaboration or for a fee, we will put the agreement in writing. |
| Co-authored publication from data generated in this work |
| 4. Are there any ethical issues we should be aware of? |
| No |
| 5. How much work is expected from CBIO and when? |
| Facilitate the computational work of the project, assist with data analysis and storage, and provide bioinformatic tools needed for the project. The sequence data will be available in at least three months for analysis. |
| 6. What type of data will be generated (e.g. sequencing, genotyping, expression, etc.) and what technology platform will be used? |
| Illumine Miseq sequencing data. |
| 7. When do you expect the data? Does it need to be transferred from somewhere else? |
| To be discussed |
| 8. How large will the data be? How long does it need to stored for, and have you made arrangements for storage? |
| No storage arrangements made yet. This is still to be finalised |
| 9. What bioinformatics analysis needs to be done? Which tools are required? |
| QC: FASTQ and cellRanger  De novo assembly: cellRanger, Bowtie2 and MAST  Data normalization: Scran  Deferentially expressed genes analysis, clustering, and gene network: cellRanger and Monocle.  Please note that these tools are suggestions |
| 10. If a collaborative model is being used, what papers are envisaged and who will the authors be? |
| We are hoping to publish at least two paper, one on latency markers and another on the latency mechanisms. |
| 11. Can we add a short description and objective of the project to the CBIO website? |
| To be discussed |

**PLEASE FORWARD THE COMPLETED FORM TO:**

[Nicola.mulder@uct.ac.za](mailto:Nicola.mulder@uct.ac.za)