The Forgotten Cancer: A Three-Pronged Approach: (1)MRI Analysis of Disease Localization, (2)Optimization of ZFN Therapy,(3)In vitro Implementation of ZFR Treatment

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Human T-Cell Lymphotropic Virus Type 1 (HTLV-I) is the first-discovered retroviral disease and has been considered globally epidemic yet has no cure or treatment. This project aims to produce a cure by (1) inhibiting trans-activation by Tax (p40), (2) optimizing gene knockout to accomplish the aforementioned using catalytic domain mutants of zinc finger nucleases (ZFNs), and (3) examining frequent HTLV-1 infection regions in the spine to be targeted by treatments. Inhibition was accomplished using zinc finger repressors (ZFR) because in vitro analysis via gel electrophoresis of digestion products proved that the ZFNs were inefficacious compared to the positive control (EcoRI). The ZFRs were incubated with Tax and CREB in a pulldown assay using vCREs, with just the TFs as a negative control. SDS-PAGE analysis revealed that the ZFR repressed as much as 80% of the TF binding to the immobilized vCRE. Lastly, magnetic resonance images (MRIs) were analyzed for spinal degeneration as well as high signal lesions, revealing that both of the former localize in the cervical and upper thoracic spinal cord. Accordingly, the potential treatment or even cure of HTLV-1—as supported by this project—would constitute ZFR delivery to target sites in the central spinal cord and immune system.