# Virtual High Throughput Screening (VHTS) of small mechanoactive molecules for controlling the mechanical stability of HIV-1 receptor

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Viral infections are one of the major causes of death worldwide. The HIV-1 virus, responsible of AIDS disease, has become an epidemic which continues to spread at an alarming rate of approximately 2 million new cases per year. Traditional cell and molecular biology have tried to fight this pathology but have proven insufficient. Molecular mechanomedicine is an emerging field in nanobiology focused on the study of the effect of newtonian mechanical forces in the structure and properties of proteins related with human health, key to which are membrane proteins such as CD4. It is believed that these proteins are subjected to mechanical forces that modify not only their tertiary structure but also their secondary structure (mechanical changes), which enable them to regulate different cell functions. In this sense, HIV-1 makes use of CD4 membrane protein as a mechanical anchor in order to infect T-lymphocites. There is experimental evidence that viral infections have a mechanical component indispensable for them to be carried out. In other words, for the infection to take place, membrane proteins need to undergo mechanical changes. The latter, can be measured by means “single molecule techniques”, such as atomic force spectroscopy (AFS). It has been proven that Ibalizumab, a humanized anti-CD4 monoclonal antibody which inhibits HIV-1 infection, binds to CD4 making it mechanically more stable. We therefore believe that a relationship between the mechanical stability of CD4 and HIV-1 infection may exist. In particular, an increase in the mechanical stability of CD4 may inhibit HIV-1 infection. With this goal in mind, we made use of VHTS to identify commercially available small molecules with the ability to control the mechanical properties of CD4. AFS experiments confirmed that our molecule candidates identified by VHTS bind efficiently to D1D2CD4 and are able to mechanically stabilize the mechanical properties of CD4, as much as or even to a higher extent Ibalizumab does.