



UNIVERSITY OF GOTHENBURG  
THE SAHLGRENSKA ACADEMY

**Abstract** - Master Thesis Project, the Pharmacy Programme

## **Identification of cell targets of new anti-viral compounds**

**Kim Stockfelt, 2009**

The enveloped Ebola virus causes lethal haemorrhagic fever for which there is no effective therapy. Previous studies indicate that cleavage of the Ebola virus glycoprotein by the acid-dependent cell protease cathepsin B is necessary, but not sufficient for infection. More recently, this lab identified small molecule inhibitors that target the post-cathepsin step. A key goal is to identify the cell target of these inhibitors and characterize their role in infection. To this end, the candidate multi-subunit vacuolar H<sup>+</sup>-ATPase that mediates acidification of endosomes was tested. The approach was to measure Ebola glycoprotein-dependent infection in cells where one of the subunits of H<sup>+</sup>-ATPase was overexpressed or knocked down. In particular, it was found that overexpression of a1 and a2 subunits enhanced infection by Ebola Zaire and Ebola Sudan viruses that were blocked by the small molecule inhibitors. Additional studies are underway to determine if a1 and a2 are direct targets of these compounds. This work establishes a protocol to evaluate the function of small molecules that block Ebola virus entry as a first step towards the development of anti-viral drugs.