

Mechanism of action of maturation inhibitors of HIV-1

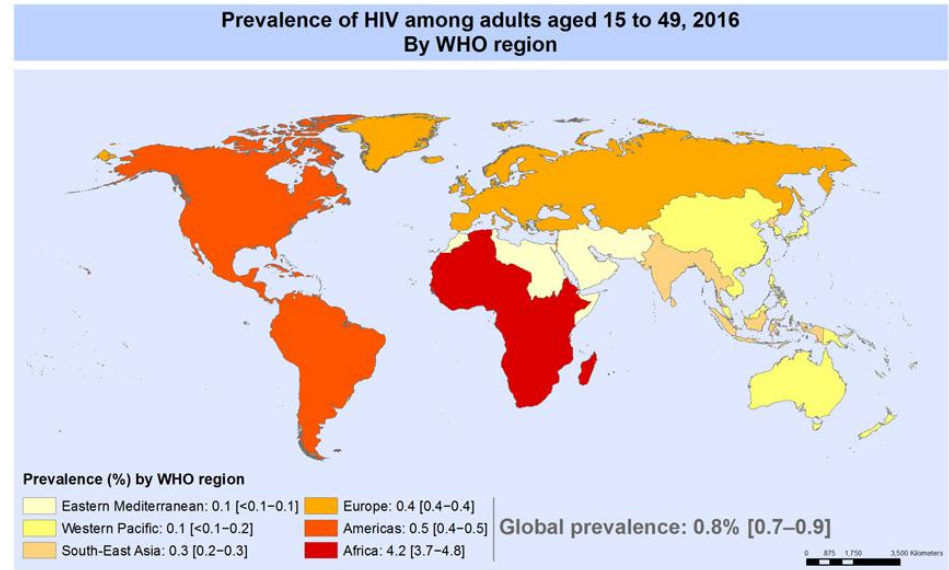
Inventors: Mark Yeager, Michael Purdy, Jakub Chrustowicz,
Tamir Gonen, Dan Shi, Johann Hattne



LICENSING & VENTURES GROUP

HIV-1

- An estimated 36 million people in the world have HIV
- It is estimated that there are 2.1 million new cases per year and that the total HIV drug market is over \$20 billion annually.
- Clinical Problem:
 - Currently, only about half of the HIV-infected patients receive anti-retroviral therapy to manage their disease



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization



© WHO 2017. All rights reserved.

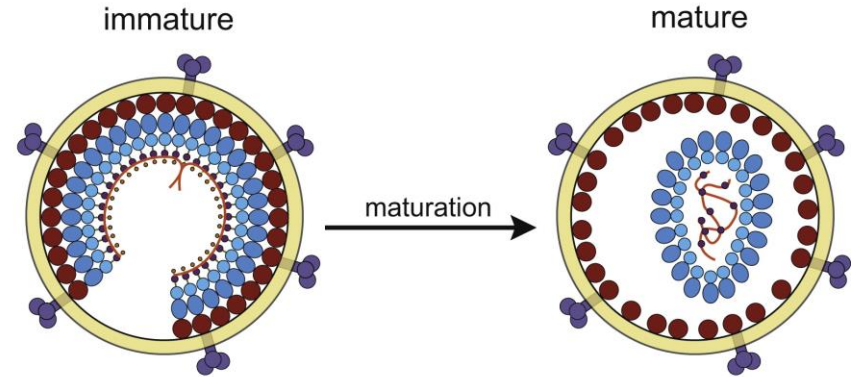
World Health Organization, 2016

HIV-1 maturation inhibitors

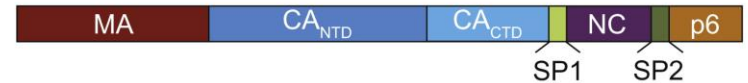
Solution: Researchers at the University of Virginia have determined the CTD-SP1 cleavage site of the Gag polyprotein of HIV-1 is a promising drug target site.

- Could aid in development of promising new class of maturation inhibitors
- Provides insight into the mechanisms of action utilized by bevirimat and other HIV-1 maturation inhibitors
- Demonstrates the capabilities of microED for structure-based drug design

HIV-1 Virion:



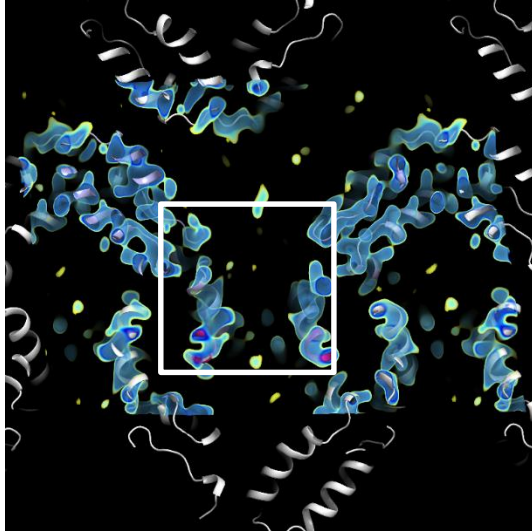
HIV-1 gag:



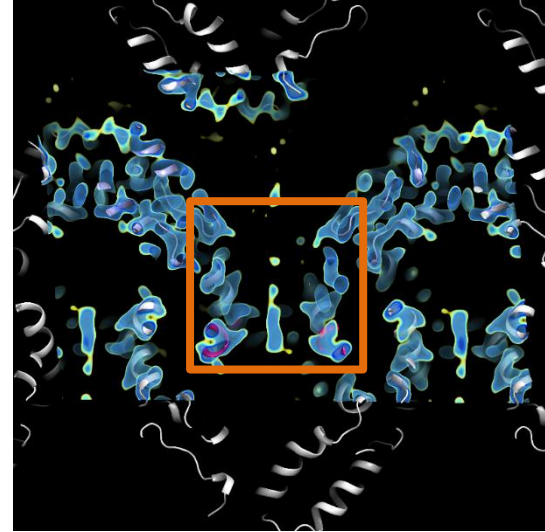
Structure 2010 10, 1483-1491.

CTD-SP1 cleavage site

Drug-free CTD-SP1



CTD-SP1-BVM



microED structure design reveals bevirimat can bind to target cleavage site CTD-SP1.

Relevant Publications

- eLife. 2016; 5: e17063. **Pornillos O**, et. al.
- Proc Natl Acad Sci USA. 2017 Nov 21;114(47):E10056-E10065. **Voth GA**, et. al.
- bioRxiv. 2017 Dec. <https://doi.org/10.1101/241182>. **Yeager M**, et. al.