ABSTRACT

FRAGMENTS OF THE PA SUBUNIT OF RNA DEPENDENT RNA POLYMERASE FROM PANDEMIC INFLUENZA VIRUS A 2009 H1N1, AND THEIR USE

The present invention relates to polypeptide fragments comprising an amino-terminal fragment of the PA subunit of a viral RNA-dependent RNA polymerase possessing endonuclease activity, wherein said PA subunit is from Influenza A 2009 pandemic HlNl virus or is a variant thereof. This invention also relates to (i) crystals of the polypeptide fragments which are suitable for structure determination of said polypeptide fragments using X-ray crystallography and (ii) computational methods using the structural coordinates of said polypeptide to screen for and design compounds that modulate, preferably inhibit the endonucleolytically active site within the polypeptide fragment. In addition, this invention relates to methods identifying compounds that bind to the PA polypeptide fragments possessing endonuclease activity and preferably inhibit said endonucleolytic activity, preferably in a high throughput setting. This invention also relates to compounds which are able to modulate, preferably to inhibit, the endonuclease activity of the PA subunit polypeptide fragment or variant thereof of the present invention and pharmaceutical compositions comprising said compounds for the treatment of disease conditions caused by viral infections with viruses of the Orthomyxoviridae family, Bunyaviridae family and/or Arenviridae family, preferably caused by viral infections with Influenza A 2009 pandemic HlNl virus. Preferably, said compounds are identifiable by the methods disclosed herein or said pharmaceutical compositions are producible by the methods disclosed herein.

Figure for publication: None