

## Accepted Manuscript

Title: Thymidine kinase and Protein kinase in drug-resistant herpesviruses: heads of a Lernean Hydra

Authors: Dimitri Topalis, Sarah Gillemot, Robert Snoeck, Graciela Andrei



PII: S1368-7646(18)30003-7  
DOI: <https://doi.org/10.1016/j.drug.2018.01.003>  
Reference: YDRUP 616

To appear in: *Drug Resistance Updates*

Please cite this article as: Topalis, Dimitri, Gillemot, Sarah, Snoeck, Robert, Andrei, Graciela, Thymidine kinase and Protein kinase in drug-resistant herpesviruses: heads of a Lernean Hydra. *Drug Resistance Updates* <https://doi.org/10.1016/j.drug.2018.01.003>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

## Thymidine kinase and Protein kinase in drug-resistant herpesviruses: heads of a Lernean Hydra

Dimitri Topalis\*<sup>1</sup>, Sarah Gillemot<sup>1</sup>, Robert Snoeck<sup>1</sup>, and Graciela Andrei<sup>1</sup>

<sup>1</sup> Rega Institute for Medical Research, KU Leuven, Herestraat 49 – box 1043, 3000 Leuven, Belgium

Dimitri Topalis: dimitrios.topalis@kuleuven.be

Sarah Gillemot: sarah.gillemot@kuleuven.be

Robert Snoeck: robert.snoeck@kuleuven.be

Graciela Andrei: graciela.andrei@kuleuven.be

\*Corresponding authors:

Dr. Dimitrios Topalis

<sup>1</sup>Rega Institute for Medical Research, KU Leuven, Herestraat 49 - box 1043, 3000 Leuven, Belgium

Telephone: +32 16 32 15 38

Email: dimitrios.topalis@kuleuven.be

### Abstract

Herpesviruses thymidine kinase (TK) and protein kinase (PK) allow the activation of nucleoside analogues used in anti-herpesvirus treatments. Mutations emerging in these two genes often lead to emergence of drug-resistant strains responsible for life-threatening diseases in immunocompromised populations. In this review, we analyze the binding of different nucleoside analogues to the TK active site of the three  $\alpha$ -herpesviruses [Herpes Simplex Virus 1 and 2 (HSV-1 and HSV-2) and Varicella Zoster Virus (VZV)] and present the impact of known mutations on the structure of the viral TKs. Furthermore, models of  $\beta$ -herpesviruses [Human cytomegalovirus (HCMV) and human herpesvirus-6 (HHV-6)] PKs allow to link amino acid changes with resistance to ganciclovir and/or maribavir, an investigational chemotherapeutic used in patients with multidrug-resistant HCMV. Finally, we set the basis for the understanding of drug-resistance in  $\gamma$ -herpesviruses [Epstein-Barr virus (EBV) and Kaposi's sarcoma associated herpesvirus (KSHV)] TK and PK through the use of animal surrogate models.

Download English Version:

<https://daneshyari.com/en/article/8436458>

Download Persian Version:

<https://daneshyari.com/article/8436458>

[Daneshyari.com](https://daneshyari.com)