



Phenotypic characterisation of cytomegalovirus DNA polymerase: a method to study cytomegalovirus isolates resistant to foscarnet

Submitted by Alexandra Ducancelle on Thu, 02/07/2019 - 15:49

Titre	Phenotypic characterisation of cytomegalovirus DNA polymerase: a method to study cytomegalovirus isolates resistant to foscarnet
Type de publication	Article de revue
Auteur	Ducancelle, Alexandra [1], Gravisse, Jérôme [2], Alain, Sophie [3], Fillet, Anne-Marie [4], Petit, Françoise [5], Sanson Le Pors, Marie-José [6], Mazon, Marie-Christine [7]
Editeur	Elsevier
Type	Article scientifique dans une revue à comité de lecture
Année	2005
Langue	Anglais
Date	Mai 2005
Numéro	2
Pagination	145-51
Volume	125
Titre de la revue	Journal of virological methods
ISSN	0166-0934
Mots-clés	Cytomegalovirus [8], Cytomegalovirus Infections [9], DNA-Directed DNA Polymerase [10], Drug Resistance, Viral [11], Foscarnet [12], Genetic Variation [13]
Résumé en anglais	<p>A phenotypic method was developed to test mutations in the human cytomegalovirus (HCMV) DNA polymerase gene (UL54) suspected to confer resistance to foscarnet. This method was used to determine the biochemical phenotype of wild-type and mutated HCMV DNA polymerases that had been synthesised in vitro as follows. The UL54 genes were amplified from foscarnet-resistant and -sensitive isolates by PCR and the products were cloned into an expression vector under the control of a T7 promoter. Mutations were introduced by site-directed mutagenesis into wild-type gene UL54 and then polymerases were synthesised by using a commercially available coupled transcription/translation system. Polymerase activity was measured with and without foscarnet by detecting the incorporation of digoxigenin-labelled nucleotides into the growing DNA chain. The results of this non-radioactive assay were consistent with those obtained with the conventional radioactive assay. It was found that the activity of polymerases containing the V715M or E756K mutations was inhibited by foscarnet at concentrations 70- and 30-fold higher than that of wild-type polymerase, respectively. Change N495K and a combination of changes K415R and S291P, both observed in foscarnet-resistant isolates, induced a 5- and 10-fold decrease in susceptibility to foscarnet, respectively. This non-radioactive phenotypic assay could be useful for the characterisation of mutations that confer HCMV resistance to foscarnet.</p>
URL de la notice	http://okina.univ-angers.fr/publications/ua18815 [14]
DOI	10.1016/j.jviromet.2005.01.005 [15]

Lien vers le document <https://www.sciencedirect.com/science/article/pii/S0166093405000236?via%...> [16]
Titre abrégé J. Virol. Methods
Identifiant (ID) 15794984 [17]
PubMed

Liens

- [1] <http://okina.univ-angers.fr/a.ducancelle/publications>
- [2] <http://okina.univ-angers.fr/publications?f%5Bauthor%5D=33751>
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- [17] <http://www.ncbi.nlm.nih.gov/pubmed/15794984?dopt=Abstract>

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