

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

2'5'-Phosphodiesterase Activity Studies with Xyloadenosine Analogs of 2-5A Cores

P. P. Torrence^a; D. Alster^a; S. Huss^b; G. Gosaelin^b; J. -L. Imbach^b

^a National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA ^b Laboratoire de Chimie BioOrganique, University des Sciences et Techniques du Languedoc, Montpellier Cedex, France

To cite this Article Torrence, P. P. , Alster, D. , Huss, S. , Gosaelin, G. and Imbach, J. -L.(1987) '2'5'-Phosphodiesterase Activity Studies with Xyloadenosine Analogs of 2-5A Cores', *Nucleosides, Nucleotides and Nucleic Acids*, 6: 1, 521 — 522

To link to this Article: DOI: 10.1080/07328318708056274

URL: <http://dx.doi.org/10.1080/07328318708056274>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

2'5'-PHOSPHODIESTERASE ACTIVITY :
STUDIES WITH XYLOADENOSINE ANALOGS OF 2-5A CORES

P.F. Torrence^{1*}, D. Alster¹, S. Huss², G. Gosselin²
and J.-L. Imbach²

¹National Institute of Arthritis, Diabetes and Digestive
and Kidney Diseases, National Institutes of Health,
Bethesda, MD 20205, USA.

²Laboratoire de Chimie BioOrganique, UA CNRS 488, Univer-
sité des Sciences et Techniques du Languedoc, Place
E-Bataillon, 34060 Montpellier Cédex, France.

Abstract. Sequential substitution of xyloadenosine into the trimeric
and tetrameric 2-5A cores¹ allows evaluation of the importance of the
3' hydroxyl groups to 2',5'-phosphodiesterase (PDE) activity.

INTRODUCTION :

A study with 3'-deoxyadenosine analogs of 2-5A and 2',5'-phosphodies-
terase (PDE) activity revealed that replacement of the 3'-hydroxyl
moiety of the penultimate nucleotide of p5'A2'p5'A resulted in a high
degree of resistance to 2',5'-PDE action.² To attempt to confirm and
extend these observations, the ability of various xyloadenosine
analogs of 2-5A cores to act as 2',5'-PDE substrates was examined.

METHODS :

Degradation studies were carried out in extracts of mouse L cells
under conditions of protein synthesis. Aliquots were removed at 30, 60,
90 and 120 minutes, heat-treated, and analyzed by HPLC using
2-chloroadenosine as an internal standard. Xyloadenosine analogs of
2-5A were prepared as described previously.¹

RESULTS :

The oligonucleotides fell into two distinct groups in regard to their
behaviour in the presence of the 2',5'-PDE.

The first group contained xyloadenosine at the 2'-termini and included

A2'p5'A2'p5'(xyloA) and A2'p5'A2'p5'A2'p5'(xyloA). These oligomers behaved as did their parent oligoadenylates in that they were equally sensitive to degradation by the 2',5'-PDE.

The second group of oligonucleotides bore a xyloadenosine residue in the penultimate nucleotide residue of the oligomer and included A2'p5'(xyloA)2'p5'(xyloA), (xyloA)2'p5'(xyloA)2'p5'(xyloA), A2'p5'A2'p5'(xyloA)2'p5'(xyloA) and (xyloA)2'p5'(xyloA)2'p5'(xyloA)2'p5'(xyloA). This group was quite resistant to 2',5'-PDE activity.

CONCLUSIONS :

- i) A ribo configuration for the 3'-hydroxyl group in the penultimate nucleotide of the 2',5'-oligonucleotide substrate is a prerequisite for the 2',5'-PDE activity.
- ii) Inversion of configuration at C-3' of the 2'-terminal residue of 2-5A core trimer or tetramer does not lead to 2',5'-PDE resistance.
- iii) These results are in accord with the previous finding that 2',5'-PDE activity depended upon the presence of a 3'-hydroxyl in the penultimate position of the oligonucleotide substrate.²

REFERENCES

1. S. Huss, G. Gosselin, A. Pompon and J.-L. Imbach, Nucleosides, Nucleotides, 5, 275 (1986).
2. D. Alster, D. Brozda, Y. Kitade, A. Wong, R. Charubala, W. Pfleiderer and P. F. Torrence, manuscript submitted for publication.