



Fig. 3 Stability of (2'-5')pppA(pA)_n and (2'-5')ppp3'dA(p3'dA)_n in HeLa cell extracts. ³H-(2'-5')pppA(pA)_n and ³²P-(2'-5')ppp3'dA(p3'dA)_n were synthesized as described in Table 1 legend. The oligonucleotides were obtained from the 0.35 M KCl eluate (DEAE-cellulose chromatography), desalted (Sephadex G-10) and concentrated *in vacuo*. The methods used to determine degradation of oligonucleotides were a modification of that of Minks *et al.*¹³. Incubation mixtures (0.125 ml) contained 0.6 parts of HeLa cell extract prepared as described previously²⁵, 2.5 mM Mg(OAc)₂, either ³²P-(2'-5')ppp3'dA(p3'dA)_n (12 μM) or ³H-(2'-5')pppA(pA)_n (5 μM), 120 mM KCl, 20 mM HEPES pH 7.4, and 1 mM dithiothreitol. Incubations were performed at 30°C. At the times indicated, 25-μl samples were withdrawn, heated for 3 min at 95°C, and the amount of undegraded oligonucleotide was determined by DEAE-cellulose chromatography as described previously¹³. Degradation of oligonucleotides was monitored as a decrease of radioactive material eluting with 0.35 M KCl compared with the zero time point (100% undegraded).

is important but not essential for the synthesis of (2'-5')pppA(pA)_n, (3) (2'-5')ppp3'dA(p3'dA)₂ is a more potent inhibitor of translation than (2'-5')pppA(pA)₂, (4) (2'-5')ppp3'dA(p3'dA)₂ and (2'-5')pppA(pA)₃ are approximately equal in their abilities to inhibit translation, and (5) enzymatically synthesized analogue (2'-5')ppp3'dA(p3'dA)_n and chemically synthesized core analogue (2'-5')3'dA-(p3'dA)₂ are not hydrolysed by the 2', 5'-phosphodiesterase in HeLa cell extracts. 3'dATP is also converted to (2'-5')ppp3'dA-(p3'dA)_n by extracts of human fibroblast interferon-treated L cells (manuscript in preparation). Enzymatically and chemically synthesized core (2'-5')3'dA(p3'dA)₂ inhibits transformation of Epstein-Barr virus (EBV)-infected lymphocytes in studies with human umbilical cord lymphocytes infected with EBV (manuscript in preparation).

The replacement of ATP with 3'dATP as a substrate for (2'-5')(A)_n synthetase has been reported from three other laboratories. Lengyel and co-workers showed that (2'-5')(A)_n synthetase from interferon-treated EAT cells can link adenylate moieties to the 2'-hydroxyl of 3'dATP¹⁵. Justesen *et al.* reported that 3'dATP is a chain terminator with respect to the addition of one 3'-deoxyadenylate moiety to either dimer or trimer (2'-5')pppA(pA)_n following 3-h incubations with rabbit reticulocyte (2'-5')(A)_n synthetase¹⁶. Minks *et al.* reported that

3'dATP inhibits the HeLa cell (2'-5')(A)_n synthetase in the presence of ATP with respect to formation of (2'-5')pppA(pA)_n (ref. 17). Baglioni and co-workers¹⁸ have also reported that the ATP analogue, 1-N⁶-ethenoATP, is converted to (2'-5')oligonucleotides which activate HeLa cell endonuclease and degrade vesicular stomatitis virus RNA. As (2'-5')oligonucleotides have been shown to inhibit mitogen-stimulated DNA synthesis in lymphocytes, as does interferon¹⁹, it is tempting to speculate that analogues of (2'-5')pppA(pA)_n may potentiate, extend or regulate these activities and could possibly be used as chemotherapeutic agents which might replace interferon.

The structure of the compound eluting at 29 ml on the DEAE cellulose column (Fig. 1a) is now under investigation.

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Erratum

In the letter 'Scale of body pattern adjusts to available cell number in amphibian embryos' by Jonathan Cooke, *Nature* **290**, 775-778 (1981), brackets in Table 1 were meant to refer to duplications of control or experimental embryos within each matched set. As these brackets are partially misaligned, they should be ignored and the data read by the use of a horizontal rule to lead the eye across the page in the absence of gaps between the data of each set.

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