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Control of Virus Replication by Cyclopentenone Prostaglandins: a Multistage Process, Associated with Induction of Heat Shock Protein Synthesis.
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Prostaglandins containing an α,β-unsaturated carbonyl group in the cyclopentane ring structure (cyclopentenone PGs) possess potent antiviral activity against a wide variety of DNA and RNA viruses in different types of mammalian cells. The antiviral activity of a long acting synthetic analog of PGA has also been shown in a mouse model in vivo. Block of virus replication can be obtained at concentrations of PGs non-toxic for the host cell and that do not inhibit the synthesis of nucleic acids and proteins in uninfected cells. While the antiviral activity appears to be related to the cyclopentenone ring structure, different effects have been shown in various experimental models. In the present report we describe the mechanism of action of two antiviral PGs, PGA_1 and Δ^{12}-PGJ_2 in mammalian cells infected with vesicular stomatitis virus (VSV). Analysis of viral proteins at different times after infection has shown a selective block of virus protein synthesis, when PG-treatment was started at an early stage of the virus replication cycle. This effect was associated with the induction of heat shock protein synthesis by antiviral prostaglandins. Studies with a temperature-sensitive mutant of VSV, ts045, which allows the control of a synchronous wave of synthesis and transport of the virus glycoprotein G to the cell surface, demonstrated that PG-treatment, started after accumulation of G protein in the RER, blocks the intracellular transport of the G protein to the cell membrane. The results show that cyclopentenone prostaglandins act at multiple levels, affecting specific events during different phases of the virus replication cycle. Interestingly the ability of the infected cell to respond to both types of PG-induced effects appears to be dependent on an efficient cellular heat shock response.

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The Remantadin Inhibition Activity at the Earliest Stages of Virus-Membrane Interaction.
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It is well known that the plasmatic membranes of the sensitive cells play a significant role on the earliest steps of the viral deproteinization and the cell penetration by viral particles. We have just shown that the proteolytic activity enchances during the interaction of purified and concentrated influenza virus with cell membranes of chicken embryons. One can suppose that the proteolytic activity of plasmatic membranes can be reduced by some proteolysis inhibitors, for example, by the anti viral preparation as remantadin is. We have studied the influence of remantadin on the proteolysis process intensity during the virus-membrane interaction, it came out that the remantadin reduces proteolytic activity of influenza virus A/Hongkong/1/68 of cell membranes of chicken embryons and virus-membrane complexes in "vitro". Thus we see that antiviral activity of remantadin is connected with the proteolytic system inhibition on the early stages of virus-cell interaction.