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WANWARANG HIRIOTE : THE EFFECT OF DIFFERENT FORMS OF NITRIC OXIDE RADICAL ON RABIES VIRUS REPLICATION. THESIS ADVISORS : SUKATHIDA UBOL, Ph.D., MOLVIBHA VONGSAKUL, Ph.D., MATHUROSE PONGLIKITMONGKOL, Ph.D. 106 p. ISBN 974-664-722-9.

Rabies or hydrophobia is the disease of the central nervous system, which causes cerebral damage and impairment of neuronal function. The pathophysiology of this disease is partially known. Death of neurons by apoptosis during rabies virus infection has been recently found. This death mechanism involves activation of caspases and up-regulation of inducible NOS (iNOS) gene expression. NO is produced in reduced form ($NO^{\bullet}$) and oxidized form (NO^{+}). In order to understand the role of $NO^{\bullet}$ and NO^{+} on rabies pathogenesis, we studied the effect of both $NO^{\bullet}$ and NO^{+} on rabies virus replication in vitro.

In this study, rabies virus infected mouse neuroblastoma cell cultures were treated with $NO^{\bullet}$ and NO^{+} generated from SNP, sodium nitroprusside, in the presence of ascorbate and SNP alone, respectively. The results showed that $NO^{\bullet}$ delayed the replication of rabies virus and production of infectious particles by 4 hours detected by FA staining and plaque assay. The level of infectious particle production was also suppressed by $NO^{\bullet}$. In contrast, NO^{+} did not show any effect on rabies virus replication. The mechanism of delay replication was investigated by monitoring rabies virus gene expression using RT-PCR and time course of viral protein synthesis by specific monoclonal antibody. It was found that $NO^{\bullet}$ suppressed and delayed expression of NS gene by 3 hours ,while expression of N, M, G, and L genes were only suppressed but not delayed. Delayed expression of NS gene subsequently led to late synthesis of NS protein.

In conclusion, we have demonstrated that NO^{+} has no effect on rabies virus replication, whereas in vitro $NO^{\bullet}$ functions as anti-rabies virus agent. This free radical molecule exerts its activity through suppression of viral gene expression but have not effect on viral protein synthesis.