S1-3

DEVELOPMENT OF LIVE VECTOR-BASED MUCOSAL VACCINE AGAINST AIDS.

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Oral polio vaccine strain Sabin 1 was manipulated to have multiple cloning site and viral specific 3C-protease cutting site at the N-terminal end of the polyprotein, named RPS-vax system. Several HIV-1 subgenomes, and their epitope-concatamers were successfully cloned into the multiple cloning site of the vector system and produced expected chimeric viruses when transfected into HeLa cells. These chimeric viruses have shown to express introduced vaccine genes efficiently during their replication in the infected cells. Expressed proteins were confirmed to retain the wild type structures at least in parts. Replication capacity of the chimeric viruses was slightly lower than that of wild type Sabin 1 likely to be due to the delay in the processing steps during their replication. Differing from the virulent Mahoney vectors, the rec-Sabin 1 chimeric viruses maintained the foreign gene stably during the serial passages. These chimeric viruses have also shown to be able to induce specific humoral immunity to the introduced vaccine proteins when inoculated into the poliovirus receptor--expressing transgenic mice through brain or intravenous routes. These results strongly suggest that the chimeric viruses expressing HIV-1 vaccine epitopes can be used as a good live mucosal vaccine candidate against AIDS.

S1-4

NOVEL REGULATION MECHANISM OF CARCINOGENESIS AND ANTI-CARCINOGENESIS IN HPV-MEDIATED CERVICAL CANCER

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HPV is strongly implicated as a causative agent in the etiology of cervical cancer. HPV-16 and HPV-18 encode two viral oncoproteins, E6 and E7, which cooperatively exert cellular immortalization and transformation by interfering with the functions of two cellular tumor suppressor proteins, p53 and Rb, respectively. Independent of p53 and pRb, other features of E6 and E7 were found. E6 binds to p73, a homologue of p53, and inactivates its transcription activity. E7 interacts with IRF-1, a putative tumor suppressor, and interferes with its transactivation function. These novel activities of HPV oncoproteins can be implicated in the HPV-mediated cervical carcinogenesis. To study anti-carcinogenesis mechanism, several cervical cancer cell lines were treated with retinoids and/or inteferons, and their effects on cell growth were evaluated. The proliferating activity was mostly reduced in HeLa cells either by RA or IFN treatment when comparing with in other cell lines tested. The molecular analysis suggests that IRF-1 be a mediator in "RA/IFN-γ $\rightarrow$IRF-1$\rightarrow$p21^{WAF1}$\rightarrow$dephosphorylation of pRb$\rightarrow$G1 arrest" pathway. In addition, the down-regulation of HPV-E6 gene expression by RA/IFN may account for the resulted increase of p53 level, which in turn leads to synergistic induction of p21^{WAF1} by cooperation with induced IRF-1.