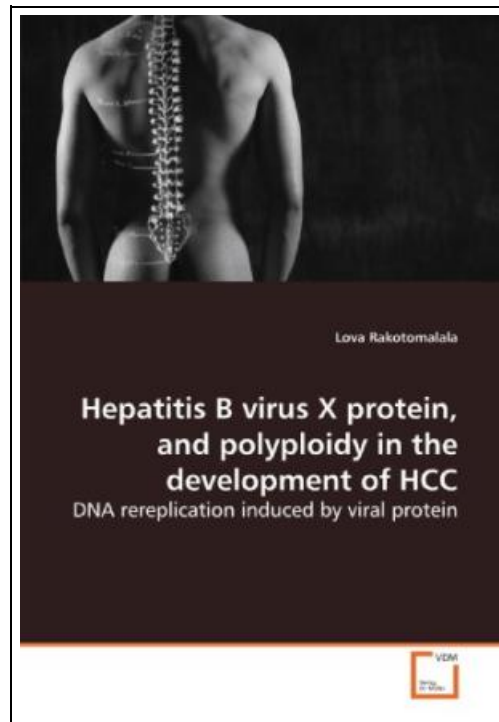


Hepatitis B virus X protein, and polyploidy in the development of HCC



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HEPATITIS B VIRUS X PROTEIN, AND POLYPOIDY IN THE DEVELOPMENT OF HCC



Condition: New. Publisher/Verlag: VDM Verlag Dr. Müller | DNA rereplication induced by viral protein | Hepatitis B Virus (HBV) X protein (pX) is implicated by an unknown mechanism in hepatocellular carcinoma (HCC) development, characterized by increased rate of chromosomal aberrations. Although most patients clear the infection and develop immunity, chronic infection in 5 to 10% infected patients lead to HCC development in the 4th to 5th decade of life. I demonstrate that tetracycline-regulated pX expression induces multipolar spindles and polyploidy (4N DNA). To understand the mechanism of pX-mediated polyploidy, I investigated whether pX promotes DNA re-replication. Dual-parameter flow cytometry demonstrates pX-dependent BrdU incorporation in cells with 4N DNA. pX also induces expression of replication initiation factors Cdc6 and Cdt1, while suppressing geminin expression, a negative regulator of re-replication. G2-phase synchronized cells exhibit pX-dependent: i) nuclear Cdc6 and Mcm5 colocalization; ii) absence of nuclear geminin; iii) increased BrdU incorporation; iv) ATR activation; v) RAD17 and H2AX phosphorylation; and vi) co-localization of H2AX with the DNA elongation factor PCNA. | Format: Paperback | Language/Sprache: english | 200 gr | 144 pp.



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