SUMMARY AND CONCLUSION
Chapter 6 SUMMARY & CONCLUSION

The main findings of the study are summarized below:

1. Both insulin and benzo-α-pyrene were found to be the stimulants for the expression of LDLR and its transcription factor SREBP2 in both HepG2 as well as Chang liver cells. Insulin keeps LDLR in functional mode and hence allows instant flow of LDL through LDLR.

2. Stimulatory effect on PBR expression was observed with insulin and benzo-α-pyrene treatment. Mitogen or mitogenic activity of carcinogen can stimulate the transporter (PBR) for cholesterol across nuclear membrane.

3. Relative increase of cholesterol concentration in cytoplasmic and nuclear compartment was found in the presence of insulin as well as benzo-α-pyrene.

4. Increased cholesterol within nucleus may be involved in the regulatory mechanism at some phases of DNA replication or cell proliferation.

5. With increasing concentrations of insulin or benzo-α-pyrene, a comparable increase in LDL uptake was observed.

6. Insulin, benzo-α-pyrene and LDL were found to increase Cyclin E and Cdk-2 expression. Increased expression of cell cycle proteins e.g. cyclin E and cdk2 implies that cholesterol loading in nuclear chromosome may be linked with cell multiplication.

7. Insulin and benzo-α-pyrene were hence found to have a stimulatory effect on cell proliferation.

Conclusion

The central dogma of this thesis is that intracellular cholesterol homeostasis is regulated in two phases – 1) at the plasma membrane level i.e. through LDL receptor, an inlet for cytoplasmic cholesterol, and 2) at the nuclear membrane site i.e. through PBR, an outlet for cytoplasmic cholesterol. But this outlet is not throwing out the cholesterol outside of the cell; rather it is depositing cholesterol in a second compartment and which is nucleus, the farmhouse for DNA synthesis and cell duplication. Normally mitogenic stimulus allow the entry of cholesterol into the nucleus in a rate control manner, whereas the same entry of cholesterol into the
nucleus by the carcinogenic dose of a mitogen is expected to vigor up without any control and this could lead tumor generation because cholesterol is reported in recent past as an associate of chromosomal habitat. The experiments in present thesis have encased the road for cholesterol from cell periphery to the target nucleus in presence of a typical mitogen e.g. insulin and the mitogenic concentration of a carcinogen viz benzo-α-pyrene.
REFERENCES


References


