It has been said that the primary function of schools is to impart enough facts to make children stop asking questions. Some, with whom the schools do not succeed, become scientists... and I never stopped asking questions."

Knut Schmidt-Nielsen
4. AIMS AND OBJECTIVES OF THIS STUDY

To study the molecular mechanism responsible for tumor progression is essential for determining the behavior and pathology of cancer. Presently, the techniques that are used to diagnose cancer do not accurately reflect progression and metastatic spread of cancer, but research has shown that the development of cancer progression and metastatic spread could be determined by the expression profiling of some proteins, which are considered as the markers. OPN is one such type of biomarker. Recent studies have demonstrated that OPN acts as an important oncogenic molecule and its over expression may be associated with tumor progression. It is considered as a lead marker for prognosis of various cancers. Enhanced expression of OPN has been detected at tumor sites and serum of patients with various types of cancer. OPN regulates the expression of several oncogenic molecules through activation of various kinases and transcription factors and controls tumor growth and metastasis. It regulates cell cycle progression and protects tumor cells from apoptosis. Recent studies have demonstrated that OPN plays important role in tumor angiogenesis. Moreover, it has been described that downregulation of OPN results in drastic suppression of in vitro as well as in vivo tumor progression. COX-2 is a membrane bound bi-functional enzyme and its expression has been found to be elevated in higher grades of various types of cancer. PGE₂ is one of the major by-products of COX-2 catalyzed reaction, produced by benign as well as the cancer cells. The mechanism by which COX-2 and PGE₂ regulate prostate cancer progression is not clearly understood.

In this study, we have demonstrated the role of OPN in regulation of NF-κB/COX-2-dependent PGE₂-mediated prostate tumor growth, metastasis and angiogenesis. The major objectives of this study are as follows.

1. To check the effect of OPN on COX-2 expression in prostate carcinoma cells.
2. To examine the status of NF-κB activation in OPN-induced COX-2 expression.
3. To elucidate the molecular/signaling mechanism by which OPN regulates COX-2 expression.
4. To examine the role of COX-2 in OPN-induced MMP-2 activation.
5. To determine the role of autocrine and paracrine pathways by which COX-2 regulate tumor cell migration, invasion, angiogenesis and tumorigenesis.
6. To investigate the role of COX-2 and its metabolite PGE\(_2\) in OPN-induced tumorigenesis.

7. To determine the status of OPN, COX-2 and other oncogenic molecules in human clinical samples, and to establish the co-relation among their expression in different grades of prostate cancer.

8. To examine the effect of PGE\(_2\) on epidermal growth factor receptor-MAPK and integrin activation.

9. To study the role of EP2 and EP4 receptors in PGE\(_2\)-induced downstream signaling.

10. To examine the role of EGFR and \(\beta3\)-integrin on AP-1 and ATF-4 activation in response to PGE\(_2\).

11. To determine the effect of PGE\(_2\) on the expression of urokinase type-1 plasminogen activator (uPA) and vascular endothelial growth factor (VEGF) expression in PC-3 cells.

12. To substantiate the role of tumor derived-PGE\(_2\) on tumor-endothelial cell interaction and angiogenesis.