

## High Expression of Cyclooxygenase-2 in High Grade Human Prostate Adenocarcinoma

(Pengekspresan Tinggi Siklooksigenase-2 dalam Adenokarsinoma Prostat Manusia Gred Tinggi)

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### ABSTRACT

*Inflammation plays an important role to the process of prostate carcinogenesis by increasing the rate of cell proliferation, which contributes to an aggressive tumour phenotype. Cyclooxygenase-2 (COX-2) has been found overexpressed in various types of cancer cells including prostate. The aim of this study was to investigate the COX-2 expressions in different types of human prostate tissues. Paraffin-embedded prostate tissues from 263 samples were examined for the expression of COX-2 marker by immunohistochemistry method. COX-2 was found highly expressed in prostate adenocarcinoma ( $p=0.001$ ) as compared to benign and normal tissues. The score of COX-2 expressions in most of normal prostate was weak 49 (77.8%), while only 16 (16%) of BPH showed strong expression. 56 cases (56%) prostate cancer showed strong COX-2 expression. Prostate cancer cases showed significant differences in staining patterns as tumour grade increased. In addition, COX-2 expression was significantly correlated with Gleason score in cancerous tissues. This study suggests that COX-2 overexpression is associated with prostate cancer and higher grade tumour.*

*Keywords: Cyclooxygenase-2 (COX-2); immunohistochemistry; inflammations; overexpression; prostate adenocarcinoma*

### ABSTRAK

*Inflamasi memainkan peranan penting dalam proses pembentukan kanser prostat melalui peningkatan kadar pembahagian sel. Inflamasi juga bertanggungjawab dalam pembentukan fenotip kanser prostat yang lebih agresif. Siklooksigenase-2 (COX-2) didapati diekspres lebih tinggi daripada aras biasa dalam pelbagai jenis sel kanser termasuk prostat. Tujuan kajian ini dijalankan adalah untuk mengkaji pengekspresan COX-2 dalam tisu prostat manusia yang berbeza. Sebanyak 263 tisu prostat tertanam parafin telah digunakan untuk mengkaji aras pengekspresan penanda COX-2 melalui kaedah imunohistokimia. Pengekspresan COX-2 didapati lebih tinggi dalam tisu adenokarsinoma prostat ( $p=0.001$ ) berbanding tisu benigna dan tisu prostat yang normal. Kebanyakan tisu prostat normal mengekspres COX-2 yang lemah 49 (77.8%) dan hanya 16 (16%) tisu BPH menunjukkan pengekspresan COX-2 yang kuat. Manakala, 56 (56%) tisu kanser prostat menunjukkan pengekspresan COX-2 yang kuat. Tisu kanser prostat juga menunjukkan perbezaan corak perwarna COX-2 yang signifikan dengan peningkatan gred tumor. Selain itu, pengekspresan COX-2 menunjukkan perhubungan yang signifikan dengan skor Gleason dalam tisu kanser. Kajian ini mencadangkan bahawa terdapat hubungan antara pengekspresan COX-2 yang sangat tinggi dengan kanser prostat dan tumor gred tinggi.*

*Kata kunci: Adenikarsinoma prostat; siklooksigenase-2 (COX-2); imunohistokimia; inflamasi; pengekspresan*

### INTRODUCTION

Prostate adenocarcinoma (PCa) is one of the most frequently diagnosed cancers among males in Malaysia. A report by National Cancer Registry (2008) showed that, prostate cancer is the fourth frequent cancer occurred and accounted for 7.3% of the total cancers occurrence among males. Out of total cases, the majority of morphologically reported cases were adenocarcinoma which is 96%. Today diagnosis of prostate cancer is commonly based on morphological interpretation by use of cell architecture, nuclear features and presence or absence of basal cell layer. Nevertheless, this method is usually not adequate in equivocal cases in which it might require histopathologists to use immunohistochemistry (IHC) staining to resolve the differential diagnosis (Varma & Jasani 2005). Despite of

the clinical importance of prostate cancer, understanding of mechanism underlying development and progression of this disease is poorly understood. Many researches have suggested that inflammation was linked to the development of tumours in several organs, including the prostate itself (Weitzman & Gordon 1993). Cyclooxygenase (COX), was referred as prostaglandin (PG) endoperoxidase synthase, is an enzyme that converts arachidonic acids to PGs and other eicosanoids. COX exists in two isoforms, namely COX-1 and COX-2. COX-1 is expressed constitutively in many tissues and cell types and involved in normal cellular physiological functions. Meanwhile, COX-2 exists as pro-inflammatory in nature and inducible by variety of factors, including growth factors, cytokines, tumour promoters and mitogens (Herschman 1991). Aberrant