A study of p53 oncogene in cases of endometrial hyperplasia

Thesis
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وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

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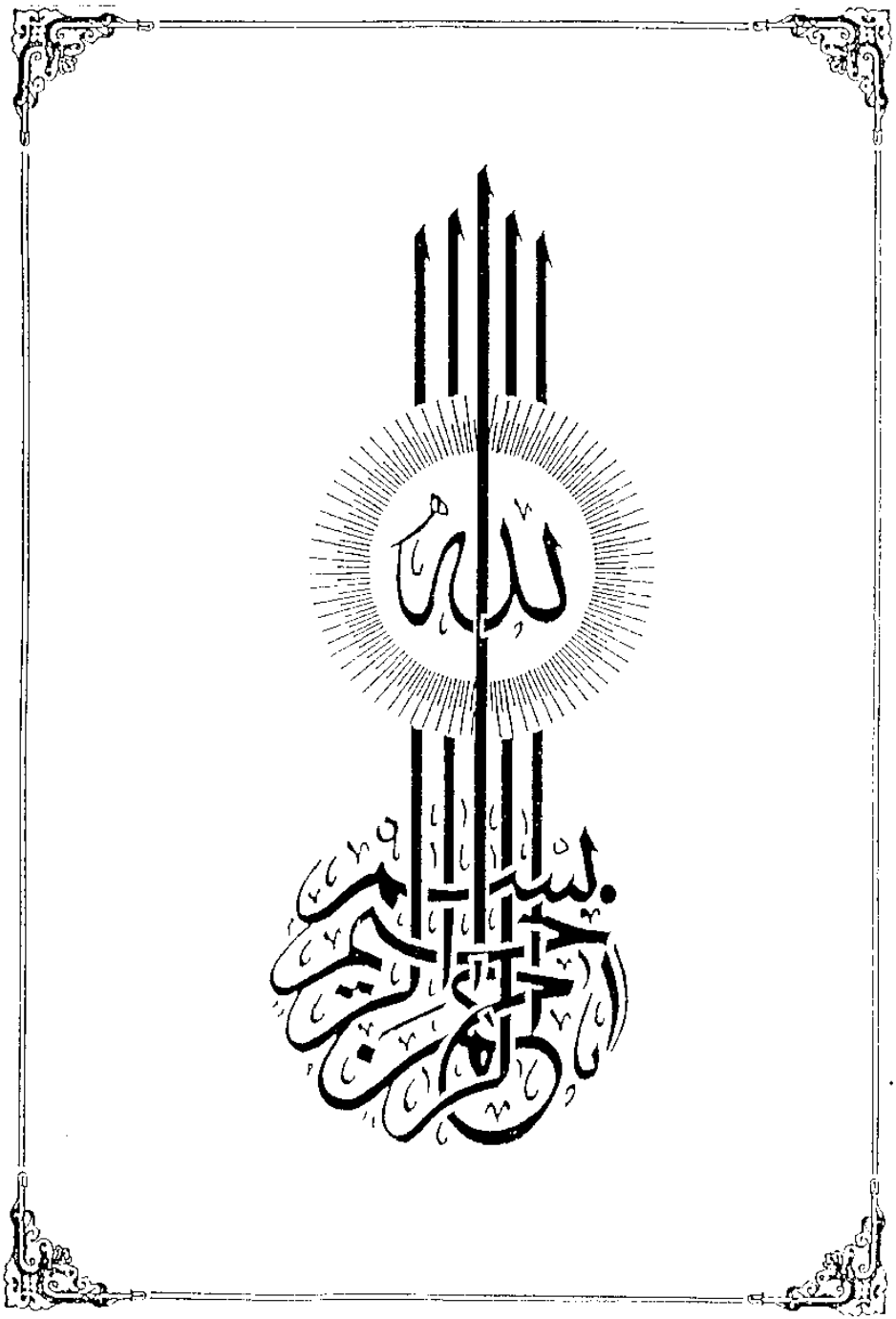
سورة التوبة آية ١٠٥



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Introduction

In no area of medicine has recombinant DNA had a greater impact than in our understanding of cancer . Although this disease has been obscure for decades , the seed for recent explosive growth in our knowledge of cancer was planted in 1911 ; in that year *Rous Peyton* discovered that filtered cell-free extracts from chicken tumors could cause new tumors when inoculated into healthy chickens . It was eventually recognized that what Rous had discovered was a tumor virus . The realization that a tumor virus with an exceedingly small genome could trigger the entire panoply of traits that characterize a cancer cell was an intellectual water shed : the task of understanding how a cell's entire growth program is rewritten in cancer now seemed a feasible one . What was not anticipated was that tumor viruses would provide a window on our own genome.(*Watson*, 1992).

A window opened wide by recombinant DNA technology . what we have learned since the tools of recombinant DNA were unleashed on the cancer problem is that our own genome is littered with genes having the potential to cause cancer and other genes having the power to block it . From the study of these genes , We have derived a greater understanding of molecular events that occur in tumor cells and we have discovered many of the players that orchestrate normal cell growth & differentiation (*Watson*, 1992).

Oncogenes

During division of the cancer cells ; they transmit the neoplastic phenotype to their daughter cells ; for that reason it has been generally assumed that the neoplastic phenotype inheritance is determined by specific genes , this assumption explains the great appeal of oncogenic viruses for cancer researches . These oncogenic viruses are capable of inducing all the pathologic and clinical changes associated with neoplastic disease and in some cases a virus can introduce single gene agent (*oncogene*) into a normal cell whose product can initiate & maintain the neoplastic state in this cell .(Neiman , 1987)

These oncogenes represent altered form of cellular proto-oncogenes which have important cellular function in normal state. Human homologues of some of these oncogenes may play a role in human cancer development and this hypothesis arouse a number of questions about nature of oncogenes , the control of their expression , the biochemical nature of their products & the mechanisms of interaction with the metabolism of the host cell (Neiman , 1987) .

Proto-oncogene

Recently molecular biologist have discovered a class of genes termed proto-oncogenes which are highly conserved during vertebrate evolution and which may provide a substrate upon which the multitude of carcinogenic stimuli can play . Over 20 proto-oncogenes have already been identified , they are normal constituents of all cells & appear to be critically important in regulation of normal cell growth and differentiation . The products of proto-oncogenes assume specific cellular location & can be divided into distinct functional families

which will be clarified in the review : they include for example growth factors and growth factor receptors.

The conversion of a proto-oncogenes ; a vital normal cellular constituents to an oncogene capable of transforming cells results from a mutation within the proto-oncogen or abnormal expression of its products (*Nienhius & Sherr*, 1987) .

Some varients of the cell growth controlling genes act as a tumor suppressor genes with their products are the negative growth regulators and their loss of function results in the expression of transformed phenotype while the oncogen products are positive effectors of transformation . (*Devita*,1993) .

P53 gene

◆ The protein **p53** was identified through its association with simian virus 40 (*SV40*) & it was the first cellular protein shown to bind to the transforming gene product of DNA virus (*Lane & Crawford* , 1979)

◆ **p53** gene appear to play an important role in controlling cell division & mutation in **p53** have been reported widely in non gynecological cancer. Unlike other cancer related genes; which become activated during carcinogenesis, it is the loss of wild type **p53** function that is though to contribute to cancer development , so this gene therefor has been considered one of the tumor suppressor genes since normal function appears to be necessary for negative control of the cell growth. (*Lane & Crawford* , 1979)

Several viral oncoproteins have been shown to interact with **p53**, it seems likely that the formation of this complexes inactivate the cellular proteins resulting in an overall effect similar to somatic mutation in **p53** ; as an example of this complexes is HPV 16 transforming protein Eb complex with protein products of **p53**. In HPV positive anal & cervical tumors the normal function of **p53** may be inhibited by these viral proteins & so mutation within **p53** gene coding sequences would not appear to be a necessary step in the genesis of these tumors .
However in HPV negative tumors from the same tissues , loss of wild type **p53** activity may only be achieved by somatic mutation of this gene (*Tidy & Werde* , 1992).

Over expression of **p53** was found in conducted study in about 20% cases of endometrial adenocarcinoma but in other type of cancer as breast & lung cancer a strong correlation between **p53** & advanced stage disease has been found (*Mathew et al* . 1992)

P53 & Endometrial hyperplasia

Aim of the work