Aim and Objectives

Aim:

It is hypothesized that several molecular mechanisms play a significant role in synergistic way in oral cancer initiation and progression. The major **aim** of the present study was to carry out comprehensive analysis of p53, the gatekeeper of human genome in conjunction with, MDM2, HPV status, hTERT, VEGF, MMP2 and MMP9 which are implicated in immortalization, angiogenesis, invasion and metastasis and have potential role in the etiopathogenesis of oral cancer.

Objectives: Major objectives of the investigation were:

1. To study *p53* and *MDM2* gene polymorphisms, mutations and HPV infection in oral cancer patients.
    - To estimate risk of oral cancer development associated with *p53* intron 3 (rs17878362), exon 4 (rs1042522) and intron 6 (rs1625895) and *MDM2* SNP309 (rs2279744) polymorphisms.
    - To analyze gene-environment interaction (*p53* and *MDM2* polymorphisms and tobacco exposure) and risk of oral cancer development.
    - To analyze association of *p53* and *MDM2* polymorphisms with clinico-pathological features, recurrence and survival of oral cancer patients.
    - To analyze gene-gene interaction (*p53* and *MDM2* polymorphisms) and risk of oral cancer development and its association with clinico-pathological features, recurrence and survival of oral cancer patients.
    - To identify frequency and type of *p53* mutations in oral cancer patients and its association with clinico-pathological features, recurrence and survival of oral cancer patients.
    - To study interactions between *p53*, *MDM2* polymorphisms and *p53* mutations and their association with clinico-pathological features, recurrence and survival of oral cancer patients.
    - To estimate the frequency of HPV infection in oral cancer patients and its association with *p53* gene status.
2. To investigate expression of genes involved in immortalization (*hTERT)*, angiogenesis (*VEGF)* invasion and metastasis (*MMPs)* in oral cancer patients.

- To evaluate *hTERT* mRNA levels in oral cancer patients and their association with clinico-pathological features, recurrence and survival of oral cancer patients.
- To estimate mRNA as well as protein levels of VEGFA, VEGFC and VEGFD in oral cancer patients and their association with clinico-pathological features, recurrence and survival of oral cancer patients.
- To estimate mRNA as well as protein levels of MMP2 and MMP9 in oral cancer patients and their association with clinico-pathological features, recurrence and survival of oral cancer patients.

3. To evaluate the correlation between *p53*, *MDM2* polymorphisms, *p53* mutations, hTERT, VEGFA, VEGFC, VEGFD, MMP2, MMP9 and their role in molecular pathogenesis of oral cancer.
    - To evaluate association of hTERT expression with *p53*, *MDM2* polymorphisms and *p53* mutations.
    - To evaluate association of VEGFA, VEGFC and VEGFD expression with *p53*, *MDM2* polymorphisms and *p53* mutations.
    - To evaluate association of MMP2 and MMP9 with *p53*, *MDM2* polymorphisms and *p53* mutations.