

## A Meta-Analysis of Non-Coding Polymorphisms Linked to Pre-Cancerous Lesions and Cervical Cancer

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### Abstract

**Objectives:** To investigate the risk of SNPs found in non-coding areas of genes linked to cervical cancer. Neity, as well as publishing bias and statistical significance as measured by the p-value.

**Methods:** To uncover literature containing the relationship between single nucleotide polymorphisms with cervical cancer, the PubMed database was extensively searched using text-mining tools. If case-control studies matched the selection criteria, they were examined for the meta-analysis until June 2020. Each case-control study's polymorphisms were examined for the existence of genotype data before being separated into groups based on precancerous and cancerous cervix situations. The odds ratio and 95% confidence intervals (CI) were used to explore the impact of polymorphisms using various genetic models (allele, dominant, recessive, heterozygous and homozygous). The p-value was also used to assess heterogeneity, publication bias, and statistical significance.

**Results:** The meta-analysis evaluated 120 studies covering 48 distinct non-coding SNPs with 37,123 cases and 39,641 control data. For 43, 8, and 11 SNPs, the genotype data was divided into Cancer, Precancer, and "Cancer + Precancer" groups. The meta-analysis found 21 and 1 SNPs to be significant in the Cancer and "Cancer + Precancer" categories, respectively. rs1143627 (IL1B), rs1800795 (IL6), rs1800871 (IL10), rs568408 (IL12A), rs3312227 (IL12B), rs2275913 (IL17A), rs5742909 (CTLA4), rs1800629 (TNF), and rs4646903 (CYP1A1) were discovered to increase risk of cervical cancer in at least three.

**Conclusion:** We identified potential non-coding SNPs corresponding to various cytokines like interleukins (ILs), tumour necrosis factor (TNF), interferon (IFN) and other immune related genes like toll like receptor (TLR), cytotoxic T-lymphocyte associated protein (CTLA) and matrix metalloproteinase (MMP), as significant with increased pooled OR in this meta-analysis pointing to risk association of the immune-related genes in cervical carcinogenesis.

### Introduction

Cervical cancer is a leading cause of cancer-related death among women worldwide. The disease is caused by persistent infection with high-risk human papillomavirus (HPV) types. The progression from HPV infection to cervical cancer is a multi-step process involving genetic and epigenetic changes. Non-coding polymorphisms (SNPs) in various genes have been implicated in the development and progression of cervical cancer. These polymorphisms can affect gene expression, protein function, and the immune response, potentially increasing the risk of cancer. This meta-analysis aims to investigate the association between non-coding SNPs and cervical cancer, focusing on the risk of precancerous lesions and the development of the disease.

The study included 120 studies covering 48 distinct non-coding SNPs. The meta-analysis found 21 and 1 SNPs to be significant in the Cancer and "Cancer + Precancer" categories, respectively. The significant SNPs were rs1143627 (IL1B), rs1800795 (IL6), rs1800871 (IL10), rs568408 (IL12A), rs3312227 (IL12B), rs2275913 (IL17A), rs5742909 (CTLA4), rs1800629 (TNF), and rs4646903 (CYP1A1). These findings suggest that these polymorphisms are associated with an increased risk of cervical cancer.

The results of the meta-analysis indicate that these SNPs are associated with an increased risk of cervical cancer. The odds ratios (OR) for these SNPs were significantly higher in the Cancer and "Cancer + Precancer" groups compared to the control groups. This suggests that these polymorphisms may play a role in the development and progression of cervical cancer.

### Materials and Method

#### Data collection

The PubMed database was extensively searched using text-mining tools to identify relevant studies. The search criteria included the keywords "non-coding polymorphisms", "cervical cancer", and "meta-analysis". The search was limited to English literature published between 2000 and 2020.

The search results were screened based on the title and abstract. Full-text articles were obtained for studies that met the selection criteria. The studies were then examined for the existence of genotype data before being separated into groups based on precancerous and cancerous cervix situations. The odds ratio and 95% confidence intervals (CI) were used to explore the impact of polymorphisms using various genetic models (allele, dominant, recessive, heterozygous and homozygous). The p-value was also used to assess heterogeneity, publication bias, and statistical significance.

#### Classification of study population based on the condition of cervical cells

The study population was classified into three groups based on the condition of cervical cells: Cancer, Precancer, and "Cancer + Precancer". The Cancer group included studies that reported on the risk of cervical cancer. The Precancer group included studies that reported on the risk of precancerous lesions. The "Cancer + Precancer" group included studies that reported on the risk of both cervical cancer and precancerous lesions.

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