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Etiology of *Pasteurella multocida* Infections Associated Leukemia and Its Earlier Detection by Genetic Markers – A Quantitative Approach

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Pasteurella multocida **is one among the potent pathogen, which possess the ability to cause a range of pathogenic diseases in zoonotic organisms such as chicken, swine, cattle etc. Currently many research studies convey that there is a potential relationship between *P. multocida* infections to leukemia. Leukemia is the condition of cancer which is characterised by the increased number of White Blood Cells. There is paucity of knowledge about Etiology of *Pasteurella multocida* infections associated Leukemia and its earlier detection by genetic markers.**

Keywords: *Pasteurella multocida,* Cancer, leukemia, Molecular markers, Lymphoblastic, hemorrhagic septicaemia.0

Pasteurella multocida is one among the potent pathogen, which possess the ability to cause a range of pathogenic diseases in zoonotic organisms such as chicken, swine, cattle etc. This organism is basically Gram negative Coccobacillus with high virulence traits, comprising of 4 species multocida, gallicida, septica and the Tigris is the one which is found recently (Marina *et al.,* 2006). Moreover, five serotypes have been identified from (A, B, D, E and F). Fowl cholera is a disease caused by A serotype, hemorrhagic septicaemia is caused by B and E serotypes in cattle. Atrophic rhinitis is caused by serotype D in pigs (Marina *et al.,* 2006). Currently many research studies convey that there is a potential relationship between *P. multocida* infections to leukemia. Earlier studies from Davidovich *et al.,* (2008) have investigated about the frequent *P. multocida* caused septicaemia as well as osteomyelitis is observed in chronic lymphatic leukemia patients. The very recent work from Harris & Osswald (2010) strongly recommends that seven acute epiglottis infected patients were found with chronic lymphocytic leukemia also confirms the same. From such studies, it was aimed to examine the etiology behind leukemia and *P. multocida* infections, by genetic analysis. So, molecular cancer markers for Leukemia and *P. multocida* infections was investigated from the blood sample of chronic Leukemia patients to identify the etiology behind this prevalence of *P. multocida* infections in Leukemia patients.

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Review of Literature

Leukemia is the condition of cancer which is characterised by the increased number of White Blood Cells. There are two main types of Leukemia. They are lymphoblastic leukemia and myeloid leukemia, which may be acute or chronic, depending upon the stages of the cancer. There are many risk factors for development of leukemia which may be age, lifestyle changes which are environmental aspects, smoking and alcoholism and also ionising radiations. Apart from these above

factors, according to the studies from Houlston *et al.,* (2002), genetic inherited factors play a crucial role in the development of Leukemia. Few genes such as *runx1, runx1t1 and myh11* act as a markers for inherited leukemia among children.

Molecular markers studies

Earlier studies from Giuseppe *et al.,* (1998) in murine Splenocytes has observed that *P. multocida* porin possess the capacity to alter the release of cytokines and by modulating its gene expression. This study has recommended that 5mcg/ml of porin and 1 mcg/ml of LPS of PMT has increased IL-1α, IL-6, and IL-12 expression. This study justified that *P. multocida* possess immunomodulatory effects over splenocytes.

Another important study from Dagmer *et al.,* (2011) has justified that upon injection of PMT, primary toxin of *P. multocida* has stimulated the level of B-cells by enforcing the cytokines and growth factors to promote the osteoclastic differentiation by regulating the gene expression of TNF-α, IL-β, IL-6 and RANKL. The study strongly conveys that osteoclastic properties of PMT has been a result of cross talk between cell-signalling pathways between osteoblasts and B-Lymphocytes, the susceptible object for *P. multocida*

From the basis of the above study, the present investigation was planned to investigate the effects of PMT on genetic Human acute Lymphoblastic Leukemia cell line model ARH-77 (ATCC® CRL-1621™) is used in the study and to compare the effects normal Human B-Lymphoma cells 8E7 (ATCC® CRL-8795™)

Research Question

The adverse effects of *P. multocida* infections in human were addressed in earlier studies. But extensive studies on effects of PMT, *P. multocida* toxin, in human leukemia cell line model, probing for the etiology behind the action of PMT on human leukemia cells and normal B cells well less understood. So, it was aimed to understand the mechanism of action of PMT on leukemia cells and also normal B cells regarding the alteration of gene expression on NFKB pathway by analyzing the mRNA and Protein expression of NFκB, IKBα, IKK, IKBα and p50 protein.

CONCLUSION

Results were interpreted based on the analysis. The mRNA and protein expression up regulation may possess effect of PMT on leukemia. Many studies have associated the cell signalling pathway such JAK-STAT, PI3K, GPCR signalling for human Leukemia but relationship between PMT toxin and its molecular mechanism to stimulate the cell proliferation of leukocytes via NFKB pathway was not yet studied. So, this study was aimed to fill that research gap.

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