Objectives: Idiopathic pulmonary fibrosis (IPF) is a serious disease characterized with progressive scarring of
the lungs in which the genetic background is supposed. The aim of our study was to investigate Th1/Th2
cytokine gene polymorphisms to evaluate their possible influence on IPF development. Then we have correlated
selected polymorphisms of IL-1, IL-4 and IL-12 groups (the selection was based on our previous results) with
clinical parameters and high resolution computed tomography (HRCT) as a markers of disease stage and
progression.
Methods: We investigated 30 patients with IPF and 103 healthy volunteers for the cytokines polymorphisms of
the IL-1 alpha, IL-1 beta, IL-1R, IL-1RA, IL-2, IL-4, IL-6, IL-10, IL-12, TNF alpha, IFN gamma, TGF beta,
IL-1 beta, IL-2, IL-4 and IL-4RA genes. The PCR-SSP method was used for measurement. Then the correlations of vital capacity(VC) and diffusing capacity for carbon monoxide(DL_{CO}), bronchoalveolar lavage
(BAL) fluid cell counts and high resolution computed tomography (HRCT) alveolar and interstitial scores with
different genotypes of groups of IL-1, IL-4, and IL-12 cytokines and their receptor antagonists. The HRCT
results were evaluated by an experienced viewer using the interstitial and alveolar score scales, which were
based on the IPF HRCT description system from Gay et al. (1998).
Results: The CT genotype of the IL-1 alpha gene promoter at position (-889) was more frequent in IPF patients
($p=0.042$, $p_{corr}=0.61$). In the IL-2, the genotypes GT at position (-330) and TT at position (+166) were more
frequent in the IPF group ($p=0.015$, $p_{corr}=0.28$). Concerning the IL-4 gene promoter region at position (-1098),
the GT was more frequently seen in IPF group and 97% of patients with IPF had the genotype GT or TT
($p=0.012$, $p_{corr}=0,26$). The CT genotype at position (-590) (IL-4) was more frequent in the IPF group ($p<0.0001$, $p_{corr}<0.0022$). The prevailing genotype in IPF patients for IL-4 at position (-33) was CT ($p<0.0001$,
$p_{corr}<0.0022$). The carriers of CT genotype at IL-1 alpha (-889) position had higher VC at the time of diagnosis. The CC genotype at this position was more frequent in patients with higher counts of HLADR+ T

lymphocytes in BAL. The GT genotype at IL-4 (-1098) position correlated with higher counts of CD4+ T
lymphocytes, and inversely the TT genotype with higher counts of CD8+ T lymphocytes in BAL fluid. The
HRCT alveolar score was more pronounced in IL-4 RA (+1902) AG heterozygotes. The HRCT interstitial score
was less severe in the IL-12 (-1188) AA homozygotes. According to progression of the HRCT interstitial score,
the CC homozygosity at IL-1 RA (mspa 111100), the AA homozygosity at IL-4 RA (+1902) and CC homozygosity at IL-4(+33) positions were more frequent in patients with stable disease compared to those with
progressive disease.
Conclusion: Our results support the idea of the pathogenic role of cytokine gene polymorphisms of IL-1 and
especially of IL-4 in the etiology and pathogenesis of IPF. We assume from our data that the gene polymorphisms of the promotor region of IL-4 at position (-1098) and (-33) and IL-1 alpha at position (-889)
are likely to play a pathogenic role in IPF and in modification of its clinical presentation and severity. Furthermore we conclude from our data that the polymorphisms of IL-4, IL-4RA, IL-1RA and IL-12 genes
(genes of cytokines with regulatory activity) might influence the phenotype of IPF as shown by measurable
changes in HRCT investigations.