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Role of microRNAs in development of chronic obstructive pulmonary disease

Abstract: Chronic obstructive pulmonary disease (COPD) is a multi-pathogenesis chronic lung disease characterized by irreversible and progressive bronchial obstruction. An important role in the development of the disease belongs to the genetic predisposition and environmental factors. Although the pathogenesis of COPD is now not well understood, it is known that oxidative stress, imbalance of the proteolysis-antiproteolysis system, immune system disorders, impaired lung repair, and apoptosis dysfunction make a significant contribution to the disease. In this review, we discuss about various molecular and cellular mechanisms of COPD including airways inflammation. Special attention is paid to the role of miRNA in the development of COPD. It is considered the possibility of using microRNAs as new biomarkers and therapeutic tools for the diagnosis and treatment of COPD.

Keywords: microRNA, chronic obstructive pulmonary disease, biomarkers, signaling pathways.

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Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory condition of the lung of high global prevalence and is associated with high morbidity and mortality [1]. Its contribution to death worldwide is predicted to increase over the course of both the current and next decade and up to 2030, COPD will become the third cause of deaths worldwide, and the prevalence is increasing in developing countries at present [2]. COPD is characterized by chronic bronchiolitis and emphysema due to the abnormal inflammatory response triggered by pollutants such as virus infection and noxious gases exposure, of which cigarette smoking (CS) is considered as the predominant factor and attributed to 80-90% of the COPD cases [3]. Cigarette smoke and other irritants inhaled into the respiratory tract may activate surface macrophages and airway epithelial cells to release multiple chemotactic mediators, particularly chemokines, which attract circulating neutrophils, monocytes, and lymphocytes into the lungs [4]. These inflammatory and structural cells release many inflammatory mediators that contribute to the pathophysiology of COPD. Also, there may be several coexisting cellular and molecular mechanisms that interact in complex ways in treating COPD [5]. Therefore it is important to identify molecular biomarkers of disease activity.

Over the last two decade have been identified small non-coding RNAs as regulators of gene expression [6]. The discovery of these small RNAs, called microRNAs (miRNAs) in the beginning of 1990s, revealed an unexpected level of gene expression regulation that has proven to be a great relevance in the regulation of numerous physiological and pathological conditions [7]. MiRNAs are assuming greater significance in research as novel regulators of gene expression, playing a central role in different pathophysiological processes. Increasing evidence supports the potential role of miRNAs as disease specific biomarkers, including COPD and other broncho-pulmonary diseases [8].

The miRNAs are endogenous non-coding small RNAs of about 19-22 nucleotides in length that function at a transcriptional and post-transcriptional level, usually resulting in gene silencing via mRNA translational repression or target degradation [9]. At present, more than 1 000 miRNAs have been identified in human. These miRNAs can regulate the expression of at least 30% of genes that control various biological functions. Each miRNA can regulate multiple target genes, while the specific target mRNA can also regulated by multiple miRNAs at the same time [10].

Increasing evidence supports the potential role of miRNA as disease-specific biomarkers, generating new tools for diagnostic, preventive or therapeutic purposes. In most solid tumors, such as gastric cancer, prostate cancer, non-small cell lung cancer, miRNA profiling has been proposed as a useful aid in the diagnosis, prediction of recurrence and assessment of a patient's prognosis in different clinical directions [11]. Many previous observations demonstrated that miRNAs have the potential of being used as biomarkers for COPD. Exploration of dysregulated expression profile of miRNAs

in distinct samples from COPD patients or model animals under different environmental exposures could be helpful for elucidating the role of miRNAs in the pathogenesis of COPD. Therefore in this short review we provided an overview of the interplay of those miRNAs with environmental risk factors of this disease. We also highlight the potential utility and limitations of miRNAs serving as diagnostic biomarkers and therapeutic targets for COPD.

Conickx et al. have investigated the miRNA profile of 523 miRNAs by qRT-PCR in lung tissue and cell-free bronchoalveolar lavage (BAL) supernatant of mice exposed to air or cigarette smoke (CS) for 4 and 24 weeks[12]. They demonstrated that after 24 weeks of CS exposure, 31 miRNAs were differentially expressed in lung tissue and metricconverterProductID78 in78 in BAL supernatant. To assess the change in cell types following CS exposure could be associated with the alteration in miRNA expression the authors correlated the miRNA expression with populations of immune cells and levels of inflammatory chemokines. It was demonstrated that after subacute CS exposure, miRNA-135b correlated strongly with percentage of dendritic cells. Following chronic CS exposure, miR-155 correlated significantly with percentage of B cells and miR-152, miR-30a-5p, miR-30c, miR-218 and miR-26a correlated with several immune cell types in lung tissue. Correlation of altered miRNA expression with the change in inflammatory profile, suggests a possible implication of these miRNAs in CS-induced inflammation.

Pinelo et al. studied miRNA expression patterns in patients with COPD and/or lung adenocarcinoma to elucidate distinct regulatory networks involved in the pathogenesis of these two smoking-related diseases [13]. Expression of 381 miRNAs was quantified by TaqMan Human MicroRNA A Arrray v metricconverterProductID2.0 in2.0 in bronchoalveolar lavage fluid samples from 87 patients classified into four groups: COPD, adenocarcinoma, adenocarcinoma with COPD, and control (neither COPD nor adenocarcinoma). 11 differentially expressed miRNAs were randomly selected for validation in an independent cohort of 40 patients. The authors demonstrated that 40 miRNAs were up-regulated in patients with adenocarcinoma, 19 of which were exclusively up-regulated in patients without COPD. Patients with adenocarcinoma and COPD showed 12 additional deregulated miRNAs, nine of which were up-regulated and three were down-regulated. In patients with COPD only, seven miRNAs were found to be up-regulated and seven down-regulated. Additionally, the COPD and adenocarcinoma with COPD groups shared five deregulated miRNA (two down-regulated and three up-regulated). Finally, the three pathologic groups shared three up-regulated miRNAs (miR-15b, miR-425 and miR-486-3p) as compared with the control group. These results contribute to unravelling miRNA-controlled networks involved in the pathogenesis of lung adenocarcinoma and COPD, and provide new tools of potential use of miRNAs as biomarkers for diagnosis and/or therapeutic purpose.

Recently Paschalaki et al. demonstrated that chronic exposure to cigarette smoke causes reduced expression of miR-126 and increases the DNA damage response (DDR) [14]. It is known that DDR contributes to the pathophysiology of aging disorders, including COPD, cardiovascular disease and cancer [15]. It was shown that miR-126 levels in lung epithelial cells negatively correlated with smoking history assessed as pack-years and positively correlated with disease severity measured as FEV1% (forced expiratory volume in 1s) predicted, suggesting miR-126 expression is down-regulated with extended exposure to cigarette smoke and increased severity of lung disease. These results identify a novel miR-126-dependent pathway controlling DDR caused by cigarette smoke, where down-regulation of miR-126 enhances ataxia-telangiectasia mutated activation and thereby promotes tissue aging and dysfunction.

A new phenotype with overlapping characteristics between asthma and COPD called asthma-COPD overlap syndrome (ACOS) is emerging among inflammation diseases [16]. Lacedonia et al. studied the expression profiling of miRNA-145 and miRNA-338 in serum and sputum of patients with COPD, asthma and ACOS [17]. They demonstrated that the expression of miRNA-338 is higher in the supernatant of different obstructive diseases than in peripheral blood, while miRNA-145 is higher only in the supernatant of asthma patients. The expression of miRNA-145 in sputum was higher in COPD patients than in controls. The results of that study do not show differences between the expression of miRNA-145 and mi-RNA-338 in ACOS patients compared to asthma or COPD patients, and this confirms that this syndrome presents some characteristics overlapping between

both diseases. The similar results were observed by Wang et al. [18]. They demonstrated the down expression of miR-145-5p and miR-338-3p, and upregulation of miR-3620-3p in plasma of patients with COPD.

Quite recently Dang et al. investigated the expression level of miR-145-5p in human lung tissue samples, and to explore its regulatory role in the apoptosis and inflammation of human bronchial epithelial cells (HBECs) following CS extract (CSE) exposure [19]. They found that miR-145-5p was significantly down-regulated in lung tissues from smokers without or with COPD compared to non-smokers. Their functional assays showed that miR-145-5p over expression remarkably alleviated CSE-induced apoptosis and inflammation response by regulating p53-mediated apoptotic signaling and pre-inflammatory factors such as necrotic factor- α (TNF- α), interleukins – IL-6,IL-8 in HBECs, whereas, down-regulation of miR-145-5p showed opposite effects. Furthermore, luciferase reporter assays verified that Kruppel-like 5 (KLF5) transcription factor was a direct target of miR-145-5p. By western blot assay was confirmed that KLF5 is up-regulated in COPD tissues and negatively associated with miR-145-5p expression. It was also shown that the CSE-induced NF- κB signaling activation was suppressed by miR-145-5p overexpression. On the basis of received results the authors suggested that the protective role of miR-145-5p on CSE-induced airway epithelial cell apoptosis and inflammation was partially through regulating KLF5-mediated activation of NF- κB signaling, which might be a potential therapeutic biomarker in COPD treatment.

As mentioned above, lung infections are a significant in smokers and COPD patients [4]. Chen et al. studied the effects of nicotinamide adenine dinucleotide phosphate 4 (NOX4) and transforming grows factors – beta (TGF- β) involved in airway remodeling of COPD. Their results demonstrated that the expressions of NOX4 and TGF- β in COPD epithelial cells and small airway smooth muscle cells are significantly enhanced. The expression of NOX4 and TGF- β are positively correlated with the severity of chronic pulmonary air flow suggesting that TGF- β and NOX4 signaling may be involved in the development of COPD airway remodeling [20]. CS and COPD lead to impaired mucociliary clearance, thereby promoting microbial colonization and lung infections. It is known that the etiology of pneumonias associated with COPD and CS is similar to that seen in cystic fibrosis [21]. Dutta et al. determined the mechanism by which cigarette smoking and TGF- β suppress cystic fibrosis transmembrane conductance regulator (CFTR) [22]. It was demonstrated that miR-145-5p plays an important role in CFTR suppression in primary bronchial epithelial cells re-differentiated at the air-liquid interface cultures treated with TGF- β1 and in small animal models exposed to cigarette smoke. The authors also demonstrated that miR-145-5p modulates another important chloride channel, SLC26A9, which physically interacts with CFTR and plays an important role in CFTR biogenesis and activation.

Regulation of miR-145 was found to be negatively controlled by pathways involving the MAP-kinases, MEK-1/2 and p38-MAPK. Overexpression of miR-145 in airway smooth muscle cells from patients with COPD suppressed IL-6 and CXCL8 (chemokine ligand) release, to levels comparable to the nonsmoker controls [23]. This finding may open a new way in COPD therapeutics by targeting of miRNA-145 and diagnosis by its detection.

Li et al. compared the expression spectrum of miRNAs in the lung homogenates of rats with COPD and normal control group [24]. COPD rat models were reproduced by smoke inhalation as well as intratracheal instillation of lipopolysaccharide (LPS). The samples of the lung were harvested, and the histopathological examination of the right lung was carried out to evaluate the degree of lung injury. Total RNA were isolated from the left lung. The miRNA expressions in lung tissue of rats with COPD or normal rats were determined by miRNA chip technology to screen the miRNA with differential expression. The data were analyzed to study the expression difference of miRNAs between the two groups, and to construct the miRNA-target network. Compared with normal control group 20 miRNA with increased expression were found in COPD model group. The study reveals that many miRNA have multiple target genes, such as miR-30c-2, miR-145, miR-181b, miR-181a ,miR-181d, and miR-199. Hierarchial clustering analysis showed that significant differences in individual miRNA in lung tissue between of two groups – COPD and control were found.

Recently Ong et al. studied age-related gene and miRNA expression changes in airways of healthy individuals [25]. RNA and small RNA sequencing was performed on bronchial biopsies of 86 healthy

individuals (age: 18-73) to determine age-related expression changes. It was shown that miR-146b-5p, miR-142-5p and miR-146a-5p expression levels were lower with increasing age and a significant enrichment of their predicted target genes was found among the genes higher expressed with increasing age. It is known that during normal ageing, lung function declines over time due to a variety of mechanisms and anatomic changes including smaller thoracic cavity, reduced respiratory muscle function and reduced mucus clearance [26].

Destruction and inability of bronchioles and lung tissue, in which inflammatory disorder plays a critical role, are the base of pathophysiology in COPD. T-cells and T-helper-17 cells demonstrate strong associations with inflammatory cascade in COPD, in which inflammatory cytokines are crucial in the early stage, such as TNF- α , IL-6 and Il-8, after the release of which the inflammatory cells are concentrated in the site of inflammation to mediate the immune response [3]. Chen et al. investigated the predicting value of miR-146a and miR-146b for acute exacerbation chronic obstructive pulmonary disease (AECOPD) and COPD, and to explore their associations with inflammatory cytokines in AECOPD and COPD patients [27]. It was shown that miR-146a and miR-146b were negatively correlated with inflammatory cytokines - TNF- α , IL-1 β , IL-6, Il-8 and LTE-4, and could be promising biomarkers for predicting the risk of AECOPD in stable COPD patients and healthy individuals.

Ding et al. by studying the miRNA expression patterns in COPD and different smoking status of Li and Han population found the expression of seven miRNAs in COPD of Li population [28]. In Han population there have only one miRNA (hsa-miR-196b-5p) were under-expressed in COPD patients.

By using next-generation sequencing Wang et al. studied the expression profiles of miRNAs in COPD patients [29]. For the study 20 representative COPD patients were separated into four groups based on increasing severity (A, B, C and D) and compared to 6 healthy controls. Compared to healthy controls 19 differentially expressed miRNAs were found in COPD patients. For all COPD groups, miR-3177-3p was down-regulated, while 17 miRNAs were up-regulated. The results revealed 21 differentially expressed miRNAs, of which miR-183-5p was continually down-regulated from A to B to D COPD groups. The authors found that four miRNAs (miR-106b-5p, miR-125a-5p, miR-183-5p and miR-100-5p) are significant for the development of COPD. The severity of COPD was attenuated by miR-106b-5p, thus suggesting this miRNA as potential target for COPD treatment.

It was demonstrated that levels of serum miR-218 were positively correlated with FEV/FVC% (forced expiratory volume in 1s/forced vital capacity) and were negatively correlated with levels of serum IL-6 or IL-8 [30]. In human bronchial epithelial cells, cigarette smoke extract reduced miR-218 expression, decreasing the inhibitory effect of miR-218 on TNFR1 (Tumor necrosis receptor 1), which resulted in enhanced NF- κ B signaling. It was concluded that in smoking-incuced COPD, miR-218, acting *via* TNFR1-mediated activation of NF- κ B, is involved in MUC5AC hyperproduction and inflammation [30]. These results reveal a mechanism for epigenetic modification by which smoking induced broncholitics, which is of practical value to control smoking-induced COPD.

The role of microRNA-218-5p in the pathogenesis of COPD was also studied by Song et al. [31]. A total of 40 COPD patients and 40 healthy controls were enrolled in this study. The COPD model of C57BL/6 mice was also developed by exposing them to cigarette smoke. The expression of miR-218-5p was detected by qRT-PCR in all the patients and mice. The serum level of IL-18 and TGF- β 1 was also detected via ELISA kit. The results showed that miR-218-5p was significantly down-regulated in patients with COPD, compared to normal subjects. There was a negative correlation between the plasma miR-218-5p level and the duration of disease with diagnosis of COPD ex-smokers. CS-induced COPD mice experiments with a miR-218-5p inhibitor demonstrated a protective role of miR-218-5p in cigarette smoke-induced inflammation and COPD. These data supported previously findings [30] that miR-218-5p play an important role in the pathogenesis of COPD.

FAIM2 (FAS apoptotic inhibitory molecule 2) has been reported to inhibit FAS-mediated the apoptosis of T-lymphocytes death which is believed to play a central role in the pathogenesis of COPD [32]. However almost nothing is known about the role of FAIM2 in T lymphocytes in the development of COPD. By bioinformatics prediction, FAIM2 was identified as a potential target of miR-322. Shen et al. carried out the experiments for identification the molecular involvement of

miR-3202 in the pathophysiology of COPD [33]. Level of miR-3202 in blood sample of non-smoker non-COPD (C), smoker without COPD (S), smoker with stable COPD (S-COPD) and smoker with acute exacerbation COPD (AE-COPD) was analyzed by qRT-PCR. Results showed that the miR-3202 was down-regulated in S,S-COPD and AE-COPD group when compared with C group. Decreased level of miR-3202 was also observed in cigarette smoke extract (CSE) treated T-cells. CSE stimulation increased INF-γ and TNF-α levels and FAIM expression whereas inhibited Fas and FasL expressions in T-lymphocytes. However, these effects were significantly suppressed by miR-3202 overexpression and enhanced by miR-3202 inhibitor. These results suggest that high level of miR-3202 in T lymphocytes may protect epithelial cells through targeting FAIM2. MiR-3202 might be used as a notable biomarker of COPD [33].

Recently Chatila et al. demonstrated substantial differences in miRnome of regulatory T (T_{reg}) cells, but not T_{eff} cells, between COPD and healthy controls [34]. The authors also shoen that miR-199a-5p is up-regulated in T_{reg} cells compared to T_{eff} cells, These findings suggest that the abnormal repression of miR-199a-5p in patients with COPD compared to unaffected smokers may be involved in modulating the adaptive immune balance in favour of a Th1 and Th17 response.

Gu et al. more recently studied the role of miR-195 in CS-induced COPD and demonstrated that miR-195 was significantly up-regulated in the lung tissues of patients with COPD compared to in never smokers [35]. miR-195 expression was also up-regulated in CS-exposed mice. A positive correlation was found between miR-195 and phosphorylation of Akt in lung tissues of COPD patients. By using publicly available databases (TargetScan and miRanda) these authors have identified PHLPP2, which is an essential phosphatase for the termination of Akt signaling and observed that inhibition of PHLPP2 enhanced Akt phosphorylation and increased IL-6 and TNF-α production in human airway bronchial epithelial cell line BEAS-2B cells, resembling the effects of miR-195 overexpression. These data demonstrate that miR-195 has a pathogenetic role in cigarette-induced COPD and regulate Akt phosphorylation by suppressing PHLPP2 expression and indicate that miR-195 is a potential therapeutic target for the treatment of cigarette-smoke induced COPD.

To analyze the miRNA expression profile in COPD, levels of serum miRNAs were profiled by qRT-PCR array system. In 20 COPD and 12 control patients were examined 72 miRNAs by qRT-PCR array. There was down-regulation of miR-20a,miR-28-3p, miR-34-5c and miR-100, and up-regulation of miR-7 compared with controls. The received results allowed to suggest that these miRNAs may have a role in COPD pathogenesis and may give clues for designing therapeutic strategy [36].

To perform a network analysis between miRNAs and mRNAs, the expression levels of miRNAs in COPD and control lung tissue samples Kim et al. carried out the integrative analysis of miRNAs. They showed that 11 miRNAs were down-regulated significantly and only one miRNA was up-regulated in the lung tissues of COPD subjects. The most significantly dysregulated miRNA in the lung tissue from COPD patients was miR-28-3p [37].

Down-regulation of the serum response factor/miR-1 axis in the quadriceps of patients with COPD was demonstrated by Lewis et al.. In this study they show that the expression of miRNAs is different in the quadriceps of patients with COPD than in control subjects. These results suggest that reduced activity of the serum response factor pathway contributes to COPD skeletal muscle dysfunction, in part by down-regulating miR-1 expression [38].

It is known that particulate matter (PM) is an aggravating risk factor of COPD exacerbation [39]. Fine particulate matter ($PM_{2.5}$) are the PM with a diameter of 2.5 μm or less. Once inhaled, $PM_{2.5}$ deposits in lung tissues inducing airway and systematic inflammation [40]. Animal experiments showed $PM_{2.5}$ accelerated lung inflammation and oxidative stress in COPD mice [41]. Recently Zhou et al. found that miR-194-3p was dramatically down-regulated in $PM_{2.5}$-cigarette smoke solution (CSS)-treated human bronchial epithelial cell cultures. Overexpression of miR-194-3p suppressed apoptosis in $PM_{2.5}$ - CSS-treated cells. These results suggested that miR-194-3p was a protective regulator involved in apoptosis pathway and a potential therapeutic target for a treatment of bronchial epithelial injury aggravation induced by $PM_{2.5}$ [42]. In order to screen COPD associated miRNAs, Zhou et al. in addition identified differentially expressed blood miRNA contrasting COPD participants without diagnose of COPD or related treatment before and matched control. The results showed that miR-495-3p and miR-223-5p significantly increased whereas, miR-194-3p decreased in

COPD patients. miR-194-3p was highly positive correlated with lung ventilation function during exposure of $PM_{2.5}$. These results clearly indicated that miR-194-3p might be a protective biomarker in $PM_{2.5}$-triggered pulmonary dysfunction such as COPD [43].

Recently Lin et. al demonstrated the role of miR-186 in relation to of hypoxia-induced factor 1α (HIF-1α) in the development and progression of COPD. After miR-186 transfection, the MRC-5 cells (human lung fibroblast cells) showed reduced proliferation and increased apoptosis. After overexpression of miR-186, they found that the HIF-1α expression level was reduced in MRC-5 cells. It was also demonstrated that miR-186 can affect apoptosis of inflammatory fibroblasts through the regulation of HIF-1α and affect the downstream signaling pathways. These data allowed to suggest that miR-186 contributes to the pathogenesis of COPD and that miR-186 is associated with HIF-1α expression in COPD [44].

It is well known that influenza A virus (IAV) infections lead to severe inflammation in the airways. Patients with COPD characteristically have exaggerated airway inflammation and a more susceptible to infections with severe symptoms and increased mortality [45]. The mechanisms that control inflammation during IAV infection and the mechanisms of immune dysregulation in COPD are unclear. It was shown that IAV infection increased the expression of miR-125a and miR-125b [46]. The authors show that A20 is a negative regulator of NF-κB-mediated induction of inflammatory but not antiviral cytokines and that A20 protein level were impaired in COPD. The impaired induction of A20 and antiviral responses in COPD were attributed to increased expression of miR-125a and miR-125b. It was suggested that A20 regulates NF-κB activation and subsequently the production of inflammatory cytokines.

CONCLUSION. Chronic obstructive pulmonary disease (COPD) is a global epidemic disease which is characterized by chronic inflammation of the lung parenchyma and peripheral airways. The pathogenesis of COPD involves many components, including hypersecretion of mucus, oxidative stress, inflammation in the airway and lungs. Cigarette smoke remains the key cause of COPD worldwide. In last decade has been made significant development in understanding the role of microRNAs in molecular mechanisms of pathogenesis of different diseases, including COPD. It was demonstrated that modulation of miRNAs via targeting various cellular and molecular pathways involved in COPD could contribute to the development of COPD. In Figure 1 we have summarized the cellular and molecular signaling pathways involved in pathogenesis of COPD with the participation of different miRNAs.

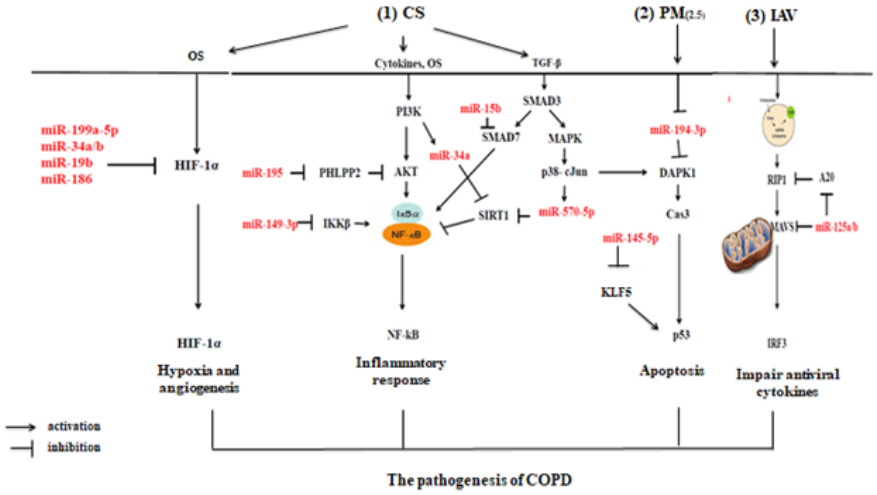

FIGURE 1 – **Cellular and molecular pathways involved in the pathogenesis of COPD. CS -Cigarette smoke, $PM_{2.5}$ - particulate matter, OS - oxidative stress, IAV - Influenza A virus are factors of COPD. TGF-β – transforming grows factors – β, HIF-1 α -hypoxia-induced factor 1α, PI3k-Phosphoinositide 3-kinase, AKT- actin, PHLPP2- PH Domain And Leucine Rich Repeat Protein Phosphatase 2, NF-kB- nuclear factor kappa B, IKK β - inhibitor of nuclear factor kappa Bkinase subunit beta, SMAD 3/7 - Similar to Mothers Against Decapentaplegic 3/7, MAPK - mitogen-activated protein kinase, SIRT1 – sirtuin 1, DAPK- death-associated protein kinase 1, Cas-3- caspase3. The miRNAs in red.**

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Роль микроРНК в развитии хронической обструктивной болезни легких

Аңдатпа Хроническая обструктивная болезнь легких (ХОБЛ) - хроническое легочное заболевание со сложным патогенезом, характеризующееся необратимой и прогрессирующей бронхиальной обструкцией. Важную роль в развитии болезни играют генетическая предрасположенность и факторы окружающей среды. Хотя патогенез ХОБЛ в настоящее время еще недостаточно изучен, известно, что значимый вклад в ее возникновение вносят окислительный стресс, дисбаланс системы протеолиза/антипротеолиза, дисфункция иммунной системы, нарушение репарации легких и апоптоза. В представленном обзоре мы суммировали сведения о различных молекулярных и клеточных механизмах, вовлеченных в воспаление и играющих ключевую роль в патогенезе ХОБЛ. Особое внимание уделено роли микроРНК в развитии ХОБЛ. Рассматривается возможность использования микроРНК в качестве новых биомаркеров и терапевтических инструментов для диагностики и лечения ХОБЛ.

Ключевые слова: микроРНК, хроническая обструктивная болезнь легких, биомаркеры, сигнальные пути.

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Өкпенің созылмалы обструктивті ауруының дамуындағы микроРНК-ның рөлі

Аннотация: Өкпенің созылмалы обструктивті ауруы (СОӨА) - қайтымсыз және үдемелі бронхиалды обструкциямен сипатталатын күрделі патогенезі бар созылмалы өкпе ауруы. Аурудың дамуында генетикалық бейімділік пен қоршаған ортаның факторлары маңызды рөл атқарады. СОӨА патогенезі қазіргі уақытта әлі жеткілікті зерттелмеген болса да, оның пайда болуына тотығу стресс, протеолиз/антипротеолиз жүйесінің дисбалансы, иммундық жүйенің дисфункциясы, өкпенің репарациясы мен апоптоздың бұзылуы елеулі үлес қосатыны белгілі. Ұсынылған шолуда қабынуға қатысатын және ӨСОА патогенезінде негізгі рөл атқаратын әртүрлі молекулалық және жасушалық механизмдер туралы мәліметтер жинақталған. Соның ішінде, ӨСОА дамуындағы микроРНҚ рөліне ерекше назар аударылды. ӨСОА диагностикалау және емдеу үшін ықтимал биомаркерлер мен терапевтік құралдар ретінде микроРНҚ-ны пайдалану мүмкіндігі қарастырылған.

Түйін сөздер: микроРНҚ, өкпенің созылмалы обструктивті ауруы, биомаркер, сигналдық жолдар.

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