**SUPPLEMENTARY TABLE 2∣**Common Chinese formulas and herbs with possible mechanisms or effects that protect COPD patients from developing lung cancer

|  |  |  |
| --- | --- | --- |
| TCM name | Main Components | Possible Mechanisms or Effects |
| *Fritillaria thunbergii*  Zhe-Bei-Mu 浙貝母 | Peimine, Peiminine | Trigger G0/G1 phase arrest and increase apoptosis by enhancing caspase-3 expression and reducing microvessel density in tumor tissues of lung cancer models [1].  Suppress the inflammatory response by mediating the expression of proinflammatory cytokines, including IL-1β, IL-6, IL-8, TNF-α, NF-κB, and their mediators TGF-β1, MMP-9, and TIMP-1 in lung tissues of COPD rat models [2]. |
| *Prunus armeniaca*  Xing-Ren杏仁 | Amygdalin, Emulsin | Inhibit quorum sensing in *Pseudomonas aeruginosa* culture and thus combat pulmonary infection [3]. |
| *Platycodon grandiflorus*  Jie-Gen桔梗 | Polygalacic, Platycodigenin, Platycoside C, Prosapogenin | Activate NK cells and decrease metastasis by inhibiting the adhesion of lung tumor cells to the basement membrane [4].  Promote cancer cell autophagy and regulate intracellular signaling to reduce proliferation in A549 cells [5]. |
| *Scutellaria baicalensis*  Huang-Qin黃芩 | Baicalin, Baicalein | Regulate the PI3K/AKT/NF-κB pathway to decrease airway remodeling in inflamed COPD models [6].  Induce cell cycle arrest and decrease free radicals and inflammatory cytokine expression [7]. |
| *Ophiopogon japonicus*  Mai-Men-Dong 麥門冬 | Methylophiopogonanone, ophiopogonin, ophiopogonanone | Block NF-κB and STAT3 signaling pathways to trigger cell apoptosis [8] and suppress oncogenic gene expression [9]. |
| *Houttuynia cordata*  Yu-Xing-Cao 魚腥草 | decanoyl acetaldehyde, lauric aldehyde, afzelin, hyperin, quercitrin | Inhibit lung inflammatory response in a mouse model of LPS-induced acute lung injury [10].  Anti-inflammatory effects via the suppression of the TLR4/NF-κB pathway in a rat model of COPD induced by cigarette smoke and LPS [11]. |
| *Salvia miltiorrhiza*  Dan-Shen 丹參 | Tanshinone IIA | Reduce the area of collagen deposition in bleomycin-induced pulmonary fibrosis and inhibit TGF-β1-triggered alveolar EMT in rat models [12, 13]. |
| *Glycyrrhiza uralensis*  Gan-Cao 甘草 | liquiritin apioside, liquiritin | Decrease proinflammatory cytokines such as IL-1β and TNF-α as well as suppress the expression of COX-2 and iNOS to reduce ALI in a mouse model of LPS-induced ALI [14]. |
| *Tussilago farfara*  Kuan-Dong-Hua 款冬花 | Tussilagone, Faradiol, Armiliot | Inhibit the production of mucin protein and downregulate mucin gene expression in airway epithelial cells via the NF-κB signaling pathway [15]. |
| *Magnolia officinalis*  Hou-Po 厚朴 | Honokiol, Magnolol | Antitumor effects include inducing cell apoptosis, anti-inflammatory and anti-oxidative mechanisms in NSCLC cells [16]. |
| Xiao Qing Long Tang  小青龍湯 | *Ephedra sinica, Paeonia lactiflora, Cinnamomum cassia, Glycyrrhiza uralensis,*  *Pinellia ternata, Zingiber officinale, Asarum sieboldii, Schisandra chinensis* | Induction of apoptosis in NSCLC cells [17].  Inhibition of proinflammatory cytokines via the NF-kB pathway [18].  Decrease serum concentrations of proinflammatory cytokines such as IL-4, IL-8, and TNF-α [19]. |
| Zhi Sou San  止嗽散 | *Platycodon grandifloras, Schizonepeta tenuifolia, Aster tataricus, Stemona sessilifolia, Cynanchum stauntonii*  *Glycyrrhiza uralensis, Citrus reticulata* | In a rat model: inhibit lung inflammation, increase expression of aquaporins, and decrease Muc5AC expression in lung [20]. |
| Mai Men Dong Tang  麥門冬湯 | *Ophiopogon japonicus, Pinellia ternata, Panax ginseng, Glycyrrhiza uralensis, Oryza sativa, Ziziphus jujuba* | Attenuates airway hyper-responsiveness and has bronchodilatory effects by relaxing bronchial smooth muscle and increasing cAMP [21, 22]. |
| Ma Xing Gan Shi Tang  麻杏甘石湯 | *Ephedra sinica, Prunus armeniaca,  Glycyrrhiza uralensis, Aqueous calcium sulfate* | Decrease IL-4, IL-8, and TNF-α in rats with COPD [23] and regulate the oxidative/antioxidative balance in bronchial and alveolar epithelium of COPD rats through deceasing the expression of r-GCS and NF-kB [24].  Relieve the bronchial contraction induced by acetylcholine/histamine [25]. |
| Ding Chuan Tang  定喘湯 | *Ginkgo biloba, Ephedra sinica, Tussilago farfara, Morus alba, Pinellia ternata, Perilla frutescens, Prunus armeniaca, Scutellaria baicalensis, Glycyrrhiza uralensis* | Suppression of inflammation through regulating IRAK/NF-κB, IRAK/AP-1 and TBK1/IRF3 pathways in lipopolysaccharide-stimulated macrophages [26]. |
| Bai He Gu Jin Tang  百合固金湯 | *Rehmannia glutinosa (dried), Rehmannia glutinosa (processed), Ophiopogon japonicus, Lilium albanicum, Paeonia lactiflora, Angelica sinensis, Fritillaria thunbergii, Glycyrrhiza uralensis, Scrophularia ningpoensis, Platycodon grandiflorus* | Improve FEV1/FVC [27] and decrease levels of IL-2 and IL-6 in tuberculosis [28]. |
| Xin Yi Qing Fei Tang  辛夷清肺湯 | *Magnolia biondii, Scutellaria baicalensis, Gardenia jasminoides, Ophiopogon japonicus, Lilium albanicum, Aqueous calcium sulfate, Anemarrhena asphodeloides, Glycyrrhiza uralensis, Eriobotrya japonica, Cimicifuga heracleifolia* | Antibacterial effects against *Streptococcus pneumonia* [29]. |
| Qing Zao Jiu Fei Tang  清燥救肺湯 | *Morus alba (leaf), Aqueous calcium sulfate, Glycyrrhiza uralensis, Sesamum indicum, Asini Corii Collas, Panax ginseng, Ophiopogon japonicus, Prunus armeniaca, Eriobotrya japonica* | Promote INF-γ and AQP5 protein expression, and decrease TNF-α expression after *Mycoplasma pneumoniae* infection in mice [30]. |
| Qing Fei Tang  清肺湯 | *Glycyrrhiza uralensis, Scutellaria baicalensis, Platycodon grandiflorus,*  *Poria, Citrus reticulata, Angelica sinensis,*  *Fritillaria thunbergii, Morus alba, Asparagus cochinchinensis, Gardenia jasminoides, Prunus armeniaca,*  *Ophiopogon japonicus, Schisandra chinensis, Zingiber officinale, Ziziphus jujuba, Bambusa tuldoides* | Enhance the defense mechanism of the lower airway in pneumonia [31] through increasing ciliary beat frequency in mouse ciliary cells [32]. |
| Xin Yi San  辛夷散 | *Ligusticum striatum, Akebia quinata,*  *Cimicifuga foetida, Angelica dahurica,*  *Glycyrrhiza uralensis, Saposhnikovia divaricata, Magnolia biondii,*  *Asarum sieboldii, Ligusticum sinense, Camellia sinensis* | Suppress serum IgE levels and increase production of IL-10, soluble intercellular adhesion molecule-1 and IL-8 in allergic rhinitis [33]. |

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