was modified by additional use of other anti-diabetic medications, BMI or HbA1c. **Results** 14,292 cases and 54,529 controls were included. Metformin was associated with 24% reduced odds of an exacerbation, its effect remained up to 180 days after the prescription date (OR=0.76, 95%CI 0.64–0.88) but there was no effect >180 days after metformin use (p>0.05). Using GLP-1 agonists with metformin had a multiplicative effect, associated with a 72% reduction in odds of an exacerbation (with GLP-1: OR=0.28, 95%CI 0.11–0.75). BMI, HbA1c and other anti-diabetic medications (DDP-4 and SGLT-2 inhibitors, sulfonylureas and insulin) were not found to influence the effect of metformin on exacerbations.

**Conclusion** Metformin reduces the risk of COPD exacerbations, but its mechanism may not be through improved systemic glycemic control or weight loss. The concurrent use of GLP-1 receptor agonists augments the effect of metformin, other anti-diabetic medication does not. Diabetes is common in COPD and metformin is relatively cheap, early use may prevent exacerbations.

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**P206 IDENTIFICATION OF NOVEL SENOLYTIC CANDIDATES FOR THE TREATMENT OF CHRONIC RESPIRATORY DISEASES WITH ACCELERATING AGING**

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**Background** Cellular senescence is a process that induces cells into a state of irreversible replicative arrest, whereby they are apoptosis-resistant, and release inflammatory mediators known as the senescence-associated secretory phenotype (SASP). Cellular senescence and the SASP potentially have a significant influence on the process of ageing and pathologies of accelerated premature-aging related chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). Senolytic agents, capable of selectively killing senescent cells by inducing apoptosis, could potentially have major implications for treating the senescence-driven accelerated ageing pathology found in COPD and IPF. The aim of this project is to identify a new class of senolytic agents.

**Methods** Compounds (0.1 and 10μM) from an FDA-approved chemical library (700 compounds) were treated 2 days after etoposide (1μM)-treated or untreated airway epithelial cells, BEAS-2B. The resazurin cell viability assay was conducted 2-days post-treatment and the ability of the compounds to eliminate senescent cells was assessed. Positive candidates were treated in double hit etoposide senescent BEAS-2B. Senescence markers p21WAF1/CIP1 and p16INK4A expression (western blotting) and positive Senescence-Associated-b-Galactosidase (SA-b-Gal) staining were assessed. SASP marker PAI (Plasminogen Activator Inhibitor)-1 was detected in supernatant using ELISA.

**Results** Single treatment with etoposide was confirmed to induce cellular senescence characterized by an increase in SA-b-Gal staining, p16INK4A and p21WAF1/CIP1 expression. After high throughput screening with this cell model, we identified 6 candidates to be able to eliminate senescent cells, but not healthy cells. Further validation revealed that Dipyridamole (DP) showed decrease in p21WAF1/CIP1 expression by 20.5% compared to etoposide control (p>0.05, n=4), where a well-established senolytic cocktail (a combination of Dasatinib and Quercetin) reduced p21WAF1/CIP1 by 27.6%. DP and Amlodipine (AL) also reduced the proportion of SA-b-Gal positive cells by 15.5% and 31.5%, respectively, compared to etoposide control. Etoposide-induced PAI-1 release was also reduced by those candidates (p>0.05) as well as DQ (57.0% reduction).

**Conclusion** DP and AL showed some potentials as senolytic agents. Further studies using primary cells obtained from patients with COPD or IPF are needed for full validation.

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**P207 SENOLYTIC EFFECTS OF TELAGLENASTAT, A GLUTAMINASE INHIBITOR, ON SENESCENT AIRWAY EPITHELIAL CELLS**

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**Background** COPD is characterized by pulmonary inflammation and accelerated lung aging, where elevated number of senescent cells are observed. Senescent cells may prevent lung repair and drive chronic lung inflammation. Telaglenastat, a non-competitive glutaminase inhibitor, is recently reported as a potential senolytic agent which removes senescent cells (Johmura et al., Science, 2021).

**Aim** Investigate the senolytic effects of Telaglenastat on airway epithelial cells.

**Methods** Immortalised bronchial epithelial cell line, BEAS-2B cells, were treated with known senescence inducer etoposide...