



REPORT FROM

# ERS International Congress 2022

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## A sticky note on a “sticky” matter

**When attending different** sessions on obstructive lung diseases and their treatment on the first day of the ERS conference, a hot topic of scientific interest and clinical relevance literally “stuck” to my attention: MUCUS! There was a huge focus on this sticky matter - a very much justified focus given the role of mucus both in pathogenesis and pathology, but also in the perceived disease burden of patients. Here is a “sticky note” of facts related to mucus in COPD and asthma;

- Mucus is not only a mere symptom of asthma and COPD - it is part of the pathology and massively influences the microbiome of the airways. This can lead to more viral exacerbations and pneumonias.
- Mucus causes cough, but cough can appear without mucus.
- Type 2 inflammation and its features of increased Mucin of type Muc5a, and substance-release by eosinophils, will not only cause the formation of mucus plugs, but also Charcot Leyden crystals which stick out of the mucus plug, attaching it to the airway wall like a piece of barbed wire.
- Mucus plugs in asthma are mainly found in the distal lobes of the lungs (51.7% of all plugs are found distally).
- Mucin in phlegm positively correlates with severity of COPD.
- Mucus hypersecretion is correlated with faster decline in lung function. Mucus plugs increase the likelihood for air trapping and lower FEV1%-predicted.
- The mucus phenotype is regarded as treatable trait in asthma.
- Problems caused by mucus can be addressed by smoking cessation, physiotherapy, azithromycin, CFTR and ENaC modulators, and mucolytics such as N-acetylcystein and hypertonic saline.
- More treatments are currently investigated targeting mucus and mucus plugs, such as monoclonal antibodies against Galectin-10 “digesting” Charcot Leyden crystals and with this, mobilizing mucus plugs; drugs targeting the Notch pathway directed against Jagged-1 and 2; drugs targeting CFTR, and more...



We also can look forward understanding more about the function of a newly discovered cell type in the airway epithelium, the Respiratory airway secretory cell (RASC; Basil et al., Nature 2022).



**Barbara Fuchs**  
Medical Manager, Nordics

## SENTINEL Project: Implementation of a maintenance and reliever treatment algorithm into practice in Hull, UK.

**At the Sunday session** “*Implementing asthma guidelines for better care of patients and planet*”, the many challenges related to SABA overuse were addressed. Of particular interest was Michael Crooks’ presentation on the SENTINEL project (SABA reduction through implementing Hull asthma guidelines) in Hull, UK. Crooks started out presenting data clearly showing the association between SABA over-reliance and the risk of exacerbations.



He pointed to the feature of SABA being a bronchodilator that effectively eases symptoms as a key driver of the challenge in changing behaviour patterns when it comes to the use of SABA as reliever. Importantly, Crooks showed evidence for SABA not being an effective treatment of the disease. In contrast SABA usage is associated with uncontrolled asthma. Data shows that Salbutamol inhalation is associated with an increase in FeNO levels, indicating no reduction in inflammation. Furthermore, Crooks pointed to another important aspect, that uncontrolled asthma correlates to harmful environmental impact. The SENTINEL project has revealed that poorly controlled asthma is associated with 3.1-fold higher per capita green-

house gas (GHG) emissions than well-controlled asthma. Moreover, SABA relievers are associated with 60% of the per capita GHG emissions from the healthcare sector, with smaller contributions from other pharmacotherapies, routine health care resource utilisation and exacerbations. Crooks discussed the paradox of SABA over-reliance considering the updated GINA guideline as well as local guidelines, where ICS/LABA is recommended as the preferred reliever therapy following the MART principle. It appears obvious that we are facing a challenge in the implementation of the guidelines.

As a measure to overcome this, the SENTINEL project has developed an implementation-ready intervention to identify and address SABA over-reliance in asthma through supported guideline implementation where the two main aims are **1)** To improve the outcomes for adult asthma patients and **2)** To reduce the environmental impact of adult asthma management. The project is ongoing, but preliminary data already suggest marked reductions in SABA prescriptions post implementation. By May 2022, SENTINEL achieved 27 609 fewer SABA inhalers used for the treatment of asthma, equivalent to a saving of 733 metric tonnes of eCO<sub>2</sub> and 966 transatlantic flights from Leeds to New York. It will be very interesting to follow the SENTINEL project also on results linked to the clinical outcomes for asthma patients.



**Ingvild Bjellmo Johnsen**

Medical Advisor, Norway

## GETomics: integrating the time axis in our understanding of chronic obstructive pulmonary disease

**At the session** on “Airway diseases”, I listened to a very interesting presentation on a topic that was new for me; GETomics: integrating the time axis in our understanding of chronic obstructive pulmonary disease. The presentation was held by professor Alvar Agusti Garcia-Navarro.



He started by saying that GETomics gives us new perspective in understanding airway disease or all human diseases in general: they have previously been explained by gene-environment interactions, but Alvar means that we have been missing an important factor and that is “time”. His gave a recent example – COVID 19. Many children which catch COVID do not have any serious symptoms, whilst the same virus can make older people very sick or even cause death. So, what is the difference? The different is time since the virus is the same and the genes amongst humans are almost the same.

This theory has been applied to airway diseases where it has been shown that as you grow older and more negative factors appear, this is leading to poor lung function. This can depend on different environmental encounters. These encounters lead to biological responses, and these responses in turn build on the previous responses; thus, the same interaction at different ages may have different outcomes. This can be applied to COPD: Most of us are born with a normal lung function and it develops normally throughout life, but if you for example smoke you can develop COPD. People that are born prematurely also may develop COPD-like symptoms, a concept called the “trajectome”. He thinks therefore that it is very important to measure lung parameters at an early age to prevent (too) late diagnosis.

Suggested reading: Agustí A, Melén E, DeMeo DL et al., Pathogenesis of chronic obstructive pulmonary disease: understanding the contributions of gene-environment interactions across the lifespan. *Lancet Respir Med.* 2022 May;10(5):512-524.



**Jenny Johansson**

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## Searching for new classes of bronchodilators – a sneak peek into the future of inhalation therapy in Asthma and COPD!

**Bronchodilators** are unquestionably important compounds in the treatment of bronchoconstriction seen in the airway smooth muscle of asthma and COPD patients. Currently, two main classes of bronchodilators (beta 2-agonists (LABA) and anticholinergics (LAMA)) are used in various inhalers treating bronchoconstriction. At this year's ERS, Professor Mario Cazzola, took us on a journey to see what we can expect of the coming years on these matters.

*But why have an interest in novel bronchodilators?*

Because bronchodilators are fundamentally important in the treatment of asthma and COPD! Thus, a potential improvement in treatment alternatives and safety profiles must be explored!

Currently, at least eight new classes of bronchodilators are in development

- Bitter taste receptor (TAS2R) agonists
- E-prostanoid receptor 4 (EP4) agonists
- Rho kinase inhibitors
- Calcilytics
- Peroxisome proliferator-activated-receptor- $\gamma$  (PPAR- $\gamma$ ) agonists
- Relaxin family peptide receptor 1 (RXFP1) agonists
- Soluble guanylyl cyclase (sGC) activators
- Pepducins

The future will show which classes will be developed for clinical use, whether they will replace or supplement existing bronchodilators. Here, it is worth highlighting the established synergistic effects of LABA/LAMA.

Suggested reading: Cazzola et al, Arch Bronconeumol. 2022 Feb;58(2):107-108. doi:10.1016/j.arbres.2021.06.005. Epub 2021 Jun 18.

**Stay tuned!**



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