SHAREABLE PDF

Eight novel variants in the *SLC34A2* gene in pulmonary alveolar microlithiasis

Åsa Lina M. Jönsson[1], Elisabeth Bendstrup[2], Susie Mogensen[1], Elizabeth J. Kopras[3], Francis X. McCormack[3], Ilaria Campo[4], Francesca Mariani[4], Amparo Escribano-Montaner[5], Are M. Holm[6], Maria del Mar Martinez-Colls[7], Guillem Pintos-Morell[7,8,9], Camille Taillé[10], Bruno Crestani[10], Ole Hilberg[2,11], Jane Hvarregaard Christensen[1,12] and Ulf Simonsen[1,12]

Affiliations: [1]Dept of Biomedicine, Aarhus University, Aarhus, Denmark. [2]Dept of Respiratory Diseases and Allergy, Aarhus University Hospital, Aarhus, Denmark. [3]Division of Pulmonary, Critical Care and Sleep Medicine, University of Cincinnati, Cincinnati, OH, USA. [4]Pneumology unit, IRCCS San Matteo Hospital Foundation, Pavia, Italy. [5]Pediatric Pneumology Unit, Clinic University Hospital, Dept of Pediatrics, Obstetrics and Gynecology, University of Valencia, Valencia, Spain. [6]Dept of Respiratory Medicine, Oslo University Hospital, Oslo, Norway. [7]Dept of Pediatrics, University Hospital Germans Trias i Pujol, Badalona, Spain. [8]Centre for Rare Diseases, University Hospital Vall d'Hebron, Barcelona, Spain. [9]Research Institute IGTP, CIBERER-GCV08, Universitat Autònoma de Barcelona, Barcelona, Spain. [10]APHP, Hopital Bichat, DHU FIRE, Pulmonology Dept, Reference Center for Rare Pulmonary Diseases, Unité Inserm 1152, Université Paris Diderot, Paris, France. [11]Medical Dept, Vejle Hospital, Vejle, Denmark. [12]Shared senior authorship.

Correspondence: Åsa Lina M. Jönsson, Dept of Biomedicine, Aarhus University, Bartholins Allé 6, Building 1242, 3rd Floor, 8000 Aarhus C, Denmark. E-mail: aasajoen@rm.dk

@ERSpublications
Eight novel variants in the *SLC34A2* gene have been identified in 14 patients with pulmonary alveolar microlithiasis (PAM), which emphasises the importance of the gene in the disease. Furthermore, a genotype–phenotype correlation in PAM may exist. http://bit.ly/3307M1p

Cite this article as: Jönsson ÅLM, Bendstrup E, Mogensen S, *et al*. Eight novel variants in the *SLC34A2* gene in pulmonary alveolar microlithiasis. *Eur Respir J* 2020; 55: 1900806 [https://doi.org/10.1183/13993003.00806-2019].

ABSTRACT

Background: Pulmonary alveolar microlithiasis (PAM) is caused by genetic variants in the *SLC34A2* gene, which encodes the sodium-dependent phosphate transport protein 2B (NaPi-2b). PAM is characterised by deposition of calcium phosphate concretions (microliths) in the alveoli leading to pulmonary dysfunction. The variant spectrum of *SLC34A2* has not been well investigated and it is not yet known whether a genotype–phenotype correlation exists.

Methods: We collected DNA from 14 patients with PAM and four relatives, and analysed the coding regions of *SLC34A2* by direct DNA sequencing. To determine the phenotype characteristics, clinical data were collected and a severity score was created for each variant, based on type and localisation within the protein.

Results: We identified eight novel allelic variants of *SLC34A2* in 14 patients with PAM. Four of these were nonsense variants, three were missense and one was a splice site variant. One patient was heterozygous for two different variants and all other patients were homozygous. Four patients were asymptomatic and 10 patients were symptomatic. The severity of the disease was associated with the variant severity.

Conclusions: Our findings support a significant role for *SLC34A2* in PAM and expand the variant spectrum of the disease. Thus, *SLC34A2* variants were detected in all patients and eight novel allelic variants were discovered. An association between disease severity and the severity of the variants was found; however, this needs to be investigated in larger patient populations.