**Methods**

**ELISA assays for CCSP and IL-8 proteins in blood and BAL.**

Blood and BAL samples collected at the time of bronchoscopy (1, 3, 6, and 12 months post transplant) were processed for CCSP and IL-8 analysis within 24hrs of collection. Plasma from blood was obtained after standard Ficoll-Paque (GE Healthcare Bio-Sciences, Uppsala, Sweden) and density gradient separation and BAL supernatant was collected following centrifugation (1000 g, 15 minutes). Commercial ELISA kits were utilized for protein quantitation of both CCSP (BioVendor, Modrice, Czech Republic) and IL-8 (BD Biosciences, CA, USA) in plasma and BAL supernatant according to manufacturer’s instructions (appropriately diluted samples were applied to specifically coated assay plates which enabled bound CCSP or IL-8 to be identified and quantified using a biotin-streptavidin colorimetric assay).

**CCSP Immunohistochemistry and quantitation**

Transbronchial biopsies (TBBx) obtained during flexible bronchoscopy performed under local anesthesia were fixed in Neutral Buffer Formaldehyde 4%, and paraffin embedded. Serial sections of the tissue were stained using an automated stainer for the CCSP protein using a rabbit polyclonal antibody (1:10,000 dilution; BioVendor, Modrice, Czech Republic). An image analyzer (Image ProPlus, Mediacybernetics, Bethesda, MD, USA) coupled to a CCD camera (Sony DXC950P, Tokyo, Japan) mounted on a light microscope (Olympus) was used for biopsy assessment. Morphometric analysis and manual cell counts of stained / non stained cells enabled assessments of epithelial thickness, epithelial area, percentage of stained cells and percentage of epithelial stained area to be made. CCSP quantitation data were corrected for epithelial thickness to take into account the airway level sampling artefact according to previously demonstrated differences in normal human airways.
Single Nucleotide Polymorphism (SNP)

Genomic DNA from both donor and recipient blood (at the time of transplantation) was isolated using a DNA extraction kit (Qiagen, Hilden, Germany). Specific PCR amplification of the CCSP 5’ untranslated region of exon 1 gene was achieved as follows: 100 ng genomic DNA was added to a Universal PCR master mix containing 10 µM of each primer 5’-TCTGGGTGCTGCTGCTA-3’ and 5’-CTGCAGCAGAGAGCCAGTG-3’(28). An aliquot of the PCR product is then loaded on a 2% agarose gel for confirmation of the 258 bp band. The PCR product is subsequently digested using restriction enzyme Sau96I, yielding two fragments 130 bp and 128 bp, digestion products were visualised on 2% agarose gel allowing for A38G polymorphism assessment according to previously published reports (1).

**SDC Figure 1.** Consecutive BAL CCSP concentrations according to A38G polymorphism. A log scale Y axis was used to help for graphical representation. Data are mean ± SEM.
SDC Figure 2a. CCSP positive epithelial cells proportions (as a percentage of epithelial cells) in TBBx obtained in LTR at 1 and 3 months post transplantation according to BOS (5a) then according to A38G polymorphism in LTR (5b). Each line is individual data.
**SDC Figure 2b.** CCSP positive epithelial cells proportions (as a percentage of epithelial cells) in TBBx obtained in LTR at 1 and 3 months post transplantation according to BOS (5a) then according to A38G polymorphism in LTR (5b). Each line is individual data.