




Pathological mucus and impaired mucus clearance in cystic fibrosis patients result from increased concentration, not altered pH

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Over length scales greater than the mesh size of the mucin polymeric network of mucus, concentration, and not pH, dominates the physical properties of mucus that are associated with cystic fibrosis airways disease <http://ow.ly/K92u30m2RDC>

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ABSTRACT Cystic fibrosis (CF) is a recessive genetic disease that is characterised by airway mucus plugging and reduced mucus clearance. There are currently alternative hypotheses that attempt to describe the abnormally viscous and elastic mucus that is a hallmark of CF airways disease, including: 1) loss of CF transmembrane regulator (CFTR)-dependent airway surface volume (water) secretion, producing mucus hyperconcentration-dependent increased viscosity, and 2) impaired bicarbonate secretion by CFTR, producing acidification of airway surfaces and increased mucus viscosity.

A series of experiments was conducted to determine the contributions of mucus concentration *versus* pH to the rheological properties of airway mucus across length scales from the nanoscopic to macroscopic.

For length scales greater than the nanoscopic, *i.e.* those relevant to mucociliary clearance, the effect of mucus concentration dominated over the effect of airway acidification.

Mucus hydration and chemical reduction of disulfide bonds that connect mucin monomers are more promising therapeutic approaches than alkalinisation.