404 Are there any sex differences in lung function of CFTR – knock out mice?

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Cystic fibrosis is the most prevalent lethal autosomal recessive disorder in Caucasians. Various organs are affected; however, death commonly results from progressive lung disease. We studied lung function (Reinhard, Mamm. Genome 2002) in 14 week old Cftrtm1HGU mice (–/– and +/–) and non-CF controls (+/+, Charles River, UK) raised under SPF-conditions so that the animals had no bacterial colonization of the lungs. There was no effect on body weight (bw)in cftr mice when compared to wt, but bw were about 30% higher in male mice (29.5±3 g vs. 22±2 g in –/– mice). Despite these differences in bw, total lung capacity (TLC), as an index for lung size, was comparable between sexes (1.3±0.1 and 1.18±0.1 ml in ♂ and ♀ –/– mice) indicating that specific TLC is higher in ♀. Both sexes of the cftr mutants exhibited a little smaller TLC than wild types (<5%, ns). Series dead space volume was not affected by the mutation (0.23±0.01 ml and 0.22±0.01 ml in ♂ + ♀ –/– mice). Compliance values of the lung tended to be smaller in mutants (e.g., in ♀: 57±7 µl/cmH_2O in –/–, 64±11 µl/cmH_2O in +/– and 71±16 µl/ cmH_2O in +/+ mice), but differences failed to be statistically significant. Gas exchange, assessed by pulmonary diffusing capacity for carbon monoxide, showed no genotype specific differences but significant sex differences in cftr mice (15±1.6 µmol/min/hPa and 12±1.5 µmol/min/hPa in ♂ and ♀ –/– mice). In summary, respiratory function exhibits distinct sex specific differences in mutants but genotype specific sig. differences were not detectable in uninfected 14 week old mice. There may be trend for deviation from reference values from control suggesting that a limited lung function may develop with age.

405 Water mobility by 3D-MR imaging in normal and CFTR KO mouse trachea

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The content and water (H_2O) mobility in airway epithelium is tighly coupled to airway function. In cystic fibrosis (CF), H_2O epithelial permeability is reduced in airways. The demand of noninvasively imaging techniques with high spatial resolution potential is rising because such imaging tools would expedite anatomical and functional phenotyping in the genetically altered mice. Magnetic resonance microscopy (MRM) is a noninvasive, inherently three-dimensional (3D) imaging technique capable of visualizing anatomical structures in the mouse and allows for interpretation of complex spatial relationships between substructures and H_2O. In this study, we explore different MR contrast parameters and signal-to-noise ratios at a 30 µm pixel size to characterize microstructure and H_2O mobility in ex vivo trachea of CF transmembrane conductance regulator (CFTR)-deficient (CFTR knockout, Cftr tm1UNC) mice and their aged-matched WT littermates. This study is performed using a Bruker MRM system at 11.7 tesla. We demonstrate for the first time the ability of 3D-MRM to map the H_2O content and mobility in trachea epithelium. From the 3D-MRM video-images, differential H_2O content was visualized in different levels of trachea in WT and CF mice. T2 MRM images depicting the H_2O rotational mobility which is related to environmental viscosity of trachea epithelium will be shown. Finally, this 3D-MRM imaging method is a valuable method for measuring H_2O permeability in airways and can serve for assessing the effects of drugs on H_2O mobility in CF airways.

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