primary studies - published, non RCT

Airway epithelial CFTR mRNA expression in cystic fibrosis patients after repetitive administration of a recombinant adenovirus.

Code: PM10545523 **Year:** 1999 **Date:** 1999 **Author:** Harvey BG

Participants

7 pairs of individuals with CF

Interventions

Ad(GV)CFTR.10 at doses of 3 x 10(6) to 2 x 10(9) plaque-forming units over 9 months by endobronchial spray

Outcome measures

Each 3-month cycle, we measured vector-derived versus endogenous CFTR mRNA in airway epithelial cells prior to therapy, as well as 3 and 30 days after therapy.

Main results

The data demonstrate that (a) this strategy appears to be safe; (b) after the first administration, vector-derived CFTR cDNA expression in the CF airway epithelium is dose-dependent, with greater than 5% endogenous CFTR mRNA levels at the higher vector doses; (c) expression is transient, lasting less than 30 days; (d) expression can be achieved with a second administration, but only at intermediate doses, and no expression is observed with the third administration; and (e) the progressive lack of expression with repetitive administration does not closely correlate with induction of systemic anti-Ad neutralizing antibodies.

Authors' conclusions

The major advantage of an Ad vector is that it can deliver sufficient levels of CFTR cDNA to the airway epithelium so that CFTR expression protects the lungs from the respiratory manifestations of CF. However, this impressive level of expression is linked to the challenging fact that expression is limited in time. Although this can be initially overcome by repetitive administration, unknown mechanisms eventually limit this strategy, and further repetitive administration does not lead to repetitive expression.

http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/767/CN-00462767/frame.html

See also

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Keywords

pharmacological_intervention; Recombinant Proteins; Gene Transfer Techniques; non pharmacological intervention - genetic& reprod;