

Nanoparticle Transport in Cystic Fibrosis (CF) Mucus by Multiple Particle Tracking (MPT)

Rationale

Optimization of physicochemical properties to allow rapid transport of gene carriers through mucosal barrier should make gene therapy more feasible for CF.

Methods

Trajectories of 100's of fluorescently-labeled polystyrene beads (100, 200, and 500 nm) embedded in CF sputum were recorded using a SIT camera mounted on an epifluorescence microscope. Positional data was converted to mean squared displacements (MSDs) and transport properties were calculated using the Stokes-Einstein relationship.

Results

Majority of particle diffusivities were more than 1000-fold less than theoretical diffusivities in water and slopes of the MSDs vs. time were < 1 , indicating transport of individual beads in CF mucus is primarily sub-diffusive. Sub-diffusive behavior may indicate the binding or trapping of particles by obstacles, such as mucin fibers. These obstacles may lead to entropic caging of particles, preventing their "free" viscous diffusion. We also found CF mucus contained heterogeneous regions with microviscosities 10-100 times smaller than macroviscosities, suggesting particles with appropriate physicochemical properties may cross this barrier in vivo.

Conclusions

Particle size and surface characteristics were found to significantly affect particle transport rates in CF mucus. Our technique allows identification of individual particles that exhibit improved transport and, therefore, should allow rational design of more effective carriers.