can be an effective way to accelerate the development prevention strategies because computational methods are relatively inexpensive and much more scalable than in vivo approaches.

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Comparison of liquid Versus dry aerosol drug delivery in a 3D printed avian trachea and mainstream bronchi model

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OBJECTIVES/SPECIFIC AIMS: This study investigates the process configuration parameters involved in targeted drug delivery to the avian respiratory system. Previously, direct intratracheal aerosol delivery in an avian model using a commercial atomizer was found to result in delivery of a high portion of the total dose into one lung lobe. We hypothesize that controlling process configuration will decrease the asymmetric distribution. METHODS/STUDY POPULATION: A 3D printed model of an avian trachea and mainstream bronchi was constructed to create a representative model for direct instillation of aerosols. Construction of the model respiratory tract included the trachea and the first mainstream bronchi bifurcation to measure left/right (L/R) distribution of aerosol delivered. Both liquid aerosol delivery (LAD) using a commercial atomizer and dry aerosol delivery (DAD) using a custom-built dry powder insufflator device were tested. Two experimental variables were controlled: (1) retraction distance from the carina and (2) centering of device shaft in the lumen of the trachea. Measurement of device efficiency (dose delivered to the 3D model at as fraction of total dose), aerosol delivery efficiency (dose captured at L/R bifurcations as a fraction of total dose), and aerosol lateralization (L/R) was conducted. RESULTS/ANTICIPATED RESULTS: The aerosol delivery efficiency for both LAD and DAD devices [73.9% (95% CI: 68.2–79.2) and 73.4% (95% CI: 55.5–91.3), respectively] did not have an appreciable difference. However, the LAD device had a higher efficiency as compared with the DAD device. The L/R distribution for the DAD device was found to be highly dependent on both retraction distance and shaft centering. Appreciable improvement in the L/R distribution was seen using the DAD device by increasing the retraction distance distal to the carina. DISCUSSION/SIGNIFICANCE OF IMPACT: The use of targeted drug delivery to treat pulmonary pathogens requires a careful design, manufacture, and therapeutic positioning of devices. In particular, clinically relevant animal models and treatment regimes requires a sound understanding of the physical processes controlling aerosol distribution in the respiratory system. By using a simulated respiratory model, many of the physical parameters of drug delivery can be tested before using a live animal model. This is especially important from an animal welfare perspective as well as an animal subject availability aspect.

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Effects of anoxia on viability and differentiation of human cardiosphere-derived cells

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OBJECTIVES/SPECIFIC AIMS: A major limitation of cardiac stem cell transplantation following myocardial infarction (MI) is poor retention of cells in the ischemic microenvironment. Our study aims to better understand and promote the survival and differentiation of human cardiosphere-derived cells (hCDCs) in anoxia, a feature of infarcted myocardium. METHODS/STUDY POPULATION: We previously demonstrated that TGFβ1 and heparin-containing hydrogels (TH-hydrogel) can promote murine CDC survival. In this study, hCDCs were incubated in either normoxia or anoxia for 8 hours with and without TH-hydrogel. In addition, hCDCs without TH-hydrogel were assessed in 16 hours of anoxia. Following incubation, hCDCs were assayed for viability using calcein dye and immunostained for CD31, a marker of endothelial differentiation. RESULTS/ANTICIPATED RESULTS: hCDCs incubated for 8 hours in anoxia in both models equally demonstrated increased survival up to 30% when compared with cells incubated in normoxia. However, in contrast to hCDCs alone, hCDCs with TH-hydrogel additionally demonstrated increased differentiation into endothelial cells in both anoxia and normoxia. We found that hCDCs alone were able to upregulate CD31 only when subjected to 16 hours of anoxia. DISCUSSION/SIGNIFICANCE OF IMPACT: We demonstrate a new, previously unknown response of hCDCs to anoxia. This induces increased viability and differentiation of hCDCs into endothelial cells. The differentiation in anoxia was time dependent and could be expedited with use of TH-hydrogel. Anoxic preconditioning of hCDCs together with the TH-hydrogel system may improve the therapeutic potential of stem cell transplantation following MI.

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Neuropilin-2 is expressed by activated alveolar macrophages and negatively regulates allergic airway inflammation

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OBJECTIVES/SPECIFIC AIMS: Allergic asthma is a chronic lung disease driven by inappropriate inflammatory responses against inhaled allergens. Neuropilin-2 (NRP2) is a pleiotropic transmembrane receptor expressed in the lung, but its role in allergic airway inflammation is unknown. Here, we characterized NRP2 expression in lung immune cells and investigated the effects of NRP2 deficiency on airway inflammation. METHODS/STUDY POPULATION: NRP2 expression by lung immune cells from NRP2 reporter mice was determined by flow cytometry. NRP2 expression by human alveolar macrophages (AM) from healthy individuals was determined by mRNA analysis and flow cytometry. Airway inflammation in NRP2-deficient mice was assessed by bronchoalveolar lavage (BAL) cytology and inflammatory gene expression in lung tissue. RESULTS/ANTICIPATED RESULTS: NRP2 expression in lung immune cells was negligible under steady-state conditions. In contrast, inhalational exposure to lipopolysaccharide (LPS) adjuvant dramatically induced NRP2 expression in AM, as 63.3% of AM from LPS-treated mice were NRP2+ compared with 1.5% of AM from control mice. Ex vivo treatment of human AM with LPS resulted in a 1.5-fold and 2.6-fold increase in NRP2 mRNA and surface protein expression, respectively. Compared to littermate controls, NRP2-deficient mice had greater numbers of BAL leukocytes and increased lung expression of the T helper type 2 cytokines IL-4 and IL-5. Furthermore, NRP2 deficiency resulted in stochastic development of allergic airway inflammation, as spontaneous airway eosinophilia was detected in 25% (2/8) of NRP2-deficient mice compared with 0% (0/8) of littermate controls. DISCUSSION/SIGNIFICANCE OF IMPACT: NRP2 is expressed by activated human and murine AM and suppresses the spontaneous development of allergic airway inflammation. These findings suggest that NRP2 may play a key role in allergic asthma pathogenesis, and could prove to be an important therapeutic target in patients with asthma and other allergic diseases.

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A transgenic retinitis pigmentosa zebrafish model for drug discovery

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OBJECTIVES/SPECIFIC AIMS: Retinitis pigmentosa (RP) is a hereditary retinal degeneration disease that affects ~1 in 4000 individuals globally, and there are currently no effective treatment options available. In order to identify potential drug treatments, we optimized our existing a behavioral assay around a transgenic zebrafish carrying a truncated human rhodopsin transgene [Tg(rho:Hsa.RH1_Q344X)]. This line was also crossed with the Tg(-3.7rho:EGFP) reporter for rod visualization. The Q344X larvae experiences significant rod photoreceptor death by 7 days postfertilization (dpf) (Nakao *et al.*, 2012). METHODS/STUDY POPULATION: To assess the vision of the Q344X zebrafish, the VMR assay was run under a dim-light condition based on recorded rod b-waves in larval fish (Moyano *et al.*, 2013) and the minimum cone activation threshold in mice (Cachafeiro *et al.*, 2010). Specifically, Q344X and control larvae at 7 dpf were placed into a 96-well plate and acclimated to a dim-light source (1.802e-05 μ W/cm^2 at 500 nm) for 1 hour. The VMR was tracked and quantified during light offset. The total distance traveled was averaged and analyzed at 1 second poststimulus. Retinas were dissected from Q344X and control larvae and whole-mounted to validate the rod degeneration in the Q344X model. RESULTS/ANTICIPATED RESULTS: We found that the Q344X larvae displayed an attenuated VMR (0.121 ± 0.041 cm) to the dim-light offset as compared with the control larvae (0.2751 ± 0.038 cm) (two-sample *t*-test; *p*-value = 4.619e-14, n = 19). Analysis of whole-mounted retinae indicated significant rod degeneration at 7 dpf compared with controls (control: 87 rods/retina, Q344X: 9.3 rods/retina, Welch two-sample *t*-test, *p*-value = 1.4e4). It is unlikely that the cones of the zebrafish contributed to this VMR since the light intensity of the assay was below the cone detection threshold of mice. As the only apparent difference between the 2 groups of larvae is significant rod degeneration, it can be concluded that the behavioral phenotype was a result of

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