performance corresponded to an age-related atrophy of type IIx/IIb muscle fibers. We conclude that force generation and endurance of the DIAm required for breathing motor function is preserved in old age, while DIAm sarcopenia does impair more forceful expulsive airway clearance and voiding behaviors.

409

Assessing the preclinical potential of the antidepressant agomelatine for Alzheimer's disease

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OBJECTIVES/GOALS: Alzheimer's disease (AD) has limited treatments and an extremely high rate of clinical trial failure. Through a collaborative effort, Agomelatine (AGO) was identified as having repurposing potential for AD. This study sets out to evaluate the preclinical potential of AGO for the treatment of AD. METHODS/STUDY POPULATION: The TgF344-AD rat model (expresses human mutant "Swedish" amyloid-precursor protein and a Δ exon 9 presenilin 1) was used to test AGO's potential to reduce cognitive deficits and neuropathology. The model was chosen due to its age-dependent progressive AD pathology and cognitive decline. Treatment with AGO at ~10 mg/kg body weight/day began at 5 months of age (pre-pathology) and continued until 11 months of age when cognitive testing (active place avoidance task) and tissue collection occurred. Immunohistochemistry was used to evaluate amyloid beta plaque burden and microglial response in the hippocampus. RESULTS/ANTICIPATED RESULTS: AGO-treated female TgF344-AD rats showed reduced cognitive deficits with an increased latency to first entrance in aPAT testing compared to nontreated transgenic littermates. There were no differences between the cognitive performance of AGO treated and untreated male TgF344-AD rats. Interestingly, this reduced cognitive deficit did not correlate with decreased amyloid beta pathology in female AGO-treated rats yet male transgenic treated rats did have decreased amyloid burden in the dentate gyrus (DG) of the hippocampus. AGO modulated microglial activation in the DG of female transgenic rats. DISCUSSION/SIGNIFICANCE OF IMPACT: AGO reduced cognitive deficits in females, but did not change their amyloid burden. This suggests that AGO could increase resilience to amyloid deposition in female rats. With the recent development of amyloid targeting drugs, novel non-amyloidogenic treatments have a large translational potential.

412

Quantitative air trapping analysis in lung transplant recipients

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OBJECTIVES/GOALS: Bronchiolitis obliterans syndrome (BOS), a form of chronic lung allograft dysfunction (CLAD) that primarily affects the small airways, is often diagnosed too late using standard pulmonary function tests. This project aims to evaluate whether quantitative air trapping analysis can serve as an early diagnostic tool for BOS. METHODS/STUDY POPULATION: We performed a retrospective analysis of 134 computed tomography scans with inspiratory and expiratory protocols from 73 lung transplant recipients (48 male, 25 female). Quantitative air trapping analysis was performed by VIDA Diagnostics using a supervised machine learning technique called disease probability measure (DPM). RESULTS/ANTICIPATED RESULTS: We found that lung transplant recipients exhibit significantly more air trapping compared to healthy controls and other small airway diseases, such as long COVID and cystic fibrosis. Notably, lung transplant recipients showed increased air trapping in the upper lobes. However, when separating participants into CLAD and non-CLAD groups, those meeting criteria for CLAD had significantly more air trapping in the left lower lobe. Additionally, only 2 out of 16 participants meeting CLAD criteria had less than 20% air trapping in their lungs, suggesting early involvement of the small airways. DISCUSSION/SIGNIFICANCE OF IMPACT: Quantitative air trapping analysis seems to be an important diagnostic modality in the early detection of lung transplant-related small airway disease. Prospective longitudinal studies are needed to evaluate the spatial pathophysiology in these patients and to determine whether early air trapping can predict the development of CLAD.

413

The epithelial–mesenchymal transition protects heterogeneous breast tumors against immune attack in multiple species

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OBJECTIVES/GOALS: Our aim was to identify how the epithelial–mesenchymal transition shields heterogeneous breast tumors against immune attack. Additionally, we endeavored to understand whether our findings were conserved in canine mammary tumors as a translational model for human breast tumors. METHODS/STUDY POPULATION: To understand interactions between quasi-mesenchymal (qM) tumor cells, epithelial (E) tumor cells, and immune cells within heterogeneous breast tumors, we utilized a preclinical mouse model established in our lab. In this system, we can precisely control the proportions of E and qM tumor cells within tumors and study what immune cells infiltrate these tumors in response, using flow cytometry and immunofluorescent staining. Using this model, we have also established cell lines to study E and qM tumor cells in vitro. Finally, we used immunohistochemistry to label immune cells in canine mammary tumors and quantified the presence of these cells in relation to the expression of epithelial and mesenchymal cellular markers. RESULTS/ANTICIPATED RESULTS: We observed that immune suppression within heterogeneous mammary tumors is driven by local, rather than systemic, effects of quasi-mesenchymal (qM) tumor cells. The presence of systemic qM-derived factors does not alter immune cell infiltration nor sensitivity to immunotherapy of epithelial (E) tumors. Furthermore, I found that the local activity of qM-derived factors within heterogeneous tumors induces

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