

fitness phenotypes within these populations. This variation underscores the limitations of single-colony testing and suggests a need for population-level resistance screening. We anticipate genomic analyses will identify genetic diversity underlying these differences, supporting a more comprehensive clinical approach to treatment. **DISCUSSION/SIGNIFICANCE OF IMPACT:** This study reveals notable intrapopulation heterogeneity in *Candida glabrata*, including variations in colony morphology, antifungal resistance, and fitness. Findings highlight genomic diversity, introduce a novel screening method for resistance, and emphasize the need for population-level testing in clinical practice.

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Quality of communication with parents of critically ill infants

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OBJECTIVES/GOALS: Communication between clinicians and parents of seriously ill infants is understudied. This study aims to 1) define high-quality communication with parents of critically ill infants and 2) evaluate the psychometric properties and validity of a measure of high-quality communication in parents of critically ill infants. **METHODS/STUDY POPULATION:** 1) Using participant observation and semi-structured interviews of 35 parents of hospitalized infants, I will conduct content analysis to describe high-quality prognostic communication with parents of infants in the pediatric intensive care unit. Using descriptions captured during participant observation and in semi-structured interviews, I will produce a novel definition of high-quality communication with parents of seriously ill infants. I will also explore parent experiences of communication by race. 2) I will validate a measure of communication quality in parents of 200 neonatal and pediatric intensive care unit patients. I will use factor analysis to evaluate the extent to which responses map onto an established construct and assess dimensionality and reliability. **RESULTS/ANTICIPATED RESULTS:** 1) I anticipate finding that identification of high-quality communication will be consistent between participant observation and interviews and will track with Wreemann's framework. I hypothesize that minoritized parents are more likely to receive low-quality communication. 2) I hypothesize that the measure of communication quality will be valid and reliable in the neonatal and pediatric intensive care units. **DISCUSSION/SIGNIFICANCE OF IMPACT:** I will explore communication quality in a novel setting for which limited data are currently available, establishing a measure for future pediatric communication research and identifying targets for interventions to improve communication quality. Better understanding of communication with parents of sick infants will lead to improved outcomes.

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Social cognition is associated with social problems in adolescents with Tourette syndrome

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OBJECTIVES/GOALS: To assess theory of mind and empathy in adolescents with Tourette syndrome (TS) and examine their

association with social problems. This study aims to extend research in social cognition to an adolescent cohort with TS and identify a potential modifiable risk factor for social problems in TS that may serve as a novel intervention target. **METHODS/STUDY POPULATION:** We will enroll 50 adolescents with TS (ages 11–17) and 50 demographically matched controls along with one parent to complete a single in-person study visit. Adolescents with TS will be recruited through the Vanderbilt Center for TS and other Tic disorders. Controls will be recruited using university listservs and flyers posted in community and primary care settings. Adolescents will complete the NEPSY-II to assess theory of mind abilities and the Multifaceted Empathy Test – Juvenile to assess empathy with negative emotions. Parents will complete the Child Behavior Checklist to assess adolescent social problems. **RESULTS/ANTICIPATED RESULTS:** Based on evidence of low self-other distinction in TS, we hypothesize TS adolescents will make more errors about the mental states of others (theory of mind) and report greater emotional reactions to faces (empathy) compared to controls. Further, greater social problems will be associated with greater disturbances in social cognition. To date, 15 adolescents with TS and 15 matched controls have completed the assessment (67% male; Mage = 14.33 in both groups). Within this sample, adolescents with TS experienced more social problems than controls (Cohen's $d = .74$, $p = .03$). There were no between-group differences in theory of mind or empathy in this pilot sample. However, higher levels of both theory of mind and empathy were linked to experiencing greater social problems in the TS sample only (p 's $< .05$). **DISCUSSION/SIGNIFICANCE OF IMPACT:** Preliminary findings suggest that while social cognition did not differ between groups, TS adolescents exhibiting high levels of theory of mind and empathy appear to struggle socially. This work could inform future interventions by highlighting the need to focus on social cognition and how these skills translate into social behaviors.

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Aging and sarcopenia of the diaphragm muscle

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OBJECTIVES/GOALS: Understand the impact of sarcopenia on the main respiratory muscle, the diaphragm (DIAM). We hypothesize that in the DIAM of older (i.e., 24 months) compared to younger (i.e., 6 months) rats, maximum specific force (P_0) is reduced, maximum shortening velocity (V_{max}) is slower, maximum power output is reduced, and endurance is improved. **METHODS/STUDY POPULATION:** Mid-costal DIAM strips were excised from 6-month ($n = 8$; 4 female and 4 male) and 24-month ($n = 8$; 4 female and 4 male) rats. The DIAM was stimulated using platinum plate electrodes, and mechanical and endurance properties were measured (at 26°C). **RESULTS/ANTICIPATED RESULTS:** In the DIAM, maximum tetanic force (P_0) decreased by ~35%, maximum velocity of shortening (V_{max}) slowed by ~20%, and peak power output was reduced by ~35% in 24-month compared to 6-month rats. During repetitive isovelocity (30% V_{max} ; approximating peak power output) contractions, endurance (the period during which power output was sustained) of the DIAM was unaffected by aging. Corresponding with previous findings, **DISCUSSION/SIGNIFICANCE OF IMPACT:** The changes in DIAM mechanical

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.

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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 pre-clinical 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.

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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.

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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