covert and overt speech production. EEG was recorded using a 64-channel Biosemi ActiveTwo system. EMG was recorded on the orbicularis orbis inferior and neck strap muscles. Overt productions were recorded with a high-quality microphone to determine overt production onset. EMG during was used to determine covert production onset. Neuroimaging: Representational Similarity Analysis (RSA), was used to probe the sound- and motor-based neural representations over sensors and time for each task. RESULTS/ANTICIPATED RESULTS: Production (motor) and perception (sound) neural representations were calculated using a cross-validated squared Euclidean distance metric. The RSA results in the speech perception task show a strong selectivity around 150ms, which is compatible with recent human electrocorticography findings in human superior temporal gyrus. Parietal sensors showed a large difference for motor-based neural representations, indicating a strong encoding for production related processes, as hypothesized by previous studies on the ventral and dorsal stream model of language. Temporal sensors, however, showed a large change for both motor- and sound-based neural representations. This is a surprising result since temporal regions are believed to be primarily engaged in perception (sound-based) processes. DISCUSSION/SIGNIFICANCE: This study used neuroimaging (EEG) and advanced multivariate pattern analysis (RSA) to test models of production (motor-) and perception (sound-) based neural representations in three different speech task conditions. These results show strong feasibility of this approach to map how the perception and production processes interact in the brain.

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Loop-mediated isothermal amplification for the detection of cytomegalovirus infection and drug resistance at the point of care†

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OBJECTIVES/GOALS: To develop a loop-mediated isothermal amplification (LAMP) assay for the detection of cytomegalovirus (CMV) infection and drug resistance. METHODS/STUDY POPULATION: We designed core and loop primers sets utilizing the NEB LAMP Primer Design Tool. Each set contained four or six primers targeting major-immediate early genes – essential for viral entry/replication – or regions known to confer resistance to the antiviral drug ganciclovir. Optimization of reactions conditions was achieved employing DNA reference materials. Reactions were visualized through a change in color as amplification reactions accumulated. Successful reaction conditions were selected based on specific amplification products in less than 60 minutes. Limits of detection were evaluated as the main performance outcome. RESULTS/ANTICIPATED RESULTS: Genomic data were extracted and used to design a series of LAMP primers (48 total) that aimed to detect specific genomic regions of CMV. Using this strategy, we successfully designed and identified eight primer sets that showed high 100% sensitivity and 100 % specificity, when detecting > 1.00 x 10^5 copies/mL of CMV gDNA. We are in the process of characterizing a new set of primers to determine the diagnostic utility of a LAMP assay in detecting selected single-nucleotide mutations at the UL97 loci. The expected outcomes at completion include: (1) the identification of LAMP primers to detect drug-resistance mutants, (2) defining optimal conditions for successful reactions, and (3) determining limits of detection for subsequent validation with clinical specimens. DISCUSSION/SIGNIFICANCE: CMV infection remains one of the most dangerous infectious agents for immunocompromised hosts, newborns, and unborn children. This study will describe a proof-of-concept LAMP assay for the genotypic detection of drug resistance in CMV-infected individuals and hence, create new avenues for selection of effective therapies to treat CMV disease.

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Computational methods for predicting drug combinations for targeting KRAS mutations relevant to non-small cell lung cancer

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OBJECTIVES/GOALS: Our goal is to develop a cost-effective approach for precision medicine treatment by providing computational predictions for new uses of currently available FDA approved, and experimental drugs for NSCLC. METHODS/STUDY POPULATION: Cell Lines: A549 (ATCC- CCL-185) Human epithelial Lung Carcinoma cells, H1792 (ATCC-CRL-5895) Human Lung Carcinoma cells. In Vitro Cytotoxicity Assay: A VybrantÂ® MTT Cell Proliferation Assay was used. Colony Formation Assay: NCI-H1792, A549 cells were seeded at a density of 500 cells/ dish, then treated with ARS-1620, Osimertinib. The Computational Analysis of Novel Drug Opportunities (CANDO): Â Herein, we employed the bioanalytic docking (BANDOCK) protocol within CANDO to calculate the compound-protein interaction scores for a library of 13,218 compounds from DrugBank against a library of 5,317 protein structures from the Protein Data Bank, resulting in a proteomic interaction signature for each compound, and identified Osimertinib as the most likely EGFR/ErbB inhibitor to synergize with ARS-1620. RESULTS/ANTICIPATED RESULTS: ARS-1620 and Osimertinib in combination displays potent anti-tumor activity as evident by a decrease in cell viability with cytotoxicity assays, as well as reduced number of colonies in the colony formation assay for both A549 and H1792 cells. By using CANDO, and cross-referencing the obtained rankings with known experimental information, we have obtained drug predictions within the context of precision medicine. Our preliminary data indicates that EGFR inhibitor Osimertinib may be most structurally similar to KRAS G12C inhibitors overall, compared to other ErbB/ EGFR inhibitors. Validations with human cancer cell lines A549 and H1792 have confirmed that Osimertinib in combination with KRAS G12C inhibitor ARS-1620 may exhibit a synergistic effect in decreasing cellular proliferation and colony formation. DISCUSSION/SIGNIFICANCE: This suggests that this innovative drug combination therapy may help improve treatment outcomes for KRAS G12C(H1792) and KRASG12S(A549) mutant cancers. Cell migration and cell invasion studies in response to treatment with Osimertinib and ARS-1620 are currently ongoing.

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