Results (if a Case Study enter NA): The agreement in accuracy between the LightCycler® 2.0 and the LightCycler® 480 was 100% for whole blood samples. For historically positive FFPE samples, LightCycler® 2.0 sensitivity and LightCycler® 480 sensitivity were 86% and 100%, respectively. Specificity and inclusivity of the assay were identical between the two instruments. The limit of detection in whole blood was 5-fold lower on the LightCycler® 480 (50 copies/µL) compared to the LightCycler® 2.0 (250 copies/µL). Mean Cp and fluorescent peak intensity values increased by 5.1% and 65-fold, respectively.
Conclusion: The study demonstrates similar performance and improved limit of detection for the Bartonella FRET hybridization probe RT-PCR assay on the LightCycler® 480 compared to the LightCycler® 2.0.

Comparison of longitudinal SARS-CoV-2 nasopharyngeal specimens reveals the transcriptomic COVIDome

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Introduction/Objective: SARS-Cov-2 is well established to introduce a cytokine-like storm among select individuals that results in multisystem failure and death. Comorbidities, age, oxygen status, and real-time appraisal of inflammatory markers in the blood have been used to risk stratify patients, however, these clinical markers do not comprehensively characterize the at-risk population or disease course. To understand the molecular underpinnings of the primary site of SARS-CoV-2 infection, here, we interrogated the transcriptomic profile of the nasopharyngeal tissue among paired SARS-CoV-2 specimens.
Methods/Case Report: We performed ribosomal depletion RNAseq on 24 primary samples, including 16 paired samples from 8 unique patients who converted between SARS-CoV-2 negative and positive status via clinical diagnostic qRT-PCR. Additional targeted qRT-PCR was performed for ACE2 and TMPRSS2 in an extension sample of 54 paired specimens from 27 unique patients who converted in their SARS-CoV-2 status on the basis of the qRT- PCR test. Differential gene expression, differential correlative expression with ACE2, and correlative expression with viral load was used to identify genes, which were integral to SARS-CoV-2 pathogenesis, so termed the COVIDome. Gene ontologies, pathways, and reactive infiltrate was assessed between specimens and compared with measures of clinical outcome using regression with appropriate correction for multiple hypotheses.
Results (if a Case Study enter NA): We observed significant enrichment for ontologies of lymphocyte activation, specifically interferon gamma signaling; (P<1E-20) and platelet activation (P<1E-5). Genes specifically enriched across all three modules included: ADAMDEC1, EPSTI1, GRIP2, IRF7, KLHDC7B, OAS3, OASL, PIK3R4, RSAD2, and XAF1. Using CIBERSORT to approximate immune cell populations from bulk RNA, we observed and enrichment for CD4 immune cells, which was associated with viral status (P<0.01) while high-risk gene signatures were associated with measures of clinical outcome (P<0.05).
Conclusion: We characterized the pathogenesis of SARS-CoV-2 in longitudinal nasopharyngeal samples of COVID- 19 patients and related these molecular manifestations with measures of clinical outcome. As proof of principal, our findings suggest additional study in a large, longitudinal extension sample is warranted to validate and assess molecular features of clinical outcome associated with SARS-CoV-2 infection.

Next generation sequencing identifies potential PARP inhibitor sensitive mutations

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Introduction/Objective: Poly ADP-ribose polymerase (PARP) inhibitors are a novel and important drug class targeting homologous recombination DNA repair defects (HRD) and have been approved for use in breast, pancreatic and ovarian cancers. Originally targeted for loss of function mutations in BRCA1 and BRCA2, many other genes are involved in the HRD pathway; Rimar et al detailed 19 DNA repair genes associated with homologous recombination and PARP inhibitor sensitivity. Our 214 gene NGS panel, Iowa Cancer Mutation Profile, includes BRCA1, BRCA2 and 15 other HRD pathway genes. We reviewed cases from the prior 12 months to determine the frequency of HRD7 pathway gene variants in various tumor types with potential PARP inhibitor sensitivity.
Methods/Case Report: Iowa Cancer Mutation Profile NGS test results from June 4, 2020 through May 7, 2021 were reviewed for variants involving ATM, ATR, BAP1, BLM, BRCA1, BRCA2, CDK12, CHEK1, CHEK2, FANCA, FANCC, FANCD2, MRE11A, NBN, PALB2, RAD51c and RAD51d, categorized as pathogenic, likely pathogenic or of unknown significance and had the tumor type identified. Additional chart review for PARP inhibitor therapy was performed in cases of breast, pancreatic, and ovarian cancer.
Results (if a Case Study enter NA): A total of 599 cases were reviewed with 234 found to have variants in genes with possible PARP inhibitor sensitivity. Of these 2% (n=8) and 11% (n=43) of variants were categorized as pathogenic or likely pathogenic while most (n=334) were categorized as variants of unknown significance. The pathogenic and likely pathogenic variants included mutations in ATM (n=13), BRCA2 (n=12), BAP1 (n=8), FANCA (n=5), BRCA1 (n=4),

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