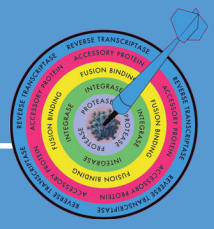

REVERSE TRANSCRIPTASE
ACCESSORY PROTEIN
FUSION BINDING
INTEGRASE
PROTEASE

ABSTRACTS

Abstract #O_01

HIV Reservoirs, Persistence and Eradication

Differential responses of memory CD4+ T cell subsets to HIV latency reversing agents

D.A. Kulpa[1], A. Talla[2], S.P. Ribeiro[2], R. Barnard[3], M. Miller[3], D. Hazuda[3], N. Chomont[4], R.P. Sekaly[2]

[1]Emory University, Pediatrics, Decatur, USA; [2]Case Western Reserve, Pathology, Cleveland, USA; [3]Merck Research Laboratories, Infectious Disease, West Point, USA; [4]University of Montreal, Microbiology, Montreal, Canada

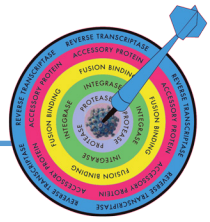
The latent HIV-1 reservoir persists in individuals on ART predominantly in three memory T cell subsets endowed with distinct functional and survival capacities, the central (TCM) transitional (TTM) and effector (TEM) memory CD4+ T subsets. Given the heterogeneous nature of the latent HIV reservoir, latency reversing agents (LRAs) used in HIV eradication strategies such as 'shock and kill' will need to address the inherent differences in the ability of each subset to respond to these compounds.

We developed a primary cell based in vitro model of HIV latency, LARA (Latency and Reversion Assay), that would facilitate the study of the mechanisms that trigger the establishment of HIV latency as well as those that lead to maintenance and latency reversion in the TCM, TTM and TEM subsets.

Transcriptional profiling showed that the CD4 T cell memory subsets retained their ex vivo gene expression profiles after LARA in vitro culture and maintained the expression of genes and pathways that define each subset. Significantly, we also showed that LARA conditions support robust HIV latency establishment and reversion in all memory CD4+ T cell subsets and reveal distinct responses to different LRAs. The protein kinase C agonist bryostatin significantly triggered latency reversal in all three subsets although the efficiency of reversal in each subset varied from 24% (TCM) to >100% (TTM) and 94% (TEM) when compared to the TCR stimulation positive control. Interleukin-15 significantly reversed latency particularly in TCM and TEM cells, but only achieved a maximum efficiency of 29% (TCM) or 37% (TEM). Interestingly, our data show that LRAs that activate pathways associated with proliferation and differentiation into TEM cells are the most efficient. By combining two different classes of LRAs, bryostatin and the acetaldehyde dehydrogenase inhibitor disulfiram, we were able to achieve a statistically significant increase in latency reversal efficiency specifically in the TCM subset to 83%, compared to bryostatin (24%) or disulfiram (19%) alone (p=0.02).

These results provide support for LRAs to have specific capacity to reactivate virus in unique T cell subsets; we also provide evidence that combination of LRAs can be used to reactivate HIV in memory subsets that are refractory to a single LRA. Knowing the efficiency with which LRAs or combinations of LRAs act on the different memory subsets is a critical prerequisite to the design of successful regimens for comprehensive reactivation of the HIV reservoirs in 'shock and kill' eradication strategies.

No conflict of interest



Abstract #O_02

HIV Reservoirs, Persistence and Eradication

HIV-1 dynamics under integrase inhibitor therapy suggests a subset of cells with slow integration

E.F. Cardozo[1], A. Andrade[2], J. Mellors[3], D.R. Kuritzkes[4], A.S. Perelson[1], R.M. Ribeiro[1]

[1]Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, USA; [2]Johns Hopkins University, Medicine, Baltimore, USA; [3]University of Pittsburgh, Medicine, Pittsburgh, USA; [4]Harvard Medical School, Brigham and Women's Hospital, Boston, USA

Introduction: The kinetics of HIV-1 decay under treatment depends on the class of antiretrovirals used. Mathematical models are useful to interpret the different profiles, providing quantitative information about kinetics of virus replication and cell populations contributing to viral decay.

Materials & Methods: We modeled proviral integration in short- and long-lived infected cells to compare viral kinetics under treatment with and without the integrase inhibitor raltegravir (RAL). We fitted the model to data of participants treated with RAL-containing regimens or with a four-drug regimen of protease and reverse transcriptase inhibitors, with frequent viral load measurements over the first month of therapy.

Results: Our model explains the existence and quantifies the three phases of decay in RAL-based regimens vs. the two phases observed in therapies without RAL. Our findings indicate HIV-1 infection is sustained by short-lived infected cells with fast integration and a short viral production period, and by long-lived infected cells with slow integration but an equally short production period. We propose that these cells represent activated and resting infected CD4+ T-cells, respectively, and estimate that infection of resting cells represent ~4% of productive infection events. RAL reveals the kinetics of integration, showing that in short-lived cells the pre-integration population has a half-life of ~7 hours, whereas in long-lived cells this half-life is ~6 weeks. We also show that the efficacy of RAL can be estimated by the difference in viral load at the start of the second phase in protocols with and without RAL.

Conclusions: Overall, we provide a mechanistic model of viral infection that parsimoniously explains the kinetics of viral load under multiple classes of antiretrovirals and predicts a novel subset of infected cells with slow integration.

No conflict of interest

Abstract #O_03

Novel Therapeutic Agents and Immunological Approaches

Anti–HIV drug candidate abx464 prevents intestinal inflammation by producing IL22 in activated macrophages

J. Tazi[1], D. Scherrer[2], H. Ehrlich[2], M. Hahne[1], K. Chebli[1]

[1]Laboratoire coopératif ABIVAX-CNRS-UM, Institut de génétique moléculaire UMR5535, Montpellier Cedex 5, France; [2]Laboratoire coopératif ABIVAX-CNRS-UM, ABIVAX, Montpellier Cedex 5, France

INTRODUCTION: Disease progression of HIV infected patients appears to be associated with mucosal damage of the gastrointestinal (GI) tract inducing bacterial translocation from the gut and subsequent inflammation. DSS-treatment is an established animal model for experimental colitis that was recently shown to induce GI-tract damage and other important features of HIV/SIV infection. Here we tested the protective properties of ABX464, a first in class anti-HIV drug candidate, that has demonstrated anti-viral activity in HIV treatment of naïve patients. ABX464 also induced a long-lasting control of the viral load in HIV infected humanized mice after treatment arrest.

MATERIAL & METHODS: A mouse model of dextran sodium sulfate (DSS)-induced colitis was used to assess the anti-inflammatory properties of ABX464. RNAseq analysis was performed on colon tissue taken from DSS-treated mice, as well as several batches of mouse bone marrow derived macrophages treated with LPS to determine the effect of ABX464 on gene expression. Anti-IL22 neutralizing antibodies were used to anneal the protective effect of ABX464 in DSS-exposed mice

RESULTS: DSS treatment results in GI barrier damages with associated microbial translocation, inflammation and immune activation. ABX464 treatment reduced both the levels of secreted inflammatory cytokines IL-6 and IFNgamma, as well as the monocyte chemoattractant protein-1 (MCP-1) in the colon. ABX464 treated DSS mice have decreased number of lesions in the colon and did not experience colon size reduction. Interestingly, the ABX464 produced long-term protection of DSS-treated mice 45 days after drug cessation despite continuous treatment with DSS. Profiling the expression of 84 RNA encoding key secreted proteins central to the immune response and other immune functions showed that ABX464 treatment of DDS mice corrects the expression of several genes to the level of mice untreated with DSS but notably induced overexpression of IL22. A comprehensive analysis of the gene expression profiles by RNAseq demonstrated that the expression of IL22 was preferentially induced by ABX464 in mouse bone marrow derived macrophages only upon stimulation with LPS. Importantly, the protective effect of ABX464 on colitis in DSS-mice was abrogated by anti-IL22 antibodies.

CONCLUSIONS: The antiretroviral drug candidate ABX464 protects DSS-treated mice from inflammation by triggering overproduction of IL22. As reduced IL-22 production in gut mucosa is an established factor in HIV and DSS-induced immunopathogenesis (), our data suggest that the anti-inflammatory properties of ABX464 may warrant exploration in both HIV and IB disease

Conflict of interest
Financial relationship(s): I have a contract with ABIVAX

Abstract #O_04

Novel Therapeutic Agents and Immunological Approaches

Development of a protease inhibitor-based single-tablet complete HIV-1 regimen of darunavir/cobicistat/emtricitabine/ tenofovir alafenamide (DCFTAF)

B. Baugh[1], E. Van Landuyt[2], S. Vanveggel[2], H. Crauwels[2], E. Dammers[2], A. Hijzen[2], E. Lathouwers[2], M. Opsomer[2]

[1]Janssen Research & Development LLC, Virology, Raritan, USA
[2]Janssen Pharmaceutica NV, Infectious Diseases, Beerse, Belgium

Introduction: DCFTAF (darunavir [DRV] 800mg, cobicistat [COBI] 150mg, emtricitabine [FTC] 200mg and tenofovir alafenamide [TAF] 10mg) is a once-a-day, single-tablet complete HIV-1 regimen in clinical development. DRV has demonstrated a high genetic barrier to resistance and has been studied in various patient populations in clinical trials. TAF, a novel prodrug of tenofovir, provides comparable efficacy to tenofovir disoproxil fumarate at one-tenth the dose, with ~90% lower tenofovir plasma concentrations and fewer bone and renal adverse events (AEs). A Phase 2 study (NCT01565850) showed non-inferior virologic efficacy of DCFTAF compared to DRV + COBI + FTC/TDF at Week 24 (FDA snapshot analysis, primary endpoint), with improved bone and renal laboratory parameters and no treatment-emergent resistance to any components of the regimen. Here we provide an update on the DCFTAF development program.

Materials & Methods: The impact of food on the bioavailability of the components of the DCFTAF single-tablet regimen was recently evaluated in a Phase 1, open-label, randomized, 2-sequence, 2-period, crossover, single-dose study in healthy volunteers (NCT02475135). The efficacy and safety of DCFTAF (administered as the single-tablet regimen) is currently under investigation in two international, randomized, Phase 3 studies: AMBER (NCT02431247) and EMERALD (NCT02269917). The primary objective of both studies is to demonstrate non-inferior efficacy of DCFTAF compared to the active control arm at Week 48 (patients will continue receiving DCFTAF beyond Week 48, providing they consent and continue to derive benefit). Primary outcome measures are the proportion of patients with confirmed virologic suppression at Week 48 (snapshot analysis) (AMBER) or confirmed virologic rebound (HIV-1 RNA ≥50 copies/mL or premature discontinuations, with a last single HIV-1 RNA ≥50 copies/mL) through Week 48 (EMERALD).

Results: When administered as DCFTAF, DRV Cmax, AUClast and AUCinf decreased by 45%, 34% and 30%, respectively, in fasted versus fed conditions. Differences in exposure to COBI, FTC and TAF in fed versus fasted conditions were not considered clinically relevant. DCFTAF was generally well tolerated in healthy volunteers; no grade 3/4 or serious AEs, deaths, or discontinuations due to AEs occurred.

In AMBER, 725 treatment-naïve HIV-1-infected adults have been randomized (1:1) to double-blind treatment with DCFTAF or DRV/COBI fixed-dose combination with FTC/TDF. In EMERALD, 1149 virologically suppressed (HIV-1 RNA <50 copies/mL) patients have been randomized (2:1) in an open-label fashion to switch to DCFTAF or remain on their current treatment regimen (protease inhibitor [PI] boosted with low-dose ritonavir or COBI + FTC/TDF).

Conclusion: The single-tablet DCFTAF regimen provides similar exposures as combined intake of the separate agents. When administered as DCFTAF, DRV exposure was decreased in fasted versus fed conditions, similar to other (co-)formulations of DRV, and the recommended intake is with food. DCFTAF is the only single-tablet complete regimen containing a PI in clinical development. The Phase 3 studies AMBER and EMERALD are fully recruited and ongoing.

Conflict of interest

Financial relationship(s): All authors are full-time employees of Janssen and potential stockholders of Johnson and Johnson.

Abstract #O_05

Drug Resistance and Modeling

Antiviral Activity of Tenofovir Alafenamide against HIV-1 with Thymidine Analog Mutation(s) and M184V

M.E. Abram[1], R.R. Ram[1], N.A. Margot[1], M.D. Miller[1], C. Callebaut[1]

[1]Gilead, Clinical Virology, Foster City, USA

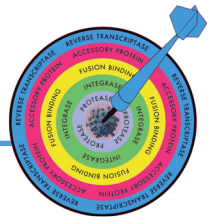
Background: Tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) are first and second generation prodrugs of tenofovir (TFV), an HIV-1 nucleotide reverse transcriptase (RT) inhibitor. TAF (25 mg) achieves ~90% lower plasma TFV levels and ~4-fold higher intracellular levels of the active phosphorylated metabolite tenofovir diphosphate (TFV-DP) compared to TDF (300 mg) which results in improved renal and bone safety. Patients whose HIV-1 has thymidine analog mutations (TAMs) in RT, previously defined as TDF-resistant, may benefit from higher intracellular levels of TFV-DP delivered by TAF. Moreover, the presence of the M184V mutation may increase susceptibility to TFV during TAF-based therapy. Here, the in vitro activity of TAF was evaluated against multiple TAMs in the presence or absence of M184V.

Methods: Site-directed mutants were constructed with all possible single, double, triple, and quadruple combinations of TAMs (M41L, D67N, K70R, L210W, T215Y, and/or K219Q) with (n=40) or without M184V (n=40). Replication capacities (RC, %WT) and antiviral drug susceptibilities (fold change [FC] EC50 relative to wild-type) were determined in replicate experiments (n=7) in acutely infected MT-2 cells using a 2-day single-cycle PR-RT HIV assay, similar to commercial assays for which TDF clinical cutoffs have been established. TAF resistance profile was further assessed in viral growth breakthrough experiments at clinically relevant drug concentrations using TAM-containing viruses.

Results: Overall, TAF fold-change EC50 ranged from 0.6 to 8.2 (median FC = 2.5) without M184V and 0.8 to 3.4 (median FC = 1.8) with M184V. Among all viruses with 1- to 4-TAMs, the addition of specific TAMs further reduced TAF susceptibility with a rank order of: T215Y > L210W ≥ M41L > D67N ≥ K70R > K219Q. Most TAM-containing viruses with M184V exhibited increased susceptibilities to TAF relative to viruses without M184V: 2-TAMs±M184V (mean = 1.2-fold), 3-TAMs±M184V (mean = 1.4-fold), and 4-TAMs±M184V (mean = 2-fold). The presence of multiple TAMs with or without M184V reduced HIV-1 replication capacity in only a few cases: M184V with M41L, T215Y, or M41L+T215Y. Based on the current TFV clinical cutoffs for TDF (FC = 1.4 and 4 for reduced and unlikely clinical response, respectively), 44/80 TAM-containing viruses (with or without M184V) exhibited FC ³ 1.4 < 4 and 7/80 viruses (3-TAMs [n=1] or 4-TAMs [n=6]; all without M184V) exhibited FC ³ 4. With the projection that the ~4-fold increase in intracellular TFV-DP concentration achieved in vivo with TAF would translate to ~4-fold greater cutoffs for TAF than TDF, only 3/80 TAM-containing viruses (4-TAMs [n=3]; all without M184V) would be predicted to exhibit reduced TAF response (FC ≥ 5.6 < 16). In viral growth breakthrough experiments, viruses with up to 4-TAMs were inhibited by TAF, but not by TFV when used at clinically relevant concentrations for TDF.

Conclusions: Multiple TAMs decrease TFV activity in vitro and may reduce TDF potency during antiretroviral therapy. However, the 4-fold higher intracellular levels of TFV-DP delivered by TAF may allow this agent to better overcome and maintain TFV activity against multiple TAMs, which is further improved in the presence of M184V.

Conflict of interest
Financial relationship(s): Employee and stock holder of Gilead



Abstract #O_06

Emerging Viruses (e.g. Zika, MERS, Noro, Ebola viruses)

In Silico Approaches Towards Broadly Active Flavivirus Protease Inhibitors

B.D. Cox[1], R.F. Schinazi[1]

[1]Emory University, Department of Pediatrics, Atlanta, USA

Introduction: Flaviviruses are mosquito-transmitted viruses with 1/3rd of the world's population at risk of infection based on the distribution of the vector. This family of viruses include tropical and emerging pathogens like West Nile Virus (WNV), Dengue Fever Virus (DENV), Japanese Encephalitis Virus (JEV), Yellow Fever Virus (YFV), and Zika Virus (ZIKV) as well as potential future threats like Omsk Virus, Usutu Virus, and Mayoro Virus. All flavivirus genomes encode a serine protease (NS3pro) responsible for processing of the viral polyprotein, and protease inhibitors for other viruses (HIV and Hepatitis C Virus) are FDA-approved therapies to mitigate infection. This study addresses conservation of druggable sites on flavivirus NS3pro and tests a method to enable design of broadly active covalent protease inhibitors.

Methods: For viruses without crystal structures, homology models of NS3pro proteins were constructed using the SwissModel server. NS3pro crystal structures and homology models were aligned and analyzed using the VMD MultiSeq tool. Free energy perturbation (FEP) calculations of protease-peptide complexes were performed using Desmond molecular dynamics with the OPLS-2005 forcefield (Schrodinger Suite, 2015).

Results: Structural alignment of available crystal structures and homology models reveals that the NS3pro active site is highly conserved among flaviviruses. A previously reported tetrapeptide based on the target sequence (Bz-Nle-Lys-Arg-Arg-CHO) exhibits modest inhibitory activity for WNV and DENV NS3pro in vitro. We developed a modified FEP approach that recaptures the divergent inhibitory potencies of tetrapeptide mutants against both DENV and WNV. This approach was used to predict structure-activity relationships for ZIKV NS3pro peptidyl inhibitors.

Conclusions: These results offer novel in silico methodology to design covalent drugs and support efforts towards a broadly active protease inhibitor for emerging and pandemic-prone flaviviruses.

No conflict of interest

Abstract #O_07

Emerging Viruses (e.g. Zika, MERS, Noro, Ebola viruses)

Jak 1/2 Inhibition Modulates Production of Replication Competent Zika Virus in Primary Human Hofbauer, Trophoblast and Neuroblastoma Cells

L. Bassit[1], C. Gavegnano[1], B.D. Cox[1], H.M. Hsiao[1], E.L. Johnson[1], M.H. Suthar[2], R. Chakraborty[1], R.F. Schinazi[1]

[1]Emory University School of Medicine, Center for AIDS Research Department of Pediatrics, Atlanta GA, USA
[2]Emory University School of Medicine & Emory Vaccine Center, Department of Pediatrics Division of Infectious Diseases & Yerkes National Primate Research Center, Atlanta GA, USA

Introduction: Mechanisms responsible for transmission of ZIKV across the placenta to the fetus are poorly understood. Herein, we define key events that modulate ZIKV infection in clinically relevant cells, including primary placental macrophages (human Hofbauer cells [HC]), trophoblasts and neuroblastoma cells.

Material & Methods: Primary HC or trophoblasts were isolated from fresh placentae. Cells were cultured ± 0.1, 1.0, or 10 µM ruxolitinib, a Jak1/2 inhibitor for 24 hr prior to infection with an MOI 1 of PRVABC59 or MR766 ZIKV (2 hr prior to removal of virus), and culture in drug free medium or 0.1, 1.0, or 10 µM ruxolitinib ± proprietary antiviral agents. Day 6 post-infection, cells were harvested for FACS (activation markers HLA-DR and CD11c) and/or RT-PCR to quantify virus. Supernatants were collected and transferred to uninfected Vero cells to confirm replication competence of virus produced. Electron microscopy was performed to determine virion integrity and coat structure from cultures. U251 neuroblastoma cells were infected as described above ± 0.1, 1.0 or 10 µM ruxolitinib and infection was quantified with FACS.

Results: HC and trophoblasts are permissive to ZIKV infection (PRVABC59 and MR766 strains) and supra-physiological concentrations of ruxolitinib, a Jak 1/2 inhibitor that increases ZIKV replication versus infection without ruxolitinib in HC and trophoblasts and human neuroblastoma cells. Infection did not decrease cell viability, and ruxolitinib- mediated increase in ZIKV production was associated with increased expression of HLA-DR and DC-SIGN on HC. Supernatants from HC and trophoblasts infected with ZIKV in the absence of ruxolitinib were unable to infect naïve Vero cells (an interferon deficient, highly permissive cell system) under normal conditions. Ruxolitinib-treated ZIKV infected HC, but not trophoblasts released infectious ZIKV in the supernatants that were able to infect naïve Vero cells. Proprietary ZIKV antiviral agents blocked ZIKV produced in ruxolitinib-treated HC and subsequent transfer to naïve Vero cells (EC50 1.7-17.3 µM). Electron microscopy demonstrated that virions produced from HC or trophoblasts in the absence of ruxolitinib produced 'thin coat' immature virions, whereas virions produced in the presence of ruxolitinib, or from Vero cells, resulted in 'thick coat' mature virions. We also demonstrated that Jak-STAT blockade conferred a significant ($p < 0.01$; One Way ANOVA) increase in ZIKV production in human neuroblastoma cells, highlighting this mechanism across target cells in vivo.

Conclusions: These data demonstrate that primary HC and trophoblasts are permissive to ZIKV infection, and that blockade of IFN-a/b production by potent, specific inhibition of Jak1/2 signaling significantly increases permissiveness of these cells to both PRVABC59 and MR766 strains, and increases HLA-DR and CD11c expression. Together, these data demonstrate that IFN-a/b signaling is likely a key factor in modulating permissiveness of placental cells to ZIKV infection. These data provide a foundation for immunomodulatory-based antiviral agents that can impact IFN-a/b signaling with a goal of prevention of transmission of virus to the unborn fetus.

No conflict of interest

Abstract #O_08

Pharmacology, Toxicology and Drug Metabolism

Predicting Antiviral Drug Toxicity Using Contractility Analysis Of Human IPSC Derived Cardiomyocytes

B.D. Herman[1], S. Tao[1], Y. Jiang[1], J. Kohler[1], R.F. Schinazi[1]

[1]Emory University School of Medicine, Center for AIDS Research Department of Pediatrics, Atlanta GA, USA

INTRODUCTION: Antiretroviral agents including some nucleoside analogs and protease inhibitors used in combination therapy for the treatment of HIV-1 infection are associated with clinical cardiomyopathies. Until recently techniques available for pre-clinical cardiac safety evaluation of candidate drugs have been insufficient to predict relevant human cardiotoxicity. In fact, many experimental drugs fail during clinical trials due to previously unrecognized cardiotoxicity. For example, a phase II study of BMS-986094 was terminated due to cardiac dysfunction in 14 of 34 patients, including one death. Additionally, a 2015 review of post-marketing adverse events for the FDA approved ribonucleotide hepatitis C virus (HCV) NS5b polymerase inhibitor sofosbuvir (SOF) revealed severe bradycardia when taken in combination with the anti-arrhythmic agent amiodarone (AMN). Advances in stem cell technology facilitated the development of a platform for in vitro evaluation of experimental drugs for potential cardiotoxicity using human induced-pluripotent stem cell derived cardiomyocytes (hPSC-CM). In the current study we validate the ability of this platform to predict human cardiotoxicity using BMS-986094 and the SOF plus AMN combination as model antiviral agents with known clinical cardiomyopathies.

MATERIALS & METHODS: To evaluate in vitro the observed cardiotoxicity of BMS-986094 and SOF+AMN we used standard toxicity assays in peripheral blood mononuclear (PBM), CEM, and Vero cells together with our recently developed hPSC-CM platform. Briefly, commercially available hPSC-CM were cultured according to manufacturer recommendations for 10 days prior to exposure to various concentrations of SOF alone or in combination with AMN. Cultures were imaged using a Perkin-Elmer spinning disc confocal microscope and 30 second videos were recorded at 14 fps using a Hamamatsu Flash 4.0 sCMOS camera and Velocity Software at 2, 4, 8, 12, 24, and 48 hr. Contractility of hPSC-CM was analyzed by manual counting and with automated motion tracking software to determine contraction rate, rhythm, and force in terms of contraction velocity.

RESULTS: SOF was not toxic (IC50 >100 μM) in standard assays in PBM, CEM, and Vero cells, whereas toxicity was observed in these cells for AMN (IC50 values of 7.1, 10.9 and 11.6 μM, respectively) and BMS-986094 (IC50 values of 4.7, 8.7, and 12.4 μM, respectively). Cultured hPSC-CM developed syncytial monolayers displaying spontaneous and synchronous beating 5-8 days post plating. At 4 hr, control hPSC-CM had an average beat rate of 37.5 ± 1.2 beats/min (bpm), a contraction to relaxation interval of 0.36 ± 0.0 sec, a contraction velocity of 2.01 ± 0.5 μm/sec, and relaxation velocity of 0.75 ± 0.2 μm/sec. All parameters modestly decreased through 48 hr likely due to exhaustion of nutrients in the media. Treatment with 10 μM and 50 μM SOF alone did not impact contraction relative to controls. However, treatment with 50 μM BMS-986094 or 10 μM SOF + AMN (0.1 μM, 1 μM, 5 μM, and 10 μM) resulted in cessation of hPSC-CM contraction 2 hr post exposure which did not recover through 48 hr.

CONCLUSIONS: Our recently developed platform to assess various hPSC-CM contractile parameters in vitro using live cell confocal microscopy and automated motion tracking software has successfully corroborated in vivo cardiomyocyte toxicity observed with BMS-986094 and the combination of SOF+AMN. These results demonstrate the utility of our hPSC-CM model for the in vitro evaluation of candidate antiviral agents.

No conflict of interest

Presentations and webcasts will be published online at:

www.infectiousdiseasesonline.com

virology education

www.virology-education.com