Articles about Covid 19 April 20-24

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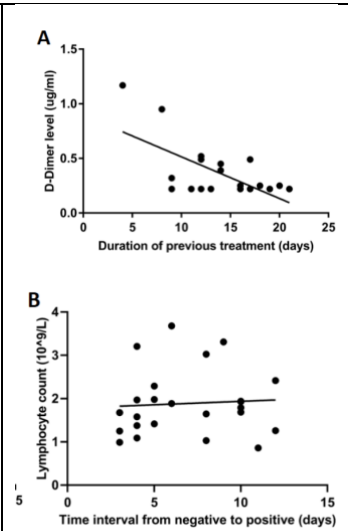
Name of Article and Link	Journal, Date	Category of Study	Question it asks	Results in Brief	Clinical Implications, Limitations	Initials
Spread of SARS-CoV-2 in the Icelandic Population	NEJM, April 20, 2020	Public Health/Epi	What is the prevalence of SARS-CoV-2 among individuals at high risk for infection (recent travel, known contact, sx) and the general population? Additionally, what do the genomes of selected individuals suggest about the introduction and spread of SARS-CoV-2 in Iceland.	13.3% of individuals targeted for testing d/t increased risk for infection (symptomatic, recent travel, known contact) tested positive for SARS-CoV2. 93% of patients who tested positive were symptomatic. Genomic testing identified most of these positives originated in Italy or Austria. 0.8% of the general population tested positive for SARS-CoV2; remained stable for the duration of screening. Genomic testing indicated most of these strains originated in the UK or US. Males tested positive more often than females; more females were tested overall. Infection rate of virus was stable from March 13 to April 1.	Infection rate has remained constant in Iceland which likely represents efficacy of social distancing measures. The genomic profile of virus strains in an initially tested high-risk group was different than a subsequent expansion to general population screening. The study authors argue that these results indicated the strain of SARS-CoV- 2 spreading among the Icelandic population came from a different source than that which was initially identified in the high-risk group. **Limitations** Nearly half the population screening group had mild respiratory symptoms which may represent self-selection bias.	CN

					People who returned from Alp ski resorts had been instructed to self-isolate and were not eligible for the study which may have skewed genomic results. Quarantined individuals were excluded from the population screening portion of the study.	
Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1	N Engl J Med 2020 March 17, 2020	Basic Science	How long does the Novel SARS-COV-2 virus remain stable as an aerosol and on surfaces compared to SARS-COV-1?	SARS- COV - 2 remained viable in aerosols throughout the duration of the experiment (3 hours), with a reduction in infectious titer from 10^3.5 to 10^2.7 TCID50 per liter of air, which was similar to SARS-COV-1. SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces, Though the virus titer was greatly reduced. on Copper, no viable SARS-CoV-2 was measured after 4 hours and on cardboard, no viable SARS-CoV-2 was measured after 24 hours	Clinical indication: This data can be used for pandemic mitigation as the SARS-COV-2 Virus demonstrated viability as an aerosol for 72 hours. It was been documented that nosocomial and superspreading events occur in this mode of transmission. Additionally, surface viability provides important information about sanitization of different objects. This could be used for infection control guidance. Limitations: There was a large standard error in the individual replicate data for cardboard. These results	JS

					should be interpreted with caution	
Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study	Travel Med. Infect. Dis. 11APR2020	Therapeutic	What's the clinical effectiveness of the combination use of hydroxychloroquine and azithromycin in COVID-19 patients?	The combination of hydroxychloroquine and azithromycin resulted in a clinical improvement and the rapid decrease in viral RNA load. In addition, the fall in culture positivity from the second day was also remarkable.	Limitations: the study is a non-comparable, uncontrolled observational study. The sample size is 80, which is relatively small. All of the study candidates only present with mild symptoms. Implications: For the treatment of COVID-19 patients with mild symptoms, the combination use of hydroxychloroquine and azithromycin can improve symptom relief. The cheap and accessible characteristics of these two drugs make them the potential candidates for standard coronavirus therapy.	XF
PCR Assays Turned Positive in 25 Discharged COVID-19 Patients	Clinical Infectious Diseases, Apr 8, 2020	Public Health/ Epi	How many hospitalized COVID-19 patients test positive again after discharge?	This study follows 172 hospitalized patients in Wuhan, China who were discharged after meeting the following criteria: 1) Normal body temperature for 3 days 2) Significant reduction of pulmonary symptoms 3) Significant improvement on chest CT 4) 2 consecutively negative RT-PCR	Implications: This study suggests that a substantial fraction of discharged patients may become PCR-positive for SARS-CoV-2 after testing negative in the hospital. This may inform disease control strategies for	NR

				results separated by at least 24 hours. Patients were tested with repeat RT-PCR every 3 days for 2 weeks following discharge. During this period, 25 patients (14.5%) tested positive for SARS-CoV-2 post-discharge and were readmitted. Average time between last negative PCR and new positive was 7.32 days. Upon 2nd admission, 8 patients (32%) experienced mild cough, while the rest were asymptomatic. The authors report negative correlation between D-dimer and duration of treatment, as well as correlation between leukocyte count at discharge and time to positive PCR, but these correlations are weak and not convincing.	patients post-discharge as well as additional criteria for discharge. Limitations: Small sample size, does not provide adequate information on the disease course/severity of the patients studied. Authors report some correlations using lab values of those who re-tested positive, but these are reported using r value instead of r-squared. The scatterplots provided suggest little-to-no correlation, and any correlation detected is likely due to a couple outliers.	

						
Symptom Screening at Illness Onset of Health Care Personnel with SARS-CoV-2 Infection in King County, Washington.	JAMA, April 17, 2020.	Other	Retrospectively, what screening questions are most accurate at identifying HCPs with SARS-CoV2?	50 HCPs were ID'd who had lab confirmed COVID19. Most common initial sx were cough (50%), fever (41.7%), and myalgias (35.4%). 8/50 subjects did not experience fever, cough, SOB, or sore throat at sx onset, among these subjects most common sx were chills, myalgia, coryza, and malaise. **64.6% worked a median of 2 days while exhibiting sx.**	Implications: The sensitive screening sx for COVID19 among HCPs include fever, cough, myalgias, chills. HCPs are still reporting to work, even after sx onset. Mask use at work may mitigate risk of transmission to colleagues or patients. Limitations: Small sample size, variations in testing criteria, limited testing availability	CN
ST-segment Elevation, Myocardial Injury, and Suspected or	Mayo Clinic Proceedings, April 13, 2020	Clinical/ diagnostic	How should COVID-19 patients whose disease course is complicated by ST	Authors propose triage algorithm to delay PCI for low risk patients with no risk factors for CAD in the setting of COVID-19 and patients	Implications: Triage algorithm can prevent unnecessary PCI in COVID-19 patients, which limits	CS 4/21

Confirmed COVID-19 Patients: Diagnostic and Treatment Uncertainties			elevation be triaged to avoid unnecessary PCI?	with complicated disease course who would not benefit from PCI in order to employ alternative diagnostic methods (Echo, CTTA) to assess cardiac function.	exposure of staff to COVID during transit of patient and limits unnecessary risk to patient undergoing unnecessary PCI. Limitations: Prevalence of ST elevation in COVID-19 patients secondary to causes other than CA occlusion is unknown and has only been reported in case studies at this time (Hu et al; Inciardi et al). The triage algorithm also relies on rapid availability of imaging modalities that may not be realistic for all healthcare systems.	
Antibody Detection and Dynamic Characteristics in Patients with COVID- 19	*Clinical Infectious Diseases*, 19 April 2020	clinical/diagnostic	Are IgM and IgG useful in diagnosis in patients with confirmed or suspected COVID-19 at 3-40 days after symptom onset?	In PCR confirmed cases, IgM and IgG were detected as early as the 4th day after symptom (sx) onset. IgM sharply increased beginning day 9 and IgG sharply increased day 11 after sx onset. Compared with RT-PCR in 66 patients with a positive RT- PCR, IgM had a sensitivity of 77.3%, specificity of 100%, PPV of 100%, NPV of 80%. IgG was 83.3.3% sensitive, 95.0% specific, PPV=94.8%, and NPV=83.8%. In 24 patients with suspected COVID-19,	Limitation: small n, study considered positive dx by RT-PCR of nasal or throat swab but throat swab is more sensitive. RT-PCR remains gold standard for dx, but antibody assays could be quicker and cheaper and may be used as a compliment in dx. IgM and IgG antibodies could be detected in the middle and later stages of disease, and	LW 4/20

				but 2 negative RT-PCRs; IgM specificity=87.5%, sensitivity=100% PPV=100%, NPV=95.2%. IgG in suspected cases was 70.8% sensitive, 96.6% specific, PPV=85.0% and NPV= 89.1%	were highly specific for COVID-19.	
Chloroquine paradox may cause more damage than help fight COVID-19	Microbes and Infection 17 April 2020	therapeutic	What is the evidence for potential harm from CHL in other viruses? What have clinical trials demonstrated for CHL in COVID19?	CHL/HCHL have been effective for many viruses including SARS-CoV in vitro. In-vivo (mostly animal models) CHL/HCHL have either had no effect or may have increased the viral replication and/or disease severity in influenza, dengue, Semliki forest virus, encephalomyocarditis virus (EMCV), Nipah and Hendra viruses, chikungunya virus, and Ebola virus. 2 studies showed increased incidence of herpes zoster in patients treated with CHL. However, mice models of milder coronaviruses have shown protection in newborn mice from mothers treated with CHL. CHL did not show anti-viral activity in mice with SARS-CoV. There have now been several clinical trials with contradictory results on the	This is a letter to the editor that reviewed previous studies of CHL; however these studies were in other viruses, many of which are not closely related to SARS-CoV-2. This letter also described the lack of clinical data for use of CHL in patients with COVID19. Two small randomized trials found benefit from CHL with azithromycin; however, some cohort studies suggested no benefit from CHL. CHL may provide some benefit but the data from clinical trials is limited. Extreme caution must be taken as self-administration	LW 4/21

				efficacy of CHL/HCHL in COVID-19 patients. The data from these trials are limited due to small sample sizes and in some cases lack of comparison groups.	of CHL can be highly toxic. Clinicians should consider treatment options with more in-vivo studies.	
COVID-19 Antibody Seroprevalence in Santa Clara County, California	MedRxiv, 4/17/20 Not peer reviewed	Public Health/Epi	What percent of the population of Santa Clara county is seropositive for antibodies against SARS-CoV-2?	3,300 adults and children in Santa Clara County, California were tested for antibodies against SARS-CoV-2 using capillary blood draw and lateral flow immunoassays. Subjects were recruited via Facebook and collection was performed in a drive-through manner. Sample over-represented white women, while under-representing men and people of Hispanic and Asian descent based on county demographics. Using pre-COVID patient controls and PCR-confirmed COVID samples, the test kit used was estimated to have 80.3% sensitivity and 99.5% specificity. Of the 3,300 subjects, 50 tests were positive (1.5%). Adjusting for test kit sensitivity and specificity, as well as weighing the sample to match Santa Clara County demographics, the seroprevalence was estimated at 2.49% - 4.16%.	Implications: This study suggests the actual number of SARS-CoV-2 infected people in Santa Clara County is 50-86 fold higher than reported with PCR testing. Based on projected deaths from COVID-19 in this county, their data also suggest an infection fatality rate between 0.12-0.2% (much lower than current estimates). However, these data also suggest that the large majority of people have not been infected with SARS-CoV-2, and therefore do not possess immunity. Limitations: This is only data from one county; other counties' infection rates will vary based on factors such as time of stay-at-home order initiation. Study design using Facebook recruitment	NR

					and drive-through testing centers skews the sample to people who use Facebook (favoring white women) and does not account for people who do not own a car. Testing kit used for this study is not yet FDA approved. This study provides no data on what percent of subjects believe they were previously ill.	
Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19	Journal of autoimmunity, 4/13/2020	Basic Science	What is ACE 2 role in viral susceptibility and post infection modulation among those with baseline lung disease/insults?	The expression of ACE2 in healthy populations and patients with underlying diseases was not significantly different. However, based on the elevated expression of ACE2 in cigarette smokers, it's possible that long-term smoking may be a risk factor for COVID-19	Clinical implications: This study will help clinicians gain insight into the pathogenesis of SARS-COV-2, and use findings to design therapeutic strategies for COVID-19. Limitations: results in this study are based on data mining and basic science and translational studies are required to confirm these models	JS

Comparative tropism, replication kinetics, and cell damage profiling of SARS-CoV-2 and SARS-CoV with implications for clinical manifestations, transmissibility, and laboratory studies of COVID-19: an observational study	The Lancet April 21, 2020	Basic science	What are the differences of cellular susceptibility, species tropism, replication kinetics, and cell damage between SARS-CoV-2 and SARS-CoV?	The cellular tropism of SARS-CoV-2 was similar to that of SARS-CoV, which showed significant virus replication in Calu3 (pulmonary; p=0·0003), Caco2 (intestinal; p=0·0009) cells, Huh7 (hepatic; p=0·012), 293T (renal; p=0·0080) cells, but moderate replication in U251 (neuronal; p=0·036) cells. Specifically, SARS-CoV-2 replicated to comparable levels in both Calu3 and Caco2 (intestinal) cells, whereas SARS-CoV replicated significantly more efficiently in Caco2 than in Calu3 cells, which supports the higher incidence of diarrhea in patients with SARS than in COVID-19 patients. The rapid viral replications in the pulmonary cell indicating the abilities of these coronaviruses to cause lower respiratory tract infection. Up to 43% of patients with COVID-19 patients developed hepatic dysfunction, and 3–7% of patients with COVID-19 developed acute kidney injury or needed renal replacement therapy. There are up to 9% of patients with COVID-19 developed confusion or dizziness, correlated with the moderate viral implication on U251 cells.	Implications: The results of this study provide the differences in clinical manifestations and transmission characteristics between SARS-CoV-2 and SARS-CoV. This information can be used to design diagnostics and research methods for COVID-19. Limitations: cell line tropism might not fully represent how SARS-CoV-2 replicates and affects human organs in the physiological state. It is essential to further characterize virus–host interactions in more physiological models, such as ex-vivo human organ tissue and human organoids from patients of different ages, sexes, and with underlying diseases. Further assessments of virus-induced damage in cardiac cells and potential animal reservoirs.	XF

				Although SARS-CoV-2 and SARS-CoV were inoculated with the same MOI, SARS-CoV-2 induced less cell damage than did SARS-CoV. However, SARS-CoV-2 showed more efficient replication in Calu3 cells than did SARS-CoV, which correlates with higher transmissibility of SARS-CoV-2.		
Family violence and COVID-19: Increased vulnerability and reduced options for support	International Journal of Mental Health Nursing, 20 April 2020	Public health	What are the risk factors and observed trends in family violence during COVID19	"Social Isolation exacerbates vulnerabilities while limiting accessible and familiar support options (van Gelder et al. 2020)." Reported in Australia, there has been an increase in demand for domestic violence services and increased reports of children not attending schools There was also a 5% increase in domestic abuse call outs by police (Kagi 2020). "At the same time in Australia, Google reported a 75% increase in internet searches relating to support for domestic abuse (Poate 2020)." There was three times the reported domestic abuse incidents in February 2020 in China	unemployment, limited resources, increased confinement at home with violent perpetrators, increased substance consumption at home, and limited social support are compounding risk factors for family violence that are increasing with prolonged widespread closures. Social-distancing is proving an effective measure for containing infection; however, we must consider the social, economic and psychological consequences, that may be severe and ultimately lead to death. These risks must	LW 4/22

				compared to the previous year (Allen-Ebrahimian 2020). "France reported a 32% - 36% increase in domestic abuse complaints following the implementation of self-isolation and quarantine measures (Reuters News Agency 2020)." In the US, increases in domestic abuse incidents ranged from 21%-35% (Wagers 2020). Alcohol sales have risen globally, and with bars and restaurants closed more are consuming at home, thus increasing risk for violence at home. During isolation, signs of abuse both physical and emotional are less visible to other people who can help such as teachers or other community members.	be weighed against the risks of infection.	

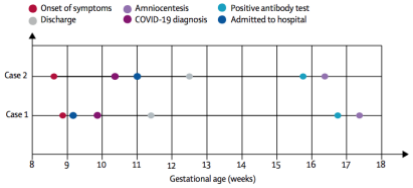
Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study	BMJ; 21 April 2020	Retrospective Cohort study	How long is viral RNA detectable respiratory, stool, serum, and urine samples? Does disease severity correlate with higher viral loads/persistent viral loads? Is viral load different between young vs old; men vs women?	The median duration of virus in stool samples (22 days, interquartile range 17-31 days) was significantly longer than in respiratory (18 days, 13-29 days; P=0.02) and serum samples (16 days, 11-21 days; P<0.001). In the respiratory samples, the median duration of virus in patients with severe disease (21 days, 14-30 days) was significantly longer than in patients with mild disease (14 days, 10-21 days; P=0.04). Viral load was highest in Respiratory samples. Severe cases had significantly higher respiratory viral load than mild cases. When cases were stratified for severe/mild, viral load was detectable significantly longer in men than women, and in old than young, in severe diseases but NOT in mild disease.	Limitations: limited sample size of n = 96, 22 mild disease and 74 with severe disease. One study site location in China, may not be generalizable to other populations. Implications: persistent viral load may be prognostic marker for disease. Longer detection rate in stool suggests role of fecal excretion in the spread of SARS-CoV-2 cannot be ignored. Supports that duration of illness in severe cases is longer in men than women, suggests could be due to difference in hormone levels[1].	CS

Tocilizumab treatment in COVID-19: A single center experience	Journal of Medical Virology, Apr 06 2020	Retrospective observational study	Is Tocilizumab (a monoclonal antibody) an effective treatment for those suffering from Covid-19	15 Covid-19 patients under Tocilizumab (toc) therapy were assessed in this retrospective study. Patients were monitored by CRP and IL-6 as a measure of inflammation. Toc therapy in all patients resulted in a decrease in serum CRP (126 --> 11.2). However, within the four critically ill patients who received only 1 dose ,3 died and one failed to show response. Serum IL-6 in all patients appeared to spike first and then decreased.	Clinical Indication: Although a single dose may not improve disease activity, repeated doses may improve the condition of critically ill patients Limitations: Small sample size of only 15 patients. Treatment duration may not be sufficient to make a conclusion.	JS 4/22

Treating hypoxemic patients with SARS-COV-2 pneumonia: Back to applied physiology	*Anaesthesia Critical Care & Pain Medicine* **Journal Pre-Proof** 16 April 2020	Other: Descriptive Cohort	Journal Pre-Proof describing observations of 82 ventilated patients in an ICU in Switzerland.	During the first 2 days of mechanical ventilation (MV), the majority surprisingly exhibited good lung compliance positive pressure MV is mainly beneficial during the first 2 days of MV, in those with preserved lung compliance due to "decreased venous return, right ventricular output, transpulmonary blood flow and finally intrapulmonary shunt. The positive impact of reverse Trendelenburg positioning on SaO2 values, in selected patients, can be spectacular." After over 48 hours of the mechanical stress of MV, or in those with chronic lung disease, patients had more classical ARDS requiring higher PEEP, a lower tidal volume, prone positioning, neuromuscular blocking agents or even ECMO.	The researchers postulate that early in SARS-CoV-2 pneumonia there is high permeability type pulmonary edema with apparently preserved lung compliance. These patients may progress to the typical ARDS phenotype. Mortality in COVID19 for those requiring MV is high (62% and 97% Cited in Wuhan) For patients early in the disease course or with transient hypoxemia we may be able to avoid invasive MV by other methods to decrease transpulmonary shunting e.g. the reverse trendelenburg position, almitrine, CPAP.	LW
The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro	Antiviral Research, 4/3/2020	Therapeutic	Can ivermectin's nuclear transport inhibitory activity be used to the effective treatment against SARS-CoV-2 in vitro?	Ivermectin is an FDA-approved anti-parasitic previously shown to have broad-spectrum anti-viral activity in vitro, including the inhibition of HIV-1 replication, DENV 1-4, West Nile Virus, Venezuelan equine encephalitis	Implications: The effectiveness of ivermectin in treating SARS-CoV-2 might come from inhibiting IMPα/β1-mediated nuclear import of viral proteins. Development of an	XF

				virus (VEEV), influenza as well as DNA virus pseudorabies virus (PRV). To test the antiviral activity, 5 µM ivermectin was add to Vero/hSLAM cells with SARS-CoV-2 isolate Australia/VIC01/2020 at a MOI of 0.1 for 2 h. The results showed a 93% reduction in viral RNA present at 24 h and a ~5000-fold viral RNA reduction at 48 h of the Ivermectin sample compared to control. In addition, no cytotoxicity is observed in either ivermectin sample or control group.	effective anti-viral for SARS-CoV-2 could help to limit the viral load, prevent severe disease progression and limit person-person transmission. Ivermectin is also FDA-approved, safe for human use. Limitations: This study is in vitro. More clinical trials using ivermectin on human need to be conducted to prove the anti-viral effects. <u>Question: Does the amount of viral RNA load correlate to the transmission ability of a type of virus?</u>	

High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation.	Obesity, 4/9/2020	Clinical	How does BMI affect the clinical course of patients hospitalized with COVID-19?	This study enrolled 124 patients admitted to the ICU at the Roger Salengro Hospital in Lille, France. When compared to a non-SARS-Cov-2 control patient population from 2019, the COVID-19 population in the ICU had significantly higher median BMI (29.6 vs. 24.0, p<.0001), while age and sex did not differ significantly. Among COVID-19 patients, those requiring invasive mechanical ventilation (IMV) had higher median BMI than those that did not require IMV (31.1 vs. 27.0, p<.001). Male sex and BMI >35 significantly increased odds ratio for requiring IMV independent of age, hypertension and diabetes.	Limitations: Only studies patients in one hospital. This region's obesity rate and the hospital's criteria for beginning mechanical ventilation will affect this study's external validity. Historical control group may not completely eliminate confounding variables, as they are patients from a different month/year. Sample size was too small to evaluate relationship between BMI and mortality. Implications: This study suggests that BMI is a key risk factor for severe COVID-19 requiring ICU admission and invasive mechanical ventilation.	NR 4/22

No SARS-CoV2 detected in amniotic fluid in mid pregnancy	Lancet, 4/22/2020	Clinical	Is there viral RNA from SARS-CoV2 detectable in the amniotic fluid of laboratory confirmed SARS-CoV2+ women in mid-pregnancy?	This study enrolled 2 women who contracted SARS-CoV2 during early pregnancy. They were at 8 weeks and 10 weeks pregnancy at the time of infection. Amniotic samples were taken during these patients' hospitalizations. Both amniocenteses were negative for SARS-CoV2 RNA PCR and IgG and IgM antibodies.  	Implications: There has been a lot of concern about the potential implications of SARS-CoV2 infection during pregnancy. It is encouraging that there was no detectable RNA via PCR or antibodies detected during amniocentesis. However, this studies has may limitations, including small sample size (N=2), young embryologic age (best age for amniocentesis is 18-20 weeks), transient nature of RNA (in Zika, another RNA virus, there are only transient positive viral PCRS on amniocentesis).	
Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved a-ketoamide inhibitors	Science, 4/22/20	Basic Science	How can crystalizing the structure of SARS-CoV-2's major protease inform design of therapeutics to inhibit viral replication?	SARS-CoV-2's main protease (M^{Pro}) is one of the best-characterized therapeutic targets in treating COVID-19, as it is responsible for processing the polypeptides produced from viral mRNA. The authors crystalized the structure of M^{Pro} and used this information to modify an a-ketoamide inhibitor to effectively inhibit SARS-CoV-2 in human lung cells *in-vitro.* Inhalation of the drug was tolerated well in mice and both	Implications: Knowing the crystalized structure of M^{Pro} will be important for developing other potential therapeutics. This study presents an optimized a-ketoamide inhibitor as one therapeutic option by inhibiting the virus' main protease. Limitations:	NR 4/23

				subcutaneous and inhaled drug produced good lung tropism.	This is an *in-vitro* study, so its results may not translate to animal models or human patients.	