PERSPECTIVES

Biological plausibility for interactions between dietary fat, resveratrol, ACE2, and SARS-CoV illness severity

Justine R. Horne and Marie-Claude Vohl
Centre Nutrition, Santé et Société (NUTRISS)-Institut sur la Nutrition et les Aliments Fonctionnels (INAF), Université Laval, Quebec City, Quebec, Canada

Submitted 13 April 2020; accepted in final form 20 April 2020

Horne JR, Vohl MC. Biological plausibility for interactions between dietary fat, resveratrol, ACE2, and SARS-CoV illness severity. Am J Physiol Endocrinol Metab 318: E830–E833, 2020. First published April 20, 2020; doi:10.1152/ajpendo.00150.2020.—The angiotensin converting enzyme-2 (ACE2) cellular receptor is responsible for the pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), thus impacting the entrance and clearance of the virus. Studies demonstrate that upregulation of ACE2 has a protective effect on SARS-CoV-2 illness severity. Moreover, animal studies demonstrate that dietary intake can modulate ACE2 gene expression and function. A high intake of resveratrol may have a protective role, upregulating ACE2, whereas a high intake of dietary fat may have a detrimental role, downregulating ACE2. As such, we postulate on the biological plausibility of interactions between dietary fat and/or resveratrol and ACE2 gene variations in the modulation of SARS-CoV-2 illness severity. We call to action the research community to test this plausible interaction in a sample of human subjects.

ACE2; coronavirus; nutrigenetics; nutrigenomics; SARS

INTRODUCTION

Severe acute respiratory syndrome coronaviruses (SARS-CoV), including the original SARS-CoV (2003) and the novel SARS-CoV-2 (2019), are highly pathogenic viruses made up of structural proteins including spike, membrane, nucleocapsid, and envelope proteins (16, 39). Eighty percent of the genetic sequence of SARS-CoV (2003) is identical to SARS-CoV-2, the virus responsible for the global pandemic caused by the infectious disease COVID-19. The pathophysiology of CoV involves receptor-binding and proteolysis; these processes result in virus-cell fusion as previously detailed elsewhere (29). A key component of virus pathogenesis for SARS-CoV involves the cellular receptor angiotensin converting enzyme-2 (ACE2) (23, 43).

Emerging research has demonstrated that dietary intake can impact the expression and function of the ACE2 gene (30, 41). Given our knowledge of the importance of ACE2 for SARS-CoV pathogenesis, coupled with preliminary knowledge about the impact of nutrition on ACE2 gene expression and function, the purpose of this paper is to present the evidence for the biological plausibility of gene-diet interactions with ACE2 modulating SARS-CoV illness severity.

Correspondence: M.-C. Vohl (marie-claude.vohl@fsaa.ulaval.ca).

BIOLOGICAL PLASIBILITY FOR GENE-DIET INTERACTIONS

ACE2 and SARS-CoV. With ACE2 as the cellular receptor for SARS-CoV, the interaction between the virus and ACE2 impacts its entrance and clearance (29, 45). ACE is responsible for the cleavage of AngI into AngII (34, 37), and following this process, ACE2 generates Ang (16, 23, 29, 30, 39, 41, 43) from a single residue cleavage of AngII and then acts as a negative regulator (8). This phenomenon has been demonstrated in mouse models, whereby disrupting the murine ACE2 gene leads to increased levels of AngII (6). ACE2 is attached to the cell membranes of lung, artery, heart, testicular, kidney, and intestinal cells (7, 8, 14). Alveolar epithelial type II cells of the lungs make up over 80% of the cells expressing ACE2 (45). ACE2 is also highly expressed on the liminal surface of intestinal epithelial cells (15), which may support the hypothesis that the COVID-19 pandemic may have begun with the consumption of an infected bat.

Acute respiratory distress syndrome is a form of acute lung injury that can result from SARS-CoV (35). With ACE2 as the cellular receptor for SARS-CoV, research demonstrates that ACE2 knockout mice are resistant to SARS-CoV infections (17, 20). Although ACE2 is needed for SARS-CoV host cell entry and replication (17), it is also important to disease progression and has been demonstrated to play a central (protective) role in determining symptom severity of acute respiratory distress syndrome (18). Accordingly, animal model research demonstrates that the disease severity of acute lung injury and acute respiratory distress syndrome were significantly more severe in mice with ACE2 inactivated or knocked out after the infection with SARS-CoV compared with the wild-type mice. The knockout mice, with loss of ACE2 expression after being infected, experienced enhanced vascular permeability, increased lung edema, neutrophil accumulation, and worsened lung function. When these mice were then treated with catalytically active recombinant ACE2 protein, these symptoms improved (18). Several other studies have also demonstrated a therapeutic effect of ACE2 treatment on acute lung injury (1, 4, 27).

As such, the ACE2 cellular receptor has been proposed as a key target for the therapeutic treatment of SARS-CoV (41, 43). The virus has a strong binding affinity to human ACE2 (22), and ACE2 is required for host cell entry and viral replication (43). Following SARS-CoV infection, ACE2 expression is downregulated (20), which may play a causal role in the pathogenesis and disease progression (17). Overall, ACE2 activity is protective against SARS-CoV pathogenesis.
Impact of dietary intake on ACE2 activity. With a lack of studies in humans [with the exception of one in vitro study in human aortic cells (28)], animal models inform our current knowledge base related to the impact of dietary factors on ACE2. ACE2 activity appears to be responsive to dietary fat and resveratrol, as further detailed below. Some preliminary research has also assessed the impact of high-fructose diets on ACE2 protein levels (3), and the impact of high-sodium diets on ACE2 receptor expression (26) but this work is only in its infancy.

The vast majority of the research on the impact of dietary intake on ACE2 activity has focused on dietary fat intake. Within these studies, the amount of dietary fat in the high-fat diet (HFD) groups varies from ~50 to 60% of total energy intake (11–13, 41). In a 10-wk dietary intervention study in mice, ACE2 gene expression was examined in a control group (76% carbohydrate, 14% protein, 10% lipids) and an HFD group, in which the HFD was rich in saturated fat (36% carbohydrate, 14% protein, 50% lipids). The mRNA levels in mice livers were assessed, and it was observed that ACE2 gene expression was reduced in the HFD group compared with the control group (11). Similarly, another study in the retroperitoneal adipose tissue of postnatal rats found that consumption of an HFD downregulated ACE2 gene expression (41). Research has also demonstrated that an HFD can lead to reduced kidney ACE2 activity only in male mice and further demonstrated that the ovariectomy of female mice fed an HFD led to reduced adipose ACE2 activity (13). These nutrition-related changes in ACE2 gene expression appear to impact further health-related outcomes. Accordingly, ACE2 deficiency resulted in increased systolic BP in male and female mice fed an HFD and promoted obesity-hypertension in female, ovariectomized mice fed an HFD (13). In a study of ACE2 knockout compared with wild-type mice fed an HFD for 16 wk, knockout mice were more susceptible to beta cell dysfunction (24).

There are, however, some inconsistencies in the literature that should be noted. In a study on mice adipose tissue, ACE2 mRNA expression, activity and protein increased in response to an HFD (12). In a study on pancreatic islet cells of wild-type and ACE2 knockout fed an HFD for 16 wk, there was no change in ACE2 gene expression specifically in response to the HFD, but the authors suggest that ACE2 gene expression was likely altered in other cells given their findings that ACE2 gene therapy improved glycemia in the mice fed an HFD (5).

Beyond an HFD, there is consistent preliminary research demonstrating the potential for resveratrol to contribute to ACE2 activity. Resveratrol is a polyphenolic compound found in plant-based foods, such as red wine, berries, grapes, cocoa, and other foods. This compound is known for its potential protective effect against a number of conditions including cancer, cardiovascular disease, and respiratory illness (2, 33, 42). To date, three studies have assessed the impact of resveratrol on ACE2 activity. In a study of rats assigned to one of five different experimental diet groups, the rats who were fed 50 mg·kg⁻¹·day of resveratrol demonstrated increased ACE2 protein level (38). In another study of mice fed an HFD compared with mice fed an HFD + resveratrol, there was significantly increased ACE2 gene expression in mice fed the HFD + resveratrol. Therefore, the addition of dietary resveratrol may help to mitigate the detrimental impacts of high-fat diets on ACE2 gene expression (30). Last, an in vitro study using human aortic smooth muscle cells demonstrated that incubation of cells with resveratrol for 24 h significantly increased ACE2 gene and protein expression (28).

Proposed gene-diet interactions of ACE2 and SARS-CoV in humans. Hypotheses about human gene-diet interactions often stem from animal model and in vitro research. The abovementioned results suggest that interactions between ACE2, dietary fat, and SARS-CoV, as well as ACE2, resveratrol, and SARS-CoV influencing illness severity are biologically plausible in

Fig. 1. Breakdown of proposed biological plausibility for interactions between dietary fat, resveratrol, angiotensin converting enzyme 2 (ACE2), and severe acute respiratory syndrome coronavirus (SARS-CoV) illness severity.
humans. Thus, we propose a potential mechanism whereby lower dietary fat and/or higher resveratrol intake may modulate responses to SARS-CoV, dependent on genetic variations in ACE2, which may then upregulate or downregulate its activity (Fig. 1). This hypothesis is supported by the abovementioned research demonstrating 1) that ACE2 plays a key role in SARS-CoV disease progression (18) and 2) the impact of diet on ACE2 expression and function (11, 13, 24, 28, 30, 38, 41). This may help to explain the vast interindividual variability observed in SARS-CoV-2 illness severity in humans (21).

Furthermore, there is an association between HFD consumption and risk of developing diabetes mellitus (DM), suggesting that individuals with DM are more likely to consume an HFD (9, 36). As such, this proposed mechanism could add to the body of knowledge seeking to explain why SARS-CoV illness severity is greater in individuals with DM as well as in individuals with hypertension (HTN) (29). In addition, ACE2 genetic variations contribute to type 2 DM and HTN risk, and thus high-risk genetic variants are more prevalent in these populations. Specific ACE2 SNPs that have been previously demonstrated to be associated with type 2 DM and HTN (rs2106809, rs4646174, rs2074192, rs4240157, rs4646188, rs1978124, rs233575, rs2158083) are of interest to future research (10, 25, 31, 32, 40, 44). One study previously explored ACE2 genetic variations between SARS-CoV-2 (2003) cases, noncases, and contact and while no significant associations were found (19), it is possible that dietary intake confounded these results. In addition, to our knowledge this study has yet to be replicated for SARS-CoV-2. Several other potential SNPs of interest were outlined in this study (19), which would be worth exploring in future research involving ACE2 and SARS-CoV illness severity.

CONCLUSION

Human studies are urgently needed to determine whether the proposed mechanism exists in a nonanimal model. If this proposed mechanism proves to be plausible in human studies, dietitians and other healthcare professionals could target dietary strategies with the aim of positively improving SARS-CoV illness severity in this current global COVID-19 pandemic.

GRANTS

MC Vohl is a Tier 1 Canada Research Chair in Genomics Applied to Nutrition and Metabolic Health. J Horne was supported through postdoctoral fellowships from the Centre Nutrition, Santé et Société (NUTRIS) and the Institut sur la nutrition et les aliments fonctionnels (INAF).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

J.R.H. conceived and designed research; J.R.H. interpreted results of experiments; J.R.H. and M.-C.V. prepared figures; J.R.H. and M.-C.V. drafted manuscript; J.R.H. and M.-C.V. edited and revised manuscript; J.R.H. and M.-C.V. approved final version of manuscript.

REFERENCES

1. Bao H, Gao F, Xie G, Liu Z. Angiotensin-converting enzyme 2 inhibits apoptosis of pulmonary endothelial cells during acute lung injury through suppressing MIR-4262. Cell Physiol Biochem 37: 759–767, 2015. doi:10.1159/000430393.

2. Bonnefont-Rousselot D. Resveratrol and cardiovascular diseases. Nutrients 8: 250, 2016. doi:10.3390/nu8050250.

3. Bundalo MM, Zivkovic MD, Romic SD, Tepavecic SN, Koricanac GB, Djuric TM, Stankovic AD. Fructose-rich diet induces gender-specific changes in expression of the renin-angiotensin system in rat heart and upregulates the ACE/AT1R axis in the male rat aorta. J Renin Angiotensin Aldosterone Syst 17: 1470320316642915, 2016. doi:10.1177/1470320316642915.

4. Chen D, Jiao G, Ma T, Liu X, Yang C, Liu Z. The mechanism of ramipril in the intervention of paragut-induced acute lung injury in rats. Xenobiotica 45: 538–546, 2015. doi:10.3109/00498254.2014.995149.

5. Chodavarapu H, Chhabra KH, Xia H, Shenoy V, Yue X, Lazartigues E. High-fat diet-induced glucose dysregulation is independent of changes in islet ACE2 in mice. Am J Physiol Regul Integr Comp Physiol 311: R1223–R1233, 2016. doi:10.1152/ajpregu.00362.2016.

6. Crackower MA, Sarao R, Oudit YG, Yagil C, Kozieradzki I, Scanga SE, Oliveire-dos-Santos AJ, da Costa J, Zhang L, Pei Y, Scholey J, Ferrari CR, Manoukian AS, Chappell MC, Baacks PY, Yagil Y, Penninger JM. Angiotensin-converting enzyme 2 is an essential regulator of heart function. Nature 417: 822–828, 2002. doi:10.1038/nature00786.

7. Donoghue M, Hsieh F, Baronas E, Godbold K, Gosselin M, Stagliano N, Leveseanu R, Breithart RE, Kanyo EJ, Timens W, Bulthuis MLC, Lely AT, Navis G, van Goor H. The novel angiotensin-converting enzyme-related carboxypeptidase (ACE2) converts angiotensin I to angiotensin 1-9. Circ Res 87: E1–E9, 2000. doi:10.1161/01.RES.87.5.e1.

8. Douglas GC, O’Bryan MK, Hudger MP, Lee DKL, Yarski MA, Smith AI, Lew RA. The novel angiotensin-converting enzyme (ACE) homolog, ACE2, is selectively expressed by adult Leydig cells of the testis. Endocrinology 145: 4703–4711, 2004. doi:10.1210/en.2004-0443.

9. Erber E, Hopping BN, Grandinetti A, Park S-Y, Kolonel LN, Maskarinec G. Dietary patterns and risk for diabetes: the multiethnic cohort. Diabetes Care 33: 532–538, 2010. doi:10.2337/dc09-1621.

10. Fan X, Wang Y, Sun K, Zhang W, Yang X, Wang S, Zhen Y, Wang J, Li W, Han Y, Liu T, Wang X, Chen J, Wu H, Hui R; Study Group for Pharmacogenomic Based Antihypertensive Drugs Selection, Effects and Side Effects, in Rural Area Chinese. Polymorphisms of ACE2 gene are associated with essential hypertension and antihypertensive effects of Captopril in women. Clin Pharmacol Ther 82: 187–196, 2007. doi:10.1038/sj.cpt.6100214.

11. Graus-Nunes F, Santos FO, Marinho TS, Miranda CS, Barbosa-da-Silva S, Souza-Mello V. Beneficial effects of losartan or telmisartan on the local hepatic renin-angiotensin system to counter obesity in an experimental model. World J Hepatol 11: 359–369, 2019. doi:10.4254/wjh.v11.4.359.

12. Gupte M, Boustany-Kari CM, Bharadwaj K, Police S, Thatcher S, Bonnefont-Rousselot D. Angiotensin-converting enzyme 2 (ACE2) in disease pathogenesis. Acta Biochim Pol 63: 417–426, 2016. doi:10.2442/pol.063000183.

13. Gupte M, Thatcher SE, Boustany-Kari CM, Yian-nikouiris F, Zhang X, Karounos M, Cassa LA. Angiotensin converting enzyme 2 contributes to sex differences in the development of obesity hypertension in C57BL/6 mice. Arterioscler Thromb Vasc Biol 32: 1392–1399, 2012. doi:10.1161/ATVBAHA.112.248559.

14. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS-CoV, one step in understanding SARS pathogenesis. J Pathol 203: 631–637, 2004. doi:10.1002/path.1570.

15. Hashimoto T, Perfot L, Rehman A, Trichereau J, Ishiguro H, Paolino M, Sigl V, Hanada T, Hanada R, Lipinski S, Wild B, Camargo SM, Singer D, Richter A, Kuba K, Fukamizu A, Schreiber S, Clevers H, Verrey F, Rosenstiel P, Penninger JM. ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. Nature 487: 477–481, 2012. doi:10.1038/nature11228.

16. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 181: 271–280, 2020. doi:10.1016/j.cell.2020.02.052.

17. Imai Y, Kuba K, Ohto-Nakanishi T, Penninger JM. Angiotensin-converting enzyme 2 (ACE2) in disease pathogenesis. Circ J 74: 405–410, 2010. doi:10.1253/circj.CJ-10-0045.

18. Imai Y, Kuba K, Rao S, Huan Y, Guo F, Guan B, Yang P, Sarao R, Wada T, Leong-Poi H, Crackerwa MA, Fukamizu A, Hui CC, Hein L,
Uhlig S, Slutsky AS, Jiang C, Penninger JM. Angiotensin-converting enzyme 2 protects from severe acute lung failure. *Nature* 436: 112–116, 2005. doi: 10.1038/nature03712.

Itoyama S, Keicho M, Hijkata M, Qu T, Phi NC, Long HT, Ha LD, Ban VV, Matsushita I, Yanai H, Kirikae F, Kirikae T, Kuratsuji T, Sasazuki T. Identification of an alternative 5′-untranslated exon and new polymorphisms of angiotensin-converting enzyme 2 gene: lack of association with SARS in the Vietnamese population. *Am J Med Genet A* 136: 52–57, 2005. doi: 10.1002/ajmg.a.30779.

Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, Huan Y, Yang P, Zhang Y, Deng W, Bao L, Zhang B, Liu G, Wang Z, Chappell M, Liu Y, Zheng D, Leibbrandt A, Wada T, Slutsky AS, Liu D, Qin C, Jiang C, Penninger JM. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. *Nat Med* 11: 875–879, 2005. doi:10.1038/nm1267.

Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents* 55: 105924, 2020. doi:10.1016/j.ijantimicag.2020.105924.

Li F, Li W, Farzan M, Harrison SC. Structure of SARS coronavirus spike receptor-binding domain complexed with receptor. *Science* 309: 1864–1868, 2005. doi:10.1126/science.1116480.

Li W, Moore MJ, Vasileva N, Sui J, Wang SK, Berne MA, Soloff SK, Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Identification of an alternative 5′-untranslated exon and new polymorphisms of angiotensin-converting enzyme 2 gene: lack of association with SARS in the Vietnamese population. *Am J Med Genet A* 136: 52–57, 2005. doi: 10.1002/ajmg.a.30779.

Lu C-L, Wang Y, Yuan L, Li Y, Li X-Y. The angiotensin-converting enzyme 2/angiotensin (1-7)/Mas axis protects the function of pancreatic β cells by improving the function of islet microvascular endothelial cells. *Int J Mol Med* 34: 1293–1300, 2014. doi:10.3892/mir.2014.1917.

Malard L, Kakinami L, O’Loughlin J, Roy-Gagnon M-H, Labbe A, Pilote L, Hamet P, Tremblay J, Paradis G. The association between the Angiotensin-Converting Enzyme-2 gene and blood pressure in a cohort study of adolescents. *BMC Med Genet* 14: 117, 2013. doi:10.1186/1471-2350-14-117.

Mao C, Liu R, Bo L, Chen N, Liz SX, Chen J, Li D, Zhang L, Xu Z. High-salt diets during pregnancy affected fetal and offspring renal function in a mouse model. *Am J Hypertens* 37: 1–27, 2014. doi:10.1016/j.ajh.2011.188.

Patnaik M, Pati P, Swain SN, Mohapatra MK, Dhwedi B, Kar SK, Ranjit M. Association of angiotensin-converting enzyme and angiotensin-converting enzyme-2 gene polymorphisms with essential hypertension in the population of Odisha, India. *Ann Hum Biol* 41: 145–152, 2014. doi:10.3109/03014460.2013.837195.

Raf A, Imran M, Butt MS, Nadeem M, Peters DG, Mubarak MS. Resveratrol as an anti-cancer agent: A review. *Crit Rev Food Sci Nutr* 58: 1428–1447, 2018. doi:10.1080/10408398.2016.1263597.

Riordan JF. Angiotensin-I-converting enzyme and its relatives. *Genome Biol* 4: 225, 2003. doi:10.1186/gb-2003-4-8-225.

Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, Stern EJ, Hudson LD. Incidence and outcomes of acute lung injury. *N Engl J Med* 353: 1685–1693, 2005. doi:10.1056/NEJMoai050333.

Shu L, Shen X-M, Li C, Zhang X-Y, Zheng P-F. Dietary patterns are associated with type 2 diabetes mellitus among middle-aged adults in Zhejiang Province, China. *Nutr J* 16: 81, 2017. doi:10.1186/s12937-017-0130-3.

Skegg LS, Dorer FE, Levine M, Lentz KE, Kahn JR. The biochemistry of the renin-angiotensin system. *Adv Exp Med Biol* 130: 1–27, 1980. doi:10.1007/978-1-4615-9173-3_1.

Tiao M-M, Lin Y-J, Yu H-R, Sheen J-M, Lin I-C, Lai Y-J, Tain YL, Huang LT, Tsai CC. Resveratrol ameliorates maternal and post-weaning high-fat diet-induced nonalcoholic fatty liver disease via renin-angiotensin system. *Lipids Health Dis* 17: 178, 2018. doi:10.1186/s12944-018-0824-3.

Walls AC, Park Y-J, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell* 181: 281–292.e6, 2020. doi:10.1016/j.cell.2020.02.058.

Yang J-K, Zhou J-B, Xin Z, Zhao L, Yu M, Feng J-P, Yang H, Ma YH. Interactions among related genes of renin-angiotensin system associated with type 2 diabetes. *Diabetes Care* 33: 2271–2273, 2010. doi:10.2337/dc10-0349.

Yu H-R, Tain Y-L, Tiao M-M, Chen C-C, Sheen J-M, Lin I-C, Li SW, Tsai CC, Lin YJ, Hsieh KS, Huang LT. Prenatal dexamethasone and postnatal high-fat diet have a synergistic effect of elevating blood pressure through a distinct programming mechanism of systemic and adipose renin-angiotensin systems. *Lipids Health Dis* 17: 50, 2018. doi:10.1186/s12944-018-0701-0.

Zhai T, Li S, Hu W, Li D, Leng S. Potential micronutrients and phytochemicals against the pathogenesis of chronic obstructive pulmonary disease and lung cancer. *Nutrients* 10: E813, 2018. doi:10.3390/nu10070813.

Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. *Intensive Care Med* 46: 586–590, 2020. doi:10.1007/s00134-020-05985-9.

Zhao Q, Gu D, Kelly TN, Hixson JE, Rao DC, Jaquish CE, Chen J, Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zuo W. Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCoV (Preprint). *bioRxiv*: 2020.01.26.919985. doi:10.1101/2020.01.26.919985.

**DIETARY FAT, RESVERATROL, ACE2, AND SARS-CoV**