



Title	A pressor dose of angiotensin II has no influence on the angiotensin-converting enzyme 2 and other molecules associated with SARS-CoV-2 infection in mice
Author(s)	王, 鈺
Citation	大阪大学, 2021, 博士論文
Version Type	
URL	https://hdl.handle.net/11094/85341
rights	
Note	やむを得ない事由があると学位審査研究科が承認したため、全文に代えてその内容の要約を公開しています。全文のご利用をご希望の場合は、 https://www.library.osaka-u.ac.jp/thesis/#closed 大阪大学の博士論文について https://www.library.osaka-u.ac.jp/thesis/#closed をご参照ください。

The University of Osaka Institutional Knowledge Archive : OUKA

<https://ir.library.osaka-u.ac.jp/>

The University of Osaka

論 文 内 容 の 要 旨
Synopsis of Thesis

氏 名 Name	Wang Yu
論文題名 Title	A pressor dose of angiotensin II has no influence on the angiotensin-converting enzyme 2 and other molecules associated with SARS-CoV-2 infection in mice (昇圧用量のアングiotenシンIIやアングiotenシンII受容体拮抗薬はマウスにおいてアングiotenシン変換酵素2およびSARS-CoV-2感染に関連するその他の分子の発現や活性に影響を与えない)
論文内容の要旨	
〔目 的 (Purpose)〕 In the early phase of the Coronavirus disease 2019 (COVID-19) pandemic, it was postulated that the renin-angiotensin-system inhibitors (RASi) increase the infection risk. This was primarily based on numerous reports, which stated that the RASi could increase the organ Angiotensin-converting enzyme 2 (ACE2), the receptor of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in rodents. RASi can theoretically antagonize the potential influence of angiotensin II (Ang II) on ACE2. However, while Ang II decreases the ACE2 levels in cultured cells, there is little evidence that supports this phenomenon in living animals. To address these issues, we conducted a cross-organ analysis of the lung, small intestine, heart, and kidney in mice infused with a lower dose of Ang II than previously reported, to understand the effect of Ang II or ARB on ACE2 and the associated molecules involved in the tissue invasion of SARS-CoV-2. 〔方 法 (Methods)〕 In this study, we tested whether physiological concentrations of Ang II or Ang II combined with its antagonist would alter the ACE2 and other molecules associated with the infection of SARS-CoV-2: TMPRSS2, Furin and TACE. Male C57BL6/J mice were administered vehicle, Ang II, or Ang II with losartan for 2 weeks. ACE2 knockout mice were used as a negative control for the ACE2 assay. 〔成 績 (Results)〕 We found that both Ang II, which elevated blood pressure by 30 mmHg, and Ang II with losartan, had no effect on the expression or protein activity of ACE2 in the lung, left ventricle, kidney, and ileum. Likewise, these interventions had no effect on ACE2, TMPRSS2, Furin and TACE. Collectively, physiological concentrations of Ang II do not modulate the molecules associated with SARS-CoV-2 infection. 〔総 括 (Conclusion)〕 Our study clearly indicated that Ang II is not a direct transcriptional regulator of ACE2 in vivo, and the effect of RASi on ACE2 might depend on their ability to repair organ injury. Therefore, this study could provide a theoretical basis for the fact that the use of RASi is not a risk in hypertensive patients in this COVID-19 era.	

論文審査の結果の要旨及び担当者

(申請者氏名) Wang Yu		
論文審査担当者	(職)	氏 名
	主 査 大阪大学教授	奥 本 宏 典
	副 査 大阪大学寄附講座教授	中 神 啓 俊
	副 査 大阪大学教授	坂 田 泰 史

論文審査の結果の要旨

昨年COVID-19が流行する早期の段階において、降圧薬のアンジオテンシンII (Angiotensin II) 受容体拮抗薬 (ARB) やACE阻害薬などレニン-アンジオテンシン (RA) 系阻害薬の服用がCOVID-19感染や病態悪化リスクを上昇させるという仮説が提唱された。RA系阻害薬がCOVID-19原因ウイルスSARS-CoV2受容体のACE2の臓器発現を増やすという過去の動物実験がその根拠として挙げられた。本研究では血圧を上昇させる低濃度のAngiotensin IIや血圧を正常化させるARB投与がACE2や他のSARS-CoV2関連遺伝子の臓器発現に及ぼす影響を検討した。結果としてAngiotensin IIやARBは肺、腎臓、小腸、心臓においてACE2や関連遺伝子 (Furin, TMPRSS2, ADAM17) の発現に影響を及ぼさないことが明らかになった。

本研究では従来の研究で報告されたRA系阻害薬によるACE2上昇作用が病態改善を介するもので、RA系阻害特異的な作用ではないことを支持するものである。この成果は、COVID-19の感染・重症化リスクの観点からも、社会的に必要性の高い知見と考えられ、博士(医学)の学位授与に値する。