# Evidence Search Service Results of your search request

## ACE 2 expression in different body tissues

**ID of request:** 22307  
**Date of request:** 16th March, 2020  
**Date of completion:** 19th March, 2020

If you would like to request any articles or any further help, please contact:  Lisa Mason at [Lisa.Mason@geh.nhs.uk](mailto:Lisa.Mason@geh.nhs.uk)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: ACE 2 expression in different body tissues. Lisa Mason. (19th March, 2020). NUNEATON, UK: George Eliot Hospital William Harvey Library.

**Sources searched**  
EMBASE (9)  
GeneDB (1)  
Google (Advanced) (1)  
MEDLINE (2)  
PubMed (2)  
PubMed Central (1)

**Date range used** (5 years, 10 years): 2017-2020 but a few earlier articles also included   
**Limits used** (gender, article/study type, etc.): English language, human   
**Search terms and notes** (full search strategy for database searches below):

HDAS search of EMBASE and Medline. Brief supplementary search of PubMed.

Please see search history for terms used.

For more information about the resources please go to: <https://geh.wordpress.ptfs-europe.co.uk>.

## Summary of Results

The following article outlines where ACE2 is expressed:

Tissue Distribution of ACE2 Protein, the Functional Receptor for SARS Coronavirus. A First Step in Understanding SARS Pathogenesis

[I Hamming](https://pubmed.ncbi.nlm.nih.gov/?term=Hamming+I&cauthor_id=15141377) [1](https://pubmed.ncbi.nlm.nih.gov/15141377/#affiliation-1), [W Timens](https://pubmed.ncbi.nlm.nih.gov/?term=Timens+W&cauthor_id=15141377), [M L C Bulthuis](https://pubmed.ncbi.nlm.nih.gov/?term=Bulthuis+ML&cauthor_id=15141377), [A T Lely](https://pubmed.ncbi.nlm.nih.gov/?term=Lely+AT&cauthor_id=15141377), [G J Navis](https://pubmed.ncbi.nlm.nih.gov/?term=Navis+G&cauthor_id=15141377), [H van Goor](https://pubmed.ncbi.nlm.nih.gov/?term=van+Goor+H&cauthor_id=15141377) PMID: 15141377 DOI: [10.1002/path.1570](https://doi.org/10.1002/path.1570)

I've included other articles discussing expression different tissues in relation to targets for therapy or in relation to the respiratory, cardiovascular, renal systems and diabetes.

I've also included links to two websites for further information on the ACE2 gene which contain links to relevant articles and data on expression.

Please get in touch if you would like the search refined or extended in any way, or if we can help further.

## Contents

[A. Synopses or Summaries](#Content2)

National Center for Biotechnology Information (NCBI)

[ACE2 angiotensin I converting enzyme 2 [ Homo sapiens (human) ]](#Research610204)

[B. Institutional Publications](#Content4)

International Union of Basic and Clinical Pharmacology

[Angiotensin-converting enzyme 2](#Research610237)

[C. Original Research](#Content5)

1. [Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target](#Research610293)
2. [High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa](#Research610294)
3. [A review of urinary angiotensin converting enzyme 2 in diabetes and diabetic nephropathy](#Research610296)
4. [The renin-angiotensin system: Going beyond the classical paradigms](#Research610295)
5. [Angiotensin-converting enzyme 2 and renal disease.](#Research610298)
6. [Comparative expression of renin-angiotensin pathway proteins in visceral versus subcutaneous fat](#Research610297)
7. [The vasoprotective axes of the renin-angiotensin system: physiological relevance and therapeutic implications in cardiovascular, hypertensive and kidney diseases](#Research609947)
8. [Circulating ACE2 in Cardiovascular and Kidney Diseases.](#Research610300)
9. [Renin-angiotensin-aldosterone (RAAS): The ubiquitous system for homeostasis and pathologies](#Research610301)
10. [The Angiotensin Converting Enzyme 2 (ACE2), Gut Microbiota, and Cardiovascular Health](#Research610292)
11. [The role of renin-angiotensin peptides in the pathogenesis of acute respiratory distress syndrome](#Research610299)
12. [The expression of renin-angiotensin system components in the human gastric mucosa](#Research610302)
13. [Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis](#Research610303)
14. [A Novel Angiotensin-Converting Enzyme-Related Carboxypeptidase (ACE2) Converts Angiotensin I to Angiotensin 1-9](#Research610132)

### [D. Search History](#SearchHistory)

## A. Synopses or Summaries

#### National Center for Biotechnology Information (NCBI)

**ACE2 angiotensin I converting enzyme 2 [ Homo sapiens (human) ]** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e38bfa4a857f674211df1f138badaa6a)

Information on ACE2 gene including expression from the Gene database produced by The National Center for Biotechnology Information (updated 13 Mar 2020).

## B. Institutional Publications

#### International Union of Basic and Clinical Pharmacology

**Angiotensin-converting enzyme 2** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a46e1ce5cfd9995db5ddeb86cc6fe03e)

## C. Original Research

1. **Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target**  
   Zhang H. Intensive care medicine 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b7d8c21bccaf5a763987a9529425d95f)

1. **High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa**  
   Xu H. International journal of oral science 2020;12(1):8.

It has been reported that ACE2 is the main host cell receptor of 2019-nCoV and plays a crucial role in the entry of virus into the cell to cause the final infection. To investigate the potential route of 2019-nCov infection on the mucosa of oral cavity, bulk RNA-seq profiles from two public databases including The Cancer Genome Atlas (TCGA) and Functional Annotation of The Mammalian Genome Cap Analysis of Gene Expression (FANTOM5 CAGE) dataset were collected. RNA-seq profiling data of 13 organ types with para-carcinoma normal tissues from TCGA and 14 organ types with normal tissues from FANTOM5 CAGE were analyzed in order to explore and validate the expression of ACE2 on the mucosa of oral cavity. Further, single-cell transcriptomes from an independent data generated in-house were used to identify and confirm the ACE2-expressing cell composition and proportion in oral cavity. The results demonstrated that the ACE2 expressed on the mucosa of oral cavity. Interestingly, this receptor was highly enriched in epithelial cells of tongue. Preliminarily, those findings have explained the basic mechanism that the oral cavity is a potentially high risk for 2019-nCoV infectious susceptibility and provided a piece of evidence for the future prevention strategy in dental clinical practice as well as daily life.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b306dfe9c1a3678a359764075a0e259b)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7bbc28d927def1c9c60fb981d0f0c3ba)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f5000ed2686791fc712bbbef01ef57ce)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=442d8c518949e89bded00f4a6be41183)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7006e1f6476c089c79fc714cc4260aed)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7006e1f6476c089c79fc714cc4260aed)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=82d127781a39911ed4f3b87466c63336)

1. **A review of urinary angiotensin converting enzyme 2 in diabetes and diabetic nephropathy**  
   Gilbert A. Biochemia Medica 2019;29(1):28-38.

Urinary angiotensin converting enzyme 2 (ACE2) is significantly increased in diabetes and diabetic nephropathy. While studies on its clinical significance are still underway, its urinary expression, association with metabolic and renal parameters has been in the recent past considerably studied. The recent studies have demystified urine ACE2 in many ways and suggested the roles it could play in the management of diabetic nephropathy. In all studies the expression of urinary ACE2 was determined by enzyme activity assay and/with the quantification of ACE2 protein and mRNA by methods whose reliability are yet to be evaluated. This review summarizes recent findings on expression of urinary ACE2, examines its relationship with clinical parameters and highlights possible applications in management of diabetic nephropathy.<br/>Copyright &#xa9; 2019, Biochemia Medica, Editorial Office. All rights reserved.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=869c537555a0fcc9247810ae40257550)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1d9c3c0e78e206f1f6c1d1e25b38a23f)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=49e5027e1bd5268f5f343de7601a2c62)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e35b1b8de43467b9f49fbdb0a6bfcbde)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fcb66b94178dd7fcb8963250b595a0e9)

1. **The renin-angiotensin system: Going beyond the classical paradigms**  
   Santos R.A.S. American Journal of Physiology - Heart and Circulatory Physiology 2019;316(5):No page numbers.

Thirty years ago, a novel axis of the renin-angiotensin system (RAS) was unveiled by the discovery of angiotensin- (1-7) [ANG-(1-7)] generation in vivo. Later, angiotensin-converting enzyme 2 (ACE2) was shown to be the main mediator of this reaction, and Mas was found to be the receptor for the heptapeptide. The functional analysis of this novel axis of the RAS that followed its discovery revealed numerous protective actions in particular for cardiovascular diseases. In parallel, similar protective actions were also described for one of the two receptors of ANG II, the ANG II type 2 receptor (AT2R), in contrast to the other, the ANG II type 1 receptor (AT1R), which mediates deleterious actions of this peptide, e.g., in the setting of cardiovascular disease. Very recently, another branch of the RAS was discovered, based on angiotensin peptides in which the amino-terminal aspartate was replaced by alanine, the alatensins. Ala-ANG-(1-7) or alamandine was shown to interact with Mas-related G protein-coupled receptor D, and the first functional data indicated that this peptide also exerts protective effects in the cardiovascular system. This review summarizes the presentations given at the International Union of Physiological Sciences Congress in Rio de Janeiro, Brazil, in 2017, during the symposium entitled "The Renin-Angiotensin System: Going Beyond the Classical Paradigms,A. in which the signaling and physiological actions of ANG-(1-7), ACE2, AT<sub>2</sub>R, and alatensins were reported (with a focus on noncentral nervous system-related tissues) and the therapeutic opportunities based on these findings were discussed.<br/>Copyright &#xa9; 2019 the American Physiological Society.

1. **Angiotensin-converting enzyme 2 and renal disease.**  
   Williams Vanessa R. Current opinion in nephrology and hypertension 2018;27(1):35-41.

PURPOSE OF REVIEWThe renin-angiotensin system (RAS) is a pivotal player in the physiology and pathophysiology of cardiovascular and renal systems. Discovery of angiotensin-converting enzyme 2 (ACE2), capable of cleaving RAS effector peptide angiotensin (Ang) II into biologically active Ang-(1-7), has increased the complexity of our knowledge of the RAS. ACE2 expression is abundant in the kidney and is thought to provide protection against injury. This review emphasizes current experimental and clinical findings that examine ACE2 in the context of kidney injury and its potential therapeutic impact for treatment of kidney disease.RECENT FINDINGSClinical studies have reported upregulation of ACE2 in urine from diabetic patients, which may be reflective of pathological shedding of renal ACE2 as suggested by mechanistic experiments. Studies in experimental models have investigated the feasibility of pharmacological induction of ACE2 for improvement of renal function, inflammation, and fibrosis.SUMMARYEmerging concepts about the RAS indicate that ACE2 is a critical regulator of angiotensin peptide metabolism and the pathogenesis of renal disease. Human recombinant ACE2 is available and may be a practical clinical approach to enzyme replacement. Elucidating precise roles of ACE2 throughout disease progression will enrich our view of the RAS and help identify novel targets and appropriate strategies for intervention.

1. **Comparative expression of renin-angiotensin pathway proteins in visceral versus subcutaneous fat**  
   Zhang Y. Frontiers in Physiology 2018;9:No page numbers.

Body fat distribution contributes to obesity-related metabolic and cardiovascular disorders. Visceral fat is more detrimental than subcutaneous fat. However, the mechanisms underlying visceral fat-mediated cardiometabolic dysregulation are not completely understood. Localized increases in expression of the renin angiotensin system (RAS) in adipose tissue (AT) may be implicated. We therefore investigated mRNA and protein expression of RAS components in visceral versus subcutaneous AT using paired samples from individuals undergoing surgery (N = 20, body mass index: 45.6 +/- 6.2 kg/m<sup>2</sup>, and age: 44.6 +/- 9.1 years). We also examined RAS-related proteins in AT obtained from individuals on renin angiotensin aldosterone system (RAAS) targeted drugs (N = 10, body mass index: 47.2 +/- 9.3 kg/m<sup>2</sup>, and age: 53.3 +/- 10.1 years). Comparison of protein expression between subcutaneous and visceral AT samples showed an increase in renin (p = 0.004) and no change in angiotensinogen (p = 0.987) expression in visceral AT. Among proteins involved in angiotensin peptide generation, angiotensin converting enzyme (p = 0.02) was increased in subcutaneous AT while chymase (p = 0.001) and angiotensin converting enzyme-2 (p = 0.001) were elevated in visceral fat. Furthermore, visceral fat expression of angiotensin II type-2 receptor (p = 0.007) and angiotensin II type-1 receptor (p = 0.031) was higher, and MAS receptor (p &lt; 0.001) was lower. Phosphorylated-p53 (p = 0.147), AT fibrosis (p = 0.138) and average adipocyte size (p = 0.846) were similar in the two depots. Nonetheless, visceral AT showed increased mRNA expression of inflammatory (TNFalpha, p &lt; 0.001; IL-6, p = 0.001) and oxidative stress markers (NOX2, p = 0.038; NOX4, p &lt; 0.001). Of note, mRNA and protein expression of RAS components did not differ between subjects taking or not taking RAAS related drugs. In summary, several RAS related proteins are differentially expressed in subcutaneous versus visceral AT. This differential expression may not alter AngII but likely increases Ang1-7 generation in visceral fat. These potential differences in active angiotensin peptides and receptor expression in the two depots suggest that localized RAS may not be involved in differences in visceral vs subcutaneous AT function in obese individuals. Our findings do not support a role for localized RAS differences in visceral fat-mediated development of cardiovascular and metabolic pathology.<br/>Copyright &#xa9; 2018 Zhang, Somers, Becari, Polonis, Pfeifer, Allen, Kellogg, Covassin and Singh.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=fd1e85ac7acac80506f556128718e185)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bcc774214a2df6bb669b2e216adf82f0)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=26f5a90d5c6b7579050b6df77a773fa3)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=26f5a90d5c6b7579050b6df77a773fa3)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=26f5a90d5c6b7579050b6df77a773fa3)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=73a32460880e59364fbb0390e1ca72a0)

1. **The vasoprotective axes of the renin-angiotensin system: physiological relevance and therapeutic implications in cardiovascular, hypertensive and kidney diseases**  
   Xiao C. Li Pharmacological Research 2018;125 (Pt A), 21-38 Nov 2017:21-38.

See sections 3.1-3.34. Section 3.3.2 mentions expression in heart, kidney,testes and smooth muscle cells.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a7edde862a1e63576fd661cdc2fc758f)

1. **Circulating ACE2 in Cardiovascular and Kidney Diseases.**  
   Anguiano L. Current medicinal chemistry 2017;24(30):3231-3241.

Angiotensin converting enzyme (ACE) 2 is a homologue of ACE that catalyzes the conversion of Angiotensin (Ang) II into Ang1-7, which induces vasodilation, anti-fibrotic, anti-proliferative and anti-inflammatory effects. Given that ACE2 counterbalances the effects of Ang II, it has been proposed as a biomarker in kidney disease patients. Circulating ACE2 has been studied in human and experimental studies under physiological and pathological conditions and different techniques have been assessed to determine its enzymatic activity. In patients with cardiovascular (CV) disease circulating ACE2 has been shown to be increased. In addition, hypertensive and diabetic patients have also shown higher circulating ACE2 activities. A study in type 1 diabetes patients found a negative association between circulating ACE2 and estimated glomerular filtration rate in male and female patients. Recently, it has been demonstrated that circulating ACE2 is increased in male patients with chronic kidney disease (CKD) and that it is independently associated with other classical CV risk factors, such as advanced age and diabetes. Furthermore, circulating ACE2 has been shown to be associated with silent atherosclerosis and CV outcomes in CKD patients. In diabetic nephropathy, experimental studies have demonstrated an increase in circulating ACE2 activity both at early and late stages of the disease, as well as a direct association with increased urinary albumin excretion, suggesting that it may be increased as a renoprotective mechanism in these patients. In this paper we will review the measurement of circulating ACE2 and its role in kidney disease, as well as its potential role as a renal and CV biomarker.

1. **Renin-angiotensin-aldosterone (RAAS): The ubiquitous system for homeostasis and pathologies**  
   Patel S. Biomedicine and Pharmacotherapy 2017;94:317-325.

Renin-angiotensin-aldosterone system (RAAS) is a vital system of human body, as it maintains plasma sodium concentration, arterial blood pressure and extracellular volume. Kidney-secreted renin enzyme acts on its substrate to form angiotensin II, a versatile effector peptide hormone. Every organ is affected by RAAS activation and the resultant hypertension, cell proliferation, inflammation, and fibrosis. The imbalance of renin and angiotensin II can result in an overwhelming number of chronic and acute diseases. RAAS is influenced by other enzymes, hormones, pumps and signaling pathways, hence, this review discusses important facets of this system, its crosstalk with other crucial factors like estrogen, thyroid, cortisol, kallikrein-kinin system, Wnt/beta-catenin signaling, and sodium-potassium pump. The nexus of RAAS with the above-discussed systems was scantily explored before. So, this review furnishes a new perspective in comprehension of inflammation diseases. It is followed by the formulation of hypotheses, which can contribute to better management of an array of pathologies plaguing mankind. Manipulation of RAAS, by bending it towards ACE2 expression can regulate endocrine functions, which can be critical for a number of pathological management. Dietary intervention can restore RAAS to normalcy.<br/>Copyright &#xa9; 2017 Elsevier Masson SAS

1. **The Angiotensin Converting Enzyme 2 (ACE2), Gut Microbiota, and Cardiovascular Health**  
   Protein & Peptide Letters 2017;24(9):827-832.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=09ef2472417de6b571355b49add64838)

1. **The role of renin-angiotensin peptides in the pathogenesis of acute respiratory distress syndrome**  
   Reddy R.M. American Journal of Respiratory and Critical Care Medicine 2017;195:No page numbers.

Background Acute respiratory distress syndrome (ARDS) is characterized by pulmonary edema, disruption of the alveolar capillary membrane and an aggressive inflammatory response. The role of renin-angiotensin (RAS) peptides in ARDS has been described in mice models. Angiotensin I [A(1-10)] is converted to angiotensin II [A(1-8)] by angiotensin converting enzyme (ACE) found in lung endothelial cells. A(1-8) can promote fibrosis and impair lung function via angiotensin II type 1a (AT<sub>1a</sub>) receptors. In a second pathway, angiotensin converting enzyme II (ACE2) converts A(1-8) to angiotensin(1-7) [(A(1-7)] and A(1-10) to angiotensin(1-9) [A(1-9)]. Mice models have shown that loss of ACE2 or A(1-7) leads to the development of severe ARDS and replacement with ACE2 or A(1-7) peptide attenuates the inflammatory response. In ARDS, lung damage may lead to the loss of ACE and ACE2 and thus decreased conversion of A(1-10) to A(1-9) or A(1-8), and ultimately A(1-7). Objectives Determine whether there is a difference in levels of RAS peptides in ARDS patients between survivors and non-survivors. Methods Patients aged 18-90 years of age were enrolled within 24 hours of diagnosis of ARDS. Plasma concentrations of RAS peptides were quantified at study entry and 24, 48, and 72 hours thereafter. Levels were determined using a validated a liquid chromatography mass spectrometry based metabolomics assay. Survivors were defined as patients that survived their initial ICU admission. A total of 28 patients with ARDS were enrolled into the study. Differences amongst the cohorts were analyzed using the Mann-Whitney U Test. Results Higher plasma concentrations of A(1-10) were observed amongst non-survivors compared to survivors (p&lt;0.05) on days 1-4 (Figure 1). Survivors had higher plasma concentrations of A(1-7) compared to non-survivors on days 1-4 but they did not reach statistical significance. Conclusions Non-survivors had significantly higher levels of A(1-10). We speculate that non-survivors may be unable to express adequate levels of ACE and ACE2 required for lung repair, hence a reduction in conversion of A(1-10) to A(1-8) and subsequently to A(1-7). A(1-10) can also metabolize to A(1-9) via ACE2, which can undergo further metabolism to form A(1-7). Further studies will determine activity of ACE and ACE2 in survivors and non-survivors. (Figure Presented).

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b213ff3418c02c513a5f70c29d170387)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b213ff3418c02c513a5f70c29d170387)

1. **The expression of renin-angiotensin system components in the human gastric mucosa**  
   Hallersund P. JRAAS - Journal of the Renin-Angiotensin-Aldosterone System 2011;12(1):54-64.

Introduction: The aim of the present study was to map the distribution of representative protein components of the renin-angiotensin system (RAS) in the human gastric mucosa. <br/>Material(s) and Method(s): Biopsies from the antral and corporal mucosa of healthy Helicobacter pylori negative and positive volunteers were assessed by histology, Western blot and immunohistochemistry for angiotensin II subtype 1 and 2 receptors (AT1R, AT2R) and other RAS components (angiotensinogen, renin, angiotensin converting enzyme, and neprilysin). Mucosal levels of myeloperoxidase (MPO) served as a protein marker of neutrophil infiltration. <br/>Result(s): AT1R and AT2R were located in a variety of cells in the human gastric mucosa, including AT1R on a subpopulation of endocrine cells in the antral mucosa. Angiotensinogen and renin were expressed by resident mesenchymal cells in lamina propria. All investigated RAS components were found in vascular endothelial cells. The AT1R protein expression was 3-4 times higher in the gastric mucosa of H. pylori positive subjects compared to the gastric mucosa of H. pylori negative subjects (p&lt;0.05). Gastric mucosal AT1R protein expression correlated positively with neutrophil infiltration (r=0.7, p&lt;0.05). <br/>Conclusion(s): Protein components of RAS are present in the human gastric mucosa. The results suggest an angiotensin II mediated impact on mucosal epithelial functions, antral endocrine properties, microvascular permeability, and gastric inflammation. &#xa9; The Authors, 2010.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b68678f7a5c16c4ddedfaed70f5e65e3)

1. **Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis**  
   Hamming I. Journal of Pathology 2004;203(2):631-637.

Severe acute respiratory syndrome (SARS) is an acute infectious disease that spreads mainly via the respiratory route. A distinct coronavirus (SARS-CoV) has been identified as the aetiological agent of SARS. Recently, a metallopeptidase named angiotensin-converting enzyme 2 (ACE2) has been identified as the functional receptor for SARS-CoV. Although ACE2 mRNA is known to be present in virtually all organs, its protein expression is largely unknown. Since identifying the possible route of infection has major implications for understanding the pathogenesis and future treatment strategies for SARS, the present study investigated the localization of ACE2 protein in various human organs (oral and nasal mucosa, nasopharynx, lung, stomach, small intestine, colon, skin, lymph nodes, thymus, bone marrow, spleen, liver, kidney, and brain). The most remarkable finding was the surface expression of ACE2 protein on lung alveolar epithelial cells and enterocytes of the small intestine. Furthermore, ACE2 was present in arterial and venous endothelial cells and arterial smooth muscle cells in all organs studied. In conclusion, ACE2 is abundantly present in humans in the epithelia of the lung and small intestine, which might provide possible routes of entry for the SARS-CoV. This epithelial expression, together with the presence of ACE2 in vascular endothelium, also provides a first step in understanding the pathogenesis of the main SARS disease manifestations. Copyright &#xa9; 2004 Pathological Society of Great Britain and Ireland. Published by John Wiley & Sons, Ltd.

1. **A Novel Angiotensin-Converting Enzyme-Related Carboxypeptidase (ACE2) Converts Angiotensin I to Angiotensin 1-9**  
   M Donoghue Circulation Research 2000;87(5):e1-5.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=ff2ea49fb5a116da9a17f8158ab85153)

### Opening Internet Links

The links to internet sites in this document are 'live' and can be opened by holding down the CTRL key on your keyboard while clicking on the web address with your mouse

### Full text papers

Links are given to full text resources where available. For some of the papers, you will need an **NHS OpenAthens Account**. If you do not have an account you can [register online](https://openathens.nice.org.uk/).

You can then access the papers by simply entering your username and password. If you do not have easy access to the internet to gain access, please let us know and we can download the papers for you.

### Guidance on searching within online documents

Links are provided to the full text of each document. Relevant extracts have been copied and pasted into these results. Rather than browse through lengthy documents, you can search for specific words as follows:

**Portable Document Format / pdf / Adobe**  
Click on the Search button (illustrated with binoculars). This will open up a search window. Type in the term you need to find and links to all of the references to that term within the document will be displayed in the window. You can jump to each reference by clicking it.

**Word documents**  
Select Edit from the menu, the Find and type in your term in the search box which is presented. The search function will locate the first use of the term in the document. By pressing 'next' you will jump to further references.

## D. Search History

|  | **Source** | **Criteria** | **Results** |
| --- | --- | --- | --- |
| 1. | EMBASE | exp "ANGIOTENSIN CONVERTING ENZYME 2"/ | 2324 |
| 2. | EMBASE | (ACE2).ti,ab | 2820 |
| 3. | EMBASE | (1 OR 2) | 3509 |
| 4. | EMBASE | exp "GENE EXPRESSION"/ | 1591103 |
| 5. | EMBASE | (3 AND 4) | 778 |
| 6. | EMBASE | 5 [DT 2017-2020] [English language] [Languages English] | 193 |
| 7. | EMBASE | (expression OR upregulation).ti,ab | 2572897 |
| 8. | EMBASE | (3 AND 7) | 1701 |
| 9. | EMBASE | 8 [DT 2017-2020] [English language] [Languages English] [Humans] | 102 |
| 10. | EMBASE | exp "HUMAN TISSUE"/ | 1249573 |
| 11. | EMBASE | (3 AND 10) | 152 |
| 12. | Medline | ("angiotensin converting enzyme 2" OR ACE2 OR "ACE 2" OR "angiotensin converting enzyme-2").ti,ab | 2219 |
| 13. | Medline | (distribution OR activity OR expression).ti,ab | 4773441 |
| 14. | Medline | (12 AND 13) | 1393 |
| 15. | Medline | 14 [DT 2017-2020] [Languages English] [Humans] | 75 |
| 16. | Medline | exp "DIPEPTIDYL-PEPTIDASES AND TRIPEPTIDYL-PEPTIDASES"/ OR exp "PEPTIDYL-DIPEPTIDASE A"/ | 17857 |
| 17. | Medline | (13 AND 16) | 9573 |
| 18. | Medline | 17 [DT 2017-2020] [Languages English] [Humans] [Clinical queries reviews-balance] | 50 |

**Disclaimer**  
We hope that you find the evidence search service useful. Whilst care has been taken in the selection of the materials included in this evidence search, the Library and Knowledge Service is not responsible for the content or the accuracy of the enclosed research information. Accordingly, whilst every endeavour has been undertaken to execute a comprehensive search of the literature, the Library and Knowledge Service is not and will not be held responsible or liable for any omissions to pertinent research information not included as part of the results of the enclosed evidence search. Users are welcome to discuss the evidence search findings with the librarian responsible for executing the search. We welcome suggestions on additional search strategies / use of other information resources for further exploration. You must not use the results of this search for commercial purposes. Any usage or reproduction of the search output should acknowledge the Library and Knowledge Service that produced it.