编号：YY006-20221212001

标题：The OM-85 bacterial lysate inhibits SARS-CoV-2 infection of epithelial cells by downregulating SARS-CoV-2 receptor expression

简介：Background: Treatments for coronavirus disease 2019, which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), are urgently needed but remain limited. SARS-CoV-2 infects cells through interactions of its spike (S) protein with angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) on host cells. Multiple cells and organs are targeted, particularly airway epithelial cells. OM-85, a standardized lysate of human airway bacteria with strong immunomodulating properties and an impeccable safety profile, is widely used to prevent recurrent respiratory infections. We found that airway OM-85 administration inhibits Ace2 and Tmprss2 transcription in the mouse lung, suggesting that OM-85 might hinder SARS-CoV-2/host cell interactions. Objectives: We sought to investigate whether and how OM-85 treatment protects nonhuman primate and human epithelial cells against SARS-CoV-2. Methods: ACE2 and TMPRSS2 mRNA and protein expression, cell binding of SARS-CoV-2 S1 protein, cell entry of SARS-CoV-2 S protein-pseudotyped lentiviral particles, and SARS-CoV-2 cell infection were measured in kidney, lung, and intestinal epithelial cell lines, primary human bronchial epithelial cells, and ACE2-transfected HEK293T cells treated with OM-85 in vitro. Results: OM-85 significantly downregulated ACE2 and TMPRSS2 transcription and surface ACE2 protein expression in epithelial cell lines and primary bronchial epithelial cells. OM-85 also strongly inhibited SARS-CoV-2 S1 protein binding to, SARS-CoV-2 S protein-pseudotyped lentivirus entry into, and SARS-CoV-2 infection of epithelial cells. These effects of OM-85 appeared to depend on SARS-CoV-2 receptor downregulation. Conclusions: OM-85 inhibits SARS-CoV-2 epithelial cell infection in vitro by downregulating SARS-CoV-2 receptor expression. Further studies are warranted to assess whether OM-85 may prevent and/or reduce the severity of coronavirus disease 2019.

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标题：Immunological memory to SARS-CoV-2 infection and COVID-19 vaccines

简介：Immunological memory is the basis of protective immunity provided by vaccines and previous infections. Immunological memory can develop from multiple branches of the adaptive immune system, including CD4 T cells, CD8 T cells, B cells, and long-lasting antibody responses. Extraordinary progress has been made in understanding memory to SARS-CoV-2 infection and COVID-19 vaccines, addressing development; quantitative and qualitative features of different cellular and anatomical compartments; and durability of each cellular component and antibodies. Given the sophistication of the measurements; the size of the human studies; the use of longitudinal samples and cross-sectional studies; and head-to-head comparisons between infection and vaccines or between multiple vaccines, the understanding of immune memory for 1 year to SARS-CoV-2 infection and vaccines already supersedes that of any other acute infectious disease. This knowledge may help inform public policies regarding COVID-19 and COVID-19 vaccines, as well as the scientific development of future vaccines against SARS-CoV-2 and other diseases.

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编号：YY006-20221212003

标题：Modifying chronic kidney disease progression with the mineralocorticoid receptor antagonist finerenone in patients with type 2 diabetes

简介：In patients with type 2 diabetes, chronic kidney disease (CKD) is the most common cause of kidney failure. With its increasing prevalence and limited treatment options, CKD is a major contributor to the global burden of disease. Although recent guidelines for the control of hypertension and hyperglycaemia, as well as the use of renin-angiotensin system inhibitors and, more recently, sodium-glucose co-transporter-2 inhibitors, have improved outcomes for patients with CKD and diabetes, there is still a high residual risk of CKD progression and adverse cardiovascular events. In this review, we discuss the recently published FIDELIO-DKD and FIGARO-DKD studies and FIDELITY prespecified individual patient analysis. Together, these studies have established finerenone, a novel non-steroidal mineralocorticoid receptor antagonist, as an effective treatment for kidney and cardiovascular protection and welcome addition to the pillars of treatment to slow CKD progression in patients with type 2 diabetes.

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标题：Consensus statement on the current pharmacological prevention and management of heart failure

简介：Introduction: This consensus statement of Australian clinicians provides new recommendations for the pharmacological management of heart failure based on studies reported since the publication of the 2018 Australian heart failure guidelines. Main recommendations: ▪Use of sodium-glucose cotransporter 2 (SGLT2) inhibitors to prevent hospitalisation for heart failure in type 2 diabetes mellitus can be extended to patients with multiple cardiovascular risk factors, albuminuric chronic kidney disease, or atherosclerotic cardiovascular disease. ▪New evidence supports the use of a mineralocorticoid receptor antagonist (finerenone) to prevent heart failure in type 2 diabetes mellitus associated with albuminuric chronic kidney disease. ▪In addition to renin angiotensin system inhibitors (angiotensin receptor neprilysin inhibitor preferred), beta blockers and mineralocorticoid receptor antagonists, an SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in all patients with heart failure with reduced left ventricular ejection fraction (LVEF ≤ 40%) (HFrEF). Lower quality evidence supports these therapies in patients with heart failure with mildly reduced LVEF (41-49%) (HFmrEF). ▪A soluble guanylate cyclase stimulator (vericiguat), selective cardiac myosin activator (omecamtiv mecarbil) and, if iron deficient, intravenous iron (ferric carboxymaltose) provide additional benefits in persistent HFrEF. ▪An SGLT2 inhibitor (empagliflozin) should be considered in patients with heart failure with preserved LVEF (≥ 50%) (HFpEF). Key changes in management from this statement: This document broadens the scope of angiotensin receptor neprilysin inhibitor use in patients with HFrEF and HFmrEF. SGLT2 inhibitor use expands to become a cornerstone therapy in HFrEF, with increasing evidence to support its use in HFmrEF and HFpEF.

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编号：YY006-20221212005

标题：Improving the residual risk of renal and cardiovascular outcomes in diabetic kidney

disease: A review of pathophysiology, mechanisms, and evidence from recent trials

简介：Based on global estimates, almost 10% of adults have diabetes, of whom 40% are estimated to also have chronic kidney disease (CKD). Almost 2 decades ago, treatments targeting the renin-angiotensin system (RAS) were shown to slow the progression of kidney disease. More recently, studies have reported the additive benefits of antihyperglycaemic sodium-glucose co-transporter-2 inhibitors in combination with RAS inhibitors on both CKD progression and cardiovascular outcomes. However, these recent data also showed that patients continue to progress to kidney failure or die from kidney- or cardiovascular-related causes. Therefore, new agents are needed to address this continuing risk. Overactivation of the mineralocorticoid (MR) receptor contributes to kidney inflammation and fibrosis, suggesting that it is an appropriate treatment target in patients with diabetes and CKD. Novel, selective non-steroidal MR antagonists are being studied in these patients, and the results of two large recently completed clinical trials have shown that one such treatment, finerenone, significantly reduces CKD progression and cardiovascular events compared with standard of care. This review summarizes the pathogenic mechanisms of CKD in type 2 diabetes and examines the potential benefit of novel disease-modifying agents that target inflammatory and fibrotic factors in these patients.

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