

Carbon dioxide's new-found signalling role could be applied to blood flow, birth and deafness

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New research reveals exactly how the body measures carbon dioxide and suggests that far from being a metabolic waste product, it could play a key role as a biological signalling molecule.

Researchers led by Professor Nick Dale in the School of Life Sciences at the University of Warwick have shown that the body senses carbon dioxide directly through the protein Connexin 26, which acts as a receptor for the gas. Connexin 26 is better known as forming a direct channel of communication between cells. This new work shows an unexpected function for Connexin 26 –as a receptor for carbon dioxide.

The study demonstrates at a molecular level exactly how Connexin 26 interacts with carbon dioxide. This finding therefore adds carbon dioxide to the list of gaseous signalling molecules, such as nitric oxide, carbon monoxide and hydrogen sulphide already known to be active in mammals.

Given that Connexin 26 is found in many tissues and organs – and, for example, mutations in it are the commonest genetic cause of deafness - the findings could have far-reaching effects as they open up potential new ways to control physiological processes such as [brain blood flow](#), breathing, hearing, reproduction and birth.

Carbon dioxide is the by-product of metabolism in all cells. Dissolved

carbon dioxide can combine with water to increase acidity in the blood. As mammals produce carbon dioxide at a fast rate, it is vital that the body measures its levels so that breathing rates can be adjusted to exhale excess carbon dioxide and thus regulate blood pH within the narrow limits compatible with life.

Until now the body's regulation of blood acid levels was thought to be triggered by measuring pH levels of the blood. However the new findings from Warwick indicate that the body can sense carbon dioxide levels directly through Connexin 26.

Professor Nick Dale said: "Carbon dioxide is the unavoidable by-product of our metabolic system - human beings and other mammals produce huge amounts of it every day.

"The exciting implication of our study is that carbon dioxide is much more than just a waste product: it can directly signal physiological information, and our work shows the mechanism by which this happens via Connexin 26.

"As Connexin 26 is present in many tissues and organs, for example the brain, skin, inner ear, liver and the uterus during pregnancy, this discovery should herald a re-evaluation of the potential for carbon dioxide signalling in many different processes such as the control of [blood flow](#), breathing, hearing, reproduction and birth."

Connexin 26 comprises six identical subunits. Carbon dioxide makes a chemical bond to the side chain a particular amino acid. This modified side chain can then form a bridge to a closely oriented amino acid in the adjacent subunit. A total of six carbon dioxide molecules can bind to make six bridges between subunits. These bridges force the Connexin 26 protein to alter its conformation thereby signalling the presence and concentration of [carbon dioxide](#).

More information: The study 'CO₂ directly modulates connexin 26 by formation of carbamate bridges between subunits' was published in the open access journal *eLife*. elifesciences.org/content/2/e01213

Provided by University of Warwick

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