Identifying a role for cellular CO2 sensor

October 21 2010

UCD Conway researchers have found that carbon dioxide (CO_2) is not only involved in climate change and a waste product of respiration in cells but also plays an active role in regulating the genes involved in inflammation and innate immunity. Their research findings were highlighted in the October 1st issue of *The Journal of Immunology*.

The levels of oxygen (O_2) and carbon dioxide (CO_2) in cells can vary dramatically in health and in diseases such as chronic inflammation, ischemia and cancer where metabolism rates are significantly altered. Elevated CO_2 levels that occur during hypoventilation of intubated patients have been found to decrease mortality associated with acute respiratory distress syndrome or endotoxin-induced acute lung injury.

Acute CO_2 sensing is a feature of specialised cells in lower animal species such as flies and rodents but little is known about the effect of altered CO_2 on gene expression. This research group, led by Conway fellow, Professor Cormac Taylor examined the effect of altered CO_2 levels on gene expression in mammalian cells against a background of inflammation.

“Our results suggest that a molecular CO_2 sensor associated with anti-inflammatory and immunosuppressive signalling may exist. We found that elevated levels of CO_2 had a profound effect on a master signalling pathway called NF-κB”, said Dr. Eoin Cummins, postdoctoral researcher and lead author on this publication.

In previous work, the Taylor group demonstrated that the NF-κB master

signalling pathway is induced by hypoxic (low O_2) conditions. In this study, the researchers now show that a central protein regulator within this pathway, IKKα reacts to CO_2 levels in a rapid, reversible and dose dependent manner.

Commenting on the significance of the research, Dr. Cummins said, "The molecular mechanism of this CO_2 sensor may provide an alternative therapeutic route in those instances when suppressing the body's innate immune system or inflammatory response is clinically desirable. We now need to decipher the exact mechanisms of this CO_2-dependent intracellular signalling pathway".

More information: *NF-{kappa}B links CO_2 sensing to innate immunity and inflammation in mammalian cells*. Eoin P. Cummins, et al. doi:10.4049/jimmunol.1000701

Provided by University College Dublin