Discovery improves understanding of early onset inflammatory disease

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Scientists at the University of East Anglia (UEA) have discovered a 'constant cloud' of potent inflammatory molecules surrounding the cells responsible for diseases such as thickening of the arteries and rheumatoid arthritis.

Published online today by The Journal of Cell Science, the findings could eventually lead to new treatments for chronic inflammatory diseases. Cardiovascular disease arising from atherosclerosis (thickening of the arteries) kills around 17 million people worldwide each year, including 120,000 people in England and Wales, while rheumatoid arthritis affects around 400,000 people in the UK.

The UEA team studied a type of white blood cell called monocytes. Monocytes play an important role in the human immune system and help protect our bodies against infection. But they can also invade tissue, triggering the early stages of common inflammatory diseases.

The researchers detected for the first time that monocytes were surrounded by a constant cloud. This cloud was found to be made up of potent inflammatory molecules called adenosine triphosphate, or ATP. Further study showed that the ATP molecules were being propelled through the cell wall by the actions of lysosomes. Lysosomes are sub-cellular compartments within blood cells which had previously been thought to only break down cell waste.

"These unexpected findings shed light on the very early stages in the

development of inflammatory diseases such as atherosclerosis and rheumatoid arthritis," said lead author Dr Samuel Fountain of UEA's School of Biological Sciences.

"We found that lysosomes are actually highly dynamic and play a key role in the way inflammatory cells function. This is an exciting development that we hope will lead to the discovery of new targets for inflammatory drugs in around five years and potential new treatments beyond that."

Dr Fountain said further study was now needed to investigate how to control the release of ATP by lysosomes in monocytes and other white blood cells, and to understand how inflammation may be affected in patients with inherited diseases involving lysosomes.

Dr Fountain is a Biotechnology and Biological Sciences Research Council (BBSRC) David Phillips Fellow and recently received £0.9m from the BBSRC to study how cells use ATP as a signalling molecule.

More information: 'Constitutive lysosome exocytosis releases ATP and engages P2Y receptors in human monocytes' by V Sivaramakrishnan (UEA), S Bidula (UEA), H Campwala (UEA), D Katikaneni (UEA) and S Fountain (UEA) is published online on July 5 by the *Journal of Cell Science*. The paper will be available here: jcs.biologists.org/content/early/recent

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