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Research finds new target in search for why statin drugs sometimes cause problems for some patients

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Research by the University of Warwick, the University Hospital Coventry and Warwickshire NHS Trust (UHCW), and Tangent Reprofiling Limited, has discovered that statin drugs interact with a gap junction protein called GJC3 that releases ATP, a major signaling molecule for inflammation in the body. This discovery provides a significant new target in the search for why statin drugs can sometimes cause harmful effects such as muscle toxicity in some patients.

Speaking on behalf of the team in the Department of Chemistry in the University of Warwick, Dr Andrew Marsh said: "Statins are powerful cholesterol-lowering medicines that are widely prescribed to reduce the burden of cardiovascular disease. Gap junction proteins are important in forming communication channels between cells and organs in the body. In this new research, two clinically used statin therapeutics have been found to interact with an important part of GJC3, a gap junction protein which acts to release ATP, a signaling molecule that is key to the body's response to injury and inflammation.

"Many people know ATP as the cell's main energy transfer molecule, but when released outside cells, ATP coordinates how tissues including our liver and muscles deal with recovery from injury. These results may give us better understanding of how some of the harmful effects of statins in some patients, such as muscle toxicity, might come about".

The new research paper entitled "Simvastatin sodium salt and fluvastatin interact with human gap junction gamma-3 protein" is published on Wednesday 10th February 2016 in the open access journal *PLOS ONE*. The study was a collaboration between scientists and clinicians at the University of Warwick, the University Hospital Coventry and Warwickshire NHS Trust (UHCW) and Tangent Reprofiling Limited.

The researchers found that the statins simvastatin sodium salt and fluvastatin were found to interact with a peptide from the gap junction protein GJC3. In work which confirmed the observed interaction, the researchers also found that certain pharmacological probes of other gap junction proteins are also bound to the peptide sequence they had identified.

University of Warwick research chemist Dr Andrew Marsh also said that: "GJC3 is present in many tissues in the body, but its role in cell signaling is poorly understood. Our work opens doors to its investigation".

Professor Donald Singer, President of the Fellowship of Postgraduate Medicine was the lead investigator of the teams working on this study in Warwick Medical School and UHCW. He commented: "Finding additional ways in which statins act at the cellular and molecular level is important for giving clues to potential new medical applications for these drugs. These results may also give us better understanding of how some of the harmful effects of statins in some patients might come about".

More information: The research refers to the open access journal *PLOS ONE* manuscript PONE-D-13-07792R2, 10 Feb 2016 and the paper was entitled Simvastatin sodium salt and fluvastatin interact with human gap junction gamma-3 protein".