Unlocking the secrets of gallstones

We know all too well from fairy tales that stones in your stomach generally aren’t good for your health. However, while the stones in these stories are placed in the wolf’s belly, the human body can cunningly produce stones by itself. How stones are formed in the body was previously unknown, despite the fact that gallstones are among the ten most common reasons for a stay in hospital. The secret behind gallstones has now been revealed by a team of researchers at the Department of Medicine 1 and 3 at Universität Erlangen-Nürnberg at FAU. The researchers’ findings have recently been published in the journal ‘Immunity’.

Gallstones and the problems they cause are very common. Around 25 million Americans as well as 6 million people in Germany have gallstones that can not only cause extremely painful colic but also life-threatening infections in the abdomen. Patients who have gallstones very often need surgery to remove them. Surprisingly, very little was known until now about how these stones form and what they comprise of. Whilst scientists have known that crystals are involved, and in the case of gallstones, these are usually crystals of cholesterol, little or no research had been conducted up to now about how gallstones are formed from microscopic crystals and the mechanism behind this process has now been discovered.

During their research, Dr. Luis Munoz, Sebastian Böltz and Prof. Dr. Martin Herrmann from the Department of Medicine 3, who collaborate in Collaborative Research Centre 1181 and were supported by a team led by Dr. Moritz Leppkes and Prof. Dr. Markus F. Neurath at the Department of Medicine 1 at FAU, had to use an unconventional approach that took them to museums, abattoirs and operating theatres. They investigated human gallstones from the collection kept at the museum at the Charité hospital in Berlin, bile from pigs from an abattoir and bile and gallstones from patients who underwent surgery to the abdomen. During the detailed investigation of these materials using modern methods, the team made a very surprising discovery. All gallstones are covered with the traces of a special type of white blood cell called neutrophil granulocytes. These cells are the body’s first form of defence and they attack bacteria and other pathogens and also identify crystals as a threat. While attempting to ingest the crystals, these cells die and cover the crystals with their genetic material like a net. These nets, or neutrophil extracellular traps (NET), wind themselves around the crystals, clump them together and thus form stones that can take on surprising proportions.

‘We observed that the nets, when released in the already sticky bile, clumped together calcium and cholesterol crystals to form gallstones. The production of gallstones can be greatly reduced or even stopped if the formation of these nets is inhibited using drugs,’ says Dr. Munoz. This discovery has opened up previously unknown options for the treatment of gallstones. A simple pharmacological approach could be especially useful, for example, the use of Metoprolol, which is a so-called beta blocker that has been used successfully for many years for the treatment of high blood pressure. Metoprolol prevents neutrophil granulocytes from entering tissue from the blood supply, thus reducing the capacity for forming nets and therefore gallstones. In addition, specific inhibitors for preventing the formation of nets from neutrophil granulocytes, so-called PAD inhibitors, are already known that can inhibit the formation of gallstones produced in experiments, thus proving the significance of the immune system for the formation of these structures. The FAU research team also emphasises that this process is significant not only for gallstones, but also for other types of
stones in the body such as kidney stones or salivary stones.

wissenschaftliche Ansprechpartner:
Further information
Dr. Luis Munoz
Phone: +49 9131 85 36990
luis.munoz@uk-erlangen.de

Originalpublikation: