Diabetes can cause a sugar coating that smothers body's immune defences

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Research led by the Warwick Medical School at the University of Warwick has found that unhealthy glucose levels in patients with diabetes can cause significantly more problems for the body than just the well-known symptoms of the disease such as kidney damage and circulation problems. The raised glucose can also form what can be described as a sugar coating that can effectively smother and block the mechanisms our bodies use to detect and fight bacterial and fungal infections.

In diabetes, patients suffer a higher risk of chronic bacterial and fungal infections but until now little has been known about the mechanisms involved. Now new research led by Dr Daniel Mitchell at the University of Warwick's Warwick Medical School has found a novel relationship between high glucose and the immune system in humans. The researchers have found that specialized receptors that recognize molecules associated with bacteria and fungi become "blind" when glucose levels rise above healthy levels. The new research may also help explain why diabetic complications can also include increased risk of viral infections such as influenza, and also inflammatory conditions such as cardiovascular disease.

The researchers looked at the similarities in chemical structure between glucose in blood and body fluids, and two other sugar called mannose and fucose. These sugars are found on the surfaces of bacteria and fungi and act as targets for receptors in our body that have evolved to detect and bind to microbial sugars to then combat the infection.

The research found that high levels of glucose outcompetes the binding of mannose and fucose to the specialized immune receptors, potentially blocking these receptors from detecting infectious bacteria and fungi. Glucose also binds in such a way that it inhibits the chemical processes that would normally then follow to combat infections. If this happens it can inhibit a range of key processes including:

- It can inhibit the function of immune system receptors called C-type lectins such as MBL (Mannose-binding lectin) which are known to bind to a sugar known as mannose that is present in the structure of infectious fungal bacterial cell walls. Unlike glucose, mannose does not exist in mammals as a free sugar in the blood.

- The loss of MBL function may also predispose the body to chronic inflammatory diseases, since MBL is involved in the processing and clearance of apoptotic cells (dying cells).

- A number of C-type lectins tat can be affected by raised glucose levels, including MBL, but also including immune cell surface receptors DC-SIGN and DC-SIGNR, are found in key parts of our circulation and vascular system such as plasma, monocytes, platelets and endothelial cells that line blood vessels. Inhibiting the function of these key molecules in those settings could contribute to diabetic cardiovascular and renal complications.

Warwick Medical School researcher Dr Daniel Mitchell said:

"Our findings offer a new perspective on how high glucose can potentially affect immunity and thus exert a negative impact on health. It also helps to emphasize the importance of good diet on preventing or controlling diseases such as diabetes. We will build on these ideas in order to consolidate the disease model and to investigate new routes to

treatment and prevention."

More information: The research will be published in the journal *Immunobiology* and is entitled "High glucose disrupts oligosaccharide recognition function via competitive inhibition: A potential mechanism for immune dysregulation in diabetes mellitus".
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