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A new test to detect reliably an autoimmune disease

In autoimmune diseases, the immune system wrongly identifies its “enemy”, and produces antibodies that attack the patient’s own cells. One of these diseases, the anti-phospholipid antibody syndrome (APS), is still poorly understood, even though it can have serious consequences. APS is caused by antibodies circulating in the blood plasma that are directed against a protein, which increase the blood’s tendency to form clots. This can lead to a range of vascular accidents, such as venous thromboses, strokes or repeated miscarriages. Although the prevalence of APS is very difficult to assess, it is likely to affect around 0.5% of the general population. Diagnosing the disease is a complicated affair: the test currently used has a number of problems in terms of variability, specificity and sensitivity. This situation, however, is set to change: researchers at the University of Geneva (UNIGE), Switzerland, and the Geneva University Hospitals (HUG) have succeeded in identifying the exact spot where the anti-phospholipid antibodies attach themselves. This means a more accurate and standardized diagnostic test can now be devised— an undeniable improvement for patients. These results can be read in the journal *Haematologica*.

In people suffering from APS, antibodies called “anti-B2GP1” attach themselves to elements found on the surface of certain cells, particularly those of the blood vessels and placenta. They bind themselves to receptors located on the cell membrane, generating a signal that produces the pro-inflammatory and pro-thrombotic factors that cause vascular accidents. By identifying the exact location where these antibodies bind, the research team at UNIGE and HUG have been able to clarify how they function. Karim Brandt, a researcher at the UNIGE Faculty of medicine, explains the importance of this discovery: “The current diagnostic tests use the entire protein, which reduces its specificity and leads to standardization issues. Consequently, two tests are required at an interval of 12 weeks after a thrombotic episode or following one or more miscarriages. Our new test specifically targets this pathogenic antibody, with rapid and more accurate results.”

An antibody with a rather special behaviour

The researchers managed to isolate a “motif”, which is a small part of the membrane protein. Motifs are recognized by the antibody, which then binds to it, like a key in a lock. In this instance, the key can open several locks, which correspond to the proteins found on the surface of the cells and induce the pathogenic effects. And if the target pro-

tein was identified as such, it is because it is the only protein in all the human proteome to have five of these motifs; it has therefore as many potential binding points for the pathogenic antibody.

Better diagnosis and better treatment

APS is usually treated with oral anticoagulants such as low-molecular-weight heparin and aspirin, long-term treatments that are not without side effects, and that must be used with caution by pregnant women. Moreover, treatment becomes very burdensome in patients suffering from the most severe form of the disease, called “catastrophic APS”. As Karim Brandt is keen to stress, the researchers are also focusing their working in this direction: “Our breakthrough could also give rise to a targeted treatment that would neutralize specific pathogenic antibodies, reducing not just their actions but also the side effects associated with the current treatment. It would involve injecting the protein motif we have identified into a patient’s circulatory system so that it explicitly binds itself to the pathogenic antibody and prevents it from causing harm.”

For the time being, the diagnostic test needs to be optimized for prototypes to be developed. To ensure its validity, the researchers will re-analyze hundreds of samples already tested with the old method and compare results.

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