Multiple sclerosis, Italian researchers discover a possible onset mechanism for the disease

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A non-pathogenic bacterium is capable to trigger an autoimmune disease similar to the multiple sclerosis in the mouse, the model animal which helps to explain how human diseases work. This is what a group of researchers from the Catholic University of Rome, led by Francesco Ria (Institute of General Pathology) and Giovanni Delogu (Institute of Microbiology), have explained for the first time in a recently published article on the *Journal of Immunology*.

Multiple sclerosis is a disease due to an inflammatory reaction provoked by the immune system. It causes the disruption of the coating of the nerve fibres in the Central Nervous System.

"We do not know what causes multiple sclerosis", explains Francesco Ria, immunologist of the Catholic University. "We know that there exist a genetic factor and an environmental factor, but we do not yet posses a satisfactory theory which can explain how exactly this environmental factor works".

Currently, there are two competing theories on the field: according to a first hypothesis, a virus hides within the brain and what causes the disease is the immunologic antiviral reaction. On the other hand, the second hypothesis states that a viral or bacterial pathogen similar to specific molecules of the Central Nervous System causes an inflammation which provokes a reaction of the immune system. This

reaction ends up destroying the brain cells. The latter is called the autoimmune hypothesis.

This is the hypothesis that the researchers coming from the Institutes of General Pathology, Microbiology and Anatomy of the Catholic University of Rome have been testing with their two-year long work. To demonstrate the viability of this idea, scientists have fooled the mouse immune system, modifying subtly a bacterium of the common family of mycobacteria (the same family to which also the bacterium causing tuberculosis belongs) to make it look like to myelin, the protein coating nerve cells. This modified mycobacterium is completely innocuous. As all external agents, though, it is capable to trigger the reaction of the T-cells of the immune systems. They intervene to destroy it. Since they are innocuous bacteria, although very common in the environment, and since they induce an immune reaction, they are the ideal bacteria scientists can use to study the environmental factor contributing, together with the genetic factor, to cause multiple sclerosis.

"Normally, T-cells cannot penetrate into the Central Nervous System", adds Rea, "because the hematoencephalic barrier prevents them from doing so. But the bacterium modifies the characteristics of the T-cells and allows them to overcome the barrier. In 15 days the bacterium disappears completely from the body".

Yet these T-cells can now enter into the brain. This way, they begin to attack the myelin of the nerve cells, and here is how the immune disease breaks out.

"We basically demonstrate - explains Rea - that in an animal model it is possible to be infected with something not carrying any disease, and later on develop a purely autoimmune disease".

Yet there is another element in this complex research, sponsored by the

Italian Association of Multiple Sclerosis (AISM). "Normally - clarifies Rea - to understand which diseases we have encountered, we measure the antibodies produced by that specific pathogen. But there is a whole world of infectious agents which do not induce the production of antibodies, as is the case in our research: mycobacteria and many other bacteria produce a very low and variable number of antibodies. It is thus very hard to establish whether a population has encountered that specific infectious agent. So, we demonstrate that those infectious agents which are more likely to produce an autoimmune reaction are just those which do not induce antibody production".

Obviously, this is only the first step to better understand the way this very complex and devastating disease works. Ria and Delogu are not stopping here: "We want to try to understand the exact characteristics which this infectious agent should have", they explain. "Might it truly be a good experimental model for multiple sclerosis? If we had prolonged the action of the bacteria, would we have favoured or hampered the development of the disease? And what about the myelin-like bacterium protein: where should it lie? On the surface, or inside? These are all questions - conclude the two researchers - which we will be trying to answer in the next years, in the hope to defeat this terrible illness. We could even imagine to develop a vaccine by which we could prevent the immune response associated to multiple sclerosis".

Provided by Catholic University of Rome