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Researchers identify a protein that controls the 'guardian of the genome'

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A new study published in the scientific journal *Proceedings of the National Academy of Sciences*(*PNAS*) sheds new light on a well-known mechanism required for the immune response. Researchers at the IRCM, led by Tarik Möröy, PhD, identified a protein that controls the activity of the p53 tumour suppressor protein known as the "guardian of the genome".

The researchers study the development of T cells and B cells, which are lymphocytes (or immune cells) that play a central role in protecting our body against infections by viruses, bacteria and other microbial agents.

"As these lymphocytes develop, they must learn how to recognize different pathogens in the body," says Dr. Möröy, Director of the Hematopoiesis and Cancer research unit at the IRCM. "Part of this process involves the breaking and rearranging of the genes responsible for producing the lymphocyte receptors that recognize these pathogens. However, when a cell's genome contains too many breaks, p53 (the "guardian of the genome") gets alerted and causes the cell to die."

"In developing immune cells, activation of p53 must be contained to avoid their premature death," explains Marissa Rashkovan, first author of the study and doctoral student in Dr. Möröy's laboratory. "We discovered that a protein called Miz-1 can exert such a function by controlling the activity of p53. More specifically, Miz-1 controls the way in which p53 gets alerted when a cell needs to die. In fact, without Miz-1, developing lymphocytes always activate the p53 protein and,

hence, never survive."

"Our study therefore helps advance our understanding of how an efficient immune response is built in our body," adds Dr. Möröy, who is also the IRCM's President and Scientific Director. "Our results show that, by controlling the activity of p53 and preventing premature cell death, Miz-1 ensures the survival of lymphocytes during their critical phase of development and, thereby, the proper functioning of our immune system."

More information: *Proceedings of the National Academy of Sciences* DOI: 10.1073/pnas.1412107111

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