Discovery brings cancer immune therapies a step closer

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Associate Professor Alex McLellan.

(Medical Xpress)—The development of new therapies to enhance the body's immune response to cancer is much closer after University of Otago scientists identified a pathway that alters the immune response in the spleen and lymph system when faced with cancerous tumour cells.

The research, just published in the internationally-respected American haematology journal *Blood*, has identified the pathway, or mechanism used when cells remove unwanted material in lipid-bound particles called exosomes. Exosomes are only 1/10,000 of a millimetre in diameter but are important in immunity as they contain proteins that can

enhance or suppress the immune response against cancer and have recently been exploited as cancer vaccines. They have also been implicated in autoimmune diseases.

Lead researcher Associate Professor Alex McLellan from Otago's Department of Microbiology and Immunology says that although the existence of exosomes has been known since the early 1970s, the fate of the released exosomes in the lymph system or blood has been poorly understood until now.

"We have discovered how exosomes are removed from circulation or lymph fluid and taken up by the immune system, and how this uptake system suppresses the immune response to these circulating particles," he says.

"In a normally functioning body this works in our favour to prevent autoimmunity, but when cancerous cells are involved you want to block this pathway to make the immune system more aggressive. Although exosomes are normally removed from circulation within minutes, we were able to induce strong immune responses to the exosomes by blocking this uptake system."

The study also is the first to record a circulation half life for exosomes.

Associate Professor McLellan, doctoral student Sarah Saunderson and colleagues found that the newly discovered mechanism uses a receptor called CD169 or sialoadhesin that is expressed on the lymph node or spleen that recognises sugars (sialic acids) present on the surface of the exosomes. In the absence of this uptake mechanism, immune responses are significantly enhanced in the spleen and lymph nodes.

"This suggests that when vesicle-uptake is working normally, inappropriate immune responses against self-tissues are prevented.

"Since tumours are also self-tissue the next application is to design small molecule inhibitors to block this pathway to enhance the body's immune response to cancer.

"The work has identified a new pathway of intercellular communication, a process that has involved seven years of work in the laboratory, and that has the potential to inform clinical developments in the fields of autoimmunity and tumour immunotherapy," says Associate Professor McLellan.

"This is relevant to all types of cancer that can be recognised by the immune system, including melanoma, and also autoimmune disorders."

Provided by University of Otago