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Unleashing the killers - new approach in Tumor Immunotherapy

Scientists at the Institute of Molecular Biotechnology of the Austrian Academy of Science (IMBA) in Vienna developed a new strategy to enhance tumor killing by the immune system in a mouse model. They published their recent findings as the cover story in the Journal of Experimental Medicine.

Our body's intrinsic defense, the immune system, does not only play a critical role in protection against foreign germs and viruses, it also monitors the development of tumors. However, cancers arise from normal cell of our body and therefore recognition by immune cells can be difficult and is often incomplete. In addition, cancer cells themselves tend to create an immune suppressive environment, thereby abrogating the anti-cancer activities of immune cells.

Researchers at the IMBA now genetically deleted the central negative regulator Cbl-b in mice, which resulted in enhanced immune function of T-cells leading to complete eradication of injected tumors in less than four weeks. Further, mice deficient in Cbl-b showed a markedly decreased incidence of spontaneous UV induced skin cancer, a model which mimics a specific type of skin cancer in humans.

The researchers could show, that transfer of genetically modified 'killer' T-cells lacking Cbl-b was sufficient to shrink tumors in other mice. Strikingly and in contrast to several other immunotherapeutic approaches, T-cells did not have to be pre-activated with tumor material or defined tumor proteins, which can be limiting; the inactivation of Cbl-b only conferred T-cells mediated tumor rejection.

Further studies will now focus on the validation of Cbl-b as a potential therapeutic target for human cancer therapy. Possible approaches would be blockade of Cbl-b by pharmacological inhibitors or by RNA interference techniques in T-cells of cancer patients followed by adoptive transfer back into the patient's blood.

However, unleashing T-cells by blockade of a negative regulator also increases the risk of autoimmune reaction and this certainly needs to be considered in a therapeutic setting.

Further studies in different cancer models as well as in human T-cells will reveal the potential of Cbl-b as new target for cancer immunotherapy.

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