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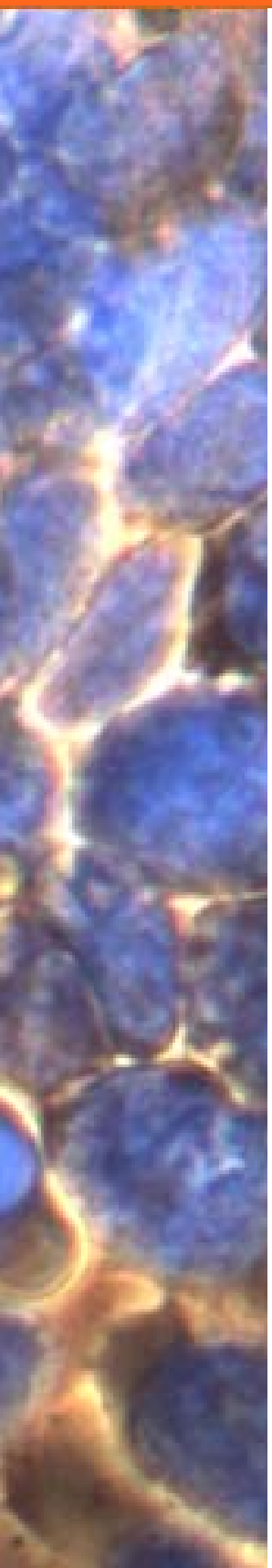
Blood Research Institute

Drug: Activated protein C (APC) for radiation and chemo protection



In Brief

Drug for radiation exposure treatment, and patient health during chemotherapy. Recombinant APC reduces immune system dysfunction upon lethal radiation doses, and prolongs survival in animal models.

Description

Activated protein C (APC) plays an important role in blood clotting, inflammation, cell death and maintaining blood vessel integrity. Recombinant human APC was sold under the brand name Xigris® (Eli Lilly) for the treatment of sepsis. Previously the drug was administered in continuous infusion. Bolus dosing discovered by inventors here addresses this bleeding problem.

Investigators have now discovered that APC provides protection to laboratory mice after lethal and sub-lethal doses of total body irradiation. Results showed significantly improved survival after exposure to radiation injury. Animals dosed with APC up to 24 hours after radiation exposure displayed improved hematologic recovery resulting in a shortened period of immune system dysfunction. Inventors predict a similar protective effect for other toxic insults to the bone marrow or rapidly dividing cells in the gut as occurs during chemotherapy. Given these results, APC has potential uses in controlling cellular toxicity during cancer treatment, and also in recovery following nuclear disaster exposure.

Inventors

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Benefits

- APC improves survival after lethal doses of radiation in animal models
- APC protective to bone marrow following injury
- Administration effective at various time points after exposure
- Bolus dosing of the drug offers more simplified use and lowers bleeding risk

Publications

Geiger, H., Pawar, S.A., Kerschen, E.J., Nattamai, K.J., Hernandez, I., Liang, H.P.H., Fernández, J.Á., Cancelas, J.A., Ryan, M.A., Kustikova, O. and Schambach, A. Pharmacological targeting of the thrombomodulin–activated protein C pathway mitigates radiation toxicity. *Nature medicine*. 2012; *18*(7), p.1123. PMID: 22729286.

Gur-Cohen, S., Itkin, T., Chakrabarty, S., Graf, C., Kollet, O., Ludin, A., Golan, K., Kalinkovich, A., Ledergor, G., Wong, E. and Niemeyer, E. PAR1 signaling regulates the retention and recruitment of EPCR-expressing bone marrow hematopoietic stem cells. *Nature medicine*. 2015; *21*(11), p.1307. PMID: 26457757.

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