Activated protein C is radioprotective

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Technology description

Activated protein C (APC) is known to play an important role in blood clotting, inflammation, cell death and maintaining blood vessel integrity. Recombinant human activated protein C was sold under the brand name Xigris for the treatment of sepsis. In October 2011, Eli Lilly pulled Xigris from the market after a large clinical study showed failure of the drug to reduce mortality in septic patients. The protective effects of the drug were offset by an increased risk of severe bleeding. Investigators have now discovered that various mutant forms of APC and naturally occurring APC provide protection to laboratory mice after lethal and sub-lethal doses total body irradiation. Animals showed significantly improved survival after exposure to up to 10Gy radiation. Animals dosed with APC up to 24 hours after radiation exposure displayed improved hematologic recovery resulting in a shortened period of immune system dysfunction following injury. Inventors predict a similar protective effect for other toxic insults to the bone marrow or rapidly dividing gut endothelium as occurs during chemotherapy. Technology is the subject of a provisional application filed late May 2012. Experimental model is whole mice exposed to total body irradiation and dosed with protein both before or after lethal doses of radiation.
Activated protein C, an FDA approved protein drug and biologically important in coagulation and inflammatory processes, has a new use in protecting subjects to radiation exposure and toxicity to the bone marrow and gut epithelium.

Application area

1. Nuclear disaster recovery
2. Uses in cancer therapies where controlling toxicity is important

Advantages

1. Various APC molecules improve survival after lethal doses of radiation in animal models
2. APC protective to bone marrow following injury
3. Administration effective at various time points after exposure
4. Bolus dosing of the drug offers more simplified use

Institution

BloodCenter of Wisconsin

Inventors

Hartmut Geiger
John Griffin Laurent Mosnier
Martin Hauer-Jensen
Hartmut Weiler