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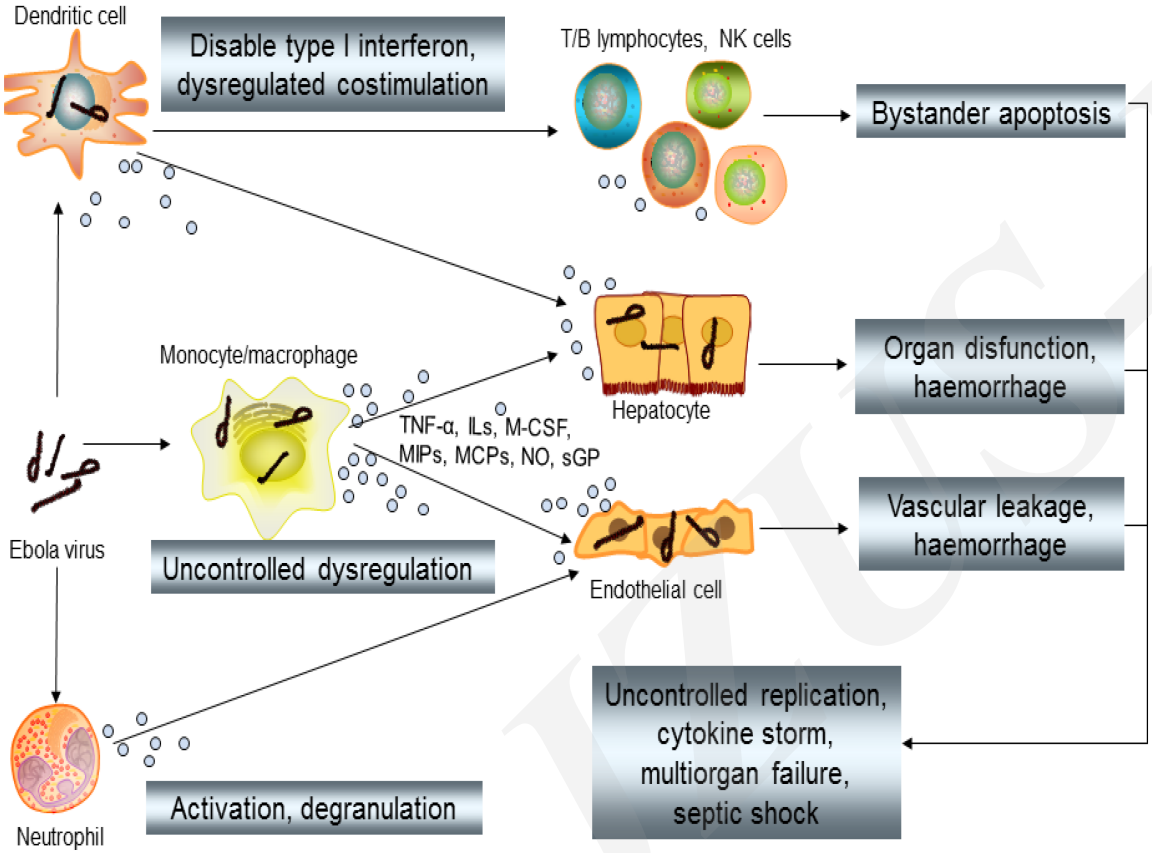
Against Ebola: type I interferon guard risk and mesenchymal stromal cell combat sepsis

Key words: Ebola, type I interferon, mesenchymal stromal cell

What makes the Ebola infection so deadly?

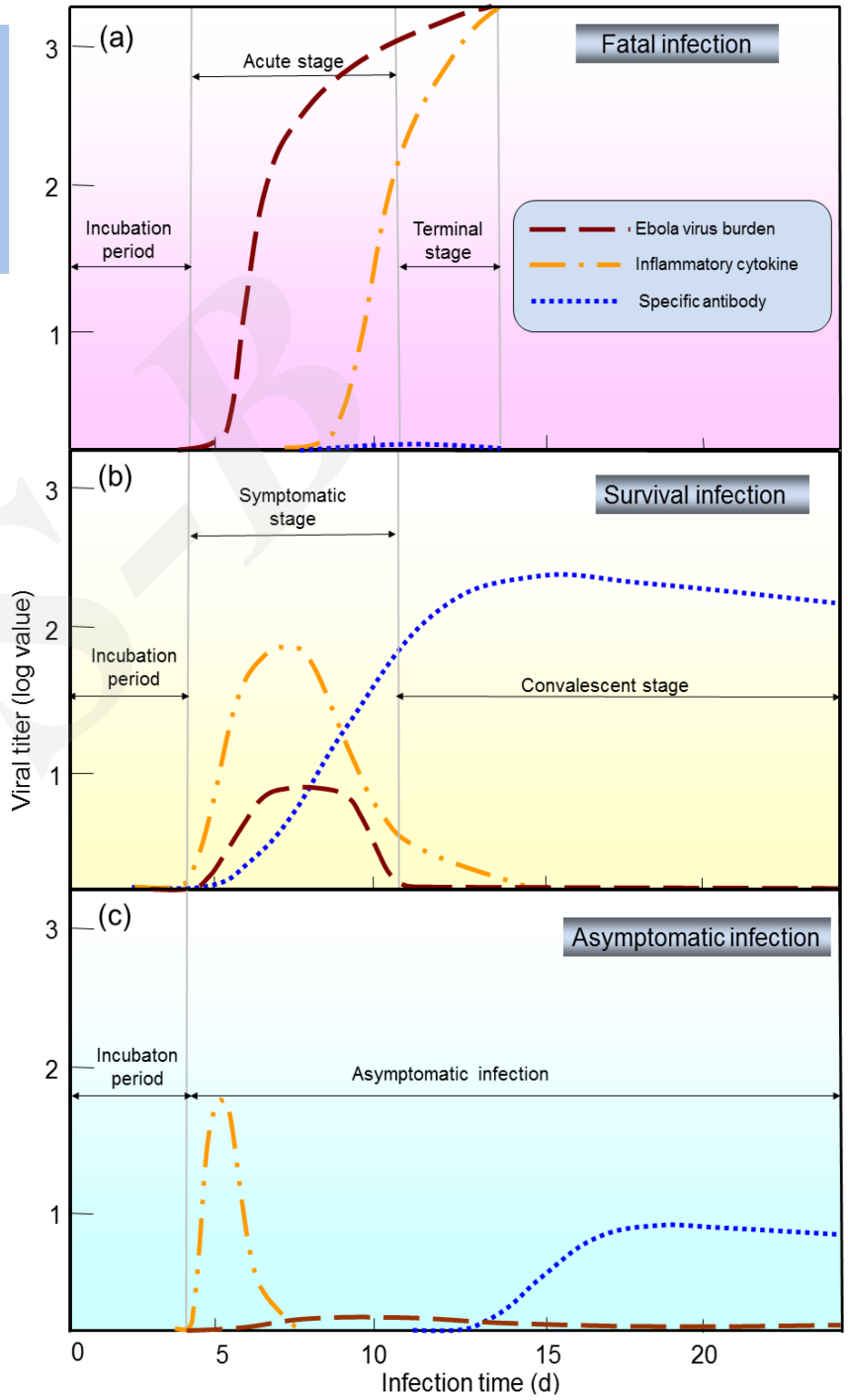


System overview of Ebola pathogenesis

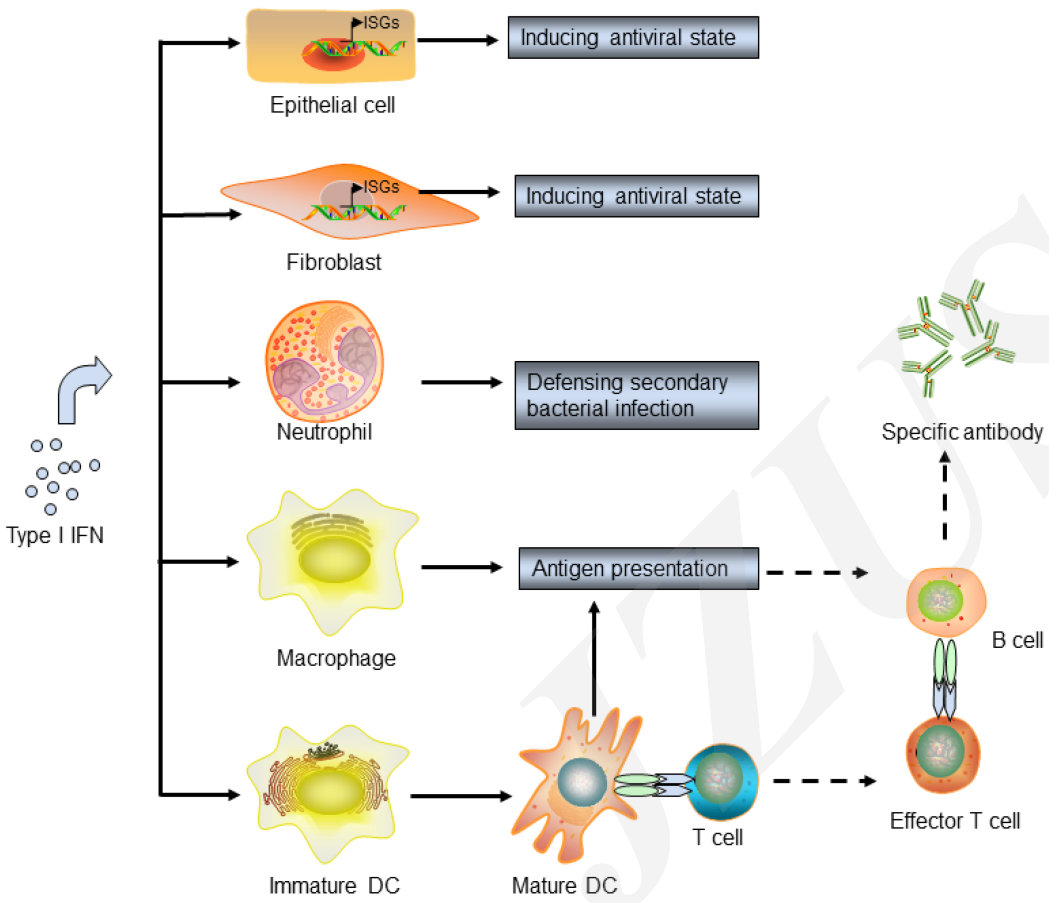
- The infection of the Ebola virus;
- The impairment of innate and adaptive immunity;
- The severe attacks of dysregulated immune system;
- Diffusive bleeding and hypotensive shock eventually kill the patients.

What are the differences among fatal, survival and symptomless infection?

- The double edges of inflammatory response;
- The distinction of specific antibodies;
- The diversity of the virus burden;
- The depletion of relevant cells;
- Some patients indeed recovered from the Ebola infection without receiving specific interventions;
- Appropriate immune responses can help the body heal itself.



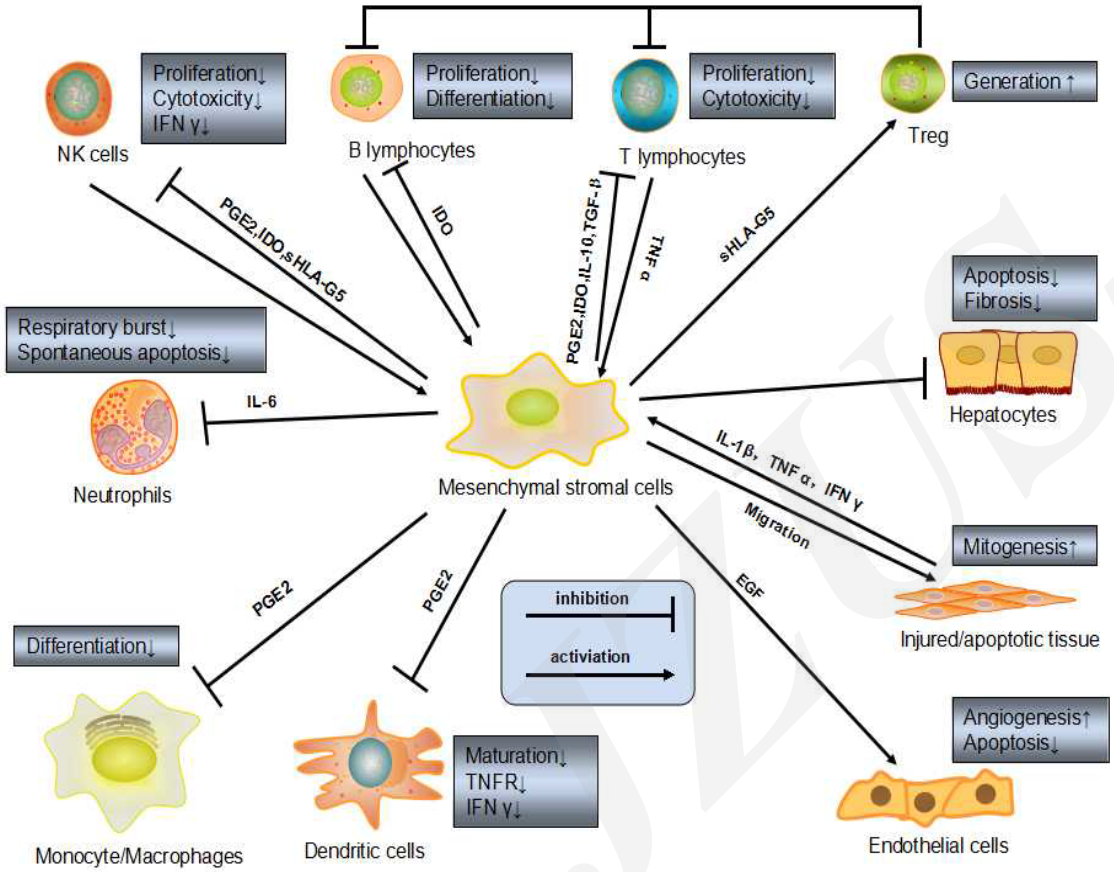
Type I interferon intervention during the incubation period may render a beneficial outcome



Type I interferon controls innate and adaptive immunity and intracellular antiviral programs.

- Type I interferons have a broad spectrum of antiviral capability that are able to fight most virus infections;
- Recombinant IFN-α2b (200 IU/ml) can suppressed Ebola replication by 100-folds in Vero cells in vitro;
- Early treatment on Ebola-infected cynomolgus with recombinant IFN-α2b delayed onset of viremia and death by several days;
- IFN-β treatment was associated with reducing the plasma and tissue viral burden, significantly increased survival time in Ebola infected macaques in vivo;
- Exogenous administration of type I interferon may induce uninfected cells into an antiviral state.
- Type I interferon might limit the spread of the Ebola virus and prolong survival if administered immediately after exposure to Ebola viruses.

Mesenchymal stromal cell therapy during the terminal stage may prevent the cytokines storm, massive cell apoptosis and septic shock



Immunological Function of MSCs on different cell types of the innate/ adaptive immunosystem. MSCs diminish damage and induce repair.

- The significant differences in fatality rate between age groups may be relavent to the consumption of age-related changes in the stem cells reservoir;
- MSCs migrate to injured tissue sites where they can inhibit the release of pro-inflammatory cytokines and promote the survival of damaged cells;
- MSCs operate through a variety of effector mechanisms on key cells of the innate and adaptive immune systems;
- MSCs can specifically communicate with the inflammatory microenvironment and this immunoregulatory function of MSCs is highly plastic ;
- It would be interesting to use the available nonhuman primate models of EVD to test such a therapeutic hypothesis.

Non-specific treatment is an essential strategy against viral diseases in the foreseeable future

- **It has been almost forty years since the first Ebola outbreak in 1976. There has been no specific therapy for even the most common human viral infection,the outlook for the development of Ebola therapeutics is not optimistic.**
- **In the symptomatic stage, the supportive care is mainly toward aggressive prevention; There is neither precaution for the incubation period nor effective medications for the terminal stage;**
- **A preventative antiviral intervention for the incubation period may lower the consequent virus burden; An immunomodulatory strategy for the terminal stage may reduce the damages caused by the cytokine storm, thus prolong the survival time of the patients;**
- **When our immune system is given sufficient time for intentionally activation when we are exposed to deadly viruses, there is a good chance that it can gear up and eliminate the viruses by itself.**