Diesel Soot Exposure Modulates Functional Differentiation and Maturation of Bone Marrow-Derived Dendritic Cells

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Dendritic Cells (DC)

- DC are present at sites where pathogens may enter the body, i.e. close to surfaces like skin and mucosal tissue.
- DC are often the first cells of the immune system to encounter pathogens.
- DC actively take up and process foreign matter.
- DC activate other immune cells to respond.
- DC are prime candidates for being influenced by environmental pollutants.
Differentiation

- DC are derived from stem cells in the bone marrow. When needed the cells travel from the bone marrow to their target organs.
- DC can be produced from bone marrow (mouse) or from blood (human) by growing cells in culture with the appropriate hormones.
- The result are immature DC, which are not yet doing anything, but are ready to go.
Maturation

- Immature DC get activated when they have contact to bacteria, viruses, or other pathogens. Activated DC migrate to the next lymph node.
- The mature DC which arrive in the lymph node are mature DC which are now ready to stimulate T cells.
- Maturation can also be mimicked in cell culture.
DC were exposed to Diesel soot (Euro 3 light duty engine), carbon black (39 nm, aggregates 122 nm), graphite (1-2 µm), and Printex XE 2 (30 nm).

The particles are not toxic at the concentrations used (40 µg/ml).

Are there relevant parameters which indicate effects of particles on the immune system?
Bone marrow cells were removed from mouse femur and cultured 10 d in presence of GM-CSF.

Expression of the DC markers CD11c, CD40, CD80, CD86 and MHCII is induced on the surface of the cells.
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From d0 +

w/o

diesel-soot

carbon black
39nm, aggregates 122nm

graphite
1-2µm

Printex XE2
30nm
CD86 - why worry?

- CD86 is a protein on the surface of activated DC.
- It delivers an important activation signal to the T cells.
- A T cell which does not get all required activation signal does not get activated a bit less! It is turned off! Permanently!
- It will have to be tested in mouse models whether this occurs in vivo.
O\textsubscript{2}⁻

From d0 -/+ LPS

w/o                      diesel-soot                        carbon black
-                          +                                    -                          +                                    -                          +

graphite                   Printex XE2
-                          +                                    -                          +                                    -                          +
Immune hormones: Cytokines

IL-10 pg/ml

IL-6 pg/ml

TNFalpha pg/ml

Particle effects
Summary

- Diesel soot inhibits immune functions of dendritic cells in some ways (CD86, TNF-alpha) but delivers activation signals as well (superoxide anions, IL-10).
- Other nanoparticles (Printex, carbon black) have similar effects on CD86 as DEP.
- The mechanisms involved have yet to be characterized.
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