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## *In vitro* and *in vivo* inflammatory effects of PAMAM dendrimers nanoparticles

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Several types of dendrimer nanoparticles (NPs) have been developed for various biomedical applications, including imaging agents and drug delivery systems. The polyamidoamine dendrimers (PAMAM) are among the most widely used and, despite their multiple functions, very few nanotoxicological studies have been performed. Since inflammation is one of the most toxic effects of NPs reported in the literature, we evaluated the impact of four generations (G) of PAMAM NPs (G0, G1, G2 and G3) on neutrophils, key player cells in inflammation. Because of the importance of neutrophil apoptosis in the resolution of inflammation, we determined if their basal apoptotic rate could be altered by the NPs. Also, we evaluated if the NPs could attract neutrophils *in vivo*. To do so, freshly isolated human neutrophils were incubated with various concentrations of NPs and the apoptotic rate was determined after 24 h by cytology and by fluorescence microscopy. For *in vivo* cell infiltration, we used the murine air pouch model in which 100 or 500 µg/ml of the NPs were administered into the pouch for 6 or 24 h. Exudates were harvested for cell counting and a fraction was used to perform western blot and zymography experiments to determine gelatinase activity. All the NPs (G0 to G3) were found to increase the apoptotic rate at a concentration greater than 100 µg/ml. Although only G1-500, G2-500 and G3-100 and 500 µg/ml were found to significantly increase the total number of leukocytes recruited *in vivo*, an increase number of neutrophils was consistently observed in all tested conditions. Results of the zymography experiments suggest a correlation between the number of neutrophils and the gelatinase activity. Unexpectedly, our results indicate that the NPs are proapoptotic *in vitro* (anti-inflammatory), but induce a neutrophilic infiltration (pro-inflammatory) *in vivo*.

### Biography

Isabelle Durocher has completed her BSc in microbiology and immunology at University of Montreal in 2013. She has recently initiated her second year of her Master at INRS-Institut Armand-Frappier.

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