

Molecular impact of functionalized nanodiamonds on *ex vivo* human immune cells response

Elisabetta Avitabile, Valentina Armuzza, Tatiana Da Ros, Lucia Gemma Delogu

University of Sassari, Via Vienna 2, 07100 Sassari, Italy, University of Trieste, Piazzale Europa, 1, 34128 Trieste
lgdelogu@uniss.it

Abstract

Carbon-based nanomaterials have been explored for biomedical applications due to their unique physicochemical properties [1]. In this context, nanodiamonds (NDs) are gaining increasing interest thanks to their biocompatibility, structure and unique electrostatic properties for several nanomedicine applications such as drug delivery, bioimaging and cancer therapy [2,3,4]. However, before any effective application of NDs, their action on the immune system is not fully clarified yet [5]. Nowadays, no comprehensive studies were performed on the immune system with NDs. In this work, we propose an integrative characterization of the molecular impact of two different types of NDs, Oxidized (-Ox) and Amino (-NH₂), on several human immune cell subpopulations such as T and B Lymphocytes, Natural killer (NK), monocytes and on red blood cells (RBCs). Both NDs showed no toxicity on RBCs and on the T and NK lymphocyte subpopulations. Only monocytes and B cells were affected by the presence of NDs-Ox at the highest concentration used while the functionalized ND-NH₂ counterpart showed no toxicity also on these cell types. NDs-Ox exposure increased proinflammatory cytokines secretion, such as IL6, IL1 β , TNF α and IL10, while we found a reduced immune cell activation in -NH₂ treated samples. On monocytes, -NH₂ showed low levels of CD25 activation marker expression compared to -Ox. To deeply analyze the molecular immune impact of NDs a gene expression analysis of 84 immune genes was performed. Intriguingly, after 24h -NH₂ reduced the expression of genes related to a strong inflammatory response such as IL10, IL5, IL4 compared to the -Ox form. These results emphasize the importance of the amino group functionalization, enhancing the biocompatibility of ND-based nanomaterials. These data are of particular interest for further translational applications of amino-functionalized NDs being possible inert materials useful for drug delivery and bioimaging applications.

References

- [1] Wang C, Li J, Amatore C, Chen Y, Jiang H, Wang XM, *Angew Chem Int Ed Engl*, 49 (2011) 11644-11648.
- [2] Tsai LW, Lin YC, Perevedentseva E, Lugovtsov A, Priezhev A, Cheng CL, *Int J Mol Sci*, 7 (2016) 1111.
- [3] Passeri D, Rinaldi F, Ingallina C, Carafa M, Rossi M, Terranova ML, Marianecchi C, *J Nanosci Nanotechnol*, 2 (2015) 972-988.
- [4] Zhang XQ, Lam R, Xu X, Chow EK, Kim HJ, Ho D, *Adv mater*, 41 (2011) 4770-4775.
- [5] Orecchioni M, Ménard-Moyon C, Delogu LG, Bianco A, *Adv Drug Deliv Rev*, 105 (2016) 163-175.