"Effect of graphene on human pluripotent and vascular cells"

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ABSTRACT

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The use of brain organoids has emerged as a novel research approach due to their ability to partially mimic early neurodevelopment and represent a tool for drug testing and disease modeling. Recently, vascularization of brain organoids has been attempted in order to increase the nutrient supply, decrease hypoxia and cell death, and importantly to establish a communication between the vasculature and neuronal cell types for their proper differentiation, neuronal migration and maturity (Zhang et al., 2018). We have succeeded in generating vascularized brain organoids using mature endothelial and mural cells. However, to increase the validity of brain organoid models by promoting an accurate human brain cytoarchitecture and cell-type representation, nanomaterials such as graphene were proposed as substrates. Graphene forms an allotropic carbon material and the 2D structure allowing its use in various biological applications (Lawani et al., 2016). Nanoparticles of graphene and graphene oxide (GO), have gained broad interest because of their unique properties and advantages: biocompatibility, flexibility and electrical conductivity (Kumar et al, 2016). In addition, graphene has been shown to act as an excellent substrate for neuronal and vascular cells promoting neurogenesis and angiogenesis (Kumar et al, 2016;Zhang et al., 2018). The focus of our research is the vascular component of the organoid, i.e. endothelial and mural cells. Prior to assembling the vascularized graphene-containing brain organoid we established the optimal type, size and concentration of graphene for use employing pluripotent stem cells, mature endothelial cells, mural cells and vascular organoids. We tested the effect of graphene on (1) pluripotent stem cell markers (NANOG and OCT3/4) (2) endothelial and mural cell growth (2) expression of mural cell phenotype markers (CALPONIN, a-SMA and SM22) and (3) formation and the sprouting of vascular organoids. Our results define the type and concentration of graphene which can now be used for the generation of vascularized brain organoids.

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