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Oxaliplatin-induced oxidative stress in isolated spermatogonial stem cells

S permatogonial stem cells (SSCs) are responsible for transmission of genetic information from males to their progeny. SSCs play pivotal roles in spermatogenesis and reproductive biology of gametes and treatment of infertility. Many chemicals have a negative impact on the SSCs, either directly, or indirectly through the somatic nursing cells. Eventually, these effects can inhibit fertility, and they may have negative consequences for the development of the offspring. Oxaliplatin is a platinum-organic drug with antineoplastic properties used for colorectal cancer and cytotoxicity due to platinum binding to DNA and the formation of intrastrand cross-links between neighbouring guanines. This study was to establish an oxidative stress model for antioxidant activity of some drugs investigated in SSCs in *in vitro* culture. The effects of oxaliplatin on SSCs were evaluated by standard cytotoxicity assays and the potential biochemical and molecular effects on the antioxidant system. Administration of oxaliplatin showed significant increases in DNA damage, p53 and *bcl-2* gene expression levels concomitant with significant decreases in endogenous antioxidant enzymes SOD, CAT and *GPx-mRNA* gene expression. Glial cell line-derived neurotrophic factor (GDNF) is important for SSC self-renewal *in vitro* and *in vivo*, so we also assessed oxaliplatin on GDNF-mediated signalling in these cells and oxaliplatin significantly decreased GDNF-mRNA and associated protein. Oxaliplatin-induced DNA damage causes an increase in intracellular superoxide anions which are reduced by the exogenous antioxidant flavonoid, quercetin. This study highlights evidence that SCCs have antioxidant and antiapoptotic properties that could reverse oxaliplatin-induced testicular toxicity, in addition to their role in spermatogenesis.

Biography

Diana Anderson (H index 54) holds the Established Chair in Biomedical Sciences at the University of Bradford. She obtained her first degree from the University of Wales and second degrees from the Faculty of Medicine, University of Manchester. She has 450+ peer-reviewed papers, 9 books, has successfully supervised 30 PhDs, is an Editorial Board Member of 10 international journals. She is Editor-in-Chief of a book series on Toxicology for the Royal Society of Chemistry. She gives key note addresses at various international meetings. She is a Consultant for many international organisations, including WHO, EU, NATO, TWAS, UNIDO, OECD.

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