

Scientific Paper:

Neurogastroenterology & Motility 23, e412 – e424, 2011

Reduced oxygen stress promotes propagation of murine postnatal enteric neural progenitors *in vitro*

C. Hegewald¹, R. Alt¹, S. Hetz¹, M. Cross², A. Acikgoez³, H. Till⁴, R. Metzger⁴, and M. Metzger¹

¹Translational Centre for Regenerative Medicine, University of Leipzig, Germany

²Division of Hematology and Oncology, University of Leipzig, Germany

³Department of General and Visceral Surgery, St. George´s Hospital Leipzig, Germany

⁴Department of Pediatric Surgery, University of Leipzig, Germany

Abstract:

Background Neural stem and progenitor cells of the Enteric Nervous System (ENS) are regarded as a novel cell source for applications in regenerative medicine. However, improvements to the current ENS cell culture protocols will be necessary to generate clinically useful cell numbers under defined culture conditions. Beneficial effects of physiologically low oxygen concentrations and / or the addition of anti-oxidants on propagation of various types of stem cells have previously been demonstrated. In this study, we tested the effects of such culture conditions on ENS stem and progenitor cell behavior.

Methods Enteric neural progenitor cells were isolated from postnatal day 3 mouse intestine and propagated either as monolayers or neurosphere-like bodies. The influence of hypoxic culture conditions and / or anti-oxidants on enteric cell propagation were studied systematically using proliferation, differentiation and apoptosis assays, whereas effects on gene expression were determined by qRT-PCR, western blot, and immunocytochemistry. **Key Results** Both hypoxic culture conditions and anti-oxidants supported a significantly improved enteric cell propagation and the generation of differentiated neural cell types. Enteric neural progenitors were shown to be specifically vulnerable to persistent oxidative stress. **Conclusion & Inferences** Our findings are consistent with previous reports of improved maintenance of brain stem cells cultured under reduced oxygen stress conditions and may therefore be applied to future cell culture protocols in ENS stem cell research.

Key-words: anti-oxidants, enteric neural progenitors, enteric nervous system, gut, hypoxia, oxygen