The regulation of the neuregulin1/ErbB system in the degenerating and regenerating nerve

The regulation of the neuregulin1/ErbB system in the degenerating and regenerating nerve

G Gambarotta[1,2], G Ronchi[1,3], K Haastert-Talini[4], BE Fornasari[1], A Crosio[5], P Pugliese[5], M El Souri[1,6], I Perroteau[1,2] , S Geuna[1,2,3]

[1] *Department of Clinical and Biological Sciences, University of Torino, Orbassano (To), Italy;*
[2] *Neuroscience Institute of Torino (NIT), Interdepartmental Centre of Advanced Studies in Neuroscience, University of Torino, Italy;*
[3] *Neuroscience Institute Cavalieri Ottolenghi (NICO), Orbassano (To), Italy;*
[4] *Institute of Neuroanatomy, Hannover Medical School, and Center for Systems Neuroscience (ZSN), Hannover, Germany;*
[5] *Reconstructive Microsurgery, Orthopedics Department, Trauma Center Hospital (CTO), University of Torino, Italy;*
[6] *Faculty of Science, Alexandria University, Egypt.*

The Neuregulin1(NRG1)/ErbB system consists of a family of soluble and transmembrane ligands and transmembrane tyrosine kinase receptors. Through the use of conditional knockout and transgenic models, it has been shown that this system is deeply involved in the myelination process during development and in the remyelination process after peripheral nerve injury, and that the different NRG1 isoforms (soluble and transmembrane) play different roles.
To better understand the role played by this system during nerve degeneration and regeneration, we analysed the expression of ErbB receptors and NRG1 in the distal portion of rat median nerves under regenerating and degenerating conditions, discriminating not only between soluble and transmembrane NRG1 isoforms, but also between alpha and beta EGF-like domain, and among a, b and c C terminus.
Five injury models characterized by a different degree of severity were analysed:
- axonotmesis (nerve crush), characterized by a mild injury followed by fast nerve regeneration;
- neurotmesis (nerve cut), followed by end-to-end repair and nerve regeneration;
- neurotmesis, with substance loss, followed by nerve autograft repair and nerve regeneration;
- neurotmesis, with substance loss, followed by empty chitosan tube graft and nerve regeneration;
- neurotmesis, followed by nerve degeneration.

Nerve ultrastructure changes in the different injury models were evaluated by electron microscopy.
Our data show that the different NRG1 isoforms and ErbB receptors are deeply regulated after peripheral nerve injury, not only at transcriptional and translational level, but also at post-transcriptional and post-translational level, thus suggesting that the finely tuned regulation of this system plays an important role in the peripheral nerve regeneration.
This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement No [278612].