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**Beta-lactam antibiotic offers neuroprotection in a spinal muscular atrophy model by multiple mechanisms**

Monica Nizzardo,a Martina Nardini,a Dario Ronchi,a Sabrina Salani,a Chiara Donadoni,a Francesco Fortunato,a Giorgia Colciago,a Marianna Falcone,a Chiara Simone,a Giulietta Riboldi,a Alessandra Govoni,a Nereo Bresolin,a,b,c Giacomo P. Comi,a,b,* Stefania Corti,a,b,*

*a*Dino Ferrari Centre, Department of Neurological Sciences, University of Milan, IRCCS Foundation Ca’ Granda, Ospedale Maggiore Policlinico, Milan, Italy, bCentre of Excellence on Neurodegenerative Diseases, University of Milan, Italy, cIRCCS Eugenio Medea, Bosso Parini, Lecco, Caps

Correspondence : Stefania Corti, Department of Neurological Sciences, University of Milan, IRCCS Foundation Ca’ Granda, Ospedale Maggiore Policlinico, Padiglione Ponti, Via Francesco Sforza 35, 20122 Milan, Italy, E-mail: stefania.corti@unimi.it

**Sonu Bhatia**
Department of Biotechnology, Panjab University, Chandigarh, INDIA

**Background**

Spinal muscular atrophy (SMA) is the most common genetic neurodegenerative disease leading to death in childhood.1 SMA is characterized by the loss of spinal cord anterior horn neurons and progressive denervation of skeletal muscles. SMA is caused by deletion or mutation of the telomeric copy of human surviv-}

Histological analysis of muscles of hind limbs for total tibialis anterior (TA), cross sectional area, total TA myofiber number and myofiber diameter was performed by the author. Spinal cord sections were subjected to immunohistochemistry using monoclonal antibodies against motoneuron specific markers SMI 32 antigen followed by secondary antibody AlexaFlour 488. Purified RNA isolated from spinal cord followed by cRNA preparation and oligonucleotide microarray hybridization. Biotinylated cRNA was hybridized to Affymetrix GeneChip Mouse Genome 430A 2.0 array at 47°C overnight and visualized on GeneArray 2500 Scanner. RNA from four groups of selected animals was reverse transcribed on Real time PCR system. Spinal cord protein was extracted from experimental animals and subjected to semi quantitative western blot. The membranes were probed with mouse anti SMN, anti EAAT2 antibody, rabbit anti BAX, anti PRG2, anti TDP 43, anti FUS and anti actin antibodies followed by use of secondary antibodies and chemiluminescence detection techniques. The staining sections and proteins density were measured with NIH Image software. Kaplan Meier analysis was used on lifespan using log rank post hoc test. ANOVA and Tukey-post hoc analysis of growth curve was performed. Student’s test was used for statistical analysis and upper significance level of 0.05 was used.

**Implications**

This study showed the neuroprotective effect of ceftriaxone on motoneurons and motor unit integrity by modification of gene expressions. The treatment of SMA mice with ceftriaxone increased survival time by 31.6%, slightly changed SMN defect mediated pathology and ameliorated motor dysfunction. A number of unregulated genes containing one or more NF-κB binding sites were observed after treatment. The author reported both GLT1 mediated reduction of excitotoxicity and activation of NRF2 related factors which may contribute to phenotypic amelioration. Out of several genes involved in transcription and RNA processing few of them including FUS, plastin 3 got down-regulated in SMN. These can be used as biomarkers to correlate with disease progression, however rel-
Evidence of these genes to disease in humans and efficacy of other drugs need to be studied.

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