ORAL COMMUNICATIONS

TARGETING P75NTR CORRECTS OXIDATIVE AND INFLAMMATORY IMBALANCES IN A CELLULAR MODEL OF RETT SYNDROME

M. Varone, M. Colardo, N. Martella, D. Pensabene, E. Bisesto, M. Segatto

Dept of Biosciences and Territory, University of Molise, Pesche, Italy

Rett syndrome (RTT) is a neurodevelopmental disorder with early onset that mainly affects females and leads to severe impairments in both cognitive and motor functions. Rather than being confined to the nervous system, RTT is now considered a multisystem disorder, as it involves not only the brain but also several peripheral tissues and organs. Growing evidence highlights a key contribution of disrupted redox balance and inflammatory pathways to the pathophysiology and progression of the disease.

The present study explores the impact of modulating the p75 neurotrophin receptor (p75NTR) through the small molecule LM11A-31 in fibroblasts obtained from RTT patients. To this end, cells were treated with 0.1 μM LM11A-31 for 24 hours, followed by molecular and biochemical analyses performed using qPCR, immunofluorescence, ELISA, and Western blot.

The data obtained indicate that LM11A-31 markedly reduces oxidative stress in RTT-derived cells. More specifically, modulation of p75NTR signaling restored the physiological levels of protein glutathionylation and decreased the expression of the pro-oxidant enzyme NADPH oxidase 4 (NOX4). In parallel, LM11A-31 treatment led to a reduction in pro-inflammatory cytokine levels and to the normalization of transcription factors that regulate antioxidant defenses and inflammatory responses.

Taken together, these results point to the potential of p75NTR-targeting compounds as therapeutic tools to counteract oxidative imbalance and inflammation in RTT. By intervening on central molecular mechanisms underlying the disorder, p75NTR modulation could represent a more integrated therapeutic approach. Additional studies will be necessary to clarify the mechanisms involved and to confirm these effects across different experimental models.