Title: **Mesenchymal stem cell transplantation overcome drug-resistant epilepsy in children - clinical observation and potential mechanism of action**

Authors: Majka M.[1], Milczarek O.[2], Badyra B.[1], Jarocha D.[1], Starowicz –Filip A.[3], Kwiatkowski S. [2]

[1] *Department of Transplantation, Institute of Pediatrics, Jagiellonian University School of Medicine, Cracow, Poland*

[2] *Department of Children Surgery, Institute of Pediatrics, Jagiellonian University School of Medicine, Cracow, Poland*

[3] *Department of Medical Psychology, Institute of Pediatrics, Jagiellonian University School of Medicine, Cracow, Poland*

Abstract:
Patients suffering from drug resistant epilepsy (DRE) are still waiting for more efficient and less toxic treatment. Recent advances in a field of cell therapy bring new options for those patients. The objective of present study was to assess the safety, feasibility, and potential efficacy of autologous bone marrow cells transplantation in pediatric DRE patients and elucidation potential mechanisms of action.

19 children with DRE were enrolled into the study. All children received combined autologous cell therapy of single bone marrow nucleated cells (BMNCs) transplantation and four rounds of bone marrow mesenchymal stem cells (BMMSCs) transplantations. The BMMSCs used in the study were a unique population derived from CD271 positive cells. Neurological evaluation included magnetic resonance imaging (MRI), electroencephalography (EEG) and cognitive development assessment using neuropsychological tests. Properties of patient's BMMSCs were also evaluated.

Intravenous and intrathecal transplantations were performed causing no adverse events, showing safety and feasibility during 6 - years follow-up. Importantly, the therapy caused neurological and cognitive improvement in all patients: significant reduction in a number of epileptic seizures (from initial 10/day to 1/week) and absence of SE episodes (from 4/week to 0/week). The therapy decreased number of discharges in EEG evaluation and caused cognitive improvement in the sphere of reaction to light and sound, in the sphere of emotions and in the sphere of motor function. Analysis of BMMSCs properties revealed expression of neurotrophic, proangiogenic and tissue remodeling factors. Their immunomodulatory potential was also shown.
Our results demonstrate the safety and feasibility of BMNCs and BMMSCs transplantations in children with DRE. Moreover, the results demonstrate that cell therapy approach brings considerable neurological and cognitive improvement for those patients due to intrinsic properties of transplanted cells.