

The review article entitled “Diagnosis and management of mucopolysaccharidosis type II 2 (Hunter syndrome) in Poland” by Zbigniew Żuber and co-authors describes the current methods of diagnosis for the management and treatment of patients affected by MPS II.

- The article has a good structure and a proper logical flow. English language is appropriate.
- In the title the focus of your article is on the diagnosis and management of MPSII in Poland. However, it seems a generic description of techniques and tests for MPSII. Probably, concepts and information more focused on Poland should be reiterated in the manuscript.
- The manuscript misses of figures. Adding at least one figure would improve the value of your article. I suggest to prepare one figure with the chemical structures of heparan and dermatan sulphates, or with the MS/MS spectra or with the chromatographic profiles of the different GAGs.
- The introduction should contain more details about the I2S protein. This may include expression levels, structure, activities etc.
- The introduction should better explain the brain features and the neurological impairment in MPS II. Furthermore, as comparison, the background misses of important references related to the neurologic and metabolic disturbances in other MPS (such as MPSIII), in which these alterations were explained by alterations in proteins involved in cytoskeleton organization, vesicle trafficking and fatty acid metabolism (please use the following refs: 10.3390/biom10030355; 10.3390/ijms21124211).
- The Diagnosis section (or the introduction for a more general description) misses of an important recall to the expanded newborn screening programs worldwide, which include laboratory analyses to detect the biochemical/molecular defects of some MPS types in order to perform early diagnosis at the neonatal age.
- Line 81: “ultra-efficient liquid chromatography” does not exist. Please, replace with high-performance liquid chromatography (HPLC).
- Line 83: replace “quantify and qualify” with “identify and quantify”
- Line 83-84: the authors comment that “Liquid chromatography can distinguish between non-neuronopathic and neuronopathic MPS II sub-types.”. What do they exactly refer to? To the ability of HPLC to discriminate retention times of different GAGs? This should be better explained.
- Line 89-90: Please, rephrase the following sentence for a better readability: “Since multiple sulfatase deficiency is also characterized by decreased I2S activity, it should be excluded by simultaneous measurement of other sulfatases to confirm I2S deficiency and the diagnosis of MPS II”

- Line 104-105: “Idursulfase does not affect the cognitive and behavioral functioning of patients with MPS II because it does not cross the blood-brain barrier” means that the treatment does not ameliorate the cognitive functions?
- Line 113: The “Treatment guidelines” continues with a series of bullet points that do not explain if there are specific guidelines depending on the age and severity of patients (as it is suggested by the authors in the first sentence at line 114). This should be better clarified.
- Line 128: “Recommendations for the initiation of enzyme replacement therapy”. An introductive one-line sentence to explain the value or importance for the existence of these recommendations should be added to help the reader to understand the story.
- Line 231: ERT abbreviation was not added next to the *enzyme replacement therapy* when it was firstly cited in the text.