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Review of Doctoral Thesis

"Clinical-epidemiological characteristics of mucopolysaccharidoses in children in the Republic of Kazakhstan" by Tulebayeva Assel Kairatovna Specialty: 6D110100 (Medicine)

PhD candidate Assel Tulebayeva has undertaken an important and burning problem concerning the prevalence, diagnosis and treatment of patients with mucopolysaccharidoses (MPS) type I, II, VI and IV in the Republic of Kazakhstan.

In my opinion this is the first such detailed study, covering clinical, biochemical, and molecular characterization of the mentioned mucopolysaccharidoses, including the effects of enzyme replacement therapy currently available.

PhD candidate Assel Tulebayeva made a retrospective analysis (from 1998 to 2016) of the prevalence of these diseases in the Republic of Kazakhstan by estimating their incidence at 0.75 per 100 000 live births. She also found the mutual ratio of the incidence of particular types of mucopolysaccharidoses showing that the most common is MPS II. These results provide a more reliable estimation of the incidence of MPS. What is notably important for prospective decisions regarding diagnostics including newborn screening and treatment of MPS patients in the Republic of Kazakhstan.

In cooperation with foreign centres, a number of new mutations, not described so far, have been identified in the Kazakh population. This allowed to establish the molecular database for the Kazakh population, but also to make a significant contribution to the general knowledge of the correlation between genotype and phenotype in these mucopolysaccharidoses. What it is interesting is that in the study population PhD candidate did not find correlation between the genotype and phenotype, showing that similar genotypes may lead to different phenotypic expression.



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Assessing the effects of enzymatic therapy, Assel Tulebayeva presented in detail all the treatment endpoints used in world standards. PhD candidate personally performed cardiological and pulmonological examinations. This adds tremendous value to her work and makes it comparable to similar studies undertaken in leading global centres.

Assel Tulebayeva's doctoral dissertation allows to develop diagnostic and therapeutic algorithms and, what is extremely important, may result in raising the awareness of physicians for patients with this group of diseases. This is of great importance for improving the diagnosis of rare diseases in general.

Moreover, Assel Tulebayeva's evaluation of the effectiveness of enzyme replacement therapy due to its specificity makes a significant contribution to the general knowledge of the effectiveness of this treatment in mucopolysaccharidoses. This all makes Assel Tulebayeva an expert in the field.

The reviewed dissertation fulfils all requirements posed on theses aimed for obtaining a PhD degree. Due to the high level of work, as well as the importance of the issue, I postulate, as a reviewer, the award of outstanding work.

Warsaw, November the 13th 2017

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