Mashhad University of
Medical Sciences

Dear professor Wojciech Miltyk,

I have reviewed this dissertation and I have the following comments and questions:

The subject of this dissertation "Complete Clinical Pharmacogenomic Profiling" has a high scientific value and great impact in the field of pharmacogenomics and pharmacogenetics. This kind of analysis prior to treatment of diseases will result in a more successful outcome for the patients.

Comments:

1. I believe that a chart similar to the chart given in the discussion section about the results of NGS variants found in this study and their correlations with diseases should be given in the result section. The significance of the variants found is illustrated more in the examples of genotype-phenotype correlations.
2. The dissertation text has some gramer and typing error that requires corrections.

Questions:

1. Because of some complexity in PGx genes like *CYP2D6* and *UGT1A1*, utilization of WGS and long read sequencing approaches are recommended as well. Please explain why did you choose WES as your selected platform for PGx variant identification in your samples.
2. As the novel discoveries and new information about gene-drug interactions may cause the already existed guidelines and recommendations to be modified as well, your PGx card and related databases/guidelines (including what you already inserted in your website tables) may need to be updated periodically. I would like to know what type of strategy you will employ to deal with such a problem?
3. The ultimate goal of PGx data analysis would be the integration of acquired result into daily clinical practice. Please explain (in your opinion) how and by whom this knowledge could be obtained faster and expected to be part of routine clinical setting in local healthcare systems.

Alireza's doctoral dissertation grade: distinction

Sincerely yours,

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