

Dear Lian-Sheng Ma,

Ref.: 64628, Review

Thank you for thinking about publishing our manuscript " Proteomics: Concepts and Applications " in the World Journal of Biological Chemistry. We've answered the major and minor points raised by the reader, and the manuscript has been updated as a result. In addition to this answer letter, we used track changes and yellow highlight to highlight the changes in the manuscript (for the references). Overall, the remarks highlighted critical questions and greatly improved the study's applicability. Our response to each of the individual comments is mentioned below.

Reviewer #1:

* Comment: "The number of human proteins reaches about one million, containing some modifications such as posttranslational modifications (PTMs). However, the human genome holds 26,000–31,000 proteins." - The first and second sentences appear to contradict each other.

** Response: Thank you for this observation. The correct sentences has been inserted.

* Comment: "Protein expression mapping uses two-dimensional (2D) gel electrophoresis combined with mass spectrometry for quantitative proteomes expression in cells, body fluids, or tissue." - The authors emphasize 2D-PAGE in combination with MS. What about 1D-PAGE (SDS-PAGE) and gel-free MS? Please describe them too.

** Response: Thank you for your suggestion. The required addition description has been added.

* Comment: "The protein separation can be considered either by "in-gel solution" or by chromatography called "off-gel". - This is not correct. What is the definition of off-gel? Do the authors mean liquid isoelectric focusing (OFFGEL) protein fractionation /gel-free proteomics? In both gel-base and gel-free LC-MS/MS, protein samples will be separated by HPLC prior to MS.

** Response: Thank you for your correction. the sentences were deleted and the right sentences has been inserted.

* Comment: Qualitative proteomics can provide information on diseases' molecular mechanisms and compare two groups such as diseased patients with healthy people. - Please provide references.

** Response: Thank you. The reference has been added.

* Comment: Please give examples of all types of proteomics

** Response: Thank you. The examples have been added.

* Comment: "Two-dimensional variations can also be used in the techniques of gel electrophoresis (2D-DIG) and sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE)." - What is 2D-DIG? The abbreviation is used without a full name. - In fact, SDS-PAGE is 1D-PAGE, isn't it?

** Response: Thank you for your comments. 2d-DIG is two-dimensional difference gel electrophoresis. We agree that SDS PAGE is 1D-PAGE and we have added more explanations.

* Comment: "Because of some limitations of a 1-Da gel, the proteins only used after some purification. So in the case of a more complex protein, the 2-DE can be used." - This is not correct. Do we really need to purify protein before applying to 1D-gel? Both 1D and 2D gel are widely used in combination of MS.

** Response: Thank you . We have deleted these sentences.

* Comment: Chromatography-based approach" - Why did the authors describe this topic? Do they misunderstand the core context of the article? How to link this topic with proteomics?

** Response: In Fact, there are two approaches are used in the separation of proteins from the mixture ,Gel-based approach and chromatography based approach. This is the reference: Coskun O. (2016). Separation techniques: Chromatography. *Northern clinics of Istanbul*, 3(2), 156–160. <https://doi.org/10.14744/nci.2016.32757>.

* Comment: Edman sequencing" - Similar to No.5., how to link this topic with proteomics?

** Response: Also , Edman sequencing is one of the earliest methods used for protein identification. The is the reference : Graves PR, Haystead TA. Molecular biologist's guide to proteomics. *Microbiology and molecular biology reviews* 2002; **66**(1): 39-63.

* Comment: Protein Identification and Validation" - This topic is not clear. Proteomics can be validate using bioinformatic tools (such as STRING or STITCH programs, Venn diagram, etc.) and wet labs (such as western blots, ELISA, etc.). Please describe them.

** Response: Thank you for your comments. The description of bioinformatics tools have been added.

* Comment: Bioinformatics in proteomics" Please describe programs generally used to analyze proteome data such as MASCOT, Panther, STRING or STITCH programs, Venn diagram, etc.

** Response: Thank you for your comments. The description of bioinformatics tools have been added.

* Comment: Please give a full name of AML

** Response: Acute myeloid leukemia.

* Comment: Some misspelled words appear. Please correct the title to be Proteomics: Concepts and Applications in Human Medicine.

** Respons: Thank you for your suggestion.