

## Narrative Review Checklist

| Section/Topic        | Item No | Item   | Reported on Page Number/Line Number | Reported on Section/Paragraph |
|----------------------|---------|--|-------------------------------------|-------------------------------|
| <b>TITLE</b>         |         |  |                                     |                               |
| Title                | 1       | Identify the report as a systematic Review of PTPRD mediated signaling pathways in hepatocellular carcinoma.   | Page1/Line7                         | -                             |
| <b>ABSTRACT</b>      |         |  |                                     |                               |
| Unstructured summary | 2.a     | Provide an unstructured summary including, as applicable: background: (HCC) is the third most common cause of cancer-related mortality worldwide, and the methods for its treatment have shown limited efficacy. (PTPRD) is an important tumor-suppressor gene that is down-regulated in HCC | Page2/Line1-2;5-7                   | Abstract/paragraph1           |
|                      | 2.b     | Objective: To explore the underlying signal transduction pathway of PTPRD in HCC   | Page2/Line1-9                       | Abstract/paragraph1           |
|                      | 2.c     | Brief summary of narrative review: We introduce the structure, functionality, and the physiological role of PTPRD and summarize the underlying signal transduction pathway of PTPRD to emphasize a hypothesis that PTPRD is a strong HCC tumor-suppressing gene.                             | Page2/Line10-15                     | Abstract/paragraph1           |
|                      | 2.d     | Implications for future research: The PTPRD-mediated signaling pathway has emerged as a promising target for the treatment of HCC.   | Page2/Line15                        | Abstract/paragraph1           |
|                      | 2.e     | Clinical practice or policy development: Efficient delivery and stability of PTPRD in conjunction with other anticancer therapeutics in vivo remain technically challenging  | Page2/Line16-20                     | Abstract/paragraph1           |
| <b>INTRODUCTION</b>  |         |  |                                     |                               |
| Rationale/background | 3       | Describe the rationale for the review in the context of what is already known: PTPRD is homozygously deleted and epigenetically downregulated in HCC, and PTPRD may be a significant tumor-  | Page3/Line 11-17                    | Introduction/paragraph1       |

|                           |     |  |                                      |                         |
|---------------------------|-----|--|--------------------------------------|-------------------------|
|                           |     | suppressor gene for HCC  |                                      |                         |
| Objectives                | 4   | Specify the key question(s) identified for the review topic:   | -                                    | -                       |
|                           | 4.a | Does PTPRD deletion promote the development of HCC? Page/3Line 13-27   | Page3/Line 13-17                     | Introduction/paragraph2 |
|                           | 4.b | Why PTPRD decreased in HCC compared with normal tissues?   | Page3/Line 18-23                     | Introduction/paragraph2 |
|                           | 4.c | Whether PTPRD inhibites the carcinogenic signaling pathway in HCC?   | Page3/Line 24-30                     | Introduction/paragraph2 |
|                           | 4.d | How does PTPRD play an inhibitory role in HCC?   | Page3/Line 31-33;<br>Page4/Line 1-11 | Introduction/paragraph3 |
| <b>METHODS</b>            |     |  |                                      |                         |
| Research selection        | 5   | Specify the process for identifying the literature search (eg, years considered, language, publication status, study design, and databases of coverage):<br><br>We searched PubMed database for published English papers on PTPRD in the past ten years. | -                                    | -                       |
| <b>DISCUSSION/SUMMARY</b> |     |  |                                      |                         |
| Narrative                 | 1). | research reviewed including fundamental or key findings;   | -                                    | -                       |
|                           | 6.a | PTPRD negatively regulates of signaling pathways in HCC, including those of STAT3/JAK, $\beta$ -catenin/TCF, the PTPRD-CXCL8 axis, the PI3K/Akt/mTOR axis, and the PD-1/PD-L1 axis.  | Page14/Line14-17                     | Conclusion/paragraph1   |
|                           | 2). | Limitations and/or quality of research reviewed:   | -                                    | -                       |
|                           | 6.b | This hypothesis lacks experiments both in vivo and in vitro.   | Page14/Line21-22                     | Conclusion/paragraph1   |
| Discuss                   | 3). | Need for future research:  | -                                    | -                       |

|         |     |  |                  |                       |
|---------|-----|--|------------------|-----------------------|
|         | 6.c | It provides a theoretical basis for future research  | Page14/Line19-21 | Conclusion/paragraph1 |
| Summary | 7   | Provide an overall interpretation of the narrative review in the context of clinical practice and/or the Nutrition Care Process for registered dietitian nutritionists, clinical practice for other health professionals, policy development and implementation, or future research. Mainly including: | -                | -                     |
|         | 7.a | PTPRD is a tumor-suppressor gene that has a crucial role in the initiation, promotion, and progression of HCC.   | Page14/Line10-13 | Conclusion/paragraph1 |
|         | 7.b | We summarize the pathological role of PTPRD and We put forward a hypothesis that PTPRD pivotal contribution to the regulation of signaling pathways in HCC, including those of STAT3/JAK, $\beta$ -catenin/TCF, the PTPRD-CXCL8 axis, the PI3K/Akt/mTOR axis, and the PD-1/PD-L1 axis.                 | Page14/Line14-19 | Conclusion/paragraph1 |
|         | 7.c | We suggest that PTPRD combined with other anticancer therapeutics may be a promising therapeutic approach against HCC  | Page14/Line19-22 | Conclusion/paragraph1 |

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\*As the checklist was provided upon initial submission, the page number/line number reported may be changed due to copyediting and may not be referable in the published version. In this case, the section/paragraph may be used as an alternative reference.