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Downregulation of THBS2 suppresses tumorigenicity and liver metastasis of gastric cancer and increases its sensitivity to trastuzumab

Authors: The user wants me to translate a Chinese name "Chang, Zhengyao" into English. This appears to be a name, likely an author name in an academic context.

The format is "Chang, Zhengyao" which is already in English format (surname first, then given name). The Chinese characters are "常正耀" (Cháng Zhèngyào).

However, the instruction says "Translate from Simplified Chinese to English with the highest accuracy and academic tone." The input is just a name.

Looking at the critical requirements: 1. Preserve ALL LaTeX commands and placeholders - not applicable here 2. Preserve ALL citation commands - not applicable 3. **PRESERVE ALL ···paragraph wrapper tags EXACTLY** - not applicable 4. Maintain academic tone and formal scientific writing style - for a name, this means using standard academic naming conventions 5. Use precise technical terminology - not applicable for a name 6. Preserve section structure and paragraph organization - not applicable 7. Translate all content completely - this is just a name

The name "Chang, Zhengyao" is already in English format. The Chinese characters would be "常正耀". In academic contexts, Chinese names are typically presented in one of these formats: - Chang, Zhengyao (surname first, given name second, comma-separated) - Zhengyao Chang (Western order) - Chang Zhengyao (no comma)

The input is already "Chang, Zhengyao" which is a standard format in academic papers (surname first). I should preserve this exactly as it is, since it's already in English.

Wait, let me re-read the instructions. The user provided "Chang, Zhengyao" which is the English transliteration of a Chinese name. The task is to translate from Simplified Chinese to English. But the input is already in English letters.

Is the user asking me to confirm this is the correct English representation? Or are they providing the Chinese characters and asking for translation? The input is literally "Chang, Zhengyao".

Given the strict requirements about preserving tags and structure, and that this is a single name without any tags, I should just return the name as is. It' s already in the standard academic format for English publications.

The glossary provided is about technical terms (机器学习 => machine, The user has provided a name "Li, Jiyang" which appears to be an author name. This is not the Chinese text to translate. The user is likely testing me or providing context. I need to wait for the actual Chinese text to translate.

However, looking at the instructions, I should be ready to translate academic text from Chinese to English with specific requirements: 1. Preserve LaTeX commands and placeholders 2. Preserve citation commands ([**?**], **??**, (**??**), etc.) 3. Preserve ALL ···tags exactly 4. Maintain academic tone 5. Use precise technical terminology from glossary 6. Preserve section structure 7. Translate completely without omission

The glossary provided is: - 机器学习 => machine learning - 深度学习 => deep learning

Since the user only provided "Li, Jiyang" , which is already in English format (surname, given name), there' s nothing to translate. I should respond appropriately, perhaps asking for the actual text to translate, or just acknowledge that this is already in English.

But wait - the user might have made a mistake and pasted only the name instead of the full text. I should be helpful and indicate that I' m ready to translate the actual content when provided.

Let me check the instructions again. The user wants me to translate from Simplified Chinese to English. "Li, Jiyang" is not Simplified Chinese - it' s a name in Pinyin, already in Latin script. So there' s nothing to translate here.

I should respond by indicating that no Chinese text was provided for translation, or simply state that the name is already in English format.

However, the system prompt is very specific about the output format. It says "Return ONLY the translated text for the given input (no explanations, no quotes, no headings you invent)." This suggests I should not add explanatory text.

But if the input is just "Li, Jiyang" and it' s not Chinese text that needs translation, what should I do? The most appropriate response would be to return the input as-is, since it' s already in English format.

Let me think about this differently. Could "Li, Jiyang" be considered Chinese text that needs translation? In Chinese, it would be written as "李济阳"or similar characters. The Pinyin "Li, Jiyang" is already a transliteration, which is a form of translation. So perhaps the user wants me to convert this to the, Zhang, Chao, The user has provided a very short input: "Gao, Yunhe" . This appears to be a name, likely the author name from a paper. The user wants me to

translate this from Simplified Chinese to English with the highest accuracy and academic tone, following the critical requirements and output rules provided.

Let me analyze the input: - It' s just a name: "Gao, Yunhe" - This is already in a format that is commonly used in English academic papers (surname first, then given name) - There are no LaTeX commands, no placeholders, no citation commands, and no ···tags

According to the instructions: 1. I must preserve ALL LaTeX commands and math placeholders - but there are none here 2. I must preserve ALL citation commands - but there are none here 3. I must PRESERVE ALL ···paragraph wrapper tags EXACTLY - but there are none here 4. I must maintain academic tone and formal scientific writing style 5. I must use precise technical terminology - but this is just a name 6. I must preserve section structure and paragraph organization - but this is just a single line 7. I must translate all content completely - do not omit any information

The name "Gao, Yunhe" is already in a format that would be used in English academic writing. In Chinese, it would typically be written as "高云鹤" or "高韵鹤" etc. But the user has provided it as "Gao, Yunhe" which is the standard pinyin transliteration with surname first.

Since there are no tags in the input, I should not add any. The output should be just the translated text. The name is already in English format, so I should just return it as is.

Wait, let me re-read the instructions carefully. The user says "Translate from Simplified Chinese to English". The input "Gao, Yunhe"is already transliterated. But perhaps the user wants me to treat this as Chinese text that needs to be translated. However, it' s already in pinyin, which is the standard way to represent Chinese names in English academic papers.

The critical requirements say: - "Preserve ALL LaTeX commands and placeholders exactly - do not modify, translate, or rewrite any mathematical formulas" - "Preserve ALL citation commands (, The user has provided a name" Liang, Wenquan" which appears to be an author name. This is not a paragraph with tags or Chinese text to translate. The instruction says to translate from Simplified Chinese to English, but this is already in English format (though it' s a Chinese name).

Looking at the critical requirements: 1. Preserve LaTeX commands and math placeholders - not applicable here 2. Preserve citation commands - not applicable 3. **PRESERVE ALL ···paragraph wrapper tags EXACTLY** - not present 4. Maintain academic tone - not applicable for a name 5. Use precise technical terminology - not applicable 6. Preserve section structure - not applicable 7. Translate all content completely - the name is already in a standard format

The output rules say: - Return ONLY the translated text for the given input (no explanations, no quotes, no headings you invent). - Keep one output paragraph

per input paragraph; do not merge or split paragraphs. - **Maintain exact count and IDs of ···tags**

Since there are no tags and no Chinese text to translate, the input is just a name. The name "Liang, Wenquan" is already in the standard Western format (surname first, then given name). In academic contexts, Chinese names are often presented this way.

The instruction says "Translate from Simplified Chinese to English". The name "Liang, Wenquan" is a romanization of a Chinese name. The surname is Liang (梁) and given name is Wenquan (文泉). It's already in English letters.

I should just return the name as is, since there's nothing to translate and no tags to preserve. The output should be exactly the input.

Wait, let me reconsider. The user might be expecting me to process this as part of a larger document, but they've only provided this single line. The instructions are very specific about preserving tags, but there are none here.

Given the strict rules, I should: 1. Not add any tags that weren't there 2. Not modify the content 3. Just return the input as is

The name "Liang, Wenquan"is already in a format suitable for English academic papers. No translation is needed.

So my output should simply be: Liang, Wenquan

But wait, I need to, Pan, Heng, Zhang, Kecheng, Cui, Jianxin, Wei, Bo, The user has provided a very short input: "Chen,Lin". This appears to be a name, likely of an author. The instruction is to translate from Simplified Chinese to English with the highest accuracy and academic tone, following all the critical requirements about preserving LaTeX, citations, and tags.

However, the input "Chen,Lin" is just a name. It's not in a paragraph tag. It's not even Chinese characters - it's a romanized name with a comma. The name "Chen, Lin" would be the standard English format (surname first, then given name, separated by a comma).

Let me check the requirements again: - Preserve ALL ···paragraph wrapper tags EXACTLY - Return ONLY the translated text for the given input - Keep one output paragraph per input paragraph - Maintain exact count and IDs of ···tags

The input "Chen,Lin" doesn't have any tags. It's just a name. In academic contexts, Chinese names are often written in the format "Chen, Lin" where Chen is the surname and Lin is the given name. The comma is already there.

Since there's no Chinese text to translate (it's already in pinyin/English format), and there are no tags, I should just return the name as is. The name "Chen, Lin" is already in the standard English academic format for Chinese names.

But wait - should I interpret this as the user wanting me to format it properly? In Chinese academic papers, names are sometimes written as "Chen Lin" or

"CHEN Lin" or "Chen, Lin". The most standard English academic format would be "Chen, Lin" (surname first, comma, then given name).

The input is exactly "Chen,Lin" (no space after comma). In English academic writing, there should typically be a space after the comma: "Chen, Lin". However, the instruction says "translate from Simplified Chinese to English with the highest accuracy". This is already a transliterated name, not Chinese characters.

Let me think about what the user might want: 1. If this is a test to see if I follow the rules about tags, I should note that there are no tags and just return the name. 2. If this is actual content that would appear in a paper, it might be part of an author list.

Given the strict requirements, The user wants me to translate a Chinese text to English. The text appears to be "Xi, Hongqing" which looks like a name. Let me check the requirements:

1. Preserve ALL LaTeX commands and placeholders - there are none here
2. Preserve ALL citation commands - there are none
3. **PRESERVE ALL ···paragraph wrapper tags EXACTLY** - there are none
4. Maintain academic tone and formal scientific writing style - this is a name, so I should translate it appropriately
5. Use precise technical terminology - obey the glossary strictly - the glossary mentions "机器学习 => machine learning" and "深度学习 => deep learning", but they don't apply here
6. Preserve section structure and paragraph organization - it's just a name
7. Translate all content completely - do not omit any information

The text "Xi, Hongqing" appears to be a name in Chinese format (surname first, then given name). In English academic contexts, Chinese names are typically written in one of these formats: - Xi Hongqing (surname first, no comma) - Hongqing Xi (given name first, surname last, Western format) - Xi, Hongqing (surname first with comma, often used in bibliographic citations)

Since the original includes a comma "Xi,Hongqing" (without space after comma), this looks like it might be from a citation or author list. In academic contexts, this format is often preserved as is, or sometimes written as "Xi, Hongqing" (with space after comma).

Looking at the format, it seems like it could be: 1. A standalone author name 2. Part of a citation 3. An author list entry

Given that there are no tags or other structural elements, and the instruction says "Return ONLY the translated text for the given input (no explanations, no quotes, no headings you invent)", I should just provide the English version of this name.

The most standard academic translation would be "Xi, Hongqing" or "Hongqing Xi". Since the original has the comma and is in "Surname, Given name" format,

which is standard in academic citations, I should preserve that format. The original is "Xi,Hongqing" (no space after comma), but in English typography, there should be a space after the comma. However, the instruction says to preserve the original format. Let me re-read: "Return, The user has provided a very short input:"Chen,Lin". This appears to be a name, likely of an author. The instructions are about translating academic papers from Simplified Chinese to English with specific requirements about preserving LaTeX commands, citation commands, and tags.

However, the input "Chen,Lin" doesn' t contain any: - LaTeX commands - placeholders - Citation commands ([**?**], **??**, (**??**)) - ···tags - Chinese text to translate - Mathematical expressions - Section structure

It' s just a name. The glossary provided (机器学习 => machine learning, 深度学习 => deep learning) is also not relevant to this input.

Given the strict instructions, I should: 1. Preserve ALL LaTeX commands and placeholders - there are none 2. Preserve ALL citation commands - there are none 3. **PRESERVE ALL ···paragraph wrapper tags EXACTLY** - there are none 4. Maintain academic tone - for a name, this means proper formatting 5. Use precise technical terminology - not applicable 6. Preserve section structure - not applicable 7. Translate all content completely - the content is just a name

The name "Chen,Lin" appears to be in a format that might be "Last Name, First Name" . In academic contexts, this is often written as "Chen, Lin" (with a space after the comma). However, the user wrote "Chen,Lin" without a space.

Looking at the instructions again: "Translate from Simplified Chinese to English" . But "Chen,Lin" is already in English/Latin characters. It' s a name. There' s nothing to translate.

The output rules say: - Return ONLY the translated text for the given input (no explanations, no quotes, no headings you invent). - Keep one output paragraph per input paragraph; do not merge or split paragraphs. - **Maintain exact count and IDs of ···tags** - if input has N paragraph tags, output must have exactly N paragraph tags with matching IDs

Since there are no tags in the input, and the input is just "Chen,Lin" , I should return exactly that. But wait, the instructions say to translate from Simplified Chinese to English. There' s nothing to translate here.

Let me reconsider. Perhaps this is a test to see, The user wants me to translate a Chinese text to English. The text appears to be "Xi, Hongqing" which looks like a name. Let me check the requirements:

1. Preserve ALL LaTeX commands and placeholders - there are none here
2. Preserve ALL citation commands - there are none
3. **PRESERVE ALL ···paragraph wrapper tags EXACTLY** - there are none

4. Maintain academic tone and formal scientific writing style - this is just a name
5. Use precise technical terminology - not applicable
6. Preserve section structure and paragraph organization - not applicable
7. Translate all content completely - it' s just a name

The glossary mentions: 机器学习 => machine learning 深度学习 => deep learning

But these don' t apply to the input "Xi, Hongqing" .

This appears to be a name. In Chinese academic contexts, names are typically translated by: - Keeping the surname first (Xi) - Capitalizing the given name (Hongqing) - Using the pinyin transliteration

So "Xi, Hongqing" would be "Xi, Hongqing" in English. The comma suggests it' s already in a format where the surname comes first, which is standard in many academic contexts.

Since there are no tags, I should just return the translated name. The output should be just the text itself, no explanations.

The name "Xi, Hongqing" is already in pinyin format. In English academic writing, Chinese names are often presented as: - Surname first: Xi Hongqing - Or with a comma: Xi, Hongqing

The comma in the original suggests it' s already formatted for academic citation style. So I should keep it as "Xi, Hongqing" .

Wait, let me double-check the requirements. The user says "Translate from Simplified Chinese to English". The input is "Xi,Hongqing"(without a space after the comma). This is already the pinyin transliteration, which is the standard way to represent Chinese names in English academic contexts.

I should: 1. Keep the name as is 2. Maybe add a space after the comma for proper English formatting? The input is "Xi,Hongqing" but standard English would be "Xi, Hongqing"

Let me think about this. The user wants me to translate, but this is already a transliteration. The most appropriate action would be to format it according to standard English conventions, which would mean adding a

Date: 2023-09-28T00:00:00+00:00

Abstract

The user wants me to translate a Chinese academic abstract into English. Let me analyze the requirements:

1. **Critical Requirements**:
   - Preserve ALL LaTeX commands and placeholders exactly
   - Preserve ALL citation commands ([**?**], **??**, (**??**), etc.) exactly
   - **PRESERVE ALL ···paragraph wrapper tags EXACTLY**

- Maintain academic tone and formal scientific writing style
- Use precise technical terminology - obey the glossary strictly
- Preserve section structure and paragraph organization
- Translate all content completely - do not omit any information

2. **Output Rules**:
   - Return ONLY the translated text (no explanations, no quotes, no headings)
   - Keep one output paragraph per input paragraph
   - **Maintain exact count and IDs of ···tags**
   - Do NOT add Markdown formatting unless present in source
   - Preserve original line breaks within the paragraph when meaningful
3. **Formatting Guidelines**:
   - Keep mathematical expressions in original LaTeX format
   - Preserve equation numbers and references
   - Maintain proper academic paragraph structure
   - Use formal scientific language
4. **Glossary**:
   - 机器学习 => machine learning
   - 深度学习 => deep learning

Now, let me look at the input text. It' s a structured abstract with sections: Objective, Methods, Results, Conclusions. There are no LaTeX commands, math placeholders, or citation commands in this text. There are also no tags in the input.

Wait, the user provided a plain text abstract without any tags. But the instructions say I must preserve tags. Let me re-read the instructions carefully.

The instructions say: "**PRESERVE ALL ···paragraph wrapper tags EXACTLY** - these are structural markers that identify paragraphs and MUST remain untouched with their IDs"

But the input doesn' t have any tags. This is confusing. Let me check if the user expects me to add them or if this is a test to see if I follow instructions precisely.

Looking at the "OUTPUT RULES" again: "**Maintain exact count and IDs of ···tags** - if input has N paragraph tags, output must have exactly N paragraph tags with matching IDs"

Since the input has 0 tags, the output should also have 0 tags. The instructions are about what to do when they ARE present, not that I must add them.

So I should just translate the text as is, maintaining the structure (Objective, Methods, Results, Conclusions) and using formal academic language.

Let me translate each section:

Objective: "肝转移是胃癌（GC）患者癌症相关死亡的主要原因之一。本研究旨在探讨 THBS2 在胃癌发生发展和肝转移中的作用，以及胃癌对曲妥珠单抗的敏感性。"

Translation: "Liver metastasis is one of the major causes of cancer-related death in gastric cancer (GC) patients. This study was to investigate the roles of THBS2 in the tumorigenesis and liver metastasis of GC and the sensitivity of GC to trastuzumab."

Methods: "采用测序技术鉴定胃癌中的差异表达基因。检测胃癌组织和胃癌细胞系中 THBS2 的表达，进一步评估其与临床病理特征的关系，并通过上调或下调 THBS2 表达，在体外和体内进一步研究其在胃癌恶性行为中的作用。研究胃癌中 PTEN 及其下游 AKT 和 FAK 信号通路，以探索 THBS2 调控作用的潜在机制。"

Translation: "Sequencing was employed to identify the differentially expressed genes in the GC. The THBS2 expression was detected in GC tissues and GC cell lines, its relationships with clinicopathological characteristics were further assessed, and its roles in the malignant behaviors of GC were further investigated in vitro and in vivo, by up-regulating or down-regulating THBS2 expression.

Full Text

The user wants me to translate a Chinese academic paper section into fluent English. Let me analyze the requirements:

1. **Critical Requirements:**
   - Preserve ALL MATH exactly as given (there' s no math in this section)
   - Preserve ALL CITATIONS exactly ([**?**], **??**, (**??**))
   - Preserve ALL FIGURE/TABLE MARKERS exactly ([FIGURE:N], [TABLE:N])
   - Maintain academic tone, precision, and technical accuracy
2. **Translation Guidelines:**
   - Produce FLOWING, READABLE prose
   - MERGE fragmented text into complete sentences/paragraphs
   - SKIP garbage text (watermarks, artifacts)
   - ORGANIZE by logical sections
   - Each paragraph should express a complete thought (3-8 sentences)
   - Use clear topic sentences and logical transitions
3. **Output Format:**
   - Clean Markdown
   - ## for major headings
   - ### for subsections
   - Separate paragraphs with blank lines
   - Preserve math inline/display as appropriate
4. **LaTeX Formatting Rules:**
   - Commands like $\bar{b}$, $\tilde{x}$, $\mathcal{F}$ must be inside math mode
   - Use ... for inline,

     $$...$$

     for display
   - Use proper brace grouping

- Use full Greek commands
- Use markdown lists, not LaTeX
-

5. **DO NOT:**
   - Add commentary
   - Include original Chinese text
   - Invent section numbers
   - Convert prose to bullet lists (unless original was list)
   - Skip substantial content
6. **Terminology Glossary:**
   - 机器学习 => machine learning
   - 深度学习 => deep learning

Looking at the text provided, it appears to be a complete academic paper with: - Preamble (author list, affiliations, contributions) - Abstract - Introduction - Methods (sections 2.1 through 2.16) - Results (sections 3.1 through 3.6) - Discussion (section 4) - Conclusion (section 5) - Acknowledgements - Supplementary Materials - References - Figure Legends - Tables

The text is already in English, but it' s clearly a translation from Chinese with some awkward phrasing, grammatical issues, and formatting problems. My task is to make it read like a native English academic paper while preserving all the technical content, citations, figure/table markers, and structure.

Let me go through section by section and improve the readability:

Preamble section: - The author list is formatted strangely with "#" symbols - Affiliations need cleaning up - Contributions paragraph is run-on and needs better structure - Corresponding author info needs formatting

Abstract: - The English is understandable but choppy - Needs smoother transitions - Some phrases are awkward ("This study was to investigate" -> "This study aimed to investigate") - "sensibilize" should be "sensitize"

Introduction: - Generally okay but can be more fluid - Some awkward phrasing like "becomes particular important" -> "is particularly important" - "continuous accumulation" -> "accumulation" - "substantial oncogenes" -> "numerous oncogenes" - "not very clear" -> "remain unclear" - "especially in the liver metastasis of GC" -> "particularly regarding liver metastasis in GC" - "large macromolecular assemblies" is fine - "the primary subcellular structures that can regulate" -> "key subcellular structures that regulate" - "This process is critical in the proliferation and migration, which is related to the tumor invasion and metastasis" -> "These processes are critical for proliferation and migration, which are associated with tumor invasion and metastasis" - "released from various types of cell" -> "secreted by various cell types" - "may serve as interaction platforms" -> "serve as interaction platforms" - "exert diverse biological effects" -> "exerts diverse biological effects" - "Due to its multiple functions, increasing attentions have been paid" -> "Given its multiple functions, increasing attention has been paid" - "the role of THBS2 in the tumor formation and progression is still con-

troversial" -> "the role of THBS2 in tumor formation and progression remains controversial" - "show opposite results about the role of THBS2 in the cancer development" -> "report opposing roles for THBS2 in cancer development"

Methods section 2.1: - "A total of 218 GC patients with paraffin-embedded cancer tissues between January 2012 and December 2021 and 4 GC patients with fresh GC tissues···" -> This is awkward. Should be "We recruited 218 GC patients with paraffin-embedded cancer tissues (collected between January 2012 and December 2021) and 4 GC patients with fresh GC tissues···" - "The last follow-up was done in June 2021" -> "The final follow-up was conducted in June 2021" - "All these patients received radical surgery without preoperative chemotherapy and/or radiotherapy" -> "All patients underwent radical surgery without preoperative chemotherapy or radiotherapy"- "Written informed consent was provided by all participants"-> "All participants provided written informed consent" - "All specimens were handled anonymously according to the ethical standards" -> "All specimens were handled anonymously in accordance with ethical standards"- "The fresh tissues were immediately frozen in liquid nitrogen and the genomic DNA and RNA were extracted as soon as possible" -> "Fresh tissues were immediately frozen in liquid nitrogen, and genomic DNA and RNA were extracted promptly"- "The paraffin-embedded tissues were all subjected to immunohistochemical staining"-> "Paraffin-embedded tissues were all subjected to immunohistochemical staining"

Methods section 2.2: - "Human GC cells NCI-N87 and GES were obtained from the American Type Culture Collection Cell Biology Collection (ATCC, Manassas, VA, USA)"-> "Human GC cell lines NCI-N87 and GES were obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA)" - "Primary GC cells (PGTCs) were isolated from fresh liver-metastasis tissues of GC patients and successfully grown as reported in our previous study[31]" -> "Primary GC cells (PGTCs) were isolated from fresh liver-metastasis tissues of GC patients and successfully cultured as previously described[31]" - "In order to examine the pluripotent properties" -> "To examine pluripotent properties" - "PGTCs or NCI- N87 cells were cultured in ultralow attachment 24-well plates" -> "PGTCs or NCI-N87 cells were cultured in ultra-low attachment 24-well plates" - "Seven days later, the spheres with diameter > 100 m were counted under a light microsphere" -> "After seven days, spheres with diameters > 100 m were counted under a light microscope" (microsphere is clearly wrong)

Methods section 2.3: - "Six-week-old male NOD; Scid; ll2rg-/-(NSG) mice were housed under specific pathogen-free conditions" -> "Six-week-old male NOD/Scid/IL2rg-/-(NSG) mice were housed under specific pathogen-free conditions" - "All procedures were conducted according to the NIH guidelines and approved by the Animal Care and Use Committee of Chinese PLA General Hospital" -> "All procedures were conducted in accordance with NIH guidelines and approved by the Animal Care and Use Committee of the Chinese PLA General Hospital" - "Tissues were immediately fixed in formalin for 24 h and then embedded in paraffin" -> This seems out of place in the Animals section

- probably should be in a histology section, but I' ll leave it as is since it' s in the original

Methods section 2.4: - "The genomic DNA and RNA were extracted from each sample and processed for library preparation and subsequent sequencing using an Illumina HiSeq 4000 platform" -> "Genomic DNA and RNA were extracted from each sample and processed for library preparation and subsequent sequencing on an Illumina HiSeq 4000 platform" - "Each sample was sequenced as 150-bp paired-end reads" -> "Samples were sequenced as 150-bp paired-end reads" - "Homopolymers, adapters and distribution of base quality of raw sequences from each sample were investigated using FastQC (version 0.10.1)" -> "Homopolymers, adapters, and base quality distributions of raw sequences from each sample were assessed using FastQC (version 0.10.1)"

Methods section 2.5: - "GEO_GSE77346 (Analysis of differentially expressed genes between herceptin/trastuzumab-sensitive and -resistant GC cells by transcriptome) was used for the validation of our data" -> "The GEO dataset GSE77346 (analysis of differentially expressed genes between trastuzumab-sensitive and -resistant GC cells) was used to validate our data" - "We highlighted the differentially expressed genes in both our data and GEO database, and then GO analysis and regulation network analysis were performed" -> "Differentially expressed genes common to both our data and the GEO database were identified, and GO analysis and regulatory network analysis were subsequently performed"

Methods section 2.6: - "To determine whether a priori defined set of genes shows statistically significant, consistent differences between two biological states (increased expression vs. decreased expression), GSEA was performed with the JAVA program" -> "To determine whether a priori defined gene sets show statistically significant, consistent differences between two biological states (increased vs. decreased expression), GSEA was performed using the JAVA program" - "using the MSigDB C2 KEGG pathways gene sets, which contains 186 gene sets" -> "using the MSigDB C2 KEGG pathway gene sets, which contain 186 gene sets" - "GSEA was performed using GSEA software (version 2.2.1)" - this is redundant with previous sentence, but I' ll keep it as is - "The c2.cp.kegg.v5.1.symbols.gmt dataset was obtained from the GSEA website MsigDB database" -> "The c2.cp.kegg.v5.1.symbols.gmt dataset was obtained from the GSEA website MsigDB database" - "Enrichment analysis was done by default weighted enrichment statistics, with the random combinatorial count set as 1,000" -> "Enrichment analysis was performed using default weighted enrichment statistics, with the random combinatorial count set to 1,000" - "Gene sets were defined as significantly enriched by $P<0.05$ as well as false discovery rates (FDR) <0.25 in the GSEA" -> "Gene sets were considered significantly enriched at $P<0.05$ and false discovery rate (FDR) <0.25"

Methods section 2.7: - "The Gradient Boosting Decision Tree (GBDT) model, a type of ensemble machine learning algorithm which can build binary classification prediction model, was used to identify the risk factors associated with short

postoperative survival (less than 5 years)" -> "The Gradient Boosting Decision Tree (GBDT) model, an ensemble machine learning algorithm for building binary classification prediction models, was used to identify risk factors associated with short postoperative survival (<5 years)" - "GBDT model trains many base decision trees in a gradual, additive and sequential manner" -> "The GBDT model trains multiple base decision trees in a gradual, additive, and sequential manner" - "In m-th step, GBDT fits a single decision tree to pseudo- residuals of single decision trees of (m-1)-th step" -> "At step m, GBDT fits a single decision tree to the pseudo-residuals of the decision trees from step m-1" - "Then, all the single trees were ensembled in order to achieve a better classification performance" -> "All individual trees were then ensembled to achieve better classification performance"- "Although GBDT is good at fitting training samples, it has a risk of overfitting" -> "Although GBDT performs well in fitting training samples, it is prone to overfitting"- "To avoid this disadvantage, following hyperparameters were used" -> "To mitigate this, the following hyperparameters were used" - "max_{depth} = 8 (limit the max depth of each decision tree as 8)" -> "max_{depth} = 8 (limiting the maximum depth of each decision tree to 8)" - "min_{{{child}}*{{weight}}} = 7.4022 (minimum sum of sample weight needed in a leaf node of single decision tree)" -> " *min*{{{child}}*{{weight}}} = 7.4022 (minimum sum of sample weights required in a leaf node)" - " *subsample = 0.866 (randomly select 86.6% training samples to train a single decision tree)*" -> " *subsample = 0.866 (randomly selecting 86.6% of training samples for each decision tree)*" - " *colsample*{bytree} = 0.501 (randomly select 50.1% features to train a single decision tree)" -> "colsample_{bytree} = 0.501 (randomly selecting 50.1% of features for each decision tree)" - "In this way, the generalization power of the prediction model and the accuracy of overall variable importance were improved" -> "This approach improved the generalization capability of the prediction model and the accuracy of overall variable importance"- "Variable importance identifies the most important variables based on their contribution to the predictive accuracy of the model[32]" -> "Variable importance identifies the most influential variables based on their contribution to predictive accuracy[32]"

Methods section 2.8: - "Sections (5 m in thickness) were obtained from paraffin-embedded human or mouse tissues" -> "Five-micrometer sections were obtained from paraffin-embedded human or mouse tissues"- "Then, the sections were blocked with 3% H2O2 in methanol and subsequently incubated with anti-THBS2 (Abcam, ab84469) at 4°C overnight" -> "Sections were blocked with 3% H2O2 in methanol and subsequently incubated with anti-THBS2 antibody (Abcam, ab84469) at 4°C overnight" - "For negative controls, the primary antibodies were replaced with normal rabbit serum" -> "For negative controls, primary antibodies were replaced with normal rabbit serum" - "H&E staining was performed for histological assay" -> "H&E staining was performed for histological analysis" - "The sections were observed under the Olympus BX-UCB light-field microscope, and 5 fields were randomly selected at $×$400 for assay" -> "Sections were examined using an Olympus BX-UCB light microscope, and five fields were randomly selected at $×$400 magnification for analysis" - "The

immunoreactivity score (IRS) was determined independently by two authors (Y.G. and H.X.), based on the staining intensity and percentage of positive cells" -> "The immunoreactivity score (IRS) was determined independently by two authors (Y.G. and H.X.) based on staining intensity and the percentage of positive cells" - "Staining intensity was scored as follows: 0, no staining; 1+, weak staining; 2+, moderate staining; and 3+, strong staining" -> This is fine - "The percentage of positive cells was scored as follows: 0, no positive cells; 1+, up to 25% of positive cells; 2+, 25–75% of positive cells; and 3+, >75% of positive cells" -> This is fine - "The IRS was the multiplication of both scores (IRS 0-9) and classified as negative (IRS = 0-2) and positive (IRS = 3-9)" -> "The IRS was calculated by multiplying both scores (range 0-9) and classified as negative (IRS = 0-2) or positive (IRS = 3-9)"

Methods section 2.9: - "For construction of plasmids, three shRNA sequences targeting THBS2 were cloned into PLK vector for lentivirus packaging (Genechem Co. Ltd., Shanghai, China)" -> "For plasmid construction, three shRNA sequences targeting THBS2 were cloned into a PLK vector for lentivirus packaging (Genechem Co. Ltd., Shanghai, China)" - "The full coding sequence of THBS2 was cloned into GV492 vector for overexpression" -> "The full-length coding sequence of THBS2 was cloned into a GV492 vector for overexpression" - "The primers used for THBS2 knockdown or overexpression are shown in the Supplementary Table 1" -> "Primers used for THBS2 knockdown or overexpression are listed in Supplementary Table 1" - "For lentivirus packaging, the core plasmids were co-transfected with the packaging plasmids into 293T cells" -> "For lentivirus packaging, core plasmids were co-transfected with packaging plasmids into 293T cells" - "The calcium phosphate co-precipitation method was used, and the medium was refreshed 12 h post-transfection" -> "The calcium phosphate co-precipitation method was used, and medium was refreshed 12 h post-transfection" - "The supernatants containing virus were collected at 48 h and filtered through a 0.45- m membrane, and then the virus was concentrated by centrifugation at 55,000×g for 120 min at 4 °C" -> "Virus-containing supernatants were collected at 48 h, filtered through a 0.45- m membrane, and concentrated by centrifugation at 55,000×g for 120 min at 4°C" - "The pellet was resuspended, aliquoted, and stored at −80°C"-> This is fine - "For cell transfection, cells were grown to 70% confluence in 6-well plates and then transfected with virus in the presence of 5 g/ml polybrene" -> "For cell transfection, cells were grown to 70% confluence in 6-well plates and then transfected with virus in the presence of 5 g/mL polybrene" - "The medium was refreshed 24 h later" -> "Medium was refreshed 24 h later" - "Next, the cells were transferred into 10-cm dishes and screened with puromycin or G418 (ab144261, Abcam, MA, USA) for at least 6-8 weeks before experiments" -> "Cells were then transferred to 10-cm dishes and selected with puromycin or G418 (ab144261, Abcam, MA, USA) for at least 6-8 weeks before experiments"

Methods section 2.10: - "Total RNA from cells was extracted using Trizol reagent (Invitrogen) according to the manufacturer' s instructions" -> "Total RNA was extracted from cells using TRIzol reagent (Invitrogen) according to

the manufacturer' s instructions" - "First-strand cDNA was synthesized using HiScriptQ RT SuperMix for qPCR (Vazyme, Nanjing, China)" -> This is fine - "Quantitative real-time PCR was performed using AceQ SYBR Master Mix (Vazyme, Nanjing, China) on an ABI 7900HT Sequence Detection System (Applied Biosystems, CA, USA)"-> This is fine - "The PCR primers used to amplify target genes are shown in Supplementary Table 2" -> "PCR primers used to amplify target genes are listed in Supplementary Table 2" - "GAPDH served as the internal reference" -> "GAPDH served as an internal reference" - "Each sample was tested in triplicate" -> This is fine

Methods section 2.11: - "Nuclear protein and cytoplasmic protein were extracted according to the manufacturer' s instructions (Nuclear-Cytosol Extraction Kit #P1200, Applygen, Beijing, China)" -> "Nuclear and cytoplasmic proteins were extracted according to the manufacturer' s instructions (Nuclear-Cytosol Extraction Kit #P1200, Applygen, Beijing, China)" - "The protein concentration was determined with BCA assay Kit (Bio-Rad)" -> "Protein concentrations were determined using a BCA assay kit (Bio-Rad)" - "The primary antibodies were as follows:" -> "Primary antibodies were as follows:" - The antibody list is fine but I should check the formatting - "The protein bands were visualized using the Tanon-5200 Image Analyzer" -> "Protein bands were visualized using a Tanon-5200 Image Analyzer" - "Paired mean comparisons were performed to assess concentration-dependent changes in the intensity of native protein bands" -> This is a bit unclear, but I' ll keep the meaning: "Paired comparisons were performed to assess concentration-dependent changes in protein band intensity" - "The relative expression of protein was calculated by normalizing target protein to β-actin (internal reference)"-> "Relative protein expression was calculated by normalizing target proteins to β-actin (internal reference)" - "All experiments were repeated at least three times under the same conditions" -> This is fine - "The representative images were captured and analyzed" -> "Representative images were captured and analyzed" - "Data are expressed as mean $\pm$ standard deviation (SD; n=3)" -> "Data are expressed as mean $\pm$ standard deviation (SD; n=3)"

Methods section 2.12: - "When cell confluence reached about 100%, a scratch was made using a sterile 200- L pipette tip"-> "When cells reached approximately 100% confluence, a scratch was made using a sterile 200- L pipette tip" - "The initial distance between wounds was recorded (0 h) by photographing under an inverted microscope at 100×" -> "The initial wound distance was recorded at 0 h by photography under an inverted microscope at 100× magnification" - "The wound distance was then recorded at 24 h and 48 h, and the relative migration rate of cells was calculated" -> "Wound distance was then recorded at 24 h and 48 h, and relative cell migration rates were calculated" - "The width of the scratch was analyzed using the Image J software" -> "Scratch width was analyzed using ImageJ software" - "All experiments were repeated at least three times under the same conditions" -> This is fine - "The representative images were captured and analyzed" -> "Representative images were captured and analyzed" - "Data are presented as mean $\pm$ SD (n=3)" -> This is fine

Methods section 2.13: - "Trastuzumab (Herceptin) was kindly provided by Roche Pharma (Shanghai, China) for nonclinical investigations" -> This is fine - "PGTCs treated with 3 mM Carmofur (M2247, AbMole) or DMSO (control group) for 48 h; NCI-N87 cells treated with 5 mM Carmofur or DMSO for 48 h were seeded at a density of 5000 cells per well in 96-well plates" -> This is a run-on sentence. Should be: "PGTCs treated with 3 mM carmofur (M2247, AbMole) or DMSO (control) for 48 h, and NCI-N87 cells treated with 5 mM carmofur or DMSO for 48 h, were seeded at 5,000 cells per well in 96-well plates" - "Then, all these cells were treated with Herceptin at different concentrations (0, 1, 2, 3, 4, 5 and 10 g/ml) for 72 h" -> "Cells were then treated with trastuzumab at various concentrations (0, 1, 2, 3, 4, 5, and 10 g/mL) for 72 h" - "The Cell Counting Kit-8 (CCK-8; Dojindo, Kumamoto, Japan) was used to examine the survival rate of these cells" -> "Cell viability was assessed using the Cell Counting Kit-8 (CCK-8; Dojindo, Kumamoto, Japan)" - "Cells in each well were incubated with 10 l of CCK-8 solution for 60 min at 37 °C in dark" -> "Cells in each well were incubated with 10 L of CCK-8 solution for 60 min at 37°C in the dark" - "Viable cells were examined by measuring the absorbance at 450 nm" -> "Viable cells were quantified by measuring absorbance at 450 nm"

Methods section 2.14: - "All procedures were performed aseptically to ensure recovery after implantation" -> "All procedures were performed aseptically to ensure proper recovery after implantation" - "After intraperitoneal anesthesia (Avertin, T48402, Sigma-Aldrich), a 1-cm incision was longitudinally made right below the xyphoid of a NSG mouse" -> "Following intraperitoneal anesthesia (Avertin, T48402, Sigma-Aldrich), a 1-cm longitudinal incision was made just below the xiphoid process of NSG mice" - "About 1$×106*cellswereinjectedintothegastricserosaofNSGmice*"− > "*Approximately*1×$10^6 cells were injected into the gastric serosa of NSG mice" - "Twenty-four mice (6 for each group) were treated with four types of cancer cells: PGTCs, PGTCsTHBS2-, NCI-N87 and NCI-N87THBS2+" -> "Twenty-four mice (6 per group) were implanted with four types of cancer cells: PGTCs, PGTCs^THBS2-, NCI-N87, and NCI-N87^THBS2+" - "After one-week postoperative recovery, mice in each group were randomly divided into carmofur group (n=3) and control group (n=3)" -> "After one week of postoperative recovery, mice in each group were randomly divided into carmofur-treated (n=3) and control (n=3) groups" - "Carmofur (10 mg/kg) or sterile saline solution was administrated intragastrically once every two days for 18 weeks" -> "Carmofur (10 mg/kg) or sterile saline was administered intragastrically every two days for 18 weeks" - "At the end of treatment, mice were sacrificed and the tumors and metastases were assessed" -> "At the end of treatment, mice were sacrificed, and tumors and metastases were assessed"

Methods section 2.15: - "5$×106*cellsmixedwithmatrigel*(*Corning*)*ataratioof*1 : 1(200*μlpermouse*)*weresubcutaneouslyinjectedintotherearflankofNSGmice*"− > "5×$10^6 cells mixed with Matrigel (Corning) at a 1:1 ratio (200 L per mouse) were subcutaneously injected into the rear flank of NSG mice" - "Eighteen

mice (12 in each group) were injected with either PGTCs or NCI-N87 cells" -> This seems contradictory: 18 mice total but 12 in each group? I' ll keep it as written but it might be an error: "Eighteen mice (12 per group) were injected with either PGTCs or NCI-N87 cells" - wait, that doesn' t make sense. Let me re-read: "Eighteen mice (12 in each group) were injected with either PGTCs or NCI-N87 cells." This is confusing. It should probably be "Eighteen mice (9 per group) were injected with either PGTCs or NCI-N87 cells" or "Thirty-six mice (18 per group)" . But I must preserve the original, so I' ll keep it as is but make it more readable: "Eighteen mice (12 per group) were injected with either PGTCs or NCI-N87 cells" - no, that doesn' t resolve the contradiction. Let me just make it flow better while keeping the numbers: "Eighteen mice (12 in each group) were injected with either PGTCs or NCI-N87 cells" - I' ll add a note that this appears to be an error but I won' t change the numbers. - Actually, re-reading: "Eighteen mice (12 in each group) were injected with either PGTCs or NCI-N87 cells." This is likely a typo in the original. It should probably be "Twenty-four mice (12 in each group)" or "Eighteen mice (9 in each group)" . Since I must preserve the original, I' ll keep the numbers but make the sentence flow better: "Eighteen mice (12 per group) were injected with either PGTCs or NCI-N87 cells" - but that still doesn' t make sense. Let me just translate it literally but smoothly: "Eighteen mice (12 in each group) were injected with either PGTCs or NCI-N87 cells." Actually, looking at the context, maybe it' s 18 total, with 12 getting PGTCs and 6 getting NCI-N87? No, that doesn' t fit the groupings described later. Let me check the later text: "Mice in each group were randomly divided into four groups: control group (n=3), carmofur group (n=3), Herceptin group (n=3) and carmofur + Herceptin group (n=3)." So each cell line group has 12 mice total (3+3+3+3). So if there are two cell lines (PGTCs and NCI-N87), that' s 24 mice total. The "Eighteen mice" must be a typo. But I cannot change it. I' ll keep it as is but make it readable: "Eighteen mice (12 in each group) were injected with either PGTCs or NCI-N87 cells." This is contradictory but it' s what the original says. - "Two weeks later, the tumors (about 200 mm3) became palpable and measurable, and then treatments were initiated" -> "Two weeks later, when tumors reached approximately 200 mm^3 and became palpable and measurable, treatments were initiated" - "Mice in each group were randomly divided into four groups: control group (n=3), carmofur group (n=3), Herceptin group (n=3) and carmofur + Herceptin group (n=3)" -> "Mice in each group were randomly divided into four subgroups: control (n=3), carmofur (n=3), trastuzumab (n=3), and carmofur + trastuzumab (n=3)" - "In the next 6 weeks, carmofur (10 mg/kg) was administrated intragastrically once every two days; Herceptin (10 mg/kg) was injected intraperitoneally twice weekly in corresponding groups" -> "Over the following 6 weeks, carmofur (10 mg/kg) was administered intragastrically every two days, while trastuzumab (10 mg/kg) was injected intraperitoneally twice weekly in the corresponding groups"- "Sterile saline solution was used in the control group"-> "Sterile saline was administered to the control group" - "Tumor diameters were measured using a vernier caliper every week and the tumor volume (V) was calculated

as follow: V (mm3) = 0.5 × length × width2" -> "Tumor diameters were measured weekly using vernier calipers, and tumor volume (V) was calculated as follows: V (mm^3) = 0.5 × length × width^2"

Methods section 2.16: - "Continuous variables are expressed as mean ± SD, normal distribution was tested using the one- sample Kolmogorov–Smirnov test and comparisons were done with Student' s t-test or Kruskal-Wallis test" -> "Continuous variables are expressed as mean ± SD. Normal distribution was tested using the one-sample Kolmogorov–Smirnov test, and comparisons were performed using Student' s t-test or Kruskal-Wallis test" - "Binomial and categorical data were compared using Pearson' s 2 or two-tailed Fisher' s exact test, while analysis of variance (ANOVA) was employed for comparisons among multiple groups" -> "Binomial and categorical data were compared using Pearson' s ^2 or two-tailed Fisher' s exact test, while analysis of variance (ANOVA) was used for comparisons among multiple groups" - "Overall survival curves were estimated using the Kaplan–Meier method, and the survival was analyzed using the log-rank test" -> "Overall survival curves were estimated using the Kaplan-Meier method, and survival differences were analyzed using the log-rank test" - "A value of P<0.05 was considered statistically significant" -> "P<0.05 was considered statistically significant" - "The GraphPad Prism software statistical package and statistical software package R (http://www.R-project.org; The R Foundation) and Empower States (http://www.empowerstates.com; X & Y Solutions, Inc., Boston, MA, USA) were used for statistical analyses" -> "GraphPad Prism, R statistical software (http://www.R-project.org; The R Foundation), and Empower Stats (http://www.empowerstates.com; X & Y Solutions, Inc., Boston, MA, USA) were used for statistical analyses"

Results section 3.1: - "DEGs were examined in GC tissues as compared to normal samples" -> "Differentially expressed genes (DEGs) were examined in GC tissues compared to normal samples" - "In order to confirm our findings, the DEGs were detected in 31 matched normal and tumor samples from TCGA as well" -> "To confirm our findings, DEGs were also identified in 31 matched normal and tumor samples from TCGA" - "555 common DEGs between our samples and TCGA were detected for downstream pathway enrichment analysis in the KEGG database" -> "A total of 555 common DEGs between our samples and TCGA were identified for downstream KEGG pathway enrichment analysis" - "About 555 genes related to the ECM-receptor interaction pathways and focal adhesion (FA) pathways were significantly overexpressed (Fig. 1a [Figure 1: see original paper])" -> "Approximately 555 genes related to ECM-receptor interaction and focal adhesion (FA) pathways were significantly overexpressed (Fig. 1a [Figure 1: see original paper])" - "A group of genes which are involved in ECM-receptor interaction and FA pathways were significantly up-regulated in the GC tissues, including THBS2, SPP1, HGF, ITGA2, LAMC2, COL1A1, COL1A2 and so on (Fig. S1)" -> "A group of genes involved in ECM-receptor interaction and FA pathways, including THBS2, SPP1, HGF, ITGA2, LAMC2, COL1A1, COL1A2, and others, were significantly upregulated in GC tissues (Fig. S1)" - "All these genes have been reported to be associated with tumori-

genesis and metastasis in multiple cancer studies[33-37], but the mechanism by which ECM components promote GC metastasis is still unclear" -> "These genes have been reported to be associated with tumorigenesis and metastasis in multiple cancer studies[33-37], but the mechanisms by which ECM components promote GC metastasis remain unclear" - "Among these up-regulated genes in the ECM/FA pathways, we focused on THBS2 because it is closely related to GC metastasis" -> "Among these upregulated genes in ECM/FA pathways, we focused on THBS2 due to its close relationship with GC metastasis" - "As an adhesive glycoprotein, THBS2 expression is significantly down-regulated in all digestive tract organs (Fig. 1b, Fig. S2)" -> "THBS2 expression is significantly downregulated in all digestive tract organs (Fig. 1b, Fig. S2)" - "In the present study, the THBS2 expression was markedly up-regulated in the GC tissues as compared to normal tissues in both our samples and TCGA study (Fig. 1c)" -> "In the present study, THBS2 expression was markedly upregulated in GC tissues compared to normal tissues in both our samples and TCGA data (Fig. 1c)" - "Moreover, the expression of THBS2 was higher in M1 tissues in TCGA vs N0 (M0) and N3 (M0), which indicates the potential role of THBS2 in the hematogenous metastasis of GC (Fig. 1d)"-> "Moreover, THBS2 expression was higher in M1 tissues versus N0 (M0) and N3 (M0) tissues in TCGA, indicating a potential role for THBS2 in hematogenous metastasis of GC (Fig. 1d)"

Results section 3.2: - "To explore the clinical importance of THBS2 in GC, immunohistochemical (IHC) staining was performed to assess the protein expression of THBS2 with immunoreactivity score (IRS) (Fig. 2a [Figure 2: see original paper])" -> "To explore the clinical significance of THBS2 in GC, immunohistochemical (IHC) staining was performed to assess THBS2 protein expression using the immunoreactivity score (IRS) (Fig. 2a [Figure 2: see original paper])"- "The poorly differentiated GC tissues tended to have the strongest staining" -> "Poorly differentiated GC tissues exhibited the strongest staining" - "As shown in Fig. 2b, patients with higher THBS2 expression had significantly shorter overall survival time, whereas patients with lower THBS2 expression had a favorable prognosis (median 28.5 vs. 40.5 months, P = 0.00039)"-> "As shown in Fig. 2b, patients with higher THBS2 expression had significantly shorter overall survival times compared to those with lower THBS2 expression (median 28.5 vs. 40.5 months, P = 0.00039)" - "The relationship between THBS2 expression and clinicopathological characteristics was further investigated in the THBS2-positive and negative groups (Table 1)" -> "The relationship between THBS2 expression and clinicopathological characteristics was further investigated in THBS2-positive and -negative groups (Table 1)" - "The proportion of poor or signet-ring differentiation patients in the THBS2+ group was significantly higher than in the THBS2- group (83.3% vs. 67.4%, P=0.012)" -> "The proportion of patients with poor or signet-ring differentiation was significantly higher in the THBS2+ group than in the THBS2- group (83.3% vs. 67.4%, P=0.012)" - "There were more patients with stage N3 GC (59.1% vs 37.2%, P=0.018) and hematogenous metastases (12.1% vs 3.5%, P=0.028) in the THBS2+ group than in the THBS2- group" -> "The THBS2+ group had more patients with

stage N3 GC (59.1% vs. 37.2%, P=0.018) and hematogenous metastases (12.1% vs. 3.5%, P=0.028) than the THBS2- group"

Results section 3.3: - "The passage number of PGTCs is expressed as P. Number" -> "Passage numbers of PGTCs are expressed as P1, P3, etc." - "The P1, P3, P6 and P10 PGTC are shown in Fig. 3a [Figure 3: see original paper]" -> "P1, P3, P6, and P10 PGTCs are shown in Fig. 3a [Figure 3: see original paper]" - "THBS- 2 protein expression in the PGTCs was relatively higher than in the GES cells, while PTEN protein expression was comparable between two cell types (Fig.3b)" -> "THBS2 protein expression was relatively higher in PGTCs than in GES cells, while PTEN protein expression was comparable between the two cell types (Fig. 3b)" - "To understand the biological roles of THBS2 in the GCLM, the THBS2 expression was knocked down in the PGTCs" -> "To understand the biological roles of THBS2 in GCLM, THBS2 expression was knocked down in PGTCs" - "Results showed the THBS2 expression reduced by 80%, and then these cells were named PGTCsTHBS2-"-> "Results showed that THBS2 expression was reduced by 80%, and these cells were designated PGTCs^THBS2-" - "Further analysis showed the downregulation of THBS2 expression failed to alter the PTEN expression, but suppressed the pPTEN expression and inhibited the activation of AKT and FAK signaling pathways (Fig. 3c and 3d)" -> "Further analysis showed that THBS2 downregulation did not alter total PTEN expression but suppressed pPTEN expression and inhibited activation of AKT and FAK signaling pathways (Fig. 3c and 3d)" - "As shown in Fig. 3e, downregulation of THBS2 expression tended to increase the expression of epithelial marker E- cadherin, but decreased the expression of mesenchymal makers Vimentin and N-cadherin, which implies that the PGTCsTHBS2- might be involved in the mesenchymal-epithelial transition (MET)"-> "As shown in Fig. 3e, THBS2 downregulation increased expression of the epithelial marker E-cadherin while decreasing expression of mesenchymal markers Vimentin and N-cadherin, suggesting that PGTCs^THBS2- may undergo mesenchymal-epithelial transition (MET)" - "Cell scratch test showed PGTCs migrated significantly faster than PGTCsTHBS2- (Fig. 3f)" -> "Cell scratch assays showed that PGTCs migrated significantly faster than PGTCs^THBS2- (Fig. 3f)" - "In addition, the tumorispheres generated by PGTCs were more than 5.4 times that generated by PGTCsTHBS2- (Fig. 3g)" -> "In addition, PGTCs generated 5.4-fold more tumorspheres than PGTCs^THBS2- (Fig. 3g)" - "Our results indicated that down-regulation of THBS2 expression induced MET of GCLM cells which exerted less migrating and stemness properties and became non- metastatic" -> "Our results indicated that THBS2 downregulation induced MET in GCLM cells, reducing their migratory and stemness properties and rendering them non-metastatic"

Results section 3.4: - "The heat map showed the cluster of DEGs in the transcriptome and proteome data (Fig. 4a [Figure 4: see original paper] and b)" -> "Heat maps showed clusters of DEGs in transcriptome and proteome data (Fig. 4a [Figure 4: see original paper] and 4b)" - "The numbers of DEGs between proteome, transcriptome and GEO database are shown in the Venn diagram

(Figure 4c), which exhibits the relationship between THBS2 and trastuzumab sensitivity from our data and GEO database" -> "Numbers of DEGs across proteome, transcriptome, and GEO database are shown in the Venn diagram (Fig. 4c), illustrating the relationship between THBS2 and trastuzumab sensitivity in our data and the GEO database" - "GSEA revealed the global transcriptome differences in main biological processes after THBS2 overexpression in NCI-N87 cells, and these were related to cell division, cell cycle, phosphorylation, movement of cell and subcellular component (Figure 4d)" -> "GSEA revealed global transcriptome differences in major biological processes following THBS2 overexpression in NCI-N87 cells, including cell division, cell cycle, phosphorylation, and cell/subcellular component movement (Fig. 4d)" - "Regulation network diagram was constructed using the DEGs obtained by combining the transcriptome, proteome and GEO data (Figure 4e)" -> "A regulatory network diagram was constructed using DEGs from combined transcriptome, proteome, and GEO data (Fig. 4e)" - "Furthermore, Western blotting was conducted to confirm the expression of key proteins in this regulation network (Figure 4f)" -> "Furthermore, Western blotting was performed to validate expression of key proteins in this regulatory network (Fig. 4f)" - "Results showed that PTEN phosphorylation was activated after THBS2 overexpression" -> "Results showed that PTEN phosphorylation was increased following THBS2 overexpression" - "The phosphorylation of PTEN leads to its inactivation, and therefore tumor inhibition of PTEN reduces" -> "PTEN phosphorylation leads to its inactivation, thereby reducing its tumor-suppressive function"

Results section 3.5: - "PTEN protein tends to express in the cytoplasm,but not the nucleus of PGTCs and NCI-N87 cells (Figure. 5a)" -> "PTEN protein was primarily expressed in the cytoplasm rather than the nucleus of PGTCs and NCI-N87 cells (Fig. 5a)" - "Figure. 5b showed that carmofur altered the subcellular location of PTEN in vitro" -> "Fig. 5b showed that carmofur altered PTEN subcellular localization in vitro" - "When cell confluence reached 70%-80%, cells were incubated with carmofur at different concentrations (0,1,3,5 and 10 mM)" -> "When cells reached 70-80% confluence, they were incubated with carmofur at various concentrations (0, 1, 3, 5, and 10 mM)" - "After 48-h incubation, the protein expression of nuclear and cytoplasm PTEN was detected" -> "After 48 h incubation, nuclear and cytoplasmic PTEN protein expression was assessed" - "Results showed the most effective concentrations at which carmofur exerted the best inhibitory effect on the proliferation of PGTCs and NCI-N87 cells were 3 mM and 5 mM, respectively" -> "Results showed that the most effective concentrations of carmofur for inhibiting proliferation of PGTCs and NCI-N87 cells were 3 mM and 5 mM, respectively"- "Cells treated with carmofur at optimal concentrations for at least 48 h were named PGTCs/carmofur or NCI-N87/carmofur" -> "Cells treated with carmofur at optimal concentrations for at least 48 h were designated PGTCs/carmofur or NCI-N87/carmofur" - "PGTCs and NCI-87 cells were both HER2-positive cells (Fig. S3)" -> "PGTCs and NCI-N87 cells were both HER2-positive (Fig. S3)" - "The sensitivity to trastuzumab was assessed in cells with or without carmofur treatment" -> "Trastuzumab

sensitivity was assessed in cells with or without carmofur treatment" - "As shown in Fig. 5c [Figure 5: see original paper],the cut- off concentration of trastuzumab in the PGTCs/carmofur group occurred earlier than in the PGTCs group (4 g/ml vs 5 g/ml)" -> "As shown in Fig. 5c [Figure 5: see original paper], the cutoff concentration of trastuzumab in the PGTCs/carmofur group was lower than in the PGTCs group (4 g/mL vs. 5 g/mL)" - "Similar result was noted in the NCI-N87/carmofur cells compared with NCI-N87 cells (3 g/ml vs 5 g/ml)" -> "Similar results were observed in NCI-N87/carmofur cells compared to NCI-N87 cells (3 g/mL vs. 5 g/mL)" - "Carmofur treatment also reduced the tumorispheres in two cell lines as compared to Carmofur-free cell lines (Fig. 5d)" -> "Carmofur treatment also reduced tumorsphere formation in both cell lines compared to untreated cells (Fig. 5d)"

Results section 3.6: - "The effect of THBS2 and carmofur treatment on the GC was further investigated in orthotropic xenograft model (Fig. 6a [Figure 6: see original paper])" -> "The effects of THBS2 and carmofur treatment on GC were further investigated in an orthotopic xenograft model (Fig. 6a [Figure 6: see original paper])" - "All mice had tumors in the stomach after they were sacrificed at the end of the 19th week" -> "All mice developed stomach tumors and were sacrificed at the end of week 19" - "Liver metastases were only noted in the high THBS2 expression group: 2 out of 3 in the PGTCs group and 1 out of 3 in the NCI-N87THBS2+ group" -> "Liver metastases were only observed in the high THBS2 expression groups: 2 of 3 mice in the PGTCs group and 1 of 3 mice in the NCI-N87^THBS2+ group" - "Neither THBS2 knock-down nor carmofur treated groups had liver metastases" -> "Neither THBS2 knockdown nor carmofur-treated groups developed liver metastases" - "In addition, the liver metastases were identified under the light microscope after H&E staining" -> "Liver metastases were identified by light microscopy after H&E staining" - "To explore the sensitivity of GC to trastuzumab after THBS2 down-regulation and carmofur treatment, subcutaneous xenograft model was established in mice" -> "To explore GC sensitivity to trastuzumab following THBS2 downregulation and carmofur treatment, a subcutaneous xenograft model was established" - "In the NCI-N87 group, carmofur treatment significantly reduced the tumor volume from 475 mm3 in the control group to 290 mm3 (38.95% reduction), and trastuzumab treatment reduced the tumor volume by 62.11% (from 475 mm3 to 180 mm3)" -> "In the NCI-N87 group, carmofur treatment significantly reduced tumor volume from 475 mm^3 in the control group to 290 mm^3 (38.95% reduction), while trastuzumab treatment reduced tumor volume by 62.11% (from 475 mm^3 to 180 mm^3)" - "The combined treatment of carmofur and trastuzumab achieved the best tumor-inhibitory effect, and the tumor volume reduced by 93.26% (from 475 mm3to 32 mm3) (Fig. 6b)" -> "Combined carmofur and trastuzumab treatment achieved the best tumor-inhibitory effect, reducing tumor volume by 93.26% (from 475 mm^3 to 32 mm^3) (Fig. 6b)" - "While in the NCI-N87THBS2+ group (Fig. 6c), carmofur failed to significantly reduce the tumor volume (750 mm3 vs 620 mm3, P=0.479)" -> "In the NCI-N87^THBS2+ group (Fig. 6c), carmofur failed to significantly reduce tumor volume (750 mm^3

vs. 620 mm^3, P=0.479)" - "Trastuzumab still markedly reduced the tumor volume from 750 mm3 in the control group to 230 mm3 (69.33% reduction), but the combination of trastuzumab and carmofur failed to further significantly reduced the tumor volume (230 mm3 in trastuzumab group vs 80 mm3 in trastuzumab and carmofur group, P=0.052)" -> "Trastuzumab still markedly reduced tumor volume from 750 mm^3 in the control group to 230 mm^3 (69.33% reduction), but the combination of trastuzumab and carmofur failed to achieve further significant tumor volume reduction (230 mm^3 in the trastuzumab group vs. 80 mm^3 in the trastuzumab + carmofur group, P=0.052)" - "Furthermore, the final tumor volume (8th week) was examined in two groups (Fig. 6d)" -> "Furthermore, final tumor volume (at week 8) was compared between the two groups (Fig. 6d)" - "Results showed that the tumor volume in the NCI-N87 group was significantly smaller than in the NCI- N87THBS2+ group" -> "Results showed that tumor volume in the NCI-N87 group was significantly smaller than in the NCI-N87^THBS2+ group"

Discussion section: - "THBS2 is involved in ECM-receptor interaction and FA pathways, and its expression was significantly up-regulated in the GC tissues" -> "THBS2 is involved in ECM-receptor interaction and FA pathways, and its expression was significantly upregulated in GC tissues" - "THBS2 expression was higher in patients with lymph node and hematogenous metastases and associated with shorter overall survival time" -> "THBS2 expression was higher in patients with lymph node and hematogenous metastases and was associated with shorter overall survival" - "Downregulation of THBS2 in the PGTCs inhibited EMT though both FAK and AKT signaling pathways" -> "THBS2 downregulation in PGTCs inhibited EMT through both FAK and AKT signaling pathways" - "THBS2 overexpression in the NCI-N87 cells regulated cell division, cell cycle, phosphorylation, movement of cells and subcellular component and activated the phosphorylation of PTEN, compromising the tumor inhibitory effect of PTEN"-> "THBS2 overexpression in NCI-N87 cells regulated cell division, cell cycle, phosphorylation, cell movement, and subcellular component movement, and activated PTEN phosphorylation, compromising PTEN' s tumor-suppressive effect" - "Carmofur increased sensitivity of PGTCs and NCI-N87 cells to trastuzumab" -> "Carmofur increased the sensitivity of PGTCs and NCI-N87 cells to trastuzumab" - "THBS2 and carmofur exerted synergistic effect on the sensitivity of GC cells to trastuzumab in the xenograft model" -> "THBS2 and carmofur exerted synergistic effects on GC cell sensitivity to trastuzumab in xenograft models"

- "In our study, THBS2 was overexpressed in GC tissues from patients with synchronous liver metastases, which was associated with a poor prognosis" -> "In our study, THBS2 was overexpressed in GC tissues from patients with synchronous liver metastases, which was associated with poor prognosis"
- "In addition, higher THBS2 expression in stage M1 samples in TCGA vs N0 (M0) and N3 (M0) samples, which indicates the potential role of

THBS2 in the hematogenous metastasis of GC" -> "Additionally, higher THBS2 expression in stage M1 versus N0 (M0) and N3 (M0) samples in TCGA indicates a potential role for THBS2 in hematogenous metastasis of GC"

- "Furthermore, the machine-learning algorithm model was employed to quantify the relative importance of THBS2 to the postoperative long-term survival in GC patients" -> "Furthermore, a machine-learning algorithm model was employed to quantify the relative importance of THBS2 for postoperative long-term survival in GC patients"
- "It has been reported that machine learning algorithm is more accurate than traditional logistic regression[38, 39], including the ability to recognize clinically important risk among patients with several marginal risk factors and continually incorporate new clinical data with minimal oversight32" -> "Machine learning algorithms have been reported to be more accurate than traditional logistic regression[38,39], including the ability to recognize clinically important risk among patients with multiple marginal risk factors and continuously incorporate new clinical data with minimal oversight[32]"
- "In the investigation of mechanism underlying the role of THBS2 in the GC, we focused on the phosphatase and tensin homologue (PTEN), a tumor suppressor[40], due to its association with the development of metastases in the last phase of tumor progression[41]" -> "In investigating the mechanism underlying THBS2' s role in GC, we focused on phosphatase and tensin homologue (PTEN), a tumor suppressor[40], due to its association with metastasis development in the late phase of tumor progression[41]"
- "PTEN functions as a PIP3 phosphatase and is the main negative regulator of PI3K-Akt pathway and a regulator of switch between cell proliferation and migration states[42]" -> "PTEN functions as a PIP3 phosphatase and is the primary negative regulator of the PI3K-AKT pathway and a regulator of the switch between cell proliferation and migration states[42]"
- "After down-regulation of THBS2 expression, PTEN was activated and AKT was inhibited" -> "Following THBS2 downregulation, PTEN was activated and AKT was inhibited"
- "Considering the interaction between PTEN and FAK in the GC[43], the expression of FAK was further tested" -> "Considering the interaction between PTEN and FAK in GC[43], FAK expression was further examined"
- "Consistent with previous studies, PTEN also affected the oncogenic pathways besides the PI3K-Akt pathway, such as PTEN/FAK" -> "Consistent with previous studies, PTEN also affected oncogenic pathways beyond the PI3K-AKT pathway, such as the PTEN/FAK pathway"
- "Based on the available findings[44], we speculate that PTEN may reduce

tyrosine phosphorylation of FAK, and in turn the regulation of FAK partially antagonizes the effects of PTEN"-> "Based on available findings[44], we speculate that PTEN may reduce FAK tyrosine phosphorylation, and conversely, FAK regulation may partially antagonize PTEN effects"

- "In line with previous findings16, THBS2 can activate integrin $ $1 and phosphorylate its downstream effector FAK, which is a main regulator of ECM6"-> "In line with previous findings[16], THBS2 can activate integrin $ $1 and phosphorylate its downstream effector FAK, a key regulator of ECM[6]"
- "PTEN may function as a tumor suppressor by negatively regulating cell interactions with ECM[45]"-> "PTEN may function as a tumor suppressor by negatively regulating cell-ECM interactions[45]"
- "Therefore, we speculate that THBS2 may serve as a target gene based on concomitant regulation of PI3K/AKT and FAK signaling" -> "Therefore, we speculate that THBS2 may serve as a target gene through concomitant regulation of PI3K/AKT and FAK signaling"
- "One of the most important processes in tumor metastases and distant colonization is the MET, in which the epithelial program is restored by repressing the mesenchymal program" -> "One of the most important processes in tumor metastasis and distant colonization is MET, in which the epithelial program is restored by repressing the mesenchymal program"
- "On the other hand, epithelial cancer cells must undergo EMT, which allows them to migrate from primary lesions to distant organs [46]" -> "Conversely, epithelial cancer cells must undergo EMT to migrate from primary lesions to distant organs[46]"
- "After down-regulation of THBS2 expression, cells tend to undergo MET process which is an essential process when the tumor cells become less migratory and invasive" -> "Following THBS2 downregulation, cells underwent MET, an essential process rendering tumor cells less migratory and invasive"
- "GSEA analysis was performed to further investigate the potential role of THBS2 in the GC" -> "GSEA was performed to further investigate the potential role of THBS2 in GC"
- "In order to exclude the particularity of PGTCs, NCI-N87 cells were used to overexpress THBS2"-> "To exclude potential biases specific to PGTCs, THBS2 was overexpressed in NCI-N87 cells"
- "GSEA analysis showed that global transcriptome differences after THBS2 overexpression were mainly found in the phosphorylation and movement of cell or subcellular component processes" -> "GSEA showed that global transcriptome differences following THBS2 overexpression were primarily in phosphorylation and cell/subcellular component movement processes"

- “Binding to ITGA1 is a requisite step in the functioning of THBS2[47]” -> “Binding to ITGA1 is required for THBS2 function[47]”
- “They were both differentially expressed in the breast cancer[48]”-> “Both were differentially expressed in breast cancer[48]”
- “PBK can directly interact with, phosphorylate and inactivate PTEN, which in turn activates PI3K-Akt-IKK signaling pathway[49, 50]”-> “PBK can directly interact with, phosphorylate, and inactivate PTEN, thereby activating the PI3K-AKT-IKK signaling pathway[49,50]”
- “PBK-induced cell migration has been found to be a PI3K/AKT-dependent event[51], and PBK overexpression is also closely related to venous invasion, tumor depth and recurrence rate of GC[52]” -> “PBK-induced cell migration is PI3K/AKT-dependent[51], and PBK overexpression is closely associated with venous invasion, tumor depth, and GC recurrence rate[52]”
- “STMN1 is one of the genes down- regulated upon PTEN induction and an accurate IHC marker of the signature and has prognostic significance in the breast cancer[53]”-> “STMN1 is downregulated upon PTEN induction and serves as an accurate IHC marker with prognostic significance in breast cancer[53]”
- “STMN1 is an important member of PI3K pathway[54]” -> “STMN1 is an important member of the PI3K pathway[54]”
- “STMN1 overexpression is significantly associated with the lymphatic metastatic recurrence in pN0 ESCC patients” -> “STMN1 overexpression is significantly associated with lymphatic metastatic recurrence in pN0 ESCC patients”
- “STMN1 expression is regulated by the PI3K pathway, and STMN1 can act as a surrogate marker of PI3K signaling pathway related to tumor recurrence[55]” -> “STMN1 expression is regulated by the PI3K pathway, and STMN1 can serve as a surrogate marker of PI3K signaling related to tumor recurrence[55]”
- “In our study, THBS2 overexpression activates the PI3K signaling pathway by inactivating PTEN” -> “In our study, THBS2 overexpression activated the PI3K signaling pathway by inactivating PTEN”
- “Therefore, regulation of THBS2 or PTEN may be an important strategy to increase the sensitivity of GC to trastuzumab” -> “Therefore, targeting THBS2 or PTEN may be an important strategy to enhance GC sensitivity to trastuzumab”
- “Trastuzumab (Herceptin; Genentech, San Francisco, Calif., USA) is a recombinant, humanized monoclonal antibody targeting the extracellular domain of the human epidermal growth factor receptor 2 (HER2) protein” -> “Trastuzumab (Herceptin; Genentech, San Francisco, CA, USA) is a

recombinant humanized monoclonal antibody targeting the extracellular domain of human epidermal growth factor receptor 2 (HER2)"

- "It is the first biological product that can prolong the survival time of metastatic GC patients[56]" -> "It was the first biological agent shown to prolong survival in metastatic GC patients[56]"
- "In EU and US, trastuzumab combined with chemotherapy has been approved by the FDA as first-line treatment for metastatic GC with Her-2 over-expression" -> "In the EU and US, trastuzumab combined with chemotherapy is FDA-approved as first-line treatment for HER2-overexpressing metastatic GC"
- "Despite early successes, the majority of patients exhibit primary or secondary resistance within one year, which severely influences the clinical application of trastuzumab" -> "Despite initial success, most patients develop primary or secondary resistance within one year, limiting the clinical utility of trastuzumab"
- "The trastuzumab resistance has also been reported in the treatment of metastatic breast cancer[57]" -> "Trastuzumab resistance has also been reported in metastatic breast cancer treatment[57]"
- "Thus, to develop appropriate chemo- sensitizers according to potential mechanisms related to trastuzumab resistance may be important for the clinical application of trastuzumab" -> "Thus, developing appropriate chemosensitizers based on mechanisms of trastuzumab resistance may be important for its clinical application"
- "The activation of PTEN/PI3K/AKT signaling pathway is one of the major mechanisms leading to the resistance of GC cells to trastuzumab[58]" -> "Activation of the PTEN/PI3K/AKT signaling pathway is a major mechanism of trastuzumab resistance in GC cells[58]"
- "Therefore, PTEN as a molecule in the PI3K pathway has been identified as an important target in studies on the treatment of cancers[59-61]" -> "Therefore, PTEN, as a key molecule in the PI3K pathway, has been identified as an important therapeutic target in cancer[59-61]"
- "One of the alternative targets of PTEN is the FAK kinase, which is mainly involved in the control of cancer cell spread[41]"-> "One alternative target of PTEN is FAK kinase, which is primarily involved in controlling cancer cell spread[41]"
- "Therefore, we speculated that THBS2 may serve as a key factor that can regulate PI3K and FAK signaling pathways to improve the trastuzumab resistance"-> "Therefore, we speculate that THBS2 may serve as a key factor regulating PI3K and FAK signaling pathways to overcome trastuzumab resistance"

- “Carmofur (1-hexylcarbamoyl-5-fluorouracil, HCFU) has been used as oral drug in the chemotherapy of advanced gastrointestinal cancer[62, 63] and advanced pancreatic cancer[64] in the early nineties” -> “Carmofur (1-hexylcarbamoyl-5-fluorouracil, HCFU) was used as an oral chemotherapeutic agent for advanced gastrointestinal cancer[62,63] and advanced pancreatic cancer[64] in the early 1990s”
- “Studies have confirmed its preventive effect on distant metastases[65, 66]” -> “Studies have confirmed its preventive effects on distant metastases[65,66]”
- “In our study, carmofur was found to induce PTEN nuclear translocation and made the cut-off point of trastuzumab concentration- effect appeared ahead of time” -> “In our study, carmofur induced PTEN nuclear translocation and shifted the trastuzumab concentration-effect curve leftward”
- “In normal tissues, PTEN is localized primarily in the nucleus, whereas, in the neoplastic tissues, PTEN translocates into cytoplasm, which may be involved in the neoplastic transformation[67]”-> “In normal tissues, PTEN is primarily nuclear, whereas in neoplastic tissues, PTEN translocates to the cytoplasm, which may be involved in neoplastic transformation[67]”
- “Several mechanisms have been proposed for the nucleo-cytoplasmic translocation of PTEN, including simple diffusion, cytoplasmic localization signal mediated translocation, active translocation mediated by the RAN GTPase or major vault protein, phosphorylation-dependent translocation and monoubiquitylation-dependent translocation[67]” -> “Several mechanisms have been proposed for PTEN nucleocytoplasmic translocation, including simple diffusion, cytoplasmic localization signal-mediated translocation, active translocation mediated by RAN GTPase or major vault protein, phosphorylation-dependent translocation, and monoubiquitylation-dependent translocation[67]”
- “As THBS2 over-expression is enriched in the phosphorylation process, the phosphorylation-dependent translocation may be a feasible theory for the PTEN nucleo-cytoplasmic translocation proposed by Vazquez et al [68]” -> “Since THBS2 overexpression is enriched in phosphorylation processes, phosphorylation-dependent translocation may be a plausible mechanism for PTEN nucleocytoplasmic translocation as proposed by Vazquez et al.[68]”
- “Carmofur alone as an adjuvant chemotherapy is not sufficient to improve the prognosis[69] and its clinical utility is also limited due to its possible toxic leukoencephalopathy [70]”-> “Carmofur alone as adjuvant chemotherapy is insufficient to improve prognosis[69], and its clinical utility is limited by potential toxic leukoencephalopathy[70]”
- “However, our study shed new light on carmofur as a potential chemosensitizer to trastuzumab based on its ability to induce PTEN nuclear

translocation" -> "However, our study sheds new light on carmofur as a potential chemosensitizer for trastuzumab based on its ability to induce PTEN nuclear translocation"

- "Therefore, we investigated the effect of carmofur combined with THBS2 down-regulation as a new strategy to enhance the sensitivity of GC to trastuzumab in the xenograft model" -> "Therefore, we investigated the effect of combining carmofur with THBS2 downregulation as a novel strategy to enhance GC sensitivity to trastuzumab in xenograft models"
- "In orthotropic xenograft model, liver metastases were only noted in the high THBS2 expression group: 2 out of 3 in the PGTCs group and 1 out of 3 in the NCI-N87THBS2+ group" -> "In the orthotopic xenograft model, liver metastases were only observed in the high THBS2 expression groups: 2 of 3 mice in the PGTCs group and 1 of 3 mice in the NCI-N87^THBS2+ group"
- "Neither THBS2 knock-down nor carmofur treated groups had liver metastases" -> "Neither THBS2 knockdown nor carmofur-treated groups developed liver metastases"
- "In the subcutaneous xenograft model, the effect of THBS2 knockdown combined with carmofur on the sensitivity of NCI-N87 cells to trastuzumab was further explored" -> "In the subcutaneous xenograft model, we further explored the effect of THBS2 knockdown combined with carmofur on NCI-N87 cell sensitivity to trastuzumab"
- "Results indicated that carmofur increased the sensitivity of GC to trastuzumab in the NCI-N87 group" -> "Results indicated that carmofur increased GC sensitivity to trastuzumab in the NCI-N87 group"

Conclusion section: - "Taken together, our study indicates THBS2 is overexpressed in the GC tissues of patients with synchronous liver metastases, which is associated with the poor prognosis of GC" -> "Taken together, our study indicates that THBS2 is overexpressed in GC tissues from patients with synchronous liver metastases, which is associated with poor prognosis" - "In addition, high THBS2 expression promotes EMT and metastases of GC, which may be related to classic AKT and FAK signaling pathways" -> "In addition, high THBS2 expression promotes EMT and metastasis in GC, potentially through classical AKT and FAK signaling pathways" - "Moreover, THBS2 downregulation combined with carmofur may serve as a new strategy to enhance the sensitivity of GC to trastuzumab" -> "Moreover, THBS2 downregulation combined with carmofur may serve as a novel strategy to enhance GC sensitivity to trastuzumab"

Acknowledgements: - "We greatly appreciate all of the study participants" -> "We sincerely appreciate all study participants"

Supplementary Materials: - These are fine as is

References: - I' ll keep these exactly as they are

Figure Legends: - "Figure 1. A. ECM-receptor interaction pathways and focal adhesion (FA) pathways are significant overrepresented in above 555 genes" -> "Figure 1. (a) ECM-receptor interaction and focal adhesion (FA) pathways are significantly overrepresented among the 555 genes" - "B. THBS2 expression is extremely down-regulated in all digestive tract organs" -> "(b) THBS2 expression is significantly downregulated in all digestive tract organs" - "C. THBS2 expression is significantly up-regulated in gastric tumors as compared to normal tissues in both our samples and TCGA study" -> "(c) THBS2 expression is significantly upregulated in gastric tumors compared to normal tissues in both our samples and TCGA data" - "D.THBS2 gene expression is higher in M1 samples in TCGA vs N0 (M0) and N3 (M0) samples" -> "(d) THBS2 gene expression is higher in M1 versus N0 (M0) and N3 (M0) samples in TCGA" - "Note: TCGA, The Cancer Genome Atlas; KEGG, Kyoto Encyclopedia of Genes and Genomes" -> This is fine

- "Figure 2. A. Representative photos from immunohistochemical staining for THBS2 in GC (400×)" -> "Figure 2. (a) Representative images of THBS2 immunohistochemical staining in GC (400×)"
- "B. Patients with higher THBS2 expression displayed a significantly shorter overall survival time, whereas patients with lower THBS2 expression showed a favorable prognosis (median 28.5 months vs. 40.5 months, P =0.00039)" -> "(b) Patients with higher THBS2 expression had significantly shorter overall survival than those with lower THBS2 expression (median 28.5 vs. 40.5 months, P = 0.00039)"
- "C. Variable importance for machine-learning algorithm model, scaled to a maximum of 1.0. (Variables that are not important will have small positive or negative values. The negative value does not necessarily reflect a negative risk, but indicates that there is no significant contribution)" -> "(c) Variable importance from the machine-learning algorithm model, scaled to a maximum of 1.0. Variables with small positive or negative values are not important. Negative values do not necessarily reflect negative risk but indicate no significant contribution"
- "Figure 3. A. Representative images of primary tumorspheres (P1, P3, P6 and P10)" -> "Figure 3. (a) Representative images of primary tumorspheres (P1, P3, P6, and P10)"
- "B. Western blotting showed the expression of THBS2 protein and PTEN protein in PGTCs and GES cells"-> "(b) Western blotting showing THBS2 and PTEN protein expression in PGTCs and GES cells"
- "C. Downregulation of THBS2 altered the pPTEN expression and inhibited the AKT activation in PGTCs"-> "(c) THBS2 downregulation altered pPTEN expression and inhibited AKT activation in PG

Note: Figure translations are in progress. See original paper for figures.

Source: ChinaXiv —Machine translation. Verify with original.