



如何進行文章 及計畫的審查

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文章审查

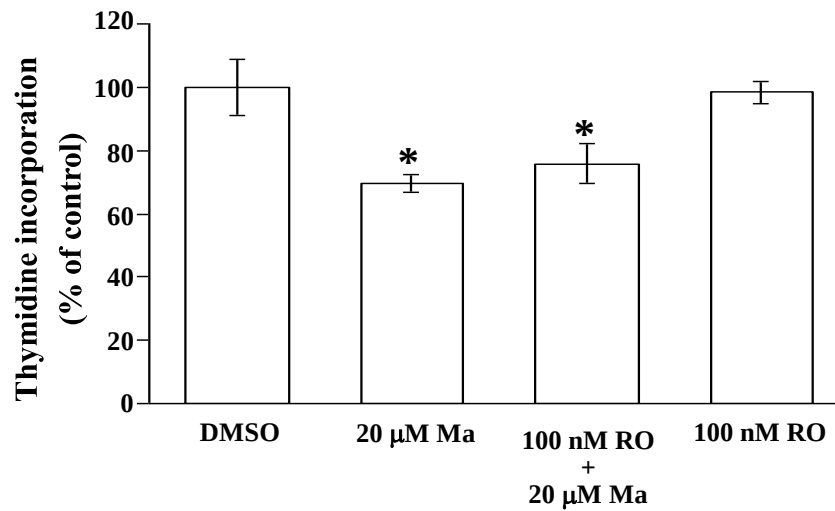
文章的好壞

- 好的數據
- 好的邏輯
- 原創性
- 文章的故事性

實驗結果的好壞

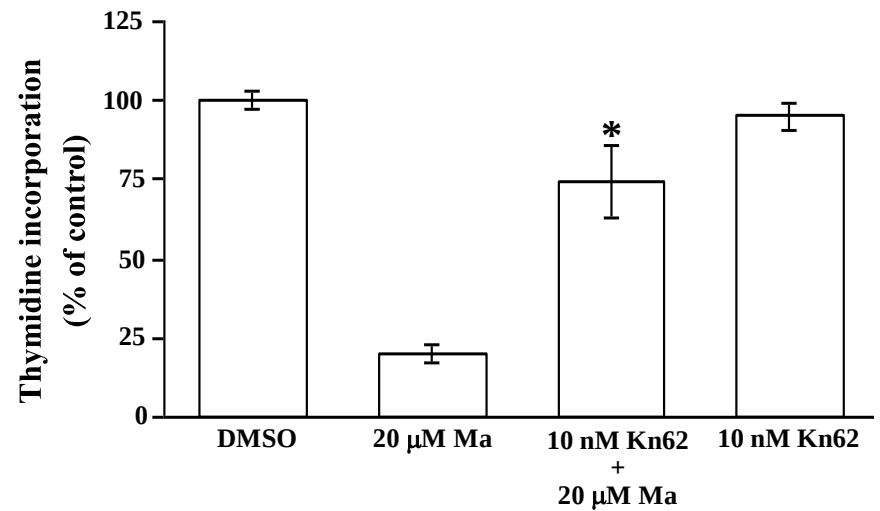
- 準確性及一致性
(Accuracy and consistency)
- 設計的嚴謹度

準確性



Ma, magnolol
RO, RO32-0432 (PKC specific inhibitor)

~~一致性~~



Ma, magnolol
Kn62, CaM kinase inhibitor

Control的設計與解讀

Positive control

Positive controls confirm that the procedure is effective in observing the effect (therefore minimizing false negatives).

**How to clarify that the
immunoreactivity negative is a
real negative or false negative**

Do smooth muscle cells in neointima express Thy-1?



What can cause false negative?

1. Experimental protocol

a. Fixation

b. Experimental procedure

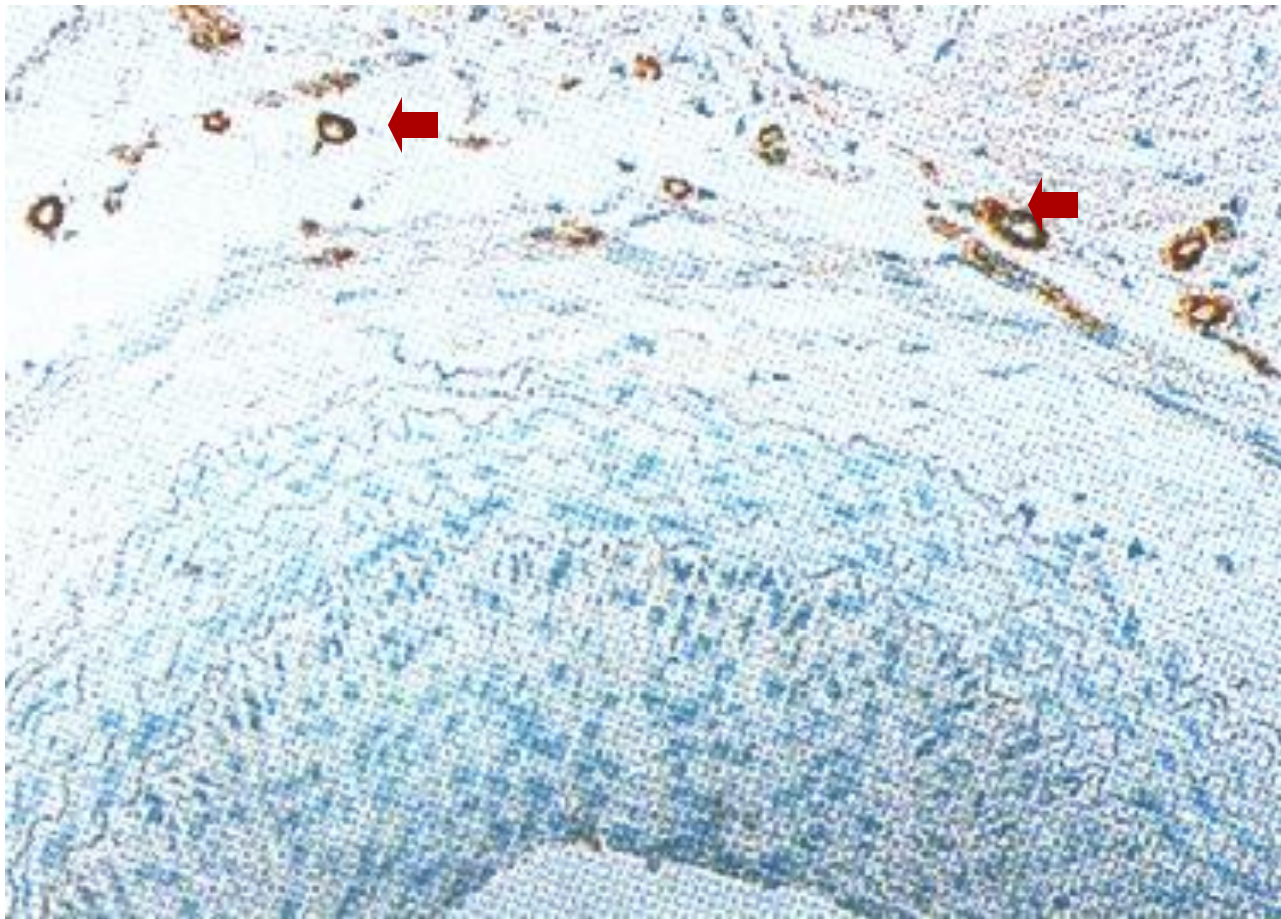
2. Chemicals

a. Antibody concentration

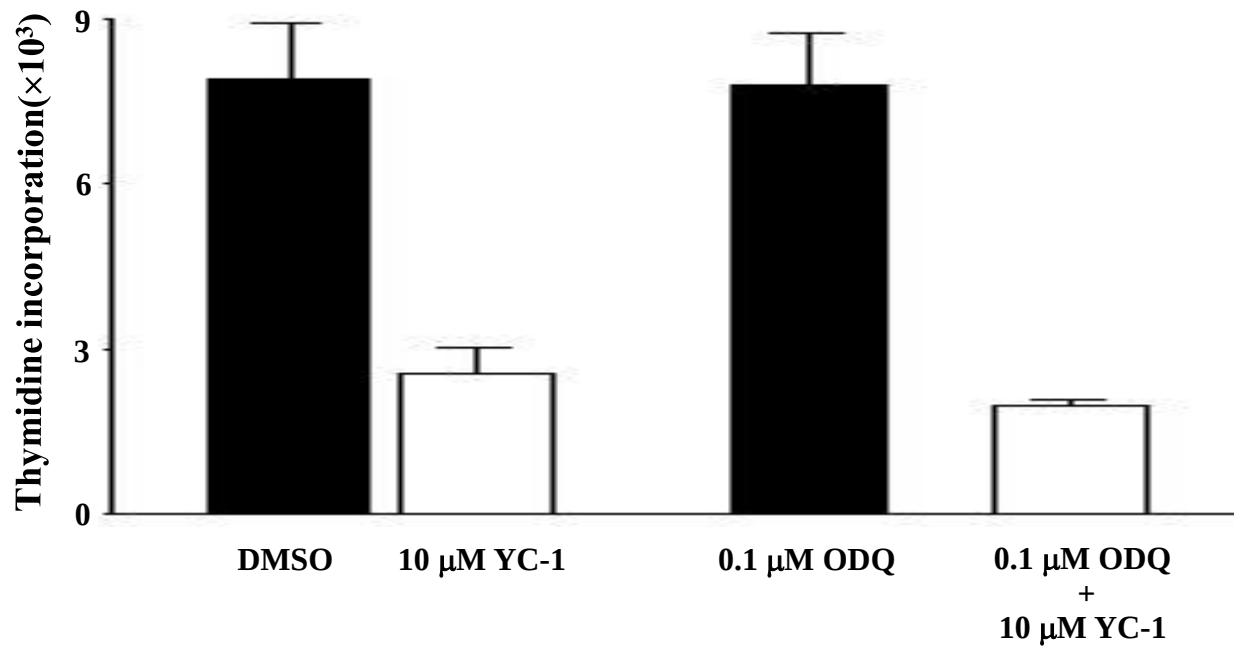
b. Expired date of chemicals

c. PH value of solutions

**Thy-1 immunoreactivity was detected
in the adventitia but not neointima**

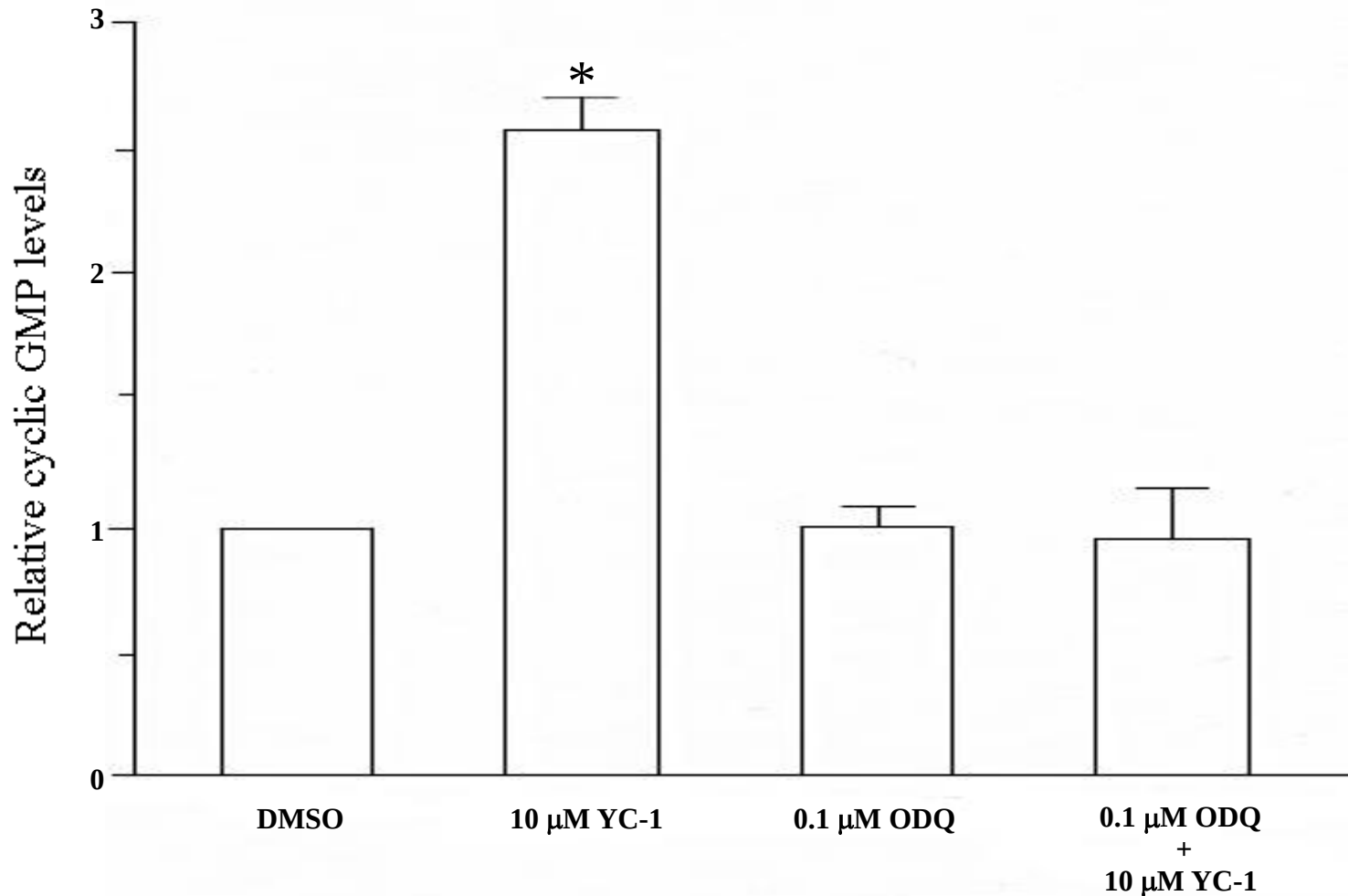


cGMP is not involved in the YC-induced [3H]thymidine incorporation inhibition in HUVEC



How to clarify that the cGMP inhibitor, ODQ, is effective?

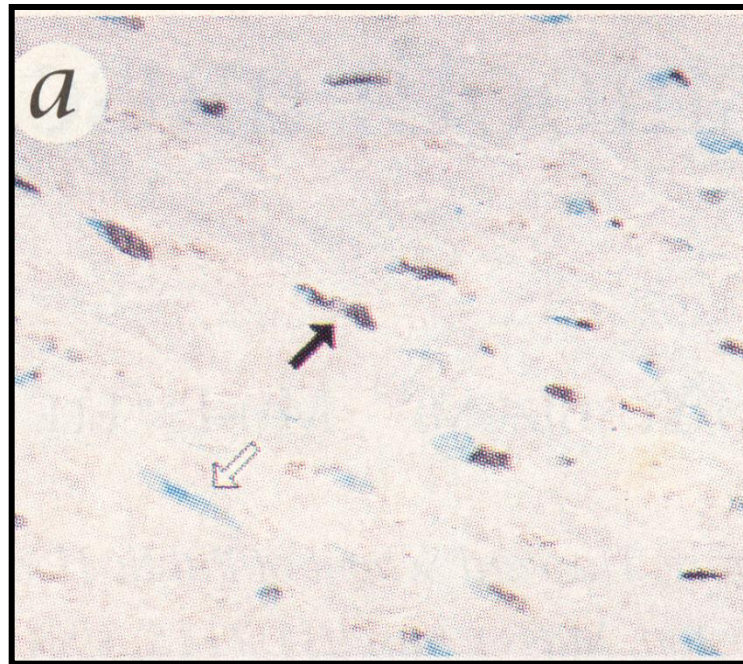
ODQ inhibits the YC-1-induced increase of cGMP level



Negative control

Negative controls confirm that the procedure is not observing an unrelated effect (therefore minimizing false positives).

Immuno-localization of progesterone receptor on the aortic smooth muscle cells



anti-P4R Ab
DAB staining

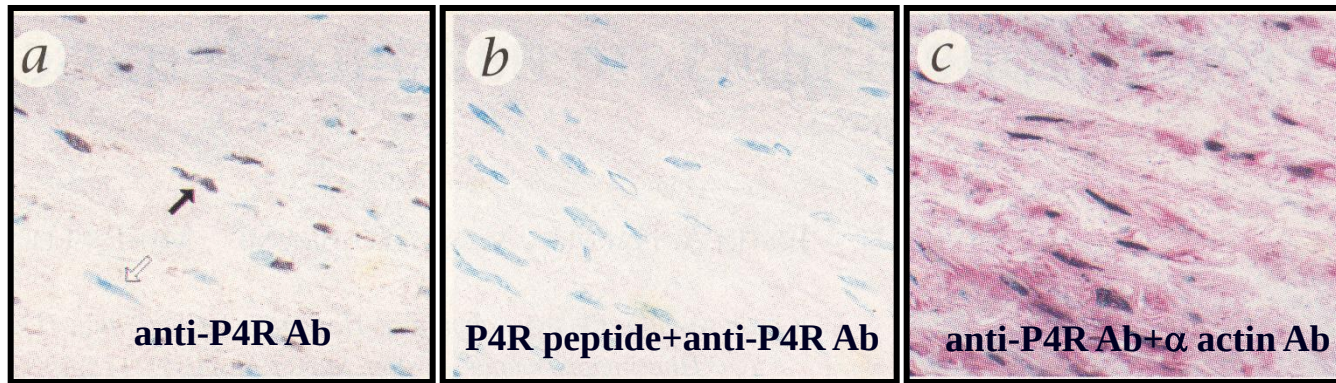
Human aorta

**How to clarify that the
immunoreactivity positive is a
real positive or false positive**

Current methods used for immunocytochemical staining negative control

- 1. Use of preimmune serum to replace the primary antibody**
- 2. To omit the primary antibody**
- 3. Antigen preabsorption**

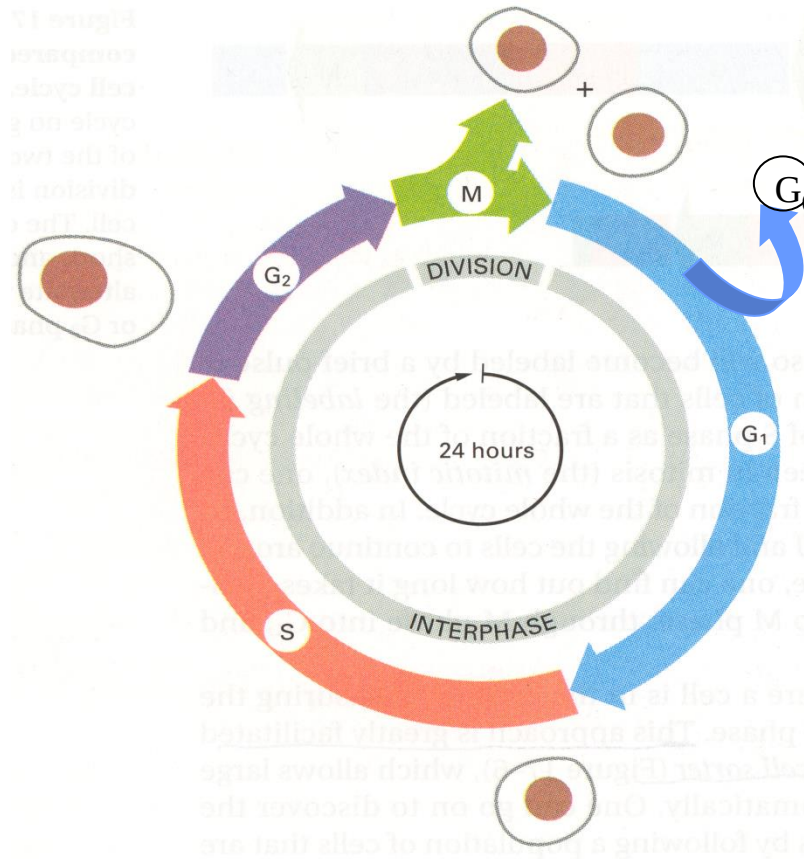
Immuno-localization of progesterone receptor on the aortic smooth muscle cells



Human aorta

Progesterone receptor-like immunoreactivity

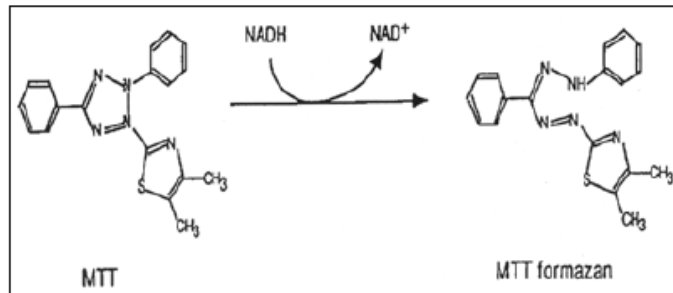
Study of cell cycle



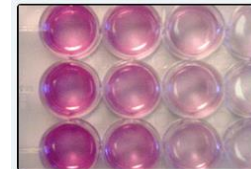
Cell synchronization

Cell proliferation assay

MTT assay



ELISA Reader



Cell survival

The manuscript “XXX” of XX et al. present the data about the signaling pathway involved in the XX-induced ferroptosis in the I/R injury. Although the authors have shown some interesting observations, some of the experimental designs are inappropriate and the findings are not sufficient to support their conclusion. To prove the involvement of NRF2/SLC7A11/GPX4 pathway in the XX-induced ferroptosis, it is important to inhibit the activities of these signaling molecules by gene knock-down technique or pharmacological inhibitors.

Major issues:

1. In the Graphical Abstract, it showed that ROS is not involved in the XX-induced ferroptosis, but it was shown that XX aggravated cardiomyocyte injury by inducing oxidative stress.
2. I/R injury is not only ferroptosis, but also apoptosis and autophagy. The authors should check whether XX affects these cell death mechanisms other than ferroptosis,
3. In Figure 1, why the XX-treated group was compared with the NACL group should be explained.
4. In Figures 2A-B, E-G, to prove that the XX-increased ROS was not an artifact, the authors should have a negative control group instead of a positive control group (H₂O₂ treatment),
5. In Figures 2J-L, the Western blots of NOX2 and NOX4 show two bands. The authors should indicate which was the right band. Moreover, the representative graph shown in Figure 2L did not match the quantitative results shown in Figures J-K.
6. In Figures 3, 4, 5 and 6, the NAC treatment alone should be included.
7. In Figure 3L, the results of TUNEL assay were not convincing
8. To prove that XX caused cardiomyocyte damage through oxidative stress, XX-increased the levels of ROS in cardiomyocytes should be demonstrated.
9. To examine the NRF2 levels in the cytosol (Fig. 5A), the membrane should also be examined the expression of PCNA to demonstrate the purity of the cytosol extraction without the nuclear contamination. Again, to examine the NRF2 levels in the nucleus (Fig. 5C), the membrane should also be examined the expression of GAPDH to demonstrate the purity of the nuclear extraction without the cytosol contamination. The same issue also existed in Figure 5K.
10. The nuclear localization of NRF2 shown in Figure 5G was not impressive. The image should be taken by confocal microscopy.
11. For the protein-protein interaction detected by co-immunoprecipitation shown in Figure 5J, Heavy chain or light chain should also be detected to serve as loading control. Moreover, there were two bands for both NRF2 and KEAP1 staining. It should be indicated which one is the right band.
12. Figures 5K, LM, and N show that si-Keap1 completely prevented the XX-reduced the protein levels of GPX4, SLC7A11 and NRF2. However, Suppl. Fig. 1 show that transfection with si-Keap1 cDNA caused only around 50% reduction of the Keap1 protein levels. The authors should have explanation on this issue.
13. This study showed that the serum XX concentration increased in AMI patients and I/R mice model. However, the serum XX concentration cannot always reflect the myocardial XX concentration. It is important for the authors to demonstrate that the XX levels increased in the heart of I/R mice.
14. The manuscript needs significant language editing for grammar and writing.

Minor issues

1. In the line 8 of Introduction, it should be “superoxide dismutase and catalase” instead of “superoxide dismutase sand catalase”
2. The bottom panels of Figure 4B were up-side down.
3. The abbreviation should be consistent. For instance, NAC and NACL were interactive used.
4. In Figure 1F-G, AAR was not defined. How AAR was measured should be described.

文章的原創性

Novelty

- being striking, original or unusual
- 避免 me too study (如法炮製)

Novelty

This proposed research project is the extension of our previous grant proposal. The findings from our previous studies of the effect of folic acid (FA) on angiogenesis sponsored by NSC 97-2320-B-038-033-MY3 have been published in two papers in *Angiogenesis* (Lin et al., 2012) and in *Biochemical Pharmacology* (Hou et al., 2012), respectively. **Demonstration of the anti-angiogenic activity of FA is a novel finding for the FA's action...** These findings suggest that female sex hormones might interfere with the actions of FA. Accordingly, the aims of this new grant proposal will be focused on studies of the interaction between female sex hormones and FA on their biological actions and treatment for diseases.

Me too study

- 換個細胞種類
 - 同類型細胞：胃癌細胞、乳癌細胞
 - 不同類型細胞：癌細胞、內皮細胞

**各種期刊有其特殊研究
方向的需求**

期刊的聲望高低對文章內容或有不同要求，但對實驗結果的準確性及一致性與設計的嚴謹度的要求則是一樣的

Decision

1. Accepted

2. Minor revision

3. Major revision

4. Rejected

計畫審查

研究計畫補助審查要點

- 計畫的創新性及重要性
- 弱點及具體建議
- 主持人之研究表現
- 總結

研究計畫補助審查要點

- 計畫的創新性及重要性
- 計畫的可行性
- 主持人的研究表現
- 計畫的撰寫

Novelty

Significance

- 主持人應點出研究成果對於學術或臨床上的重要性
- 臨床議題的計畫較容易點出其重要性

弱點及具體建議

- 嚴謹的實驗設計及邏輯
- 主持人具有相關議題的文章發表
- 具備足夠的Preliminary data
- 擁有計畫執行的技術與設備
- 擁有適當的共同或協同主持人

Preliminary data

- 支持計畫執行的可行性
- 不能是已發表的Data

主持人的技術

- 主持人具有相關技術的Publications
- 具有相關技術的共同或協同主持人

計畫共同主持人

協助計畫的順利進行

- 支援實驗所需要的技術
- 資深且學術有聲望的來協助
- 不要找太多共同主持人，有獨立性不夠之嫌

主持人之研究表現

- 論文發表情形
- 計畫的執行率

論文發表情形

- 論文發表的質與量
- 研究主題的連貫性
- 研究的獨立性

論文發表的質與量

- 對年輕學者的審查不會太過對文章質的要求，但有連貫性主題的文章會有加分效果
- 對資深學者文章的質與量都會要求

論文主題的連貫性

- 對年輕學者的審查不會太過對文章主題連貫性的要求，但有高品質的文章會有加分效果
- 對資深學者文章主題的連貫性會要求
- 如果要變換研究的主題，最好有充足的Rationale、Preliminary data、及Some related publications

計畫的執行率

過去補助計畫的成果

- 論文發表
- 專利

研究的獨立性

- 對年輕學者的審查不會太過苛責是否有通訊作者文章，如有會有加分效果
- 對資深學者會要求為文章的通訊作者
- 不要有太多的共同第一或通訊作者
(過多文章為共同通訊作者不是好現象)