Dr Shigeo Ohta of this Ms is the leader research of hydrogen in biomedicine. He published many important papers including the Foundational paper in 2007. in this mini review, Based on a recent new study by Professor He qianjun's team, which is that iron porphyrin is the molecular target of hydrogen action, he proposed the idea that Nrf2 is activated by hydrogen through this action. The effect of hydrogen on Nrf2 activation has long been reported, but there is no suitable theoretical explanation. The author proposes that if this view can be confirmed experimentally, it will be of great value to promoting the research on the medical mechanism of hydrogen gas.

Since 2007, the most important mechanistic explanation for the biological effect of hydrogen is selective antioxidant, which is also a hypothesis proposed by the Dr Shigeo Ohta team. The hypothesis is that hydrogen can selectively neutralize hydroxyl radicals and reduce oxidative damage, thus playing various medical biological roles. But as the size of the study has increased, it has been found that some effects cannot be explained by selective antioxidant use alone. For example, the long-term effect of short-time action, the improvement of endogenous antioxidant capacity in realistic biological systems such as activated antioxidant systems. The most important representative of the endogenous antioxidant system activation is the increased transcriptional activity of Nrf 2. The authors of this manuscript, based on the latest evidence on the chemical basis of the transcriptional activity of Nrf 2, is very encouraging.

 Given the high theoretical value of this Ms and the author is a leader in this field, I personally recognize this Ms.

Some minor point

We in abstract should be I，as this Ms has only one auther。“We propose that, instead of low doses, the relieved oxidative potent of •OH can serve as a hermetic-like to activated Nrf2. ”

Aing is the focus of this journal, from the perspective of paper compliance, of course, this is good. But the importance of oxidative stress and endogenous antioxidant is not limited to Aging. It is suggested that the authors can explore the value of this hypothesis from the perspective of broader significance, such as cancer, tissue ischemia and reperfusion injury, and drug toxicity.

Suggested to add a cartoon of Nrf 2-keap transcriptional activity, which can make this article more complete and exciting.