Lessons from Nobel laureate Gregg Semenza's retractions

Minh-Hoang Nguyen, AISDL

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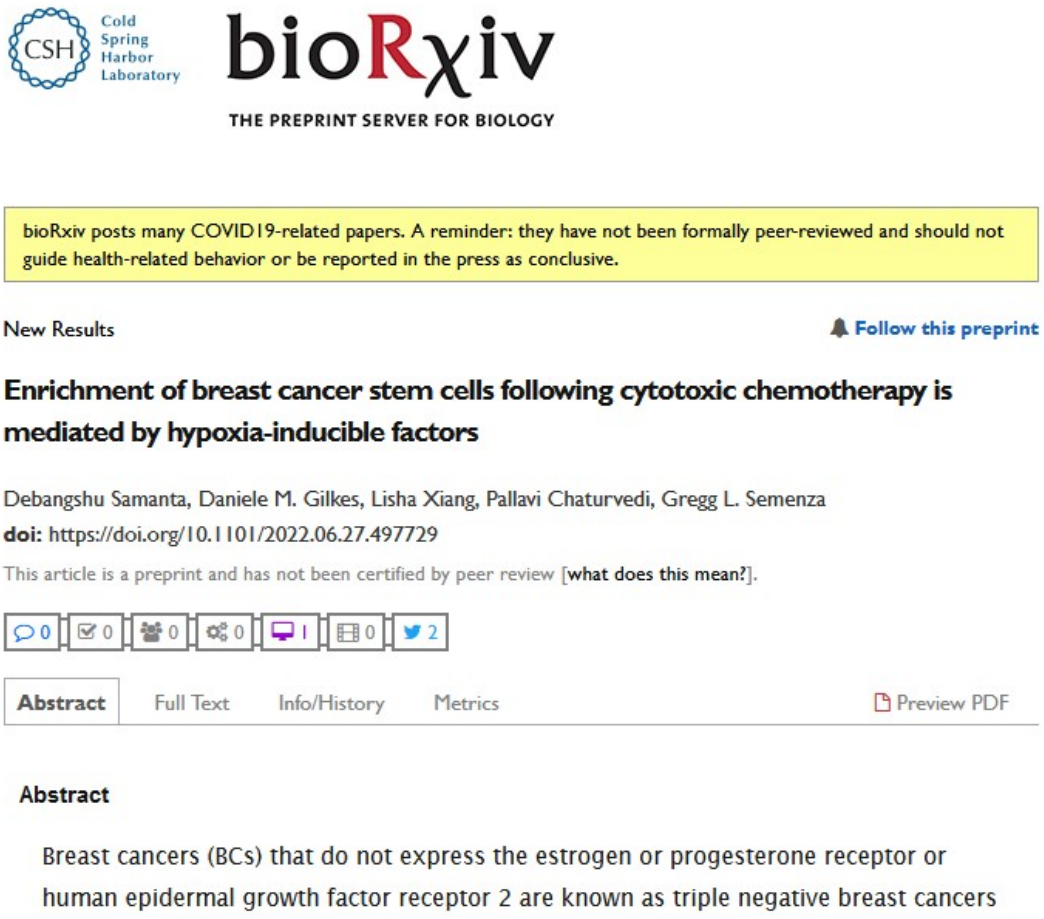
On September 3, 2022, Retraction Watch reported that four articles published in the *Proceedings of the National Academy of Sciences* (PNAS) had been retracted on the same day (02 September 2022) [1]. More notable is that all four articles were co-authored by a preeminent researcher on the molecular mechanisms of oxygen regulation – Gregg Semenza [2-5]. Semenza shared The Nobel Prize in Physiology or Medicine 2019 with William Kaelin and Peter Ratcliffe for "their discoveries of how cells sense and adapt to oxygen availability."

Although retraction might give a bad impression at first glance, the transparent retraction notices have shown the honesty and self-correcting spirit of the world-renowned teams of scientists. In the retracted papers' notices, the authors outlined they were retracting the articles with clear details of the reasons behind their decisions. The reasons for retracting four articles are similar: concerns with some published images. In addition, the authors also declared to conduct confirmatory experimentation for two studies and update the correct version of the image to ensure the validity of the papers' overall conclusions. The confirmatory experimentations and updated image can be found on bioRxiv:

• Confirmatory experimentation for 'Mutual antagonism between hypoxia-inducible factors 1? and 2? regulates oxygen sensing and cardio-respiratory homeostasis': https://www.biorxiv.org/content/10.1101/2022.07.11.499380v1

• Confirmatory experimentation for 'Anthracycline chemotherapy inhibits HIF-1 transcriptional activity and tumor-induced mobilization of circulating angiogenic cells': https://www.biorxiv.org/content/10.1101/2022.06.15.492526v1

• Updated figures for 'Hypoxia-inducible factors are required for chemotherapy resistance of breast cancer stem cells': https://www.biorxiv.org/content/10.1101/2022.06.27.497729v1



https://www.biorxiv.org/content/10.1101/2022.06.27.497729v1

Major lessons can be learned from this retraction event. The scientific and technological foundations in which humans often take pride in advancing their civilization are not perfect. Even the academic elites, like Nobel laureates (e.g., Gregg Semenza, Frances Arnold), editors, and reviewers of most prestigious scientific journals (e.g., PNAS, Lancet, The New England Journal of Medicine), can still have mistakes. In the coming era, more flaws in scientific conduct might be identified as a result of the soaring publication number. Perhaps, we should be more modest and start to adapt to the changes soon [6].

Considering retractions as error-detection and -correction tools can be a good alternative, as "retractions are not intrinsically bad: they are a practical way to correct for human fallibility and strengthen the scientific enterprise" [7].

References

[1] Oransky I. (2022). Nobel Prize winner Gregg Semenza retracts four papers. *Retraction Watch*. Available from: https://retractionwatch.com/2022/09/03/nobel-prize-winner-gregg-semenza-retracts-four-papers/

[2] Xiang L, et al. (2022). Retraction for Gilkes et al., Hypoxia-inducible factors mediate coordinated RhoA-ROCK1 expression and signaling in breast cancer cells. *PNAS*, 119(38), e2213288119. https://www.pnas.org/doi/full/10.1073/pnas.2213288119

[3] Yuan G, et al. (2022). Retraction for Yuan et al., Mutual antagonism between hypoxia-inducible factors 1? and 2? regulates oxygen sensing and cardio-respiratory homeostasis. *PNAS*, 119(38), e2213287119. https://www.pnas.org/doi/full/10.1073/pnas.2213287119

[4] Lee K, et al. (2022). Retraction for Lee et al., Anthracycline chemotherapy inhibits HIF-1 transcriptional activity and tumor-induced mobilization of circulating angiogenic cells. *PNAS*, 119(38), e2213285119. https://www.pnas.org/doi/full/10.1073/pnas.2213285119

[5] Samanta D, et al. (2022). Retraction for Samanta et al., Hypoxia-inducible factors are required for chemotherapy resistance of breast cancer stem cells. *PNAS*, 119(38), e2213289119. https://www.pnas.org/doi/full/10.1073/pnas.2213289119

[6] Vuong QH. (2022). *Mindsponge Theory*. AISDL. https://books.google.com/books?id=OSiGEAAAQBAJ

[7] Vuong QH. (2020). Reform retractions to make them more transparent. *Nature*, 582, 149. https://www.nature.com/articles/d41586-020-01694-x