

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 65758

**Title:** Unveiling the morphogenetic code: A new path at the intersection of physical energies and chemical signaling

**Reviewer's code:** 05685664

**Position:** Peer Reviewer

**Academic degree:** DDS, MS, MSc, PhD

**Professional title:** Research Scientist

**Reviewer's Country/Territory:** Brazil

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-03-15

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-04-25 13:40

**Reviewer performed review:** 2021-05-02 23:01

**Review time:** 7 Days and 9 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

Riccardo Tassinari, Claudia Cavallini, Elena Olivi, Valentina Taglioli, Chiara Zannini, Carlo Ventura have submitted an interesting editorial titled “Unveiling the morphogenetic code: a new path at the intersection of physical energies and chemical signaling”. In my personal opinion it is a fluently written manuscript which provides important information regarding the role of physical energies and chemical signaling in the morphogenetic code, which consists of the mechanisms and information structures by which networks of cells represent and dynamically regulate the target morphology of the system. However, I have few comments: 1. I suggest developing a figure to summarize the theme proposed in the editorial. 2. In the following paragraph, “Considering the diffusive properties of such physical stimuli, we may also envision a novel strategy of regenerative medicine relying upon the reprogramming of stem cells in situ, where they are resident in all tissues of the human body.” There are several types of stem cells with different cell potency, in this paragraph the authors are referring to all types of stem cells? I suggest that these concepts are not accurately addressed in the paper and it can make confusion to the readers. 3. I suggest to add the reference that supports the following paragraphs: a. “Bioelectricity is a term coined to identify the ability of electric fields endogenously generated in living cells to afford modulation of biological patterning from the cellular up to the tissue and organ level. In all the cells and tissues, a part of electrically driven signaling originates from ion channels and related ion fluxes. The differential distribution of resting potential across tissues represents an ancestral and conserved modality, highly integrated and connatural with chemical structures, in the establishment of cell signaling networks. Bioelectricity plays a major role in the scaling up dynamics responsible for embryogenesis, and tissue regeneration, while altered non-coherent bioelectrical patterning appears to be involved in the onset of



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degenerative or malignant states.”; b. “Burr was a fantastic visionary pioneer of studies that only today are creating progressive evidence for the existence of a morphogenetic field and for the need to believe in this potential as an unprecedented chance to access a real comprehensive view on how biological systems acquire coherence. Burr focused on their capability to create dynamically evolving shapes that, while sharing enormous similarities with the simplest microorganisms and our eukaryotic cells, nevertheless entail the evolutionary unfolding not only to complexity, like in multicellular organisms, but to the deeper meaning of biological forms and shapes. This includes the inherent susceptibility of biological forms and shapes to create further contexts and being then guided by those contexts to orchestrate the coherent morphologies and functions of the entire individual. A fundamental merit of Burr was not only his pioneering work, but his ability to bring science at a subtle line where science itself should find the courage to accompany the scientist to the unrestrainable need of merging with other disciplines, like Arts, Philosophy and Religion, in the effort of accepting other view points to explore the mystery of Life and Universe”. 4. Additionally, I would like to congratulate the authors for the editorial and say that I was left with a doubt: can the advent of “omic” technologies contribute in any way to the understanding of the morphogenetic code in the light of chemical signaling and physical energies?

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**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** South Korea

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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In the manuscript for the editorial, the authors demonstrated the most recent evidences of the morphogenetic code for cellular electric fields, electromagnetic and light radiation, as well as nano-mechanical oscillations. In the paper, there were divided into “three courses” about related studies including evidence, modern tool and new notion. It is a reasonable suggestion for the cellular regulation of bioelectrical signaling. Therefore, this manuscript might be appropriate for its publication after satisfying following minor concerns. 1. The authors should describe a “three courses” focusing on stem cell regulation (eg. stem cell maintenance, differentiation, survival et al...) for the purpose of the WORLD JOURNAL OF STEM CELLS. 2. It is necessary to mention the role of bioelectricity according to the difference in physical energy. 3. Core tip should be written not to exceed 100 words. 4. In the submission guide for editorial, “Citing more than five references in a single citation, even when separated by a hyphen, should be avoided” is mentioned. Please follow the rules and adjust the citation including the INTRODUCTION section (citation [2-9]).