

COMMENTARY

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Commentary: FSH and various forms of FSH receptors: distribution and their functions in gonads and extra-gonadal tissues

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FSH is central to reproduction and regulates ovarian production of steroid hormones which in turn regulate endometrial growth/receptivity/regeneration/remodeling. However, these well defined boundaries of the 70s and 80s are now blurring with steroid hormone receptors being reported in the hematopoietic system and FSHR on several extragonadal sites including cancers in multiple tissues [1], and in the endometrium, myometrium, cervix, and placental [2] and hematopoietic system [3, 4]. Female patients being subjected to FSH therapy for stimulating their ovaries show effective mobilization of stem cells in their peripheral blood [5].

Bhartiya's group reported that FSH treatment enhanced hematopoiesis in the bone marrow by almost 72h in 5-FU treated mice [6]. How does FSH exerts its pleiotropic effects? What is the significance of FSHR3 and how significant it is functionally compared to the canonical FSHR1? Ovarian cancer cells do not exhibit cAMP signaling upon treatment with FSH [7].

Ratajczak and Bhartiya groups have published data to show FSHR expression on very-small embryonic-like stem cells (VSCLs) [4, 8] in reproductive tissues and surprisingly FSH treatment upregulated alternately spliced FSHR3 more significantly compared to the canonical FSHR1. Similarly, Sullivan et al. [9] reported FSHR3 to

be the predominant isoform in sheep ovaries. It did not come as a surprise to see a special issue focused on different facets of FSH/FSHR biology published in 2020 wherein experts raised several concerns regarding extragonadal expression of FSHR [10]. They doubt the results and think these to be due to technical shortfalls [11].

Currently held belief written in golden letters in reproductive biology textbooks is the fact that initial follicle growth is gonadotropin independent and FSHR are not expressed on primordial follicles and that FSH acts on granulosa cells in the ovaries and Sertoli cells in the testes [12].

Bhartiya's group points this as a 'misconcept' and points out this discrepancy has surfaced because of initial studies used only FSHR1 specific primers to detect FSHR in various types of follicles which will not detect FSHR3.

We are pleased to publish two review articles in the Journal of Ovarian Research on FSH/FSHR biology authored by Bhartiya's group from ICMR-National Institute for Research in Reproductive Health, Mumbai, INDIA. The group has attempted to provide explanation to various concerns raised by Rahman's group [11]. Since these articles question several basic existing paradigms in the field of reproductive biology including ovarian biology, further discussions and comments will be welcome and we will be pleased to publish in JOVR.

Acknowledgements

Not applicable.

Authors' contributions

Both SSK and MZR reviewed the both the review articles published by Dr. Bhartiya in the Journal of Ovarian Research and wrote the commentary. The author(s) read and approved the final manuscript.

This comment refers to the article available at <https://doi.org/10.1186/s13048-021-00880-3>.

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Funding

This work was supported by NIH grant T32 HL134644 to SSK and MZR.

Competing interests

The authors declare that they have no competing interests.

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Published online: 30 October 2021

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Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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