Acta Scientific Neurology (ISSN: 2582-1121)

Volume 6 Issue 3 March 2023

Perspective

Perspectives in Pituitary Stem Cells: Their Biologic Properties in Pituitary Diseases, Latest Approaches, and Future Aspects

Duru Baykal, Ömer Sönmez and Aydin Sav*

Department of Medical Pathology, School of Medicine, Yeditepe University, Turkey

***Corresponding Author:** Aydin Sav, Department of Medical Pathology, School of Medicine, Yeditepe University, Turkey.

DOI: 10.31080/ASNE.2023.06.0601

Received: January 31, 2023

Published: February 13, 2023

What are the types of pituitary stem cells (PSS)? The pea-sized pituitary gland located at the sella turcica is made up of two main structures: anterior pituitary (adenohypophysis) and posterior pituitary (neurohypophysis) [1]. Adenohypophysis encompasses the stem cell candidates of the gland, which are: folliculostellate cells, follicular cells, marginal zone cells, side population cells, pituitary colony-forming cells, sex-determining region Y (SRY) box 2+ (SOX2+) cells, and glial cell line-derived neurotrophic factor family receptor alpha 2/Prophet of POU domain class 1 transcription factor/Stem cells (GFRa2/Prop1/SCs) [2]. There is compelling evidence on behalf of all of these cell groups being the stem cells (SCs) of the pituitary, but the findings are still controversial, and more research is needed.

Expectations: Treatments involving SCs show promising results. The SC research concerning the pituitary gland is a new development in this area are incredible and worth digging deeper into since pituitary pathologies affect a large portion of the population.

Where are PSS located? Pathological clues on the diseases are obtained by different expressions of pituitary stem cell (PSC) markers. These are primarily located at the lumen of the adenohypophyseal primordium Rathke's pouch and anterior pituitary parenchyma, which is suggestive of the presence of multiple niches. The most widely investigated markers are SOX2, Neuroepithelial stem cell protein (Nestin), stem cell antigen 1 (Sca-1), E-cadherin, S100, Prop1, Octamer-binding transcription factor 4 (Oct4), Bmi1, CD133, Beta-catenin, Paired Box Protein 6 (Pax6), Notch2, Notch3, POU domain, class 1 transcription factor 1 (Pit1), p57, T box transcription factor (TpiT), and Aryl Hydrocarbon Receptor Interacting Protein (AIP). Each of them is expressed in different physiological and pathological conditions, such as embryonal development, cell differentiation, migration, renewal, and tumorigenesis [3,4].

In which processes do PSSs take place? The plasticity of the pituitary gland due to the PSCs has a crucial role in the gland's adaptation process for the requirements of the human body in different periods during life. Hypothalamo-pituitary axis responds to the demands during the neonatal period, puberty, adulthood, and other physiological and pathological processes like lactation, stress, or trauma [5].

Their Roles in neoplastic and non-neoplastic processes? Regardless of the subject, SC research promises many crucial opportunities in medicine. Pituitary-related disorders are interpreted in two different groups; Pituitary tumors and pituitary disorders related to hormonal imbalances. The established factors regarding genetic hypopituitarism are homeobox expressed in ES cells 1 (HESX1), bicoid homeodomain factors (PITX1 and PITX2), LIM homeobox 3 (LHX3), LIM homeobox 4 (LHX4), SOX2 and Pit1 mutation [6].

Molecular network of PSS: The activation of SCs might be crucial for the development and proliferation of tumors. There is a widespread opinion that tumor SCs and SCs are related, although the findings are not conclusive yet [6,7]. The Wingless-related integration site (WNT) signaling promotes the proliferation process of cells, which is regulated by SOX2+ cells [8,9]. SOX2+ cells become activated as the tumor develops. However, it is still unknown whether SCs are the cause of tumors or whether their activation is a response to carcinogenesis [6]. The activation of the senescence-associated pathway (SASP) after mutant cells enter senescence, which results in the production of mitogens, cytokines, and chemokines, is one of the mechanisms implicated in tumor formation, according to recent articles [10]. Mouse model research is used to support the influence of SASP activation. Tumor formation has not been seen in mice with low SASP responses [11]. The Hippo signaling pathway is a key participant in carcinogenesis. Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding

motif (TAZ) were negatively affected by this tumor suppressor Hippo pathway. These essential effectors inhibit apoptosis and encourage proliferation [10]. It has been noted that YAP/TAZ is expressed more prominently in poorly differentiated pituitary tumors, such as null-cell adenomas, adamantinomatous craniopharyngiomas (ACPs), and papillary craniopharyngiomas (PCPs). These effectors, in contrast, are either not expressed at all or are just weakly expressed in different adenomas. Therefore, using this route as a target for cancer treatment needs to be evaluated [12]. As was already mentioned, kinases are crucial in the development of pathologies. In one study, one of the basic kinases, Large tumor suppressor kinase 1 (LATS1), was removed, and pituitary abnormalities, such as pituitary hyperplasia and hormone insufficiency, were seen as another significant illustration of the significance of kinases [13].

Recent advancement in PSS research: The clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9 (CRISPR/Cas9) genome editing method and organoid formation are the two key tools for understanding PSC biology. The ethical aspect of collecting the material from fetuses has been a controversial matter [14]. Organoids are three-dimension entities that are produced from the SC of tissue under specific circumstances. The primary issue with organoids is the inability to produce certain hormones, even though this exciting technology promises a lot of development [15,16]. Human-induced pluripotent cells are used to create a working hypothalamus-pituitary axis that appears to be quite similar to the one in humans [17]. The CRISPR/Cas9 genome editing approach appears to be the current best way. This method gives us a great chance to identify the genes responsible for diseases, which may lead to the discovery of new treatment modalities. It has previously been indicated that improvements in several hormone deficits were observed following CRISPR/Cas9 gene regulation on the orthodenticle homeobox 2 (OTX2) gene, which is a gene responsible for congenital pituitary hypoplasia [18].

Conclusion: It is significant to note that with the advancements in pituitary stem cell research, transplanting stem cells and being able to cure numerous pituitary pathologies may be possible in the future.

Bibliography

1. Alatzoglou KS., *et al*. "Development of the Pituitary Gland". *Comprehensive Physiology* 10.2 (2020): 389-413.

2. Vankelecom H. "Pituitary stem cells drop their mask". *Current Stem Cell Research and Therapy* 7.1 (2012): 36-71.

3. Yoshida S., *et al*. "Characterization of murine pituitary-derived cell lines Tpit/F1, Tpit/E and TtT/GF". *Journal of Reproduction and Development* 60.4 (2014): 295-303.

4. Sav A. Pituitary Stem/Progenitor Cells: Their Enigmatic Roles in Embryogenesis and Pituitary Neoplasia - A Review Article. J Neurol Disord (2014) 2: 146. doi:10.4172/2329-6895.1000146.

5. Laporte E., *et al*. "Pituitary Remodeling Throughout Life: Are Resident Stem Cells Involved?" *Frontiers in Endocrinology (Lausanne)* 11 (2021): 604519.

6. Nys C and Vankelecom H. "Pituitary disease and recovery: How are stem cells involved?" *Molecular and Cellular Endocrinology* 525 (2021): 111176.

7. Vankelecom H. "Pituitary Stem Cells: Quest for Hidden Functions. 2016 Jul 27. In: Pfaff D, Christen Y, editors". *Stem Cells in Neuroendocrinology*. Cham (CH): Springer (2016).

8. Le Tissier PR., *et al*. "A New Perspective on Regulation of Pituitary Plasticity: The Network of SOX2-Positive Cells May Coordinate Responses to Challenge". *Endocrinology* 163.8 (2022): bqac089.

9. Russell JP., *et al*. "Pituitary stem cells produce paracrine WNT signals to control the expansion of their descendant progenitor cells". *Elife* 10 (2021): e59142.

10. Russell JP., *et al*. "Basic Research Advances on Pituitary Stem Cell Function and Regulation". *Neuroendocrinology* 107.2 (2018): 196-203.

11. Gonzalez-Meljem JM., *et al*. "Stem cell senescence drives age-attenuated induction of pituitary tumours in mouse models of paediatric craniopharyngioma". *Nature Communications* 8.1 (2017): 1819.

12. Xekouki P., *et al*. "Non-secreting pituitary tumours characterised by enhanced expression of YAP/TAZ". *Endocrine-Related Cancer* 26.1 (2019): 215-225.

13. St John MA., *et al*. "Mice deficient of Lats1 develop soft-tissue sarcomas, ovarian tumours and pituitary dysfunction". *Nature Genetics* 21.2 (1999): 182-186.

14. Lara-Velazquez M., *et al*. "Stem cell therapy and its potential role in pituitary disorders". *Current Opinion in Endocrinology, Diabetes and Obesity* 24.4 (2017): 292-300.

15. Cox B., *et al*. "Organoids from pituitary as a novel research model toward pituitary stem cell exploration". *Journal of Endocrinology* 240.2 (2019): 287-308.

16. Camilletti MA., *et al*. "From Pituitary Stem Cell Differentiation to Regenerative Medicine". *Frontiers in Endocrinology (Lausanne)* 11 (2021): 614999.

17. Kasai T., *et al*. "Hypothalamic Contribution to Pituitary Functions Is Recapitulated *In vitro* Using 3D-Cultured Human iPS Cells". *Cell Reports* 30.1 (2020): 18-24. e5.

18. Matsumoto R., *et al*. "Congenital pituitary hypoplasia model demonstrates hypothalamic OTX2 regulation of pituitary progenitor cells". *Journal of Clinical Investigation* 130.2 (2020): 641-654.