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Letter to the Editor

Transforming growth factor β (TGF-β): is there a different role with regard to distinct phenotypes of endometriosis?

Dear Editor,

we recently read an interesting original research entitled "The involvement of multifunctional TGF-β and related cytokines in pathogenesis of endometriosis" by Sikora et al. published in your journal [1]. In this manuscript, the authors investigated the role of transforming growth factor β (TGF-β) in the pathogenesis of endometriosis, evaluating peritoneal and serum levels of this cytokine by ELISA in women with and without endometriosis. Notably, Sikora et al. found higher levels of TGF-β1, TGF-β2, TGF-β3 in both samples of women with endometriosis (n = 51) compared to control (n = 15).

Overall, it has been reported in literature that TGF-β superfamily controls several cellular functions, including cell growth, cell proliferation, cell differentiation and apoptosis; this group of proteins is expressed and finely regulated in eutopic endometrium during the menstrual cycle, and it contributes to endometrial cell proliferation and matrix remodeling [2].

With specific regard to endometriosis, high serum and peritoneal levels of TGF-β may be responsible for inducing formation of fibrotic tissue that is widely documented in endometriotic lesions (in particular in nodules of deep infiltrating endometriosis) and that may also lead to the development of pelvic adhesions [3]. Additionally, it has been demonstrated that TGF-β is able to modulate the activity of T regulator lymphocytes, whose activity and role are still controversial regarding to the pathogenesis of endometriosis [4].

Overall, it has been thoroughly demonstrated in literature that alterations of immune response (among which, intrinsic alterations compromising the abnormal production of cytokines) are likely to be involved in the pathogenesis and the establishment of endometriotic lesions [5]; for this reason, we found this original research interesting and innovative.

Despite of strong congratulating with Sikora et al., we would report an important methodologic concern on this study. The authors correctly reported the mean disease severity of patients affected according to standardized revised American Society for Reproductive Medicine (rASRM) classification. In our opinion, they should report if peritoneal nodules, ovarian endometriomas or nodules of deep infiltrating endometriosis as well as the combination of these were present in the women included in the study. In fact, as deeply demonstrated in the last years, these three phenotypes of endometriosis present peculiar clinical and molecular characteristics, and thus, they may differ from each other by numerous pathogenetic aspects [5]; for example, we deem that a different expression of TGF-β and other molecules involved in matrix remodeling may be distinct between patients presenting peritoneal implants and those presenting deep infiltrating endometriosis. In particular, nodules of this latter phenotype are known to be characterized by a larger content of fibrotic tissue and vessels [6].

In summary, the data of Sikora et al. [1] demonstrate that TGF-β may contribute to the pathogenesis and development of endometriosis. Understanding the complex mechanisms of this chronic hormonal disease has paved the way to the improvement of the currently existing therapeutic options and the investigation of possible alternative targets [7]. In the near future, it would be of interest targeting this molecule for treating cell culture of endometriosis and animal models with experimental induced-disease. Anyway, at the moment, specific inhibitors of this cytokine have never been tested in this setting [8].

Conflict of interests

The Authors declare that there is no conflict of interest.

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References

[1] J. Sikora, M. Smycz-Kubanska, A. Mielczarek-Palacz, I. Bednarek, Z. Kondera-Anasz, The involvement of multifunctional TGF-beta and related cytokines in pathogenesis of endometriosis, Immunol. Lett. 201 (2018) 31–37.
[2] R.L. Jones, C. Stoikos, J.K. Findlay, L.A. Salamonsen, TGF-beta superfamily expression and actions in the endometrium and placenta, Reproduction 132 (2) (2006) 217–232.
[3] C. Dela Cruz, F.M. Reis, The role of TGFbeta superfamily members in the pathophysiology of endometriosis, Gynecol. Endocrinol. 31 (7) (2015) 511–515.
[4] S. Saito, A. Nakashima, M. Ito, T. Shima, Clinical implication of recent advances in our understanding of IL-17 and reproductive immunology, Expert Rev. Clin. Immunol. 7 (5) (2011) 649–657.
[5] P. Vercellini, P. Vigano, E. Somigliana, L. Fedele, Endometriosis: pathogenesis and treatment, Nat. Rev. Endocrinol. 10 (5) (2014) 261–275.
[6] C. Tosti, S. Pinzauti, P. Santulli, C. Chapron, F. Petraglia, Pathogenetic mechanisms of deep infiltrating endometriosis, Reprod. Sci. 22 (9) (2015) 1053–1059.
[7] S. Ferrero, G. Evangelisti, F. Barra, Current and emerging treatment options for endometriosis, Expert Opin. Pharmacother. 19 (10) (2018) 1109–1125.
[8] F. Barra, C. Scala, V. Mais, S. Guerriero, S. Ferrero, Investigational drugs for the treatment of endometriosis, an update on recent developments, Expert Opin. Investig. Drugs 27 (5) (2018) 445–458.

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