

REPLY



We thank the authors for acknowledging the importance of our systematic review about the use of regenerative medicine as a possible treatment for fecal incontinence¹ and for the very relevant comments related to our work.

Indeed, the field of regenerative medicine is still evolving, and the mechanisms through which regeneration can be promoted are still being unraveled. The alternative paradigm about muscle tissue regeneration that is proposed by the authors might be valid; however, we think that it is just one of many other possibilities and that the readers should be aware of this.

Stem cells have the amazing property of being able to differentiate into other cell types. But tissue regeneration is a very dynamic process, and we know now that this property of stem cells, alone, is not enough. The entire microenvironment of the tissue has to be regenerated; the stem-cell niche microenvironment can promote or inhibit tissue regeneration. Autocrine, paracrine, and juxtacrine signals can all have an effect on stem-cell responses. Changes in the stiffness, pH, and even oxygen content within the microenvironment have all been shown to stir stem-cell fates into different directions.

The field of stem-cell research is expanding rapidly, and our understanding of these (and other) factors in tissue development and regeneration is growing as new technologies emerge. To have a better idea of the complexity of the situation and where the field is heading, we would like to refer the reader to a recent review by Tewary M et al.²

One must also be aware that while the exact mechanisms behind tissue regeneration by stem cells remain unclear, functional results in human trials are promising, as described in our review.³ Even though clinical studies do not clarify cellular mechanisms, they demonstrate the effectiveness of the treatment and therefore the relevance for clinical practice.

We believe that this link between biomedical research and clinical practice is crucial to make new technologies transferable. Because we understand the rules/factors that regulate stem-cell fate choices, we would be able to design better and more translational treatments. Hopefully in the not so far future. ■

Wiep R. De Ligny, BSc
Department of Obstetrics and Gynecology
Radboud University Medical Center
Nijmegen, The Netherlands
Wiep.deLigny@radboudumc.nl

Manon H. Kerkhof, MD, PhD
Department of Gynecology and Reconstructive Pelvic Surgery
Curilion Women's Health Clinic
Haarlem, The Netherlands

Alejandra M. Ruiz-Zapata, MSc, PhD
Departments of Obstetrics and Gynecology and Urology
Radboud Institute of Molecular Life Sciences
Radboud University Medical Center
Nijmegen, The Netherlands

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