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Cellular senescence in usual type uterine leiomyoma

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Reply to the Editor:

We are grateful for the comments from Markowski et al regarding our recent publication on cellular senescence in uterine leiomyoma (1). Based on their recent study conducted in 22 leiomyomas by qRT-PCR (2), Markowski et al pointed out that 1) large leiomyomas had significantly high β -galactosidase expression; 2) there was no difference between β -galactosidase and Ki-67 expression. These two findings were different from those in our recent study published in this journal (1). The differences between these two studies are interesting and related to the question of how senescence happens in leiomyomas.

Markowski et al proposed that senescence in leiomyomas can be the results in balance of leiomyoma growth and oncogene stress through regulating HMGA2-P53-CDKN1A axis (2). We like this idea of oncogene induced senescence in leiomyomas and this was supported in HMGA2 positive tumors, but was unclear in HMGA2 negative tumor population (the later accounting for about 70% of leiomyoma population). In addition, the role of aging-related senescence in leiomyoma maybe equally important (3). For examples, loss of telomere was found to be common in leiomyomas (4), the rate of senescence was higher in older women and there is no difference in the level of senescence between HMGA2 positive and HMGA2 negative tumors (1).

In terms of tumor size and senescence, we have two comments. First, although we found a trend of high level of senescence in smaller tumors and low senescence in larger ones, the findings were statistically insignificant ($p>0.05$) due to large standard errors (1). Second, sampling in different regions of large tumors may be impact the results due to possibly regional effects on gene expression (5). We collected tumor sections of all large tumors from the region next to the peripheral zone, where higher rates of cell proliferation and ER and PR expression than central zone were noted (5). We assume that the selection of tissue samples may affect the results.

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Ki-67 is a cell proliferative marker that is highly expressed in proliferative cells (G1 to M). Immunohistochemistry stain for Ki-67 is a very sensitive method which can detect a low level of Ki-67 positive cells, such as usual type leiomyomas with Ki-67 index of 1-5%. We are not certain whether Ki-67 expression detected by RT-PCR and immunohistochemical stain can be compared if tumors have low levels of Ki-67, particular at individual cell level.

Acknowledgments

We acknowledge the contribution of the study by Markowski et al in this subject and the role of cellular senescence in relation to leiomyoma growth deserves further investigations.

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