OLYMPUS

THIS IS NOT **BEER.**

This is an ethanol dewetting pattern on a glass-air interface captured with a 10X X Line objective.

Image: © Karl Gaff

Breaking barriers in optical performance.

See the truth
with Olympus X Line

Scan the code to discover more.

X LINE

Contact your Olympus sales representative or visit **www.olympus-lifescience.com/307-xline** to learn more.

Table 1. Experimental data analysis

	Number	H-caldesmon expression	
		Positive	Negative
Normal ovarian granulosa cells	10	0	10
Adult granulosa cell tumours	22	20	2
Normal ovarian theca cells	10	10	0
Fibrothecomas	31	31	0

pathological diagnosis, H-caldesmon is considered at present to be a marker of smooth muscle cells and related tumours. Although it was found that H-caldesmon was involved in the formation of tumour vasculature, there are few studies concerning caldesmon expression in other tumours.[4,5]

The results of our present study demonstrate that H-caldesmon, though previously considered to be a specific marker for smooth muscle, is also a positive marker for ovarian adult granulosa cell tumours and fibrothecoma. Other studies have shown that desmin, which is an intermediate filament protein expressed in smooth muscle, skeletal muscle and cardiac muscle cells, could be expressed in some sex cord-stromal tumours.[6,7] Combined with our findings, these sex cord-stromal tumours, including adult granulosa cell tumours and fibrothecoma, might have myogenic differentiation characteristics.

At present, the pathogenesis of granulosa cell tumour and fibrothecoma is not clear. Some studies have found that thecoma originates from the ovarian medulla, and mutant *FOXL2* of granulosa cells is a potential driver in the pathogenesis of adult granulosa cell tumours.[8,9] Another interesting finding of our study is that H-caldesmon-positive signals are localised on the cell membrane in adult granulosa cell tumour and fibrothecoma. The probable molecular mechanisms involved in tumorigenesis and progression remain to be studied.

Acknowledgements

This project was funded by the Natural Science Foundation of Shandong Province, China (Grant no. ZR2015HQ013).

Competing interests

The authors declare that they have no conflicts of interest.

Author contributions

All authors contributed equally to the manuscript.

Guohua Yu
Guimei Qu

Department of Pathology, Affiliated Yantai Yuhuangding Hospital, Qingdao University, Yantai, China

1. Sobieszek A. Helical model of smooth muscle myosin filament and the ribbons made of caldesmon: history revisited. *Eur. Biophys. J.* 2016; **45**; 861–867.
2. Frid MG, Shekhonin BV, Koteliansky VE, Glukhova MA. Phenotypic changes of human smooth muscle cells during development: late expression of heavy caldesmon and calponin. *Dev. Biol.* 1992; **153**; 185–193.
3. Ueki N, Sobue K, Kanda K, Hada T, Higashino K. Expression of high and low molecular weight caldesmons during phenotypic modulation of smooth muscle cells. *Proc. Natl Acad. Sci. USA* 1987; **84**; 9049–9053.
4. Zheng PP, van der Weiden M, Kros JM. Differential expression of Hela-type caldesmon in tumour neovascularization: a new marker of angiogenic endothelial cells. *J. Pathol.* 2005; **205**; 408–414.
5. Comin CE, Dini S, Novelli L, Santi R, Asirelli G, Messerini L. h-Caldesmon, a useful positive marker in the diagnosis of pleural malignant mesothelioma, epithelioid type. *Am. J. Surg. Pathol.* 2006; **30**; 463–469.
6. Zekioglu O, Ozdemir N, Terek C, Ozsaran A, Dikmen Y. Clinicopathological and immunohistochemical analysis of sclerosing stromal tumours of the ovary. *Arch. Gynecol. Obstet.* 2010; **282**; 671–676.
7. Santini D, Ceccarelli C, Leone O *et al.* Smooth muscle differentiation in normal human ovaries, ovarian stromal hyperplasia and ovarian granulosa-stromal cells tumors. *Mod. Pathol.* 1995; **8**; 25–30.
8. Nocito AL, Sarancone S, Bacchi C, Tellez T. Ovarian thecoma: clinicopathological analysis of 50 cases. *Ann. Diagn. Pathol.* 2008; **12**; 12–16.
9. Shah SP, Köbel M, Senz J *et al.* Mutation of FOXL2 in granulosa-cell tumors of the ovary. *N. Engl. J. Med.* 2009; **360**; 2719–2729.

In reply to: Lawless *et al.* Stalk versus base invasion in pT1 papillary cancers of the bladder: improved substaging system predicting the risk of progression

DOI: 10.1111/his.13374

Sir: We read with interest the article by Lawless *et al.* that was very recently published in *Histopathology*.[1]

The authors divided tumours into base-focal and base-extensive cases, relying on the criterion of whether or not there was a single focus <1 mm in size (i.e. field diameter of a 20× objective lens), thus confirming the threshold adopted in our study on pT1 bladder urothelial carcinoma,[2] kindly quoted by Lawless *et al.* This size enabled patient stratification in terms of risk of progression in both studies[1,2] and in others too,[3] underscoring the value of T1 substaging that has recently emerged from a broad meta-analysis.[4] Lawless *et al.* adopted very stringent selection criteria, thus reinforcing the clinical benefit of this threshold (86% of tumours >1 mm in sizeprogressed during the follow-up, as opposed to 33% of those <1 mm in size), despite their relatively small number of cases. Consequently, we are not sceptical about the possibility of an objective measurement gaining 'wide acceptance'.[1] The T1 m/e subdivision of 0.5 mm proposed by van Rhijn *et al.*[5] gained acceptance too, although we judge this depth of invasion to be probably excessively shallow, because of the uneven thickness of the lamina propria, which reaches up to 3 mm in the cupola.[6] Moreover, a 1-mm cut-off is technically practical (approximately the field diameter of a 20× objective), and with this threshold the few invasive low-grade carcinomas are placed in the focally (<1 mm) invasive category, as documented by Chang *et al.*[3]

Almost all T1 cases could be substaged with a quantitative approach, which is practical and reproducible, as the authors recognised.[1] The bladder anatomy offers no stable, micrometrically fixed anatomical parameters,[7] owing to the variability of the muscularis mucosae and vascular plexus, and this prevents widespread use of the T1a/b subdivision based on infiltration of the anatomical structures.[8] Regarding the interesting suggestion that a 'stalk invasion only' category be introduced, this could be a further step forwards, although fragmentation and loss of orientation in the transurethral resection (TUR) might hinder this approach: it would sometimes be difficult to separate such a category from the 'focal base invasion' category, particularly in small tumours. Finally, we believe that the role of early re-TUR should not be underestimated.[9] This second-look procedure is not used routinely (in 8% of patients in the Lawless *et al.* study; in 79% in our study), but, in cases of T1 carcinoma in early re-TUR, the size of the residual foci of infiltration should be added to the original TUR for a complete assessment and final substaging.[2,6]

Conflicts of interest

The authors have no conflicts of interest to disclose.

Carlo Patriarca[1]
Rodolfo Hurle[2]
Piergiuseppe Colombo[3]
Maurizio Colecchia[4]
Massimo Freschi[5]
Giario Conti[6]
Guido Petracco[1]
Renzo Colombo[7]

[1]*Department of Pathology, Azienda Ospedaliera Sant'Anna, Como,* [2]*Department of Urology,* [3]*Department of Pathology, Humanitas Research Hospital, Rozzano (MI),* [4]*Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori,* [5]*Department of Pathology, Ospedale San Raffaele, Milan,* [6]*Department of Urology, Azienda Ospedaliera Sant'Anna, Como, and* [7]*Department of Urology, Ospedale San Raffaele, Milan, Italy*

1. Lawless M, Gulati R, Tretiakova M. Stalk versus base invasion in pT1 papillary cancers of the bladder: improved substaging system predicting the risk of progression. *Histopathology* 2017; **71**; 406–414.
2. Patriarca C, Hurle R, Moschini M *et al.* Usefulness of pT1 substaging in papillary urothelial bladder carcinoma. *Diagn. Pathol.* 2016; **11**; 6. https://doi.org/10.1186/s13000-016-0466-6
3. Chang WC, Chang YH, Pan CC. Prognostic significance in substaging of T1 urinary bladder urothelial carcinoma on transurethral resection. *Am. J. Surg. Pathol.* 2012; **36**; 454–461.
4. Martin-Doyle W, Leow JJ, Orsola A, Chang SL, Bellmunt J. Improving selection criteria for early cystectomy in high-grade t1 bladder cancer: a meta-analysis of 15,215 patients. *J. Clin. Oncol.* 2015; **33**; 643–650.
5. van Rhijn BW, van der Kwast TH, Alkhateeb SS *et al.* A new and highly prognostic system to discern T1 bladder cancer substage. *Eur. Urol.* 2012; **61**; 378–384.
6. Paner GP, Montironi R, Amin MB. Challenges in pathologic staging of bladder cancer: proposals for fresh approaches of assessing pathologic stage in light of recent studies and observations pertaining to bladder histoanatomic variances. *Adv. Anat. Pathol.* 2017; **24**; 113–127.
7. Paner GP, Ro JY, Wojcik EM, Venkataraman G, Datta MW, Amin MB. Further characterization of the muscle layers and lamina propria of the urinary bladder by systematic histologic mapping: implications for pathologic staging of invasive urothelial carcinoma. *Am. J. Surg. Pathol.* 2007; **31**; 1420–1429.
8. Angulo JC, Lopez JI. The importance of the depth of invasion in stage T1 bladder carcinoma: a prospective cohort study. *J. Urol.* 1997; **157**; 800–803; discussion 804.
9. Colombo R, Hurle R, Moschini M *et al.* Feasibility and clinical roles of different substaging systems at first and second transurethral resection in patients with T1 high-grade bladder cancer. *Eur. Urol. Focus* 2016; **pii**; S2405–4569(16)30064-5. https://doi.org/10.1016/j.euf.2016.06.004. [Epub ahead of print]