**ABSTRACT**

**Background:** Octamer-binding transcription factor 4A (OCT4A) is essential for cell pluripotency and reprogramming both in humans and mice. To date, however, the function of human OCT4 in somatic and/or tumour tissues is largely unknown.

**Methods:** RT-PCR was used to identify full-length splice forms of *OCT4* transcripts in normal and cancer cells. A FLAG-tagged OCT4 genomic transgene was used to identify OCT4-positive cancer cells. A potential role for OCT4 in somatic cancer cells was examined by cell ablation of OCT4-positive cells using promoter-driven diphtheria toxin A. *OCT4* and secreted phosphoprotein 1 (*SPP1*) transcripts in early-stage lung adenocarcinoma tumours were analysed and compared with pathohistological features.

**Results:** The results show that, unlike in murine cells, *OCT4A* and *OCT4B* variants are transcribed in both human cancer cells and in adult tissues such as lung, kidney, uterus, breast, and eye. We found that *OCT4A* and *SPP1C* are co-expressed in highly aggressive human breast, endometrial, and lung adenocarcinoma cell lines, but not in mesothelial tumour cell lines. Ablation of OCT4-positive cells in lung adenocarcinoma cells significantly decreased cell migration and *SPP1C* mRNA levels. The OCT4A/SPP1C axis was found in primary, early-stage, lung adenocarcinoma tumours.

**Conclusions:** Co-expression of OCT4 and SPP1 may correlate with cancer aggressiveness, and the OCT4A/SPP1C axis may help identify early-stage high-risk patients with lung adenocarcinoma. Contrary to the case in mice, our data strongly suggest a critical role for OCT4A and SPP1C in the development and progression of human epithelial cancers.