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### **Isolation of tumour stem-like cells from benign tumours.**

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**BACKGROUND:** Cancerous stem-like cells (CSCs) have been implicated as cancer-initiating cells in a range of malignant tumours. Diverse genetic programs regulate CSC behaviours, and CSCs from glioblastoma patients are qualitatively distinct from each other. The intrinsic connection between the presence of CSCs and malignancy is unclear. We set out to test whether tumour stem-like cells can be identified from benign tumours.

**METHODS:** Tumour sphere cultures were derived from hormone-positive and -negative pituitary adenomas. Characterisation of tumour stem-like cells in vitro was performed using self-renewal assays, stem cell-associated marker expression analysis, differentiation, and stimulated hormone production assays. The tumour-initiating capability of these tumour stem-like cells was tested in serial brain tumour transplantation experiments using SCID mice. **RESULTS:** In this study, we isolated sphere-forming, self-renewable, and multipotent stem-like cells from pituitary adenomas, which are benign tumours. We found that pituitary adenoma stem-like cells (PASCs), compared with their differentiated daughter cells, expressed increased levels of stem cell-associated gene products, antiapoptotic proteins, and pituitary progenitor cell markers. Similar to CSCs isolated from glioblastomas, PASCs are more resistant to chemotherapeutics than their differentiated daughter cells. Furthermore, differentiated PASCs responded to stimulation with hypothalamic hormones and produced corresponding pituitary hormones that are reflective of the phenotypes of the primary pituitary tumours. Finally, we demonstrated that PASCs are pituitary tumour-initiating cells in serial transplantation animal experiments. **CONCLUSION:** This study for the first time indicates that stem-like cells are present in benign tumours. The conclusions from this study may have applications to understanding pituitary tumour biology and therapies, as well as implications for the notion of tumour-initiating cells in general.

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