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"Dysregulation of prolactin cell proliferation in health and disease"

The aim of this study is to understand how prolactin (PRL) cell proliferation and apoptosis is regulated normally, and dysregulated in adenoma formation. Little is known about mechanisms generating pituitary tumours, but as p8 has been recently implicated in prolactinomas. We will test whether p8 is necessary or sufficient for normal PRL cell plasticity in lactation/weaning and for generating or maintaining prolactinomas.We recently showed dopamine transporter (DAT) expression in PRL cells during weaning. We will test whether DAT regulates PRL cell survival, and if its suppression causes expanded PRL cell populations to persist and/or proliferate in adenomas. In an *ex vivo/in vivo* approach, pituitary cells will be isolated from normal or transgenic mice, transduced *in vitro* to alter p8 or DAT expression, and then translanted into recipient pituitaries. In an *in vivo* approach, pituitaries will be directly transduced *in situ* by microinjection of pseudotyped ALSV lentiviruses, into transgenic virus-receptor mice, achieving specific cell targeting. Fluorescent markers distinguish transplant from host cell types and between transduced, and untransduced cells. Mice will be examined for growth, pituitary morphology, PRL production, PRL cell proliferation and apoptosis, and 3D. This project will increase our basic understanding of pituitary cell proliferation and apoptosis under physiological conditions, and offer new insights into the dysregulation of PRL cells leading to prolactinomas, of clinical interest.