Hormonal aspects of antler growth regulation

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Abstract

Deer antlers are the only mammalian organ that completely regenerates and therefore they became an object of rising interest as a potential model for bone growth and development. In recent years, it has been confirmed that annual regeneration of the antler is initiated from the stem cell niche localised in the pedicle periosteum. Antlers grow to the length at the tip. Only a little is known about endocrine stimulation of antler growth and some discrepancy has arisen between *in vivo* and *in vitro* studies over the decades. As the secondary sexual character, the antler cycle timing and growth are linked to seasonal levels of testosterone. Since the levels are at their minimum during the antler growth phase, according to many mainly *in vitro* studies, insulin-like growth factor-1 (IGF-1) tends to be accepted as the "antler stimulating hormone".

Since the conclusion about the role of IGF-1 was contradictory to previous opinions and also in contrast with our own experience, we aimed to verify the role of IGF-1 *in vitro*. Our experiments were based on existing *in vivo* studies demonstrating the importance of testosterone, even in its low levels, and on the hypothesis that testosterone should be the "antler stimulating hormone". We performed *in vitro* experiments on cells derived from the growing antler tips of the red deer (*Cervus elaphus*) at various antler growth stages. Within *in vitro* cultivations we studied the effects of different factors such as antler sampling day, male individuality, passaging, concentration of foetal calf serum (FCS) and length of the experiment on the intensity of the antler cell proliferation. We found that all these factors not only significantly influenced the cell proliferation, but depending on these factors the intensity of proliferative response of cells from different individuals or under hormonal treatments was significantly changed. Next we studied the effects of various hormonal treatments as testosterone, IGF-1 and estradiol, as well as effect of antisteroids Cyproterone acetate, Flutamide and ICI 182,780, on antler cell proliferation. None of the treatments caused consistent proliferative response. However, testosterone and, partially, estradiol stimulated the proliferation in several cases. On the other hand, the stimulating effect of IGF-1 was not confirmed in our experiments, as IGF-1 either did not affect the antler cell proliferation or even inhibited it in some cases. We isolated STRO-1 positive mesenchymal stem cells from the mixed antler cell cultures but we could not perform hormonal experiments with the cells, as we were unable to obtain sufficient amounts of the positive cells for our experiments. Despite this, our results suggest that the sex steroids are mitogenic for antler cells *in vitro* and might play an important role in the stimulation of antler growth.

Our results are in accordance with many physiological and behavioural studies. They support the inevitable role of testosterone in the antler re-growth phase and suggest that the primary cultures may better represent the *in vivo* conditions and processes that occur in regenerating antlers.

Keywords: red deer, Cervus elaphus, antler growth, antler cells, testosterone, IGF-1