REDUCED LEVELS OF ADRENAL STEROIDOGENIC ACUTE REGULATORY PROTEIN (StAR) DO NOT LIMIT STEROIDOGENESIS IN ALDOSTERONE PRODUCING CELLS

Songül Süren Castillo
Istanbul University, Faculty of Science, Department of Biology, Zoology Section, 34459-Verneciler, Istanbul, Turkey. E-mail: songulsuren@yahoo.com

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ABSTRACT: The insulin-like growth factors (IGFs) actions are thought to be mainly due to the activation of the type I IGF receptor, which is homologous to the insulin receptor (IR) in structure\(^1\). Mature IGF-I and IGF-II are composed of four domains and share extensive sequence and structural similarity. The IGF-II C and D domains confer high-affinity binding to the IR-A and IR-B, whereas the C and D domains of IGF-I do not\(^2\). The sole structural determinant for the differential ability of IGF-I and IGF-II to induce autophosphorylation of specific IR tyrosine residues and activate downstream signalling molecules is the C domain\(^1\). On the basis of this knowledge, frogs (\textit{Rana ridibunda}) were injected with IGF-II C-peptide (2.5 mg/0.2 ml), whereas control animals were injected with Ringer solution (0.2 ml). The adrenal glands were removed at 12 and 24 h after injection and fixed, embedded in paraffin wax and Epon, and examined by immunohistochemistry and transmission electron microscopy to investigate the regulation of frog adrenal steroidogenic cell activity. Sections were stained with hematoxylin and eosin for overall tissue analysis and, in parallel, serotonin and steroidogenic acute regulatory (StAR) protein were localized using the streptavidin–biotin complex technique. At 12 and 24 h after injection of IGF-II C-peptide, a decrease of serotonin immunoreactivity in chromaffin cells (which secrete serotonin) and a decrease of StAR protein immunoreactivity in steroidogenic cells were observed. Electron microscopic observations show an increase in the activity of the steroidogenic cells producing aldosterone. Besides its action on the secretory activity of the adrenal gland, IGF-II C-peptide causes proliferation of steroidogenic cells at 24 h. Therefore, the reduced levels of StAR protein are not a limiting factor of steroidogenesis for aldosterone producing cells. In conclusion, in addition to its direct effect on aldosterone production, a possible indirect effect of IGF-II C-peptide through activation of chromaffin cells in frog adrenal glands may occur. These observations suggest that IGF-II C-peptide may play an important role in the regulation of steroidogenic cell activity.

REFERENCES