Acception of Estrogen and Progestin Receptor Complexes by Hepatocyte Nuclei in Irradiated Female Rats

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Ionizing radiation in doses of 0.5 and 1.0 Gy modifies cytosol estrogen- and progestin-receptor complexes decreasing their acception by hepatocyte nuclei in the liver of γ-irradiated female rats.

Key Words: *γ-irradiation; steroid hormones; receptors; nuclear acception*

Steroid hormones specifically and selectively bind cytoplasmatic receptor proteins in target cells. The resultant steroid-receptor complexes (SRC) after activation are translocated into the nuclei and bind chromatin and DNA. Modulation of SRC interactions with the nucleus can essentially modify the biological action of steroid hormones [3-5] causing postradiation changes in cell functioning [1].

Published reports about SRC interactions with nuclei and chromatin describe experiments with nonfractionated homogenate and crude nuclear fraction without irradiation. We studied the interactions between SRC and nuclei and compared biological activities of SRC isolated from the liver cytosol of irradiated and intact female rats.

MATERIALS AND METHODS

Female Wistar rats aged 6 months were exposed to acute irradiation on an IGUR device (^{137}Cs dose power of 6.2 CGy/min). The animals were decapitated, the liver was removed and homogenized in buffer A (20 mM Tris-HCl, 1.5 mM EDTA, pH 8.2) at 0°C. Homogenates were used for isolation of nuclei and SRC.

Methods for isolation and purification of cell nuclei and SRC binding were described previously [1], DNA was measured as described elsewhere [6]. Labeled steroids [2,4,6,7]-^{3}H-estradiol with activity of 65-85 Ci/mol and [1,2,6,7]-^{3}H-progesterone with activity of 62-80 Ci/mol (Izotop, St. Petersburg) served as the ligands.

The estrogen- and progestin-receptor complexes (ERC and PRC, respectively) were then used for investigating their interactions with liver cell nuclei after a single acute γ-irradiation. The binding of purified SRC from liver cytosol of intact 6-month female rats and liver cell nuclei from intact and γ-irradiated animals was evaluated in incubation media (NaCl) with increasing ionic strength.

Results were statistically processed using Student's *t* test.

RESULTS

Increasing of NaCl concentration to 0.2-0.4 M led to an essential decrease in the number of SRC bound to the nuclei (Fig. 1). Increasing of NaCl concentration above 0.4 M did not notably modify the elution of SRC bound to liver cell nuclei. This is characteristic of all groups of animals. SRC acception by hepatocyte nuclei was the lowest in female rats exposed to a dose of 1.0 Gy. Similar interactions were observed in experiments with purified liver SRC from 6-month-old irradiated females and liver cell nuclei from irradiated and intact animals. Increasing of NaCl concentration above 0.2-0.4 M did not decrease the number of SRC bound to the nuclei, while the minimum SRC binding was observed with the nuclei of irradiated animals.

Interactions of SRC with the nuclei from intact and γ-irradiated animals were studied by incubating

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equal volumes of purified SRC from liver cytosol or uterus of 6-month-old intact rats with the same volumes of hepatocyte nuclei from intact and γ-irradiated female rats on days 3, 10, and 30 after exposure (1.0 and 0.5 Gy). On day 3 after irradiation, hepatocyte nuclei possessed the minimum SRC-acception capacity (Table 1).

Binding of SRC by cell nuclei notably increased 30 days after γ-irradiation in a dose of 1.0 Gy. The capacity of nuclei to acception of SRC in rats exposed to a dose of 0.5 Gy on days 10 and 30 was almost the same as in intact 6-month-old rats.

The same time course was observed in experiments with liver SRC obtained on day 30 after γ-irradiation (Table 1). A different picture was observed in experiments with crude SRC. The acceptor capacity of hepatocyte nuclei essentially decreased in experiments with the cytosol of experimental animals on day 3 after γ-irradiation in a dose of 1.0 Gy, this decrease being most pronounced on days 3 and 10 after irradiation in a dose of 1.0 Gy (Table 1). This was characteristic of both ERC and PRC.

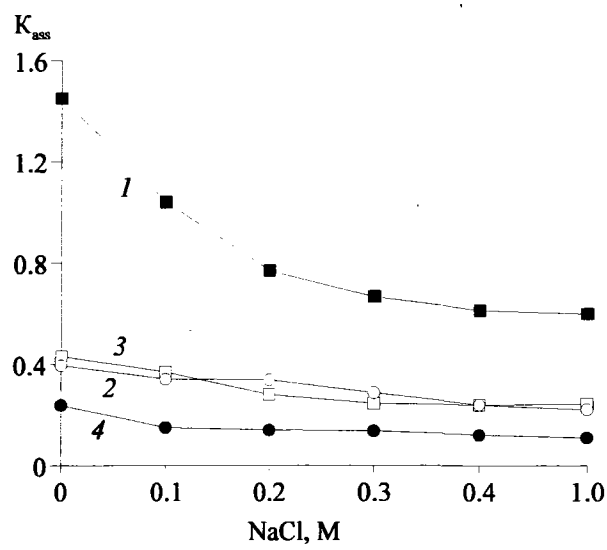

Fig. 1. Binding of purified estrogen- (*1, 2*) and progestin-receptor complexes (*3, 4*) from liver cytosol of intact 6-month rats with hepatocyte nuclei from intact (*1, 3*) and γ-irradiated (*2, 4*) female rats in medium with different NaCl concentrations.

TABLE 1. Acception of SRC (dpm/μg DNA) by Hepatocyte Nuclei from 6-Month-Old Irradiated Female Rats (*M±m*)

Parameter		Control	Time after irradiation, days					
			3		10		30	
			0.5 Gy	1.0 Gy	0.5 Gy	1.0 Gy	0.5 Gy	1.0 Gy
Acception of initial cytosolic SRC from intact rat liver	ERC	12.2±2.6	9.4±2.7	7.2±1.8*	11.4±3.2	8.8±2.5	12.0±2.8	11.6±3.0
	PRC	9.6±1.8	7.4±1.6	6.0±1.2*	8.7±1.7	7.3±1.8	8.4±1.6	8.0±1.7
Acception of cytosolic SRC from irradiated rats	ERC	10.0±2.6	7.9±1.3	5.5±0.8*	9.4±2.1	7.1±1.6	11.1±2.4	10.0±2.2
	PRC	8.2±1.6	6.6±1.0	4.7±0.6*	7.1±1.2	6.6±0.9	6.9±1.3	6.0±0.9
Acception of own SRC	ERC	12.2±2.6	8.1±2.0	6.7±1.7*	10.4±2.6	7.4±2.0*	10.7±2.5	9.8±2.3
	PRC	9.6±1.8	6.1±1.5*	5.6±1.1*	7.4±1.4	6.4±1.4*	8.7±1.7	7.9±1.4

Note. *$p<0.05$ *vs.* the control.

Hence, comparative analysis of SRC interactions with the nuclei from intact and γ-irradiated rats showed decreased acceptor capacity of hepatocyte nuclei in irradiated animals, particularly during the early periods after exposure, and a decreased number of activated SRC in the cytosol of irradiated rats in the immediate periods after exposure. Since steroid hormones act as coordinators of organ and tissue functions in the organism, the observed changed in SRC acception in target cells can serve as the molecular basis for modulation in the organ and tissue response to endocrine factors in irradiated organism.

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