The testosterone contents of the blood and gonads are reliable indices of the hormonal activity of testes in a male body. Testosterone is involved in the formation of the male phenotype and maintenance of the reproductive function in male mammals. The hormone is synthesized by Leydig cells of the testes, its production being controlled by pituitary luteinizing hormone (LH) [1].

Chorionic gonadotropin (CG), which is produced by the placenta during pregnancy, is a functional analog of LH. This is a glycoprotein hormone a molecule of which consists of two noncovalently bound subunits (αCG and βCG). The αCG subunit is identical to the α subunit of LH, follicle-stimulating hormone, and thyrotropic hormone. The βCG subunit is specific for CG; however, it is highly (about 80%) homologous to the β subunit of LH. The CG molecules of humans and many other species are considerably homologous to one another [2].

There are LH/CG receptors (LHCGRs) on the surface of Leydig cells. LHCGR activation leads to testosterone release by Leydig cells via activation of the cAMP pathway, causing an increase in the production of steroidogenesis enzymes [3].

CG is widely used in medicine and agriculture for stimulation of the testicular function. Preparations of CG are prescribed to men with spermatogenesis disorders and deficiency of androgens or gonadotropic hormones of various etiologies [4–8]. CG is used for stimulation of testicular steroidogenesis and spermatogenesis in domestic animals, including cattle, and in breeding fur animals, fish, and amphibians in captivity [9–12].

An individual pharmacological response to a pharmaceutical drug is known to depend on many factors, such as sex, age, concomitant diseases, simultaneously administered drugs, diet, unhealthy behaviors, etc. The genetic potential (hereditary differences in the response to drugs) is another important factor affecting drug efficacy [13]. However, the genetic predisposition to a specific response to individual drugs remains the main, and largely unexplored, problem of pharmacogenetics.

Inbred mouse strains are suitable models for studying genetic differences in the responses to drugs. In particular, the genetic variation of the testicular hormonal responsiveness to the stimulation of the testicular function with CG remains poorly understood. Pharmacological studies using a wide range of inbred mouse strains allows the genetic differences in the effects of drugs to be imitated.

Osadchuk and Svechnikov [14] demonstrated differences between six inbred mouse strains in the testosterone production by unstimulated and CG-stimulated isolated Leydig cells in vitro. However, the results obtained in vitro require further testing in vivo, which would give an idea about the genetic differences in testicular responsiveness to CG under the influence of all regulatory mechanisms of the hypothalamic–pituitary–testicular system.

The purpose of this study was to determine the genetic differences in the hormonal testicular respon-
siveness to in vivo steroidogenesis stimulation with CG in adult male mice of eight inbred strains (A/Sn, CBA/ Lac, CC57Br, C57Bl/6J, DBA/2J, GR, PT, and YT). The hormonal response of the testes to CG was estimated by the testosterone contents of the blood serum and testes as related to the genetic variation of the body and testis weights.

MATERIALS AND METHODS

Animals and experimental procedures. Experiments were performed on 252 three-month-old male mice of the inbred strains A/Sn, CBA/Lac, CC57Br, C57Bl/6J, DBA/2J, GR, PT, and YT. The mice were kept under the standard conditions in the vivarium of the Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences at a constant temperature of 24°C, with an unlimited access to food and water. One-month-old mice were separated by the genotype and the CG administration being the factors showed significant effects of the genotype ($F_{7, 221} = 3.56, p < 0.001$), CG ($F_{7, 221} = 700.84, p < 0.001$), and interaction between the factors ($F_{7, 221} = 2.45, p < 0.05$). Without CG administration, the blood testosterone level was the same in males of all the eight strains; however, CG administration revealed genetic differences (Fig. 1a). The blood testosterone level was the highest in A/Sn mice and the lowest in CBA/Lac mice.

Two-way ANOVA of the testosterone content of the testes (the genotype and the CG administration being the factors) showed significant effects of the genotype ($F_{7, 221} = 23.31, p < 0.001$), CG ($F_{7, 221} = 751.39, p < 0.001$), and interaction between the factors ($F_{7, 221} = 22.56, p < 0.05$). Without CG administration, the testosterone content of the testes was the same in males of all the eight strains; however, CG administration revealed genetic differences (Fig. 1b). The testosterone content of the testes was the highest in PT mice and the lowest in DBA mice.

Under the baseline conditions (without CG administration), the testosterone contents of the blood and testes were significantly correlated with each other ($r = 0.78, p < 0.05$); after CG administration, there was no significant correlation between the testosterone contents of the blood and testes.

Figure 2 shows the testis and body weights in mice of the eight inbred strains. We found differences between strains in the body weight ($F_{7, 245} = 39.78, p < 0.001$) and testis weight ($F_{7, 245} = 114.79, p < 0.001$) (Fig. 2). There was no significant relationship of the testicular responsiveness to CG administration with either the body weight or the testis weight.

DISCUSSION

We have demonstrated genetic variation of the testicular responsiveness to CG, a classical stimulator of the testicular function widely used in medicine and stock breeding. A number of factors could make a substantial contribution to the formation of this genetic variation. Genetic differences in the activities of steroidogenesis enzymes have been established to be one of these factors [15]. Genotype-dependent differences in metabolism of testosterone precursors (pregnenolone and progesterone) have been found to result from hereditary differences in the activities of microsomal enzymes, including 3β-hydroxysteroid dehydrogenase/isomerase, microsomal cytochrome P450, and 17-ketosteroid reductase [15]. The authors have demonstrated that the rate of in vitro testosterone production by Leydig cells of the testes under the conditions...