IMPACT OF RONCOLEUKIN (RIL-2) ON THE LYMPHOCYTE-TRIGGERING ACTIVITY OF MACROPHAGES AFTER TRAUMATIC BRAIN INJURY IN VARIOUSLY AGED RATS

S.N. Shanin¹, N.B. Serebryanaya¹, ², ³, T.A. Filatenkova¹, E.E. Fomicheva¹

¹ Institute of Experimental Medicine, Saint Petersburg, Russia;
² Saint Petersburg State University, Saint Petersburg, Russia;
³ North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia

IL-1β is involved in both brain damage process and the mechanisms of brain regeneration processes. The goal of the present research is to measure the change in the production of lymphocyte-activating factor (LAF) after experimental traumatic injury (TBI) in variously aged rats and evaluate the possibility to correct LAF production with roncoleukin (rIL-2). LAF activity in the supernatants of peritoneal macrophages of injured rats was measured by its ability to have comitogenic effect on the proliferation of rat thymocytes stimulated by suboptimal lectin doses. LAF stimulation index was defined as ratio of stimulated to unstimulated levels of LTF. Results and discussion. The strongest suppression of macrophages’ cytokine-producing function was found in older rats after TBI. rIL-2 injection significantly reversed the injuries caused by TBI even in older rats. These data confirm that exogenic IL-2 is able to activate the functional characteristics of innate immunity cells and that is has a normalizing effect on the immune cells of the older animals.

Keywords: lymphocyte-activating factor; traumatic brain injury; roncoleukin.

Introduction. IL-1β is involved in both brain damage process and the mechanisms of brain regeneration [1]. IL-1β also has immunoprotective effect on immunosuppression induced by glucocorticoids and stress after trauma [2]. Along with other proinflammatory cytokines, IL-1β is produced by peritoneal macrophages. Their activity may be measured with the lymphocyte-activating factor (LAF) test. The goal of the present research is to measure the change in the production of lymphocyte-activating factor (LAF) after experimental traumatic brain injury (TBI) in variously aged rats and evaluate the possibility to manage LAF production with roncoleukin (rIL-2).

Material and methods. After TBI (inflicted by a falling weight) the animals were injected with rIL-2 (30 mg/kg, 3 days). LPS-induced macrophage was used to induce LAF. LAF activity in supernatants was measured by their ability to have comitogenic effect on the proliferation of rat thymocytes stimu-
lated by suboptimal lectin doses [3]. The extent of proliferation was measured by the fluorescence of the restored resazurin. The unit of LAF activity was defined as its amount in ml enough to increase thymocyte proliferation by 50% of the value of its maximal stimulation by Concanavalin A in suboptimal dose in the given test system. Stimulation index (SI) of LAF production shows the ratio of stimulated (stLAF) to unstimulated (unstLAF) level of LAF.

**Results and discussion.** It was found that on day 7 after TBI, macrophages of young rats responded by increasing the production of unstLAF. Stimulation of macrophages didn’t increase the production of LAF. With injection of rIL-2 on day 7 and 14 after TBI, macrophages of young rats responded by increasing the production of stLAF (SI 1.86–2.85). The cells of older animals didn’t respond by increasing LAF production (SI ~ 1) on day 7 and 14 after TBI. Older injured rats that received rIL-2 injection showed significant stLAF increase only by day 14 after TBI (SI = 1.72).

These results show that the strongest suppression of microphages’ cytokine-producing function was found in older rats after TBI. The impact of age on the secretion of cytokines and chemokines by macrophages was not clearly defined. Most rodent-based researches have revealed an age-related decrease in the secretion of anti-inflammatory cytokines and chemokines extracted from microphages [4]. Our research has shown that rIL-2 injection significantly increased LAF production in young injured rats. In older rats, this effect was not as visible but by day 14 of observations the index of stLAF production was restored to normal levels. These data confirm that exogenic IL-2 is able to activate the functional characteristics of innate immunity cells and that is has a normalizing effect on the immune cells of the older animals.

### References