Секция «Тезисы на английском языке»

Participation of urokinase system in activation and proliferation of regulatory T-lymphocytes in vivo

Научный руководитель – Semina Ekaterina Vladimirovna

Maria Kulebyakina Alexandrovna

Аспирант

Московский государственный университет имени М.В.Ломоносова, Факультет фундаментальной медицины, Кафедра биологической и медицинской химии, Москва, Россия

E-mail: mariaakuleb@gmail.com

Regulatory T-lymphocytes (Treg) is a subpopulation of T-lymphocytes which restrain immune response and limit autoimmune reactions in the body. Dysfunction of Treg can lead to the development of autoimmune diseases or to an excessively strong immune response to infection. Discovering of new ways for modulation of Treg activity may be useful for treating a wide range of pathologies including mentioned above.

Urokinase (uPA) and urokinase receptor (uPAR) are the components of the plasminogen activation system. The urokinase system can trigger cascades of extracellular proteolysis and intracellular signaling which activates migration, proliferation and cell differentiation. Recently it has been reported that urokinase plays a distinct role in Treg functioning. In particular, uPA expression increases more than 100-fold during Treg activation. Moreover, experimental suppression of uPA in Tregs leads to reduction of their suppressor activity and to lower expression of the Treg-specific transcription factor FOXP3. Newertheless, it is still unknown if these processes are significant for the development of immune response in vivo. Besides, the molecular mechanism of participation of uPA and involvement of uPAR in the regulation of Treg function are still not clear.

In order to assess the effect of uPA and uPAR on lymphocyte proliferation, we analyzed the total number and ratio of various T-lymphocyte subpopulations (CD8+, or cytotoxic T-lymphocytes, and CD25+, or activated T-lymphocytes) in the spleen of wild-type (WT) mice, as well as in the spleen of uPA-knockout (uPA-KO) and uPAR- knockout (uPAR-KO) transgenic mice. For this purpose we performed immunofluorescent staining of spleen cell suspensions using antibodies to CD8 and CD25. In addition, we performed an immunofluorescent staining of spleen cells with antibodies to FOXP3. Stained cells were analyzed by flow cytometry (FACSCanto II, BD Biosystems).

We have found that the number of CD8 + T-lymphocytes in the spleen of uPA-KO and uPAR-KO mice was significantly higher comparing to WT mice (5.72 $\pm$ 0.89 mln for uPA-KO, 1.46 $\pm$ 0.44 mln for WT, 9.84 $\pm$ 0.2 mln for uPAR-KO, 4.07 $\pm$ 0.28 mln for WT). Furthermore, in the spleen of uPA-KO and uPAR-KO mice there was a significant increase in the number of T-lymphocytes expressing CD25 on their membrane (4.73 $\pm$ 0.04 mln for uPA-KO, 1.76 $\pm$ 0.55 mln for WT, 25, 2 $\pm$ 3.6 mln for uPAR-KO, 2.75 $\pm$ 0.88 mln for WT). Besides that, in uPA-KO and uPAR-KO the number of FOXP3+ Treg was reduced comparing to WT, (0.56 $\pm$ 0.15 mln for uPA-KO, 1.0 $\pm$ 0.129 mln for WT, 0.684 $\pm$ 0.24 mln for UPAR-KO, 1.32 $\pm$ 0.18 mln for WT).

Our data shows that the urokinase system regulates lymphoproliferation, and that the lack of uPA and uPAR may cause Treg dysfunction. It can be suggested that uPA and uPAR regulate Treg development and functioning, the processes which are known to play an important role in the restraining of immune response and controlling of autoimmune reactions.