ImmunoTools IT-Box-Cy55M-Award 2013

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Polyreactive antibodies and regulatory B cells in LPS-induced sepsis

Our main research topic is the therapeutic potential of intravenous immunoglobulins (IVIG) with induced polyspecificity in experimental LPS sepsis. Induced polyspecificity can be achieved by mild oxidizing treatment of immunoglobulins with ferrous ions (Fe^{2+}). Intravenously injected Fe^{2+}–treated immunoglobulins had protective effect in mice with experimental LPS sepsis, whereas non-treated immunoglobulins had no protective activity. A recent finding by Rauch et al.(1) regarding the control of sepsis might be in relation with the explanation of this protective effect. They found a small regulatory subpopulation of mouse B1 cells (called innate response activator – IRA B cells) which develop from the peritoneal B1 cells upon binding of LPS and migration to the spleen where they secrete GM-CSF.

In vitro stimulation of mouse peritoneal B1 cells with LPS in the presence of Fe^{2+}–treated IVIG induced more IRA B cells than in the presence of non-treated immunoglobulins(2). Additionally, suppressing the prolifertaion of peritoneal B1 cells, abrogated, in a dose dependent manner, the effect of stimulation with LPS and Fe^{2+}–treated immunoglobulins. In vivo, staining of the peritoneal cells with CellTraceViolet^{TM} (partially inhibiting proliferariton) proved suppressive to IRA B cell differentiation and in survival analysis abbrogated completely the effect of Fe^{2+} treated IVIG in mice with LPS sepsis. The mechanism of action of the polyspecific antibodies is unclear, as well as how IRA B cells are capable to control the cytokine storm in sepsis. Our results suggest that the control of experimental mouse sepsis might be through binding of the polyspecific immunoglobulin on the surface of B1 cells and enhancing their survival, proliferation and differentiation to IRA B cells.

Winning cytokines from the ImmunoTools *IT-Box-Cy55M* would give us chance to perform in vitro experiments aimed to examine the role of B cell activating factors such as CD40-ligand and IL-5 on mouse B1 cells when they are simultaneously cultured with these factors, LPS and polyspecific immunoglobulins. Additionally, we are interested to check the effect of IRA B1 presence on effects of rmGM-CSF, IL-17 and IL-10 added to the cultures of mouse splenocytes.

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References

1. Rauch, P. J., A. Chudnovskiy, et al. (2012). "Innate response activator B cells protect against microbial sepsis." Science **335**(6068): 597-601.
2. Djoumerska-Alexieva, I., S. Pashova, et al. (2012). "The protective effect of modified intravenous immunoglobulin in LPS sepsis model is associated with an increased IRA B cells response." Autoimmun Rev.

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