

Quality Award Winner (Non-Trainee Category):**Mechanistic approach to describe multiple effects of regulatory molecules on cell dynamics process in immune response**

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Objectives: To develop mechanistic approach enabling to describe multiple effects of cytokines, chemokines and other regulatory molecules on immune cell proliferation, differentiation, migration, apoptosis and cytokine production; to derive formula describing multiple effects of activators, inhibitors and (de-)sensitizers and to explore the ways of integration of the formula in systems pharmacology models of immune response and identification of its parameters against *in vitro* data.

Methods: General principles of receptor theory are applied to develop an approach for description of multiple effects of regulatory molecules on cell dynamics. The formula describing the combined effect of activators, inhibitors and (de-)sensitizers is derived within the framework of quasi-equilibrium approach and represents an upgrade of the multiple effect description implemented in Immune Response Template database [1] constructed by Institute for Systems Biology Moscow. Parameters of the formula are fitted against *in vitro* data from multiple sources using the Hook-Jeeves method as implemented in the DBSolve Optimum package [2].

Results: The formula derived within the framework of the mechanistic approach enables successful description of the multiple effects of regulatory molecules on cell dynamics of immune cells. The ways to integrate the formula within systems pharmacology models describing immune response and to identify its parameters against *in vitro* data are proposed. The approach is applied to describe cell dynamics of lymphocytes and eosinophils (Fig 1).

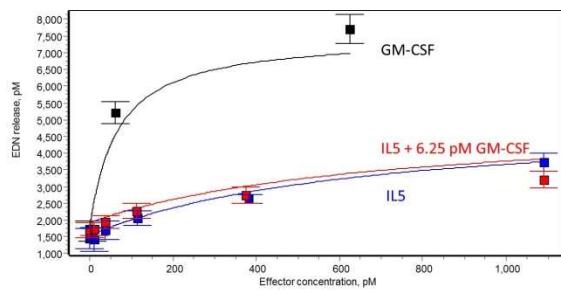


Figure 1. Effect of GM-CSF (black), IL5 alone (blue) or in combination with 6.25 pM of GM-CSF (red) on release of eosinophil-derived neurotoxin. Data taken from [3].

Conclusions: The approach allows to successfully describe effect of multiple activators, inhibitors and (de)sensitizers on cell dynamics of immune cells.

References:

1. Nikitich A, Demin O Jr, Demin O. 2016. ASCPT. San Diego, CA.
2. Gizzatkulov N, et al. BMC Systems Biology, 2010, 4 (109): 1-11
3. Horie S, et al. J Allergy Clin Immunol 1996;98:371-81