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# BIOTECHNOLOGY OF TUMOR GROWTH RESTRICTION: M3 MACROPHAGE "SWITCH" PHENOTYPE AND ANTIGEN-REPROGRAMMED LYMPHOCYTES

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**Many tumors produce anti-inflammatory cytokines, which reprogram antitumor M1 macrophages to protumor M2 macrophages via activation of transcription factors, STAT3, STAT6, and SMAD3. Earlier we showed that M1 macrophages with inhibited STAT3, STAT6, and SMAD3 (M3 phenotype) responded to the action of protumor, anti-inflammatory cytokines by increasing production of antitumor, proinflammatory cytokines and thus, preserved their antitumor properties. In vivo, the tumor also disorders the antigen presentation by macrophages and prevents formation of antigen-specific T and Th1 lymphocytes with strong antitumor properties. We hypothesized that presentation of tumor antigens to lymphocytes by M3 macrophages in vitro, in absence of tumor cells, could result in an effective antitumor programing of the lymphocytes. It can be expected that a composite pool of M3 macrophages and in vitro antigen-reprogramed lymphocytes would effectively restrict tumor growth. We showed that the antitumor effect of M3 macrophages depended on timing of their administration following the onset of solid tumor development. In early administration, M3 macrophages partially restricted the tumor development. In late administration, M3 macrophages restricted the tumor growth but to a significantly less extent. Adding antigen-reprogramed lymphocytes to M3 macrophages resulted in complete inhibition of tumor growth both in vitro and in vivo, both in early and late administration. The fact that M3 macrophages and antigen-reprogramed lymphocytes completely suppressed tumor growth makes it very promising to develop a clinical biotechnology for reducing the tumor growth by prior in vitro antitumor programing of the immune response.**

## Biography

Malyshev Igor is a Head of the Department of Pathophysiology and Head of the Laboratory of Cell Biotechnology, Medical School at the Moscow State University of Medicine and Dentistry; 2. Head of the Laboratory of Stress, Institute of General Pathology and Pathophysiology, Moscow and 3. Adjunct Professor of Biomedical Sciences, University of North Texas Health Science Center, USA. He is a Member of the board of directors of the International Society for Adaptive Medicine and an Editorial board member of Journal of Biosciences and Medicines. He has published 3 books and monographs and 153 full length articles. Research Interests: immunity, cancer, stress and adaptation

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