LycoMab™ – a monoclonal antibody vector to deliver and potentiate anti-proliferative and pro-apoptotic lycopene to treat prostate cancer

Prostate cancer is one of the leading forms of male cancer and cancer-related mortality. There is a need to develop new therapeutic approaches to treat this disease.

It has been established *in vitro* that *trans*-lycopene has an anti-proliferative effect and can also trigger apoptosis of cancer cells, including prostate cancer. Although the prostate has a significant level of expression of carotenoid receptors, patients with prostate cancer have a lycopene deficiency, in particular in affected tissues.

LycoMab™ is a new approach, not only to facilitate delivery of lycopene to the prostate, but also potentially co-deliver other synergetic pharmaceuticals for the treatment of the prostate and other forms of cancer.

Structure and Functionality

LycoMab™ is a mouse monoclonal IgM antibody mAb 6B9 against *trans*-lycopene. Its complex with lycopene has the ability to bind with two different sites on the cellular membrane - carotenoid and Fc-one. This would provide an additional delivery level of lycopene into the cells.

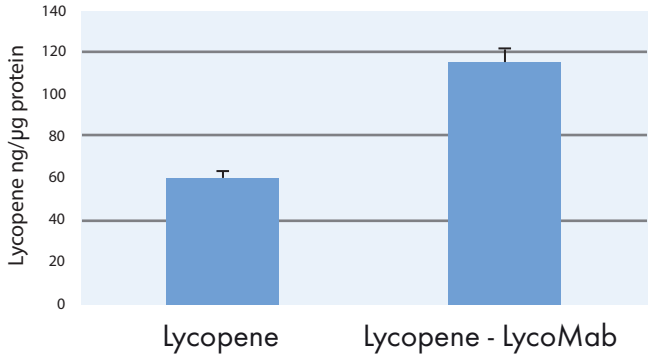
Moreover, IgM is a polyvalent molecule and can bind up to five ligands. This provides an opportunity to create a hybrid platform constructed from immunoglobulins of different specificity. For example, LycoMab™ with an incorporated Fab fragment from another antibody, which is capable of binding another synergetic anti-cancer pharmaceutical, would be able to carry and concentrate this molecule together with lycopene in the prostate.

In addition, the potential of the hybrid LycoMab™ could be further potentiated and extended by co-hybridisation with tissue cancer specific antibodies.

Vector for Intracellular Delivery of Lycopene

In a B10.MLM cell culture experiment it was demonstrated that immune complexes of mAb 6B9 with *trans*-lycopene could provide a significantly higher intracellular level than when this carotenoid was incubated at the same concentration but in a free form, fig. 1.

Figure 1. Lycopene concentration in microsomal fraction after 16 hours of incubation



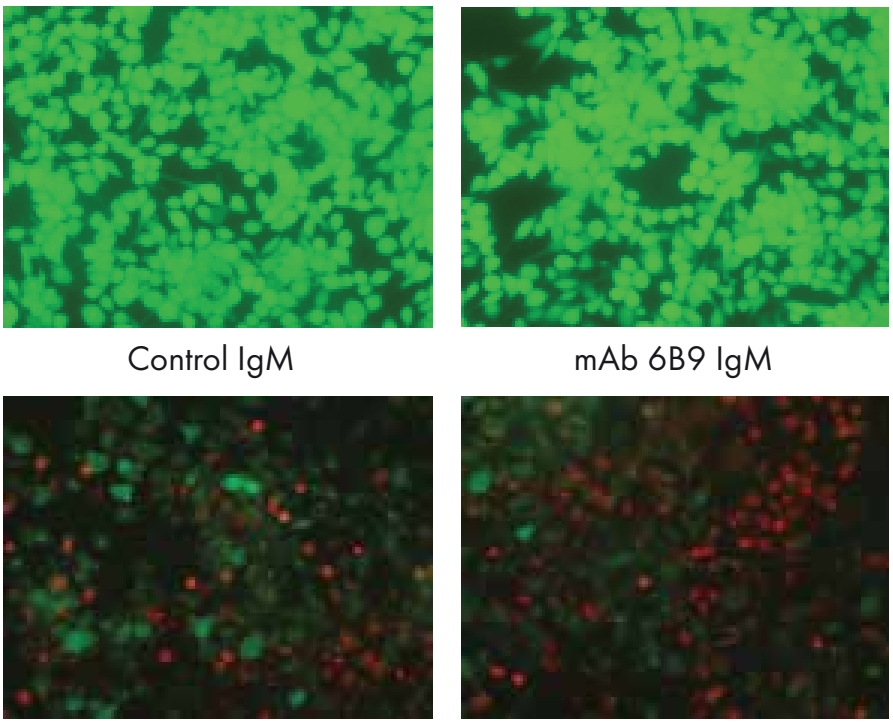
Ivan M. Petyaev, Naylia A. Zigangirova, Valeriy V. Tsibezov, Elena Y. Morgunova, Natalia E. Bondareva, Nigel H. Kyle, and Yuriy K. Bashmakov - Association with Monoclonal Antibody Promotes Intracellular Delivery of Lycopene. MONOCLONAL ANTIBODIES IN IMMUNODIAGNOSIS AND IMMUNOTHERAPY (2018) V. 37, Number 3, DOI: 10.1089/mab.2018.0010

Promotion of Anti-Proliferative and Pro-Apoptotic Lycopene in Prostate Cancer Cell

A series of in vitro experiments were undertaken on prostate adenocarcinoma cancer cell culture PC-3. It was demonstrated that the apoptotic cell death rate at 72 hours of treatment with 1μM *trans*-lycopene, or with its blend with irrelevant IgM, was 19-21%. At the same time point the cell death rate for treatment with the same concentration of lycopene, but in the form of its immune complex LycoMab™, was 48%.

A similar potentiating effect was observed in all concentrations of lycopene studies, 2, 4, 8 and 16μM. The results obtained with propidium iodide staining (fig. 2) were in good agreement with the cell viability assay.

Figure 2. Propidium iodide staining of PC3 cells incubated with LycoMab lycopene 8μM, 48h; fluorescent microscopy at 535nm, ×1000



Ivan M Petyaev, Naylia A Zigangirova, Valery A Tsibezov, Elena Y Morgunova, Nigel H Kyle, Elena D Fedina, Yuriy K Bashmakov - ASSOCIATION WITH MONOCLONAL ANTIBODY PROMOTES ANTI-PROLIFERATIVE AND PRO-APOPTOTIC EFFECTS OF LYCOPENE IN PROSTATE CANCER CELLS. Submitted for Publication (2018).

Next Step

The main objective at the next step is to find funding and/or partners to take LycoMab™ to an animal study programme and expand its pre-clinical dossier.

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