92nd Annual Meeting, American Association for Cancer Research March 24-28, 2001, New Orleans, LA, Volume 42, March 2001

## MGN-3, a Novel Antitumor Agent

Koichi Uyemura, Ken Tachiki, Mamdooh Ghoneum, Takashi Makinodan, Nalini Makhijani, and Dean Yamaguchi.

Drew University of Medical and Science, Los Angeles, CA, Greater Los Angeles VA Healthcare System, Los Angeles, CA, UCLA Medical School/Greater Los Angeles VA Healthcare System, Los Angeles, CA and UCLA School of Medicine/Greater Los Angeles VA Healthcare System, Los Angeles, CA.

There is great interest among health care professionals to explore the value of naturally derived biological response modifiers to enhance immune function. MGN-3 is a biological response modifier that is an Arabinoxylan compound which is a polysaccharide containing hemicellulose-B extract of rice bran, modified by enzymes from Shiitake mushrooms reported previously to be a potent immunomodulator. We have previously shown that treatment with MGN-3 had an augmentory effect on natural killer (NK) cell activity in healthy control subjects, in patients with breast cancer, and in patients infected with HIV-1.

In these studies, an effect on NK cell activity was noted as early as 4 weeks and did not show hyporesponsiveness with continued treatment for over 12 months, with absence of notable side effects. In present study, we demonstrate a direct effect on MGN-3 on tumor cell growth and cytokine production. Preliminary results showed that incubation of a breast cancer cell line (MCF-7) with MGN-3 arrested tumor cell growth, whereas control MCF-12A cells grown in a media in the absence of added MGN-3 continued to increase in cell number.

Employing flow cytometry procedures, results showed that after 16 hours of treatment of MCF-7 cells with MGN-3 a marked stimulation in production of interleukin 10 (IL-10). ELIZA analyses of the culture media bathing the cells 16 hours after treatment with MGN-3 also showed an increase in IL-10 production, little change in INF-g concentration. However, a marked elevation in interleukin-12 was also observed at 16 hours.

In conclusion, our findings indicate that MGN-3 acts by not only enhancing the activity of NK cells as previously reported, but also through a direct action on tumor

cell production of cytokines. The production of cytokines such as IL-10 by cancer cells to alter the activity of the immune system is well known.

Our findings indicate that the biological response modifier MGN-3 can alter the production and secretion of cytokines such as IL-10 and IL-12 by cancer cells such as MCF-7; and thereby the activity of the immune system. Findings that treatment of cultures of MCF-7 cells with MGN-3 also can arrest cell growth.

MGN-3, commercially known as Bio Bran, was provided by Daiwa Pharmaceutical Company, Ltd. Tokyo, Japan. Work in this direction is in progress. Supported in part by VA Medical Research Funds and by funds provided by Daiwa Pharmaceutical Company, Ltd, Tokyo, Japan.