Genetically Optimized Banana Lectin for the Treatment of Influenza

Steven King, Shyamala Ganesan, Maureen Legendre, E. Bart Tarbet, Dawn Reyna, Richard Lister, Eric Simon, Narayanan Surendran, Elke Lipka, and David Markovitz.

Influenza virus vaccines and current antiviral drugs only partially control epidemics and are likely to be ineffective during a pandemic when a new pathogenic influenza virus enters the population. To develop a new drug to treat influenza, we genetically optimized a lectin (BL-84) and examined its influenza antiviral activity, PK profile, and exploratory toxicity. *In vitro*, BL-84 had potent (low nanomolar) antiviral activity against multiple influenza virus strains and showed synergy with oseltamivir. Most importantly, BL-84 was highly active in treating lethal influenza infection when administered systemically in a mouse model. All mice survived infection when treated IP with 5mg/kg of BL-84 administered once daily for 5 days beginning 4h post-challenge with significant survival when treatment was delayed until 72h post-infection. PK analysis underscored the highly promising characteristics of BL-84 with significant concentrations expected in lungs, the target organ for influenza therapeutics, and a long terminal half-life (~80h) supportive of single dose administration. To explore single dose toxicity, mice were dosed IP with BL-84 at 50, 100, or 200 mg/kg. Adverse effects were limited to a slight dose-dependent weight loss, however hematology and histological evaluations of kidney, liver, lung, intestine and spleen appeared normal. Repeat IP dosing also produced no overt toxicity, and while mice developed anti-BL-84 antibodies, those did NOT neutralize BL-84's antiviral activity *in vitro* or *in vivo*. BL-84 represents a new influenza treatment that targets different virus pathways to circumvent current treatment limitations, create combination therapy possibilities, and potentially outperform available antiviral drugs in the marketplace.