

2nd Glycobiology World Congress

August 29-31, 2016 Atlanta, USA

Discovery of WecA inhibitors for development of new TB drugs for dormant *Mycobacterium tuberculosis* infections

Michio Kurosu

University of Tennessee Health Science Center, USA

The emergence of multidrug-resistant (MDR) strains of *Mycobacterium tuberculosis* (Mtb) seriously threatens TB control and prevention efforts. In general TB chemotherapy, treatment length can be up to two years for infections of MDR strains and can be longer for extensively drug-resistant (XDR) strains. Thus, it is an important program to discover promising approaches to the shortening of current TB drug regimen. Mechanisms that enter non-replicating (or dormant) state of Mtb are accounted for a significant factor that requires long-term chemotherapy and new drugs that target non-replicating Mtb are likely to revolutionize TB chemotherapy. WecA, a phosphotransferase that catalyzes the transformation of prenyl-diphosphoryl-GlcNAc from UDP-GlcNAc and decaprenylphosphate, is essential in growth of Mtb under aerobic conditions and to survive for Mtb in macrophages under oxygen-depleted conditions. Our group developed a convenient assay method against WecA using the modified enzymatic substrates and an assay method to determine bactericidal effect of molecules against intracellular Mtb. As the results of screening of capuramycin-based analogs via our methods, we identified strong WecA inhibitors (low nanomol range concentrations) that kill replicating and non-replicating Mtb. The details of assay development and *in vitro* assay data for the identified anti-mycobacterial WecA inhibitors will be presented.

mkurosu@uthsc.edu

Alcohol abuse & protein glycosylation with special emphasis on apolipoprotein J

Raj Lakshman

The George Washington University, USA

National Institutes on Alcohol Abuse and Alcoholism (NIAAA) estimates, 14 million Americans meet the diagnostic criteria for alcohol abuse. Therefore, it is critical to identify, develop and validate a viable “biomarker” for alcohol abuse. While plasma carbohydrate-deficient transferrin (CDT) is considered a gold standard as marker for chronic alcohol consumption, it is valid only when daily consumption exceeds 60 g. and is less sensitive in women than in men drinkers. Therefore, it would be desirable to have a specific and sensitive marker for alcohol consumption per se. We have established that chronic alcohol consumption (CAC) down-regulates Gal- β -1,4GlcNAc α 2, 6-sialyltransferase mRNA (ST6Gal1 mRNA) both in animals and in human alcoholics leading to the appearance of sialic acid-deficient glycoproteins such as Apolipoprotein J (APOJ). Since sialic acid index of plasma Apo J (SIJ: moles of sialic acid/mole of Apo J) is seven times more than that for transferrin (28 vs. 4) we postulated that SIJ would be a more sensitive marker for CAC than CDT. We have correlated plasma SIJ in drinkers and non-drinkers with the %CDT. The correlation of plasma SIJ with %CDT showed 13.3 % of variance in common; $r=0.365$ (non-parametric Spearman or parametric Pearson). We have established that there was a positive correlation of alteration in SIJ with alcohol consumption, detoxification, abstinence, and relapse in human alcoholics. More importantly, SIJ was decreased by 50-57% ($P<0.01$) in both male and female alcoholics. We therefore suggest that SIJ is a viable marker for early detection of chronic alcohol consumption.

Raj.Lakshman@va.gov