



BİLKENT UNIVERSITY
MOLECULAR BIOLOGY AND GENETICS
DEPARTMENTAL SEMINAR

**"Immunoglobulin G glycosylation; its regulation by sex hormones
and contribution to rheumatoid arthritis"**

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Immunoglobulin G (IgG) is a major immune related protein in circulation and has a conserved complex-type N-glycosylation at the Fc region. This glycan can have at least 32 structures that alter protein conformation and thereby modulate effector function of IgG via interaction with Fc gamma receptors and complement components. This diverse glycan structures were investigated with respect to gender, age, and disease status such as rheumatoid arthritis (RA) using human samples and mouse model of RA, K/BxN with High-Performance Liquid Chromatography. Initial investigation of a proinflammatory glycan structure, which lacks galactose (G0F), indicates a difference between female and male with respect to age with an inflection point at the time of menopause among females but not males using 713 samples from healthy donors. This observation was followed by analyzing possible effect of gonadal steroids on IgG G0F. G0F is assessed in healthy adults subjected to endocrine manipulation: 58 postmenopausal women randomized to estrogen, raloxifene or placebo; 22 premenopausal women deprived of gonadal hormones with leuprolide and randomized to estrogen or placebo; and 80 healthy men deprived of gonadal hormones using goserelin acetate and randomized to testosterone or placebo, with or without anastrozole to block conversion of testosterone to estrogen. Results show that estrogen reduced G0F in postmenopausal women, while leuprolide increased G0F in premenopausal women in a manner fully reversible by estrogen. Men treated with goserelin acetate demonstrated an increase in G0F, reversed by testosterone but only if conversion to estrogen was not blocked by anastrozole. Given the fact that, RA affects female more than male with a ratio of 3 to 1, G0F

is investigated in a cohort established from RA patients and compared to age and gender matched healthy controls. According to the results, G0F is heavily presented in RA patients compared to controls, correlates with diseases activity, and enriches in anticitrulline autoantibody pool. In DoDSR cohort, G0F aberrancy predates the onset of arthritis and the diagnosis of RA (3.5 years). In K/BxN, IgG glycosylation is different between female and male mouse and G0F is heavily presented in K/BxN mouse compared to healthy control and IgG with G0F is produced by lymph node. According to the results presented here, IgG glycosylation is a dynamically regulated process with respect to age, gender, and disease activity. In more detail, estrogen regulates galactosylation of IgG in both women and men, and begins to illuminate the in vivo regulation of IgG glycans and defines a new pathway by which gender modulates immunity and possibly contributes to RA pathophysiology.

Date-Time : Monday, October 10, 2016 – at 15:40

Place : SBZ-14

Host : Doç. Dr. Işık Yuluğ