2.01 Establishing Diurnal Variation of Inflammatory Markers in Genetic COPD

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Background: Genetic COPD is characterised by Apha-1 antitrypsin deficiency (AATD). The most common clinical manifestations of severe AATD is emphysema, cirrhosis and liver cancer, and panniculitis. The circadian rhythm is a 24-hour cycle of daily oscillations in physiology. These circadian variations have been characterised in common acute phase reactants in healthy humans but not yet investigated in COPD.

Methods: Heparinised venous peripheral blood was obtained at 8:00, 13:00, and 20:00 from stable AATD patients, and healthy MM controls. CRP and FBC analysis was performed with whole blood, and cytokines analysis from plasma and monocyte supernatant with and without LPS stimulation at three different time points using ELISA. Our panel was comprised of TNF- α Soluble IL-6 receptor (sIL-6R), IL-10, TNF-α, Soluble TNF receptor (sTNFR1), IL-β, IL-17, IL-10.

Results: White cell differentiation shows statistically significant circadian changes only in severe AATD deficiency (ZZ phenotype) with a rise in neutrophils, monocytes, and lymphocytes, in the evening (p= 0.01) (table.1). In monocyte supernatants, IL-β shows the most increase in LPS response in each time point in ZZ patients. Clock genes show a circadian pattern of expression in the MM cohort that collaborates with previous studies[1]. These patterns were partially lost in the ZZ group.

Conclusion: Neutrophils, lymphocytes and monocytes increase in the evening in ZZ AATD compared to other groups. Plasma cytokine expression can subtly vary between MM, MZ and ZZ groups.

Keywords: Alpha-1 Antitrypsin, COPD, Circadian Rhythm

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Figure 1. Full blood count analysis with automated haematology analyser demonstrates circadian variation in total white cell count in all cohorts (MM, MZ, ZZ). Cell differentiation shows statistically significant circadian changes only in the ZZ cohort with rise in neutrophils, Monocytes, and lymphocytes in the evening (p= 0.01).