3082 Diacylglycerol-mediated Signaling of Neutrophils in Diabetics with or without Periodontal Disease

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Diabetes mellitus is a metabolic disorder characterized by hyperglycemia. Diacylglycerols (DAG) are a group of second messenger molecules involved in the regulation of neutrophil functions. DAG mass can be modified in diabetic cells through direct activation of endogenous signaling pathways and receptor mediated events triggered by advanced glycation endproducts (AGE). OBJECTIVE: The aim of this study was to evaluate total DAG content, and DAG kinase (DAGK) activity in neutrophils of diabetic patients with periodontal disease. METHODS: Diabetic subjects with periodontitis (N=15) were compared to matched-healthy subjects (N=15) with no periodontal disease. Peripheral blood neutrophils were isolated and total lipid was extracted. DAG content was measured by its phosphorylation to radioactively labeled phosphatidic acid (PA). For DAGK activity, the cells were suspended in lysis buffer and the conversion of external DAG substrate into PA was measured by the uptake of radioactivity as above. RESULTS: Total DAG levels were significantly higher in diabetic neutrophils compared to healthy individuals (diabetes = 9, healthy = 9) ($p<0.05$). There was also a parallel reduction of DAGK activity in neutrophils from diabetic patients (diabetic = 6, healthy = 6) ($p<0.05$). Stimulation of the cells with fMLP (1mM) led to an increase in DAG mass in neutrophils of both diabetics and controls of equal magnitude. CONCLUSIONS: Total DAG mass is elevated in diabetic neutrophils while DAGK activity is reduced. Increased DAG mass has a direct effect on cell function through protein kinase C activation, thereby priming the cell to a hyperactive phenotype. Taken together with our previous observation that superoxide generation in diabetic neutrophils is significantly greater than controls, we suggest that the priming of diabetic neutrophils through the hyperglycemic condition and AGE may play an important role in the increased tendency of destructive form of periodontitis in diabetics. Supported by USPHS Grants DE13191 and DE14478.