Metabolic profile of Affinofile cells presenting differential CCR5 levels

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The cysteine-cysteine chemokine receptor 5 (CCR5) is found on the surface of various cells, and a number of different mutations have been described that affect their expression and hence their levels, which ultimately affects their or the cell's function. While there are many structural and immune studies published on CCR5, metabolic studies however, especially in the context of in the absence of inflammation, are limited. Additionally, clinical samples harbouring CCR5 mutations and varying levels of the receptor, are also scarce. Affinofile cells, engineered from human embryonic kidney (HEK) cells, express varying levels of CCR5, and when cultured serve as a useful tool for investigating metabolic differences under differential CCR5 expression. Flow cytometric analysis confirmed the Affinofile cells to be viable and express low and high CCR5 levels, respectively, post-induction with Ponesterone A. Mass spectrometric data subjected to chemometric (ES+ANOVA) and pathway analysis revealed that as the receptor levels increased, from low to high CCR5, that the TCA cycle, protein and FA metabolism was most affected, with methionine and carbohydrate synthesis more so at high CCR5 levels. Methionine serves as a precursor for several intermediates involved in the TCA cycle, and the synthesis of the antioxidant glutathione, and is also involved in the methylation of DNA and RNA crucial for cell proliferation and differentiation. Our study further indicates that a shift to higher CCR5 levels, increases the metabolic processes associated with energy production, antioxidant synthesis and other CCR5-specific processes (chemotaxis, elevated glycolysis, inflammation etc.). The metabolic changes measured here thus support and will aid in a further understanding of the functional-related expression of CCR5, a molecule that has in recent years shown immense translational potential in HIV/AIDSand other infectious diseases.

Keywords: Cysteine-Cysteine chemokine receptor 5, CCR5, Affinofile, metabolism