



# Personality and gene expression: Do individual differences exist in the leukocyte transcriptome?



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## KEYWORDS

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## Summary

**Background:** The temporal and situational stability of personality has led generations of researchers to hypothesize that personality may have enduring effects on health, but the biological mechanisms of such relationships remain poorly understood. In the present study, we utilized a functional genomics approach to examine the relationship between the 5 major dimensions of personality and patterns of gene expression as predicted by 'behavioural immune response' theory. We specifically focussed on two sets of genes previously linked to stress, threat, and adverse socio-environmental conditions: pro-inflammatory genes and genes involved in Type I interferon and antibody responses.

**Methods:** An opportunity sample of 121 healthy individuals was recruited (86 females; mean age 24 years). Individuals completed a validated measure of personality; questions relating to current health behaviours; and provided a 5 ml sample of peripheral blood for gene expression analysis.

**Results:** Extraversion was associated with increased expression of pro-inflammatory genes and Conscientiousness was associated with reduced expression of pro-inflammatory genes. Both associations were independent of health behaviours, negative affect, and leukocyte subset distributions. Antiviral and antibody-related gene expression was not associated with any personality dimension.

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*Conclusions:* The present data shed new light on the long-observed epidemiological associations between personality, physical health, and human longevity. Further research is required to elucidate the biological mechanisms underlying these associations.

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## 1. Introduction

Personality is commonly defined as a cluster of individual psychological attributes (e.g., thoughts, feelings and behaviours), which are typically stable across time and situations and give rise to enduring individual differences. Multivariate analyses have generally identified 5 major dimensions of human personality – Neuroticism, marked by a tendency towards negative affect; Extraversion characterized by high levels of sociability and appetitive motivation; Openness to Experience, which reflects general curiosity, creativity, and an orientation towards intellectual and aesthetic pursuits; Agreeableness, reflecting general likability and even temperament; and Conscientiousness, reflecting planfulness, caution, and harm avoidance (McCrae and Costa, 2004). The temporal and situational stability of personality has led generations of researchers to hypothesize that personality may have enduring effects on health (Eysenck, 1991; Friedman, 2008). Some large epidemiological studies have found associations between personality characteristics and measures of disease or longevity (Weiss and Costa, 2005; Nakaya et al., 2010; Chapman et al., 2011), but the biological mechanisms of such relationships remain poorly understood.

Several causal models have been invoked to explain associations between personality and health (Friedman, 2008), including common causation by underlying individual differences in genetics or early life experience (Cohen et al., 2003; MacMurray et al., 2013; Napolioni et al., 2014); effects of personality on health behaviours (e.g., smoking, alcohol consumption, physical activity: Turiano et al., 2012); differential proclivity to risky situations or environments (Cohen et al., 2003); effects of personality-related stress responses on biological function (Vedhara and Irwin, 2005; Miller et al., 2009a), and reverse causation of individual differences in behaviour by individual differences in health or inflammatory biology (Dantzer et al., 2008; Eisenberger et al., 2010).

One body of theoretical analysis suggests that individual differences in the vigour of biological immune responses may come to be associated with individual differences in personality traits that serve as a sort of ‘behavioural immune response’ (Schaller and Murray, 2008; Thornhill et al., 2010; Schaller, 2011). According to this theoretical approach, individuals who have relatively weak biological immune responses are hypothesized to show stronger behavioural immune responses such as avoidance of strangers (i.e., Introversion), reduced exploratory behaviour (i.e., low Openness to experience), and greater harm-avoidant behaviour (i.e., Conscientiousness). Recent genetic association studies have supported this hypothesis in documenting increased levels of Introversion in people carrying immune response gene polymorphisms that confer increased vulnerability to infectious diseases (MacMurray

et al., 2013; Napolioni et al., 2014). Conversely, allostatic physiology (Sterling, 2004) suggests that biological immune defences may be up-regulated in individuals who experience extended exposure to threat or stress and might thus experience an elevated risk of injury or infection, or in highly sociable individuals who face increased exposure to communicable diseases (Cole et al., 2011; Cole, 2013; Slavich and Cole, 2013).

Despite a wealth of theoretical explanation for links between personality and health, the biological mechanisms mediating those relationships remain poorly defined. Some studies have reported associations between measures of personality and specific endocrine and immune parameters such as catecholamine neurotransmitters from the sympathetic nervous system (SNS) and glucocorticoid hormones from the Hypothalamic-Pituitary-Adrenal (HPA)-axis (Miller et al., 1999; Rutledge, 2006; Molloy et al., 2008; Reinhard et al., 2012). Studies have also reported associations between some personality dimensions such as Extraversion and Conscientiousness and expression of pro-inflammatory mediators (e.g., cytokines) or biomarkers (e.g., C-reactive protein) that have been linked in particular to ageing and longevity (Finch, 2007; Chapman et al., 2009; Sutin et al., 2010; Millar et al., 2013). However, little work has directly examined the leukocyte gene regulatory systems that govern immune cell function and thus regulate the inflammatory dynamics that contribute to disease (e.g., cardiovascular disease, cancer incidence and progression, neurodegenerative diseases) or the antibody- and antiviral gene expression programs that mediate host resistance to infection.

In the present study, we utilized a functional genomics approach to identify relationships between the 5 major dimensions of human individual differences in personality and broad patterns of gene expression in human leukocytes. Previous research has linked stress, threat, and adverse socio-environmental conditions to a conserved transcriptional response to adversity (CTRA) characterized by up-regulated transcription of pro-inflammatory genes and a complementary down-regulation of genes mediating the production of Type I interferon antiviral responses and IgG antibodies (Irwin and Cole, 2011; Antoni et al., 2012; Cole et al., 2012; Cole, 2013). This profile is hypothesized to represent an anticipatory immunological response to increased risk of injury during periods of experienced threat (Irwin and Cole, 2011; Antoni et al., 2012; Cole et al., 2012; Cole, 2013). Based on the ‘behavioural immune response’ theory (Schaller and Murray, 2008; Thornhill et al., 2010; Schaller, 2011), we hypothesized that pro-inflammatory gene expression would be up-regulated in extraverts and people with high levels of openness to experience (both of whom would be expected to experience elevated risk of injury/infection) and down-regulated in conscientious

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