

# Evidence of Associations Between Cytokine Gene Polymorphisms and Quality of Life in Patients With Cancer and Their Family Caregivers

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An increasingly recognized patient-reported outcome in oncology is quality of life (QOL) (Trask, Hsu, & McQuellon, 2009). A substantial proportion of the interindividual variability in QOL in patients with cancer (Montazeri, 2008; Singh, Trabulsi, & Gomella, 2010) and their family caregivers (FCs) (Kim & Given, 2008; Kitrungrote & Cohen, 2006) is not explained by demographic characteristics (Bloom, Stewart, Chang, & Banks, 2004; Lam, Ye, & Fielding, 2012), disease severity (Mehnert, Lehmann, Graefen, Huland, & Koch, 2010; Paika et al., 2010; Zenger et al., 2010), or treatment burden (Deshields, Potter, Olsen, Liu, & Dye, 2011; Reeve et al., 2012). Several lines of evidence suggest that genetic factors may account for some of the interindividual differences in QOL (Nes, Roysamb, Tambs, Harris, & Reichborn-Kjennerud, 2006; Romeis et al., 2000, 2005).

Findings from twin studies (Nes et al., 2006; Romeis et al., 2000, 2005) suggested that genetic predisposition influences QOL. In these twin studies, heritability accounted for 11%–35% of the variance in QOL. For example, in one study that measured QOL using the SF-36® (Romeis et al., 2005), additive genetic factors accounted for 17%–33% of the variance in each of the SF-36 subscales. However, the specific genetic variations associated with interindividual differences in QOL remain unknown. Given these initial findings, experts in the fields of QOL and genomics established an international Consortium for Genetics and Quality of Life Research and called for studies to identify the molecular mechanisms that underlie interindividual differences and changes in QOL (Sprangers et al., 2009). Given the potentially large number of genes that could be involved in QOL, the consortium encouraged a focused approach to the investigation of genetic variations in biologic pathways (e.g., candidate gene studies).

Although research on the relationships between genetics and QOL is in its infancy, a substantial amount of evidence suggests that genetic variations in

**Purpose/Objectives:** To identify latent classes of individuals with distinct quality-of-life (QOL) trajectories, to evaluate for differences in demographic characteristics between the latent classes, and to evaluate for variations in pro- and anti-inflammatory cytokine genes between the latent classes.

**Design:** Descriptive, longitudinal study.

**Setting:** Two radiation therapy departments located in a comprehensive cancer center and a community-based oncology program in northern California.

**Sample:** 168 outpatients with prostate, breast, brain, or lung cancer and 85 of their family caregivers (FCs).

**Methods:** Growth mixture modeling (GMM) was employed to identify latent classes of individuals based on QOL scores measured prior to, during, and for four months following completion of radiation therapy. Single nucleotide polymorphisms (SNPs) and haplotypes in 16 candidate cytokine genes were tested between the latent classes. Logistic regression was used to evaluate the relationships among genotypic and phenotypic characteristics and QOL GMM group membership.

**Main Research Variables:** QOL latent class membership and variations in cytokine genes.

**Findings:** Two latent QOL classes were found: higher and lower. Patients and FCs who were younger, identified with an ethnic minority group, had poorer functional status, or had children living at home were more likely to belong to the lower QOL class. After controlling for significant covariates, between-group differences were found in SNPs in *interleukin 1 receptor 2 (IL1R2)* and *nuclear factor kappa beta 2 (NFKB2)*. For *IL1R2*, carrying one or two doses of the rare C allele was associated with decreased odds of belonging to the lower QOL class. For *NFKB2*, carriers with two doses of the rare G allele were more likely to belong to the lower QOL class.

**Conclusions:** Unique genetic markers in cytokine genes may partially explain interindividual variability in QOL.

**Implications for Nursing:** Determination of high-risk characteristics and unique genetic markers would allow for earlier identification of patients with cancer and FCs at higher risk for poorer QOL. Knowledge of these risk factors could assist in the development of more targeted clinical or supportive care interventions for those identified.

**Key Words:** quality of life; cytokines; genetics; growth mixture modeling; family caregivers; radiation therapy

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