Table 2. Common biological pathways, candidate genes and biomolecular markers associated with quality of life domains *(Genes are included in this table if association is found with at least 2 QoL domains)

<table>
<thead>
<tr>
<th>Biological Pathways</th>
<th>Candidate genes</th>
<th>Quality of life domain</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokine-cytokine receptor interaction</td>
<td><em>IL-1β</em></td>
<td>• General health</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Physical functioning</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (2, 3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (4-6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anti-depressant response</td>
<td>• (7)</td>
</tr>
<tr>
<td></td>
<td><em>IL-6</em></td>
<td>• Overall quality of life</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• General health</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Physical functioning</td>
<td>• (1, 8-10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (11-13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (13-15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (4-6, 11, 16-18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
<td>• (13)</td>
</tr>
<tr>
<td></td>
<td><em>IL-8</em></td>
<td>• Pain</td>
<td>• (19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (4, 20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
<td>• (21)</td>
</tr>
<tr>
<td></td>
<td><em>TNF-α</em></td>
<td>• Physical functioning</td>
<td>• (1, 9, 22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (11, 13, 21, 23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (2, 14, 24)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (7, 16)</td>
</tr>
<tr>
<td></td>
<td><em>CRP</em></td>
<td>• Fatigue</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (12, 25)</td>
</tr>
<tr>
<td></td>
<td><em>IL-1RN</em></td>
<td>• General health</td>
<td>• (17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Physical functioning</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - depression</td>
<td>• (1)</td>
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<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td><em>IL-1RA</em></td>
<td>• Fatigue</td>
<td>• (12, 21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (3, 26)</td>
</tr>
<tr>
<td>Biological Pathways</td>
<td>Candidate genes</td>
<td>Quality of life domain</td>
<td>Literature</td>
</tr>
<tr>
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</tr>
<tr>
<td></td>
<td><strong>IL-10</strong></td>
<td>• General health • Physical functioning • Fatigue • Pain • Emotional functioning – Depression • Cognitive functioning</td>
<td>• (1) • (1) • (1) • (13) • (4, 5, 18, 24, 27) • (18)</td>
</tr>
<tr>
<td>Dopaminergic synapse</td>
<td><strong>COMT</strong></td>
<td>• Fatigue • Pain • Emotional functioning – Depression • Emotional functioning – Positive affect • Cognitive functioning • Social functioning</td>
<td>• (28) • (29-39) • (40) • (41)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD2</strong></td>
<td>• Emotional functioning – Depression • Emotional functioning – Anxiety • Social functioning</td>
<td>• (40, 49) • (49) • (49-51)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD4</strong></td>
<td>• Physical functioning • Fatigue • Emotional functioning depression • Cognitive functioning • Social functioning</td>
<td>• (52) • (46) • (53) • (54) • (55)</td>
</tr>
<tr>
<td></td>
<td><strong>DAT1</strong></td>
<td>• Physical functioning • Fatigue • Cognitive functioning</td>
<td>• (56, 57) • (46) • (46) • (58) • (59)</td>
</tr>
<tr>
<td></td>
<td><strong>CREB1</strong></td>
<td>• Pain • Emotional functioning – Depression</td>
<td>• (58) • (59)</td>
</tr>
<tr>
<td>Dopaminergic synapse/Serotonergic synapse</td>
<td><strong>MAOA</strong></td>
<td>• Emotional functioning – depression • Emotional functioning – positive affect • Social functioning</td>
<td>• (53, 60) • (61) • (62)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td><strong>5-HTT</strong> (SLC6A4)</td>
<td>• Physical functioning • Pain • Emotional functioning – depression • Emotional functioning – anxiety • Emotional functioning – positive affect • Cognitive functioning • Social functioning</td>
<td>• (63) • (39, 64-66) • (67-75) • (70, 76-80) • (81) • (70) • (82)</td>
</tr>
<tr>
<td>Biological Pathways</td>
<td>Candidate genes</td>
<td>Quality of life domain</td>
<td>Literature</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>• Overall quality of life</td>
<td>• (83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (84)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - anxiety</td>
<td>• (83)</td>
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<td></td>
<td>• TPH1</td>
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<tr>
<td>Neurotrophin signaling pathway</td>
<td>• BDNF</td>
<td>• Physical functioning</td>
<td>• (85, 86)</td>
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<td>• Emotional functioning – depression</td>
<td>• (5, 7, 59, 87-90)</td>
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<td>• Cognitive functioning</td>
<td>• (45, 85, 86, 91)</td>
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<td>• OXTR</td>
<td>• Social functioning</td>
<td>• (92)</td>
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<td>• Emotional functioning – depression</td>
<td>• (93, 94)</td>
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<td></td>
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<td>• Emotional functioning – anxiety</td>
<td>• (95)</td>
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<tr>
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<td></td>
<td>• Emotional functioning – loneliness</td>
<td>• (96)</td>
</tr>
<tr>
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<td></td>
<td>• Social functioning</td>
<td>• (82, 97-100)</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>• APOE</td>
<td>• Physical functioning</td>
<td>• (101-106)</td>
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<td></td>
<td>• Emotional functioning – Depression</td>
<td>• (107-109)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
<td>• (45, 110-116)</td>
</tr>
<tr>
<td>Neuroactive ligand-receptor interaction</td>
<td>• OPRM1</td>
<td>• General health</td>
<td>• (117)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (118-124)</td>
</tr>
<tr>
<td></td>
<td>• AVPR1A</td>
<td>• Emotional functioning</td>
<td>• (41)</td>
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<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (125)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – depression</td>
<td>• (126)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (97, 98, 127-130)</td>
</tr>
<tr>
<td>Glutathione metabolic pathway</td>
<td>• DPYD</td>
<td>• Physical functioning</td>
<td>• (131)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (131, 132)</td>
</tr>
</tbody>
</table>

*Biological pathways are according to KEGG (Kyoto Encyclopaedia of Genes and Genomes), http://www.genome.jp/kegg/ or Genecards, http://www.genecards.org/*

REFERENCES


patient sample; candidate gene study

patient sample + healthy individuals; candidate gene study (buccal swab)


population-based; candidate gene study


patient sample + healthy individuals; candidate gene study


review


patient sample; biomolecular markers

NEW REFERENCE Dec 2013


patient sample + healthy individuals; candidate gene study

NEW REFERENCE Dec 2013


healthy individuals; candidate gene study

NEW REFERENCE Sep 2013


patient sample; candidate gene study

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healthy individuals; candidate gene study

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population-based; candidate gene study


patient sample; biomolecular marker

review

patient sample; candidate gene study

patient sample; candidate gene study

meta-analyses

population-based; GWAS

patient sample; candidate gene study

patient sample; candidate gene study

patient sample + healthy individuals; candidate gene study

patient sample; biomolecular marker

population-based; candidate gene study

NEW REFERENCE Sep 2013

patient sample + healthy individuals; candidate gene study

patient sample + healthy individuals; candidate gene study

NEW REFERENCE Dec 2013

population-based; candidate gene study

NEW REFERENCE Dec 2013


patient sample; candidate gene study


patient sample + healthy individuals; candidate gene study


patient sample; candidate gene study (saliva)


healthy individuals; candidate gene study


patient sample; candidate gene study (saliva)


patient sample; candidate gene study


healthy individuals; candidate gene study


population-based; candidate gene study


patient sample + matched healthy individuals; candidate gene study


patient sample; candidate gene study
*patient sample; candidate gene study*

*patient sample; candidate gene study*

*patient sample, candidate gene study (buccal swab)*

*review*

*review*

*review*

*patient sample + healthy individuals; candidate gene study*

*patient sample + healthy controls; candidate gene study (buccal swab)*  
**NEW REFERENCE Dec 2013**

*patient sample + healthy controls; candidate gene study (saliva)*  
**NEW REFERENCE Dec 2013**

*review*

*healthy individuals; candidate gene study (saliva)*

*patient sample; candidate gene study*
48. Waugh CE, Dearing KF, Joormann J, et al.: Association between the catechol-O-
methyltransferase Val158Met polymorphism and self-perceived social acceptance
healthy individuals; candidate gene study (saliva)

49. Lawford BR, Young R, Noble EP, et al.: The D2 dopamine receptor (DRD2) gene is
associated with co-morbid depression, anxiety and social dysfunction in untreated
patient sample; candidate gene study

patient sample; candidate gene study

between quantitative measures of childhood problem behaviors and DRD2/Taql
patient sample + healthy individuals; candidate gene study

healthy individuals; candidate gene study (buccal swab)

review

54. Szekely A, Balota DA, Duchek JM, et al.: Genetic factors of reaction time
performance: DRD4 7-repeat allele associated with slower responses. Genes Brain
Behav 10:129-136, 2011
healthy individuals; candidate gene study (buccal cells)

receptor (DRD4) gene and approach-related personality traits: meta-analysis and
meta-analyses; population based; candidate gene study (swab samples)

healthy individuals; candidate gene study (saliva)

processing in attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc
Psychiatry 51:722-732, 2012
patient sample + matched controls; candidate gene study (blood or mouth swab)

healthy individuals; GWAS; replication analyses with external cohorts
NEW REFERENCE Sep 2013

59. Juhasz G, Dunham JS, McKie S, et al.: The CREB1-BDNF-NTRK2 pathway in
depression: multiple gene-cognition-environment interactions. Biol Psychiatry
69:762-771, 2011
population-based; candidate gene study (buccal)
*patient sample; candidate gene study*

*population-based; candidate gene study (saliva)*

*population-based; candidate gene study*

*patient sample; candidate gene study*

*patient sample + healthy individuals; candidate gene study*

*patient sample; candidate gene study*

*healthy individuals; candidate gene study*

*population-based; candidate gene study (saliva)*

*population-based; candidate gene study (buccal swab)*

*meta-analysis*

*healthy individuals; candidate gene study*

*NEW REFERENCE Dec 2013*

patient sample + healthy individuals; candidate gene study


review


population-based; candidate gene study


meta-analyses


healthy individuals; candidate gene study

NEW REFERENCE Sep 2013


healthy individuals; candidate gene study


healthy individuals; candidate gene study (saliva)


healthy individuals; candidate gene study (buccal swab)


healthy individuals; candidate gene study (buccal swab)


meta-analyses


population-based; candidate gene study (saliva)


healthy individuals; candidate gene study (cheek cells)
patient sample; candidate gene study

population-based; candidate gene study

patient sample; candidate gene study

NEW REFERENCE Dec 2013

patient sample; candidate gene study (buccal swab); biomolecular markers

NEW REFERENCE Sep 2013

review

patient sample + healthy individuals; candidate gene study

patient sample + healthy individuals; candidate gene study

patient sample; candidate gene study

NEW REFERENCE Dec 2013

healthy individuals; candidate gene study

patient sample; candidate gene study

review


healthy individuals; candidate gene study

NEW REFERENCE Sep 2013


patient sample; candidate gene study

NEW REFERENCE Sep 2013


patient sample; candidate gene study


meta-analyses


patient sample + healthy individuals; candidate gene study


patient sample; candidate gene study


healthy individuals; candidate gene study

NEW REFERENCE Dec 2013


healthy individuals; candidate gene study

NEW REFERENCE Dec 2013


population-based; candidate gene study

NEW REFERENCE Dec 2013


population-based; candidate gene study

NEW REFERENCE Dec 2013


patient sample + healthy controls; candidate gene study

NEW REFERENCE Dec 2013

population-based; candidate gene study


healthy individuals; candidate gene study


patient sample; candidate gene study


patient sample; candidate gene study


patient sample; candidate gene study


healthy individuals (autopsy); candidate gene study


patient sample; candidate gene study


healthy individuals; candidate gene study


patient sample; candidate gene study


healthy individuals; candidate gene study (oral specimen)


patient sample + healthy individual (autopsy); candidate gene study (frozen hypothalamus)
review

patient sample; candidate gene study

patient sample + healthy individuals; candidate gene study

healthy individuals; candidate gene study (mouthwash sample)

patient sample; candidate gene study