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>&lt;br&gt;• <em>IL-1β</em></td>
<td>&lt;br&gt;• General health&lt;br&gt;• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning - Depression&lt;br&gt;• Anti-depressant response</td>
<td>&lt;br&gt;(1) &lt;br&gt;(1) &lt;br&gt;(1) &lt;br&gt;(2, 3) &lt;br&gt;(4-6)</td>
</tr>
<tr>
<td></td>
<td>&lt;br&gt;• <em>IL-6</em></td>
<td>&lt;br&gt;• Overall quality of life&lt;br&gt;• General health&lt;br&gt;• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning - Depression&lt;br&gt;• Social functioning&lt;br&gt;• Cognitive functioning</td>
<td>&lt;br&gt;(1) &lt;br&gt;(1) &lt;br&gt;(1, 8-10) &lt;br&gt;(11-13) &lt;br&gt;(13-15) &lt;br&gt;(4-6, 11, 16-18) &lt;br&gt;(1) &lt;br&gt;(13)</td>
</tr>
<tr>
<td></td>
<td>&lt;br&gt;• <em>IL-8</em></td>
<td>&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning - Depression&lt;br&gt;• Cognitive functioning</td>
<td>&lt;br&gt;(19) &lt;br&gt;(4, 20) &lt;br&gt;(21)</td>
</tr>
<tr>
<td></td>
<td>&lt;br&gt;• <em>TNF-α</em></td>
<td>&lt;br&gt;• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning - Depression&lt;br&gt;• Social functioning</td>
<td>&lt;br&gt;(1, 9, 22) &lt;br&gt;(11, 13, 21, 23) &lt;br&gt;(2, 14, 24) &lt;br&gt;(7, 16)</td>
</tr>
<tr>
<td>• inflammation</td>
<td>&lt;br&gt;• <em>CRP</em></td>
<td>&lt;br&gt;• Fatigue&lt;br&gt;• Emotional functioning - Depression</td>
<td>&lt;br&gt;(1) &lt;br&gt;(12, 25)</td>
</tr>
<tr>
<td>• anti-inflammatory</td>
<td>&lt;br&gt;• <em>IL-1RN</em></td>
<td>&lt;br&gt;• General health&lt;br&gt;• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning - depression&lt;br&gt;• Social functioning</td>
<td>&lt;br&gt;(17) &lt;br&gt;(1) &lt;br&gt;(1) &lt;br&gt;(1) &lt;br&gt;(1) &lt;br&gt;(1)</td>
</tr>
<tr>
<td></td>
<td>&lt;br&gt;• <em>IL-1RA</em></td>
<td>&lt;br&gt;• Fatigue&lt;br&gt;• Pain</td>
<td>&lt;br&gt;(12, 21) &lt;br&gt;(3, 26)</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>
<td></td>
<td><strong>IL-10</strong></td>
<td>• General health&lt;br&gt;• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning – Depression&lt;br&gt;• Cognitive functioning</td>
<td>• (1)&lt;br&gt;• (1)&lt;br&gt;• (1)&lt;br&gt;• (13)&lt;br&gt;• (4, 5, 18, 24, 27)&lt;br&gt;• (18)</td>
</tr>
<tr>
<td>Dopaminergic synapse</td>
<td><strong>COMT</strong></td>
<td>• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning – Depression&lt;br&gt;• Emotional functioning – Positive affect&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
<td>• (28)&lt;br&gt;• (29-39)&lt;br&gt;• (40)&lt;br&gt;• (41)&lt;br&gt;• (42-46)&lt;br&gt;• (47, 48)</td>
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<tr>
<td></td>
<td><strong>DRD2</strong></td>
<td>• Emotional functioning – Depression&lt;br&gt;• Emotional functioning – Anxiety&lt;br&gt;• Social functioning</td>
<td>• (40, 49)&lt;br&gt;• (49)&lt;br&gt;• (49-51)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD4</strong></td>
<td>• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Emotional functioning depression&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
<td>• (52)&lt;br&gt;• (46)&lt;br&gt;• (53)&lt;br&gt;• (54)&lt;br&gt;• (55)</td>
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<tr>
<td></td>
<td><strong>DAT1</strong></td>
<td>• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Cognitive functioning</td>
<td>• (56, 57)&lt;br&gt;• (46)&lt;br&gt;• (46)</td>
</tr>
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<td></td>
<td><strong>CREB1</strong></td>
<td>• Pain&lt;br&gt;• Emotional functioning – Depression</td>
<td>• (58)&lt;br&gt;• (59)</td>
</tr>
<tr>
<td>Dopaminergic synapse/Serotonergic synapse</td>
<td><strong>MAOA</strong></td>
<td>• Emotional functioning – depression&lt;br&gt;• Emotional functioning – positive affect&lt;br&gt;• Social functioning</td>
<td>• (53, 60)&lt;br&gt;• (61)&lt;br&gt;• (62)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td><strong>5-HTT (SLC6A4)</strong></td>
<td>• Physical functioning&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning – depression&lt;br&gt;• Emotional functioning – anxiety&lt;br&gt;• Emotional functioning – positive affect&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
<td>• (63)&lt;br&gt;• (39, 64-66)&lt;br&gt;• (67-75)&lt;br&gt;• (70, 76-80)&lt;br&gt;• (81)&lt;br&gt;• (70)&lt;br&gt;• (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>
<td></td>
<td>TPH1</td>
<td>• Overall quality of life</td>
<td>(83)</td>
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<td></td>
<td></td>
<td>• Fatigue</td>
<td>(83)</td>
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<td></td>
<td></td>
<td>• Pain</td>
<td>(83)</td>
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<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>
</tr>
<tr>
<td>Neurotrophin signaling pathway</td>
<td>BDNF</td>
<td>• Physical functioning</td>
<td>(85, 86)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – depression</td>
<td>(5, 7, 59, 87-90)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
<td>(45, 85, 86, 91)</td>
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<td>OXTR</td>
<td>• Social functioning</td>
<td>(92)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – depression</td>
<td>(93, 94)</td>
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<td></td>
<td>• Emotional functioning – anxiety</td>
<td>(95)</td>
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<td></td>
<td></td>
<td>• Emotional functioning – loneliness</td>
<td>(96)</td>
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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>
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<tr>
<td></td>
<td>AVPR1A</td>
<td>• Emotional functioning</td>
<td>(125)</td>
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<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>(126)</td>
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<td></td>
<td></td>
<td>• Emotional functioning – depression</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/](http://www.genome.jp/kegg/) or Genecards, [http://www.genecards.org/](http://www.genecards.org/)

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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*

_healthy individuals; candidate gene study (saliva)_


_patient sample; candidate gene study_


_patient sample; candidate gene study_


_patient sample + healthy individuals; candidate gene study_


_healthy individuals; candidate gene study (buccal swab)_


_review_


_healthy individuals; candidate gene study (buccal cells)_


_meta-analyses; population based; candidate gene study (swab samples)_


_healthy individuals; candidate gene study (saliva)_


_patient sample + matched controls; candidate gene study (blood or mouth swab)_


_healthy individuals; GWAS; replication analyses with external cohorts_

**NEW REFERENCE Sep 2013**


_population-based; candidate gene study (buccal)
*patient sample; candidate gene study*

**NEW REFERENCE Dec 2013**

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

*population-based; candidate gene study*

*patient sample; candidate gene study*

**NEW REFERENCE Dec 2013**

*patient sample + healthy individuals; candidate gene study*

*patient sample; candidate gene study*

*healthy individuals; candidate gene study*

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

**NEW REFERENCE Dec 2013**

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

**NEW REFERENCE Dec 2013**

*meta-analysis*

**NEW REFERENCE Dec 2013**

*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*

review


healthy individuals; candidate gene study (saliva)


population-based; candidate gene study


review


review


healthy individuals; candidate gene study (saliva)


healthy individuals; candidate gene study (saliva or cheek cells)


healthy individuals; candidate gene study

NEW REFERENCE Sep 2013


population-based; candidate gene study

NEW REFERENCE Dec 2013


healthy individuals; candidate gene study

NEW REFERENCE Dec 2013


healthy individuals; candidate gene study

NEW REFERENCE Sep 2013

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