**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):**

Last Update September 2013

<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&lt;br&gt;• pro-inflammatory</td>
<td>• <em>IL-1β</em></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;• Anti-depressant response</td>
<td>• (1)&lt;br&gt;• (1)&lt;br&gt;• (1)&lt;br&gt;• (2, 3)&lt;br&gt;• (4, 5)</td>
</tr>
<tr>
<td></td>
<td>• <em>IL-6</em></td>
<td>• 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>• (1)&lt;br&gt;• (1)&lt;br&gt;• (1, 7)&lt;br&gt;• (8-10)&lt;br&gt;• (10-12)&lt;br&gt;• (4, 5, 8, 13-15)&lt;br&gt;• (1)&lt;br&gt;• (10)</td>
</tr>
<tr>
<td></td>
<td>• <em>IL-8</em></td>
<td>• Pain&lt;br&gt;• Emotional functioning - Depression&lt;br&gt;• Cognitive functioning</td>
<td>• (16)&lt;br&gt;• (4, 17)</td>
</tr>
<tr>
<td></td>
<td>• <em>TNF-α</em></td>
<td>• Physical functioning&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning - Depression&lt;br&gt;• Social functioning</td>
<td>• (1, 7, 19)&lt;br&gt;• (8, 10, 18, 20)&lt;br&gt;• (2, 11)&lt;br&gt;• (6, 13)</td>
</tr>
<tr>
<td>• inflammation</td>
<td>• <em>CRP</em></td>
<td>• Fatigue&lt;br&gt;• Emotional functioning - Depression</td>
<td>• (9)&lt;br&gt;• (14)</td>
</tr>
<tr>
<td>• anti-inflammatory</td>
<td>• <em>IL-1RN</em></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;• Social functioning</td>
<td>• (1)&lt;br&gt;• (1)&lt;br&gt;• (1)&lt;br&gt;• (1)</td>
</tr>
<tr>
<td></td>
<td>• <em>IL-1RA</em></td>
<td>• Fatigue&lt;br&gt;• Pain</td>
<td>• (9, 18)&lt;br&gt;• (3, 21)</td>
</tr>
<tr>
<td>Biological Pathways</td>
<td>Candidate genes</td>
<td>Quality of life domain</td>
<td>Literature</td>
</tr>
<tr>
<td>---------------------</td>
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</tr>
<tr>
<td>IL-10</td>
<td></td>
<td>General health, Physical functioning, Fatigue, Pain, Emotional functioning – Depression, Cognitive functioning</td>
<td>(1), (1), (1), (10), (4, 5, 15, 22), (15)</td>
</tr>
<tr>
<td>Dopaminergic synapse</td>
<td>COMT</td>
<td>Fatigue, Pain, Emotional functioning – Depression, Emotional functioning – Positive affect, Cognitive functioning, Social functioning</td>
<td>(23), (24-34), (35), (36), (37-39), (40, 41)</td>
</tr>
<tr>
<td></td>
<td>DRD2</td>
<td>Emotional functioning – Depression, Emotional functioning – Anxiety, Social functioning</td>
<td>(35, 42), (42), (42-44)</td>
</tr>
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<td></td>
<td>DRD4</td>
<td>Physical functioning, Fatigue, Emotional functioning – depression, Cognitive functioning, Social functioning</td>
<td>(45), (39), (46), (47), (48)</td>
</tr>
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<td></td>
<td>DAT1</td>
<td>Physical functioning, Fatigue, Cognitive functioning</td>
<td>(49, 50), (39), (39)</td>
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<td></td>
<td>CREB1</td>
<td>Pain, Emotional functioning – Depression</td>
<td>(51), (52)</td>
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<tr>
<td>Dopaminergic synapse/</td>
<td>MAOA</td>
<td>Emotional functioning – depression, Emotional functioning – positive affect, Social functioning</td>
<td>(46), (53), (54)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td>5-HTT (SLC6A4)</td>
<td>Pain, Emotional functioning – depression, Emotional functioning – anxiety, Emotional functioning – positive affect, Social functioning</td>
<td>(34, 55-57), (58-62), (63-67), (68), (69)</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>Biological Pathways Candidate genes</td>
<td>TPH1</td>
<td>- Overall quality of life</td>
<td>(70)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Fatigue</td>
<td>(70)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Pain</td>
<td>(70)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Emotional functioning - Depression</td>
<td>(71)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Emotional functioning - anxiety</td>
<td>(70)</td>
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<tr>
<td>Neurotrophin signaling pathway</td>
<td>BDNF</td>
<td>- Emotional functioning – depression</td>
<td>(5, 6, 52, 72-74)</td>
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<tr>
<td></td>
<td></td>
<td>- Cognitive functioning</td>
<td>(38, 75)</td>
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<td></td>
<td>- Social functioning</td>
<td>(76)</td>
</tr>
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<td></td>
<td>OXTR</td>
<td>- Emotional functioning – depression</td>
<td>(77, 78)</td>
</tr>
<tr>
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<td></td>
<td>- Emotional functioning – anxiety</td>
<td>(79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Emotional functioning – loneliness</td>
<td>(80)</td>
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<td></td>
<td>- Social functioning</td>
<td>(69, 81-84)</td>
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<td>APOE</td>
<td>- Physical functioning</td>
<td>(85-88)</td>
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<td>- Emotional functioning – Depression</td>
<td>(89-91)</td>
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<tr>
<td>Neuroactive ligand-receptor interaction</td>
<td>OPRM1</td>
<td>- General health</td>
<td>(92)</td>
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<td></td>
<td></td>
<td>- Pain</td>
<td>(93-99)</td>
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<td></td>
<td>- Emotional functioning</td>
<td>(36)</td>
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<td></td>
<td>- Social functioning</td>
<td>(100)</td>
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<td></td>
<td>AVPR1A</td>
<td>- Emotional functioning – depression</td>
<td>(101)</td>
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<td>- Social functioning</td>
<td>(81, 82, 102-105)</td>
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<td>Glutathione metabolic pathway</td>
<td>DPYD</td>
<td>- Physical functioning</td>
<td>(106)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Fatigue</td>
<td>(106, 107)</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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   population-based; candidate gene study

   patient sample + healthy individuals; candidate gene study

   review

   patient sample + healthy individuals; candidate gene study

   patient sample; candidate gene study

NEW REFERENCE Sep 2013

   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; 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
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)

population-based; candidate gene study (saliva)

population-based; candidate gene study

patient sample + healthy individuals; candidate gene study

patient sample; candidate gene study

healthy individuals; candidate gene study

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*population-based; candidate gene study*


*review*


*patient sample + healthy individuals; candidate gene study*


*patient sample + healthy individuals; candidate gene study*


*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

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

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*