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>• <em>IL-6</em></td>
<td>• Pain</td>
<td>• (1, 2, 3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (4, 5)</td>
</tr>
<tr>
<td></td>
<td>• <em>IL-8</em></td>
<td>• Fatigue</td>
<td>• (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (10)</td>
</tr>
<tr>
<td></td>
<td>• <em>CRP</em></td>
<td>• Pain</td>
<td>• (16)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - Depression</td>
<td>• (4, 17)</td>
</tr>
<tr>
<td></td>
<td>• <em>TNF-α</em></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>
</tr>
<tr>
<td></td>
<td>• <em>IL-1RN</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>• <em>IL-1RA</em></td>
<td>• Fatigue</td>
<td>• (9, 18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (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>
<td>-----------------</td>
<td>------------------------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td><strong>IL-10</strong></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>• (10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – Depression</td>
<td>• (4, 5, 15, 22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
<td>• (15)</td>
</tr>
<tr>
<td>Dopaminergic synapse</td>
<td><strong>COMT</strong></td>
<td>• Fatigue</td>
<td>• (23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
<td>• (24-34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – Depression</td>
<td>• (35)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD2</strong></td>
<td>• Emotional functioning – Depression</td>
<td>• (36)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – Anxiety</td>
<td>• (37-39)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD4</strong></td>
<td>• Physical functioning</td>
<td>• (42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (42-44)</td>
</tr>
<tr>
<td></td>
<td><strong>DAT1</strong></td>
<td>• Emotional functioning – Depression</td>
<td>• (45)</td>
</tr>
<tr>
<td></td>
<td><strong>CREB1</strong></td>
<td>• Physical functioning</td>
<td>• (35, 42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (36)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning</td>
<td>• (42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
<td>• (46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (47)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning</td>
<td>• (48)</td>
</tr>
<tr>
<td></td>
<td><strong>MAOA</strong></td>
<td>• Emotional functioning</td>
<td>• (49, 50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• depression</td>
<td>• (34, 50)</td>
</tr>
<tr>
<td></td>
<td><strong>5-HTT</strong> (SLC6A4)</td>
<td>• Emotional functioning – depression</td>
<td>• (39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Positive affect</td>
<td>• (39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning</td>
<td>• (52)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Depression</td>
<td>• (53)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Positive affect</td>
<td>• (54)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td><strong>5-HTT</strong></td>
<td>• Pain</td>
<td>• (34, 55-57)</td>
</tr>
<tr>
<td></td>
<td><strong>(SLC6A4)</strong></td>
<td>• Emotional functioning – depression</td>
<td>• (58-62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – anxiety</td>
<td>• (63-67)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – positive affect</td>
<td>• (68)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
<td>• (69)</td>
</tr>
<tr>
<td>Biological Pathways</td>
<td>Candidate genes</td>
<td>Quality of life domain</td>
<td>Literature</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>--------------------------</td>
</tr>
</tbody>
</table>
|                                         | • *TPH1*        | • Overall quality of life  
• Fatigue  
• Pain  
• Emotional functioning - Depression  
• Emotional functioning - anxiety | • (70)  
• (70)  
• (70)  
• (71)  
• (70) |
| Neurotrophin signaling pathway          | • *BDNF*  
• *OXTR* | • Emotional functioning – depression  
• Cognitive functioning  
• Social functioning  
• Emotional functioning – anxiety  
• Emotional functioning – loneliness  
• Social functioning | • (5, 6, 52, 72-74)  
• (38, 75)  
• (76)  
• (77, 78)  
• (79)  
• (80)  
• (69, 81-84) |
| Alzheimer’s Disease                     | • *APOE*        | • Physical functioning  
• Emotional functioning - Depression | • (85-88)  
• (89-91) |
| Neuroactive ligand-receptor interaction | • *OPRM1*  
• *AVPR1A* | • General health  
• Pain  
• Emotional functioning  
• Social functioning  
• Emotional functioning – depression  
• Social functioning | • (92)  
• (93-99)  
• (36)  
• (100)  
• (101)  
• (81, 82, 102-105) |
| Glutathione metabolic pathway           | • *DPYD*        | • Physical functioning  
• Fatigue | • (106)  
• (106, 107) |

*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/)
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 + 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**


_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_


_patient sample + healthy individuals; candidate gene study_


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


healthy individuals; candidate gene study (mouthwash sample)


patient sample; candidate gene study