Table 2. Quality-of-life domains per common biological pathway and candidate genes: June 10, 2013

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><strong>IL-1β</strong></td>
<td>General health</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical function</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fatigue</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td><strong>IL-6</strong></td>
<td>Pain</td>
<td>(2, 3)</td>
</tr>
<tr>
<td></td>
<td><strong>IL-8</strong></td>
<td>Emotional function - Depression</td>
<td>(4, 5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-depressant response</td>
<td>(6)</td>
</tr>
<tr>
<td></td>
<td><strong>TNF-α</strong></td>
<td>General health</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical function</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td><strong>CRP</strong></td>
<td>Fatigue</td>
<td>(7-9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emotional function - Depression</td>
<td>(9-11)</td>
</tr>
<tr>
<td></td>
<td><strong>IL-1RN</strong></td>
<td>Social function</td>
<td>(4, 5, 7, 12-14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive function</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td><strong>IL-1RA</strong></td>
<td>Pain</td>
<td>(1)</td>
</tr>
<tr>
<td>• inflammation</td>
<td><strong>IL-10</strong></td>
<td>Emotional function - Depression</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive function</td>
<td>(1)</td>
</tr>
<tr>
<td>• anti-inflammatory</td>
<td><strong>IL-1RN</strong></td>
<td>General health</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical function</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td><strong>IL-1RA</strong></td>
<td>Fatigue</td>
<td>(8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain</td>
<td>(8, 17)</td>
</tr>
<tr>
<td></td>
<td><strong>IL-10</strong></td>
<td>Emotional function - Depression</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive function</td>
<td>(1)</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>Dopaminergic synapse</td>
<td>• COMT</td>
<td>• Fatigue • Pain • Emotional function – Positive affect • Cognitive function • Social function</td>
<td>• (21, 22) • (23-33) • (34) • (35-37) • (38, 39)</td>
</tr>
<tr>
<td></td>
<td>• DRD4</td>
<td>• Physical function • Fatigue • Emotional function – depression • Cognitive function • Social function</td>
<td>• (40) • (37) • (41) • (42) • (43)</td>
</tr>
<tr>
<td></td>
<td>• DAT1</td>
<td>• Physical function • Cognitive function</td>
<td>• (44, 45) • (37)</td>
</tr>
<tr>
<td>Dopaminergic synapse/ Serotoninergic synapse</td>
<td>• MAOA</td>
<td>• Emotional function – depression • Emotional function – positive affect • Social function</td>
<td>• (41) • (46) • (47)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td>• 5-HTT (SLC6A4)</td>
<td>• Pain • Emotional function – depression • Emotional function – anxiety • Emotional function – positive affect • Social function</td>
<td>• (33, 48-50) • (51, 52) • (53-57) • (58) • (59)</td>
</tr>
<tr>
<td></td>
<td>• TPH1</td>
<td>• General health • Fatigue • Pain • Emotional function – anxiety</td>
<td>• (60) • (60) • (60) • (60)</td>
</tr>
<tr>
<td>Neurotrophin signaling pathway</td>
<td>• BDNF</td>
<td>• Emotional function – depression • Cognitive function • Social function</td>
<td>• (5, 6, 61-64) • (36, 65) • (66)</td>
</tr>
<tr>
<td></td>
<td>• OXTR</td>
<td>• Emotional function – depression • Emotional function – anxiety • Emotional function – loneliness • Social function</td>
<td>• (67, 68) • (69) • (70) • (59, 71-74)</td>
</tr>
</tbody>
</table>
### Biological Pathways

<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>Neuroactive ligand-receptor interaction</td>
<td>• OPRM1</td>
<td>• Fatigue</td>
<td>• (22)</td>
</tr>
<tr>
<td></td>
<td>• AVPR1A</td>
<td>• Pain</td>
<td>• (75-81)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional function</td>
<td>• (34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social function</td>
<td>• (82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional function – depression</td>
<td>• (83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social function</td>
<td>• (71, 72, 84-87)</td>
</tr>
<tr>
<td>Glutathione metabolic pathway</td>
<td>• DPYD</td>
<td>• Physical function</td>
<td>• (88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
<td>• (88, 89)</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/)

### 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*

   *population-based; candidate gene study*

   *patient sample; biomolecular marker*


*patient sample; candidate gene study (saliva)*

22. Zwinderman A, Sprangers MA, Baas F, et al.: Genes selected for their relevance to pain or cachexia are also associated with fatigue and pain: Evidence from the European Pharmacogenetic Opioid Study. Submitted, 2013
*patient sample; candidate gene study*

*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


patient sample + healthy individuals; candidate gene study


review


healthy individuals; candidate gene study (saliva)


patient sample; candidate gene study


healthy individuals; candidate gene study (saliva)


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)

   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

   review

   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*


*review*


*patient sample + healthy individuals; candidate gene study*


*patient sample + healthy individuals; candidate gene study*


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


*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)

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