<table>
<thead>
<tr>
<th>Biological Pathways</th>
<th>Candidate genes</th>
<th>Quality of life domain</th>
<th>Literature</th>
</tr>
</thead>
</table>
| Cytokine-cytokine receptor interaction  
  • pro-inflammatory | **IL-1β**  
  • **IL-6**  
  • **IL-8**  
  • **TNF-α** | **General health**  
  • **Physical functioning**  
  • **Fatigue**  
  • **Pain**  
  • **Emotional functioning - Depression**  
  • **Anti-depressant response**  
  • **Overall quality of life**  
  • **General health**  
  • **Physical functioning**  
  • **Fatigue**  
  • **Pain**  
  • **Emotional functioning - Depression**  
  • **Social functioning**  
  • **Cognitive functioning**  
  • **Pain**  
  • **Emotional functioning – Depression**  
  • **Social functioning**  
  • **Fatigue**  
  • **Pain** | • (1)  
  • (1)  
  • (1)  
  • (2, 3)  
  • (4, 5)  
  • (1)  
  • (10)  
  • (1)  
  • (1)  
  • (1)  
  • (7)  
  • (10-12)  
  • (4, 5, 8, 13-15)  
  • (1)  
  • (10)  
  • (1)  
  • (1)  
  • (1, 7, 19)  
  • (8, 10, 18, 20)  
  • (2, 11)  
  • (6, 13)  
  • (1)  
  • (16)  
  • (4, 17)  
  • (18)  |
| • inflammation | **CRP** | **Fatigue**  
  • **Emotional functioning - Depression** | • (9)  
  • (14) |
| • anti-inflammatory | **IL-1RN** | **General health**  
  • **Physical functioning**  
  • **Fatigue**  
  • **Pain**  
  • **Emotional functioning - depression**  
  • **Social functioning** | • (1)  
  • (1)  
  • (1)  
  • (1)  
  • (1)  
  • (1)  |
| • inflammation | **IL-1RA** | **Fatigue**  
  • **Pain** | • (9, 18)  
  • (3, 21) |
<table>
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<tr>
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<tbody>
<tr>
<td><strong>IL-10</strong></td>
<td></td>
<td>General health</td>
<td>(1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Physical functioning</td>
<td>(1)</td>
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<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 –</td>
<td>(4, 5, 15, 22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depression</td>
<td></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 –</td>
<td>(35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depression</td>
<td>(36)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD2</strong></td>
<td>Emotional functioning –</td>
<td>(35, 42)</td>
</tr>
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<td>Depression</td>
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<tr>
<td></td>
<td></td>
<td>Emotional functioning –</td>
<td>(42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anxiety</td>
<td>(42-44)</td>
</tr>
<tr>
<td></td>
<td><strong>DRD4</strong></td>
<td>Physical functioning</td>
<td>(45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fatigue</td>
<td>(39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emotional functioning</td>
<td>(46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>depression</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Cognitive functioning</td>
<td>(47)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Social functioning</td>
<td>(48)</td>
</tr>
<tr>
<td></td>
<td><strong>DAT1</strong></td>
<td>Physical functioning</td>
<td>(49, 50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fatigue</td>
<td>(39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive functioning</td>
<td>(39)</td>
</tr>
<tr>
<td></td>
<td><strong>CREB1</strong></td>
<td>Pain</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></td>
</tr>
<tr>
<td>Dopaminergic synapse/</td>
<td><strong>MAOA</strong></td>
<td>Emotional functioning</td>
<td>(46)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td></td>
<td>– depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emotional functioning –</td>
<td>(53)</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
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<td>Social functioning</td>
<td>(54)</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td><strong>5-HTT</strong> (SLC6A4)</td>
<td>Pain</td>
<td>(34, 55-57)</td>
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<td>Emotional functioning</td>
<td>(58-62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– depression</td>
<td>(63-67)</td>
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<td></td>
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<td>Emotional functioning</td>
<td>(68)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– anxiety</td>
<td>(69)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emotional functioning</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>– positive affect</td>
<td></td>
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<td></td>
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<td>Social functioning</td>
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</tr>
</tbody>
</table>
| TPH1                                        | ● TPH1          | • Overall quality of life  
• Fatigue  
• Pain  
• Emotional functioning - Depression  
• Emotional functioning - anxiety                      | ● (70)      |
|                                             |                 |                                                                                        | ● (70)      |
|                                             |                 |                                                                                        | ● (70)      |
|                                             |                 |                                                                                        | ● (71)      |
|                                             |                 |                                                                                        | ● (70)      |
| Neurotrophin signaling pathway              | ● BDNF          | • Emotional functioning – depression  
• Cognitive functioning  
• Social functioning                      | ● (5, 6, 52, 72-74) |
|                                             |                 |                                                                                        | ● (38, 75) |
|                                             |                 |                                                                                        | ● (76)      |
|                                             | ● OXTR          | • Emotional functioning – depression  
• Emotional functioning – anxiety  
• Emotional functioning - loneliness  
• Social functioning                      | ● (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         | • General health  
• Pain  
• Emotional functioning  
• Social functioning                      | ● (92)      |
|                                             | ● AVPR1A        | • Emotional functioning – depression  
• Social functioning                      | ● (93-99)  |
|                                             |                 |                                                                                        | ● (36)      |
|                                             |                 |                                                                                        | ● (100)     |
| Glutathione metabolic pathway               | ● DPYD          | • Physical functioning  
• Fatigue                      | ● (101)     |
|                                             |                 |                                                                                        | ● (81, 82, 102-105) |

*Biological pathways are according to KEGG (Kyoto Encylopaedia 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)


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)

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

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**


**review**


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*