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


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NEW REFERENCE Sep 2013


patient sample + healthy individuals; candidate gene study


patient sample; candidate gene study


patient sample + healthy individuals; candidate gene study

sympathetic nervous and mucosal immune systems in breast cancer survivors.

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
   review

60. Grabe HJ, Schwahn C, Mahler J, et al.: Moderation of adult depression by the
   serotonin transporter promoter variant (5-HTTLPR), childhood abuse and adult
   traumatic events in a general population sample. Am J Med Genet B
   Neuropsychiatr Genet 159B:298-309, 2012
   population-based; candidate gene study

61. Munafo MR, Brown SM, Hariri AR: Serotonin transporter (5-HTTLPR) genotype and
   meta-analyses

   healthy individuals; candidate gene study

   NEW REFERENCE Sep 2013

   healthy individuals; candidate gene study

   polymorphism modulates the retention of fear extinction memory. Proc Natl Acad
   healthy individuals; candidate gene study (saliva)

   transporter function affects human fear expression indexed by fear-potentiated
   healthy individuals; candidate gene study (buccal swab)

66. Osinsky R, Losch A, Hennig J, et al.: Attentional bias to negative information and
   5-HTTLPR genotype interactively predict students’ emotional reactivity to first
   healthy individuals; candidate gene study (buccal swab)

   in the promoter region of the serotonin transporter gene and biased
   attention for emotional information: a meta-analysis. Biol Psychiatry 71:373-379,
   2012
   meta-analyses

68. De Neve JE: Functional polymorphism (5-HTTLPR) in the serotonin transporter
   gene is associated with subjective well-being: evidence from a US nationally
   population-based; candidate gene study (saliva)

69. Bakermans-Kranenburg MJ, van Ijzendoorn MH: Oxytocin receptor (OXTR) and
   serotonin transporter (5-HTT) genes associated with observed parenting. Soc
   Cogn Affect Neurosci 3:128-134, 2008
   healthy individuals; candidate gene study (cheek cells)

70. Jun SE, Kohen R, Cain KC, et al.: TPH gene polymorphisms are associated with
   disease perception and quality of life in women with irritable bowel syndrome. Biol
   Res Nurs, 2012
   patient sample; 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 (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


healthy individuals; candidate gene study (mouthwash sample)


patient sample; candidate gene study