<table>
<thead>
<tr>
<th>Biological pathways</th>
<th>Candidate gene/ marker</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)  
• (4-6) |
| | • **IL-6** | • Overall quality of life  
• General health  
• Physical functioning  
• Fatigue  
• Pain  
• Emotional functioning - depression  
• Social functioning  
• Cognitive functioning | • (1)  
• (1)  
• (1, 8-12)  
• (13-16)  
• (15, 17-19)  
• (4-6, 13, 20-22)  
• (1)  
• (15, 23) |
| | • **IL-8** | • Pain  
• Emotional functioning - depression  
• Cognitive functioning | • (24)  
• (4, 25)  
• (26) |
| | • **TNF-α** | • Physical functioning  
• Fatigue  
• Pain  
• Emotional functioning - depression  
• Social functioning | • (1, 9, 27)  
• (13, 15, 26, 28)  
• (2, 17, 29)  
• (7, 20) |
| • inflammation | • **CRP** | • Fatigue  
• Emotional functioning - depression | • (1)  
• (14, 30, 31) |
| • anti-inflammatory | • **IL-1RN** | • General health  
• Physical functioning  
• Fatigue  
• Pain  
• Emotional functioning - depression  
• Social functioning | • (21)  
• (1)  
• (1)  
• (1)  
• (1)  
• (1) |
| | • **IL-1RA** | • Fatigue  
• Pain | • (14, 26)  
• (3, 32) |
<table>
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<tr>
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<th>Candidate gene/ marker</th>
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</thead>
<tbody>
<tr>
<td>IL-10</td>
<td></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>(15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emotional functioning</td>
<td>(4, 5, 22, 29, 33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>– depression</td>
<td>(22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive functioning</td>
<td></td>
</tr>
</tbody>
</table>

Dopaminergic synapse

<table>
<thead>
<tr>
<th>Candidate gene/ marker</th>
<th>Quality of life domain</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMT</td>
<td>Fatigue</td>
<td>(34)</td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>(19, 35-45)</td>
</tr>
<tr>
<td></td>
<td>Emotional functioning – depression</td>
<td>(46-48)</td>
</tr>
<tr>
<td></td>
<td>Emotional functioning – anxiety</td>
<td>(47)</td>
</tr>
<tr>
<td></td>
<td>Cognitive functioning</td>
<td>(49)</td>
</tr>
<tr>
<td></td>
<td>Social functioning</td>
<td>(50-56)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(57-59)</td>
</tr>
</tbody>
</table>

| DRD2                  | Emotional functioning – depression | (46, 60) |
|                       | Emotional functioning – anxiety   | (60)      |
|                       | Cognitive functioning             | (61)      |
|                       | Social functioning                | (60, 62, 63) |

| DRD4                  | Physical functioning            | (64)      |
|                       | Fatigue                          | (54)      |
|                       | Pain                              | (65)      |
|                       | Emotional functioning depression  | (66, 67)  |
|                       | Cognitive functioning             | (68)      |
|                       | Social functioning                | (69)      |

| DAT1                  | Physical functioning            | (70, 71)  |
|                       | Fatigue                          | (54)      |
|                       | Pain                              | (72)      |
|                       | Cognitive functioning             | (54)      |

| CREB1                 | Pain                              | (73)      |
|                       | Emotional functioning – depression | (74, 75)  |

| GCH1                  | Pain                              | (76, 77)  |
|                       | Social functioning                 | (78)      |

RNA transport

<table>
<thead>
<tr>
<th>Candidate gene/ marker</th>
<th>Quality of life domain</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMR1</td>
<td>Physical functioning</td>
<td>(79)</td>
</tr>
<tr>
<td></td>
<td>Cognitive functioning</td>
<td>(80)</td>
</tr>
<tr>
<td>Biological Pathways</td>
<td>Candidate gene/ marker</td>
<td>Quality of life domain</td>
</tr>
<tr>
<td>------------------------------------------</td>
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<td>------------------------------------------------------------</td>
</tr>
<tr>
<td>Serotonergic synapse</td>
<td><strong>5-HTT</strong> <em>(SLC6A4)</em></td>
<td>• Physical functioning&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning – depression&lt;br&gt;• Emotional functioning – anxiety&lt;br&gt;• Emotional functioning – positive affect&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
</tr>
<tr>
<td></td>
<td><strong>TPH1</strong></td>
<td>• Overall quality of life&lt;br&gt;• Fatigue&lt;br&gt;• Pain&lt;br&gt;• Emotional functioning – depression&lt;br&gt;• Emotional functioning – anxiety</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>
</tr>
<tr>
<td></td>
<td><strong>CACNA1C</strong></td>
<td>• Emotional functioning – depression&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
</tr>
<tr>
<td></td>
<td><strong>VMAT2</strong></td>
<td>• Emotional functioning – depression&lt;br&gt;• Cognitive functioning</td>
</tr>
<tr>
<td>Neurotrophin signaling pathway</td>
<td><strong>BDNF</strong></td>
<td>• Physical functioning&lt;br&gt;• Emotional functioning – depression&lt;br&gt;• Emotional functioning – anxiety&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
</tr>
<tr>
<td></td>
<td><strong>OXTR</strong></td>
<td>• Emotional functioning – depression&lt;br&gt;• Emotional functioning – anxiety&lt;br&gt;• Emotional functioning – loneliness&lt;br&gt;• Cognitive functioning&lt;br&gt;• Social functioning</td>
</tr>
<tr>
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<td>-----------------------------------------------------------</td>
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<tr>
<td>Alzheimer’s Disease</td>
<td>• APOE</td>
<td>• Physical functioning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cognitive functioning</td>
</tr>
<tr>
<td>Neuroactive ligand-receptor interaction</td>
<td>• OPRM1</td>
<td>• General health</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pain</td>
</tr>
<tr>
<td></td>
<td>• AVPR1A</td>
<td>• Emotional functioning</td>
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<td>• Social functioning</td>
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<tr>
<td></td>
<td></td>
<td>• Emotional functioning – depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social functioning</td>
</tr>
<tr>
<td>Glutathione metabolic pathway</td>
<td>• DPYD</td>
<td>• Physical functioning</td>
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<tr>
<td></td>
<td></td>
<td>• Fatigue</td>
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<tr>
<td>Metabolic pathway</td>
<td>• MTHFR</td>
<td>• Physical functioning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning – depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emotional functioning - loneliness</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; biomolecular markers

patient sample + healthy individuals; candidate gene study

healthy individuals; candidate gene study

patient sample; candidate gene study

healthy individuals; candidate gene study

population-based; biomolecular markers
NEW REFERENCE Mar 2014

healthy individuals; biomolecular markers
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population-based; candidate gene study

patient sample; biomolecular marker

review

population-based; candidate gene study
NEW REFERENCE Jun 2014


**patient sample; candidate gene study**


**patient sample; candidate gene study**


**review**

**NEW REFERENCE Jun 2014**


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**NEW REFERENCE Mar 2014**


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patient sample + matched healthy individuals; candidate gene study

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patient sample; candidate gene study

patient sample; candidate gene study

patient sample, candidate gene study (buccal swab)

review

review

population-based + replication sample; candidate gene study (buccal swab)
NEW REFERENCE Mar 2014

healthy individuals; candidate gene study
NEW REFERENCE Jun 2014

review

patient sample + healthy individuals; candidate gene study

patient sample + healthy controls; candidate gene study (buccal swab)

**patient sample + healthy controls; candidate gene study (saliva)**


**review**


**healthy individuals; candidate gene study (saliva)**


**healthy individuals; candidate gene study**

**NEW REFERENCE Mar 2014**


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**NEW REFERENCE Jun 2014**


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   healthy individuals; candidate gene study (buccal swab)

   patient sample; candidate gene study

   review

   population-based; candidate gene study

   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; candidate gene study (mouth wash sample)

   healthy individuals; GWAS; replication analyses with external cohorts

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

*patient sample; candidate gene study*  
**NEW REFERENCE Mar 2014**

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**NEW REFERENCE Mar 2014**

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*patient sample + healthy individuals; candidate gene study*

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NEW REFERENCE Mar 2014


population-based; candidate gene study (saliva)


population-based; candidate gene study (buccal swab)


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healthy individuals; candidate gene study


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review


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meta-analyses


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NEW REFERENCE Jun 2014


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NEW REFERENCE Mar 2014

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NEW REFERENCE Jun 2014


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NEW REFERENCE Mar 2014


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NEW REFERENCE Jun 2014


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NEW REFERENCE Jun 2014


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meta-analyses


population-based; candidate gene study (saliva)


healthy individuals; candidate gene study (cheek cells)

healthy individuals; candidate gene study

NEW REFERENCE Jun 2014


patient sample; candidate gene study


population-based; candidate gene study


patient sample; candidate gene study


population-based; candidate gene study (saliva)


population-based; candidate gene study


population-based; candidate gene study; mouth wash


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NEW REFERENCE Mar 2014


review


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NEW REFERENCE Mar 2014


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healthy individuals; candidate gene study

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review

review

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population-based; candidate gene study


patient sample + healthy individuals; candidate gene study

NEW REFERENCE Mar 2014


review


review


healthy individuals; candidate gene study (saliva)


healthy individuals; candidate gene study (saliva or cheek cells)


healthy individuals; candidate gene study


population-based; candidate gene study


healthy individuals; candidate gene study


healthy individuals; candidate gene study


healthy individuals; 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


healthy individuals + replication cohort; candidate gene study (buccal + whole blood)
NEW REFERENCE Jun 2014

patient sample + healthy individuals; candidate gene study
NEW REFERENCE Mar 2014

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