Quadra-stable Dynamics of p53 and PTEN in the DNA damage response

S1 Data File

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3 Children's Cancer Institute, Porto Alegre, RS, Brazil

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Code of the model in .sbml format.

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```
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```
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        </qual:transition>
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                negative" qual:id="tr_p53_K_in_5"/>
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    <qual:input qual:qualitativeSpecies="Caspase" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_p21_in_19"/>
    <qual:input qual:qualitativeSpecies="AKT" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_p21_in_23"/>
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```

```
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        <qual:input qual:qualitativeSpecies="p53_K" qual:transitionEffect="none" qual:sign="
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          <qual:input qual:qualitativeSpecies="RB" qual:transitionEffect="none" qual:sign="
              negative" qual:id="tr_Myc_in_13"/>
          <qual:input qual:qualitativeSpecies="E2F1" qual:transitionEffect="none" qual:sign="
              positive" qual:id="tr_Myc_in_14"/>
          <qual:input qual:qualitativeSpecies="AKT" qual:transitionEffect="none" qual:sign="
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        <qual:listOfOutputs>
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        <qual:input qual:qualitativeSpecies="AMPK_MAPK" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_Cdc25_in_2"/>
        <qual:input qual:qualitativeSpecies="PTEN" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_Cdc25_in_22"/>
        <qual:input qual:qualitativeSpecies="Wee1" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_Cdc25_in_29"/>
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            </math>
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      </qual:listOfFunctionTerms>
    </qual:transition>
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        <qual:input qual:qualitativeSpecies="Cdc25" qual:transitionEffect="none" qual:sign="positive" qual:id="tr_Cdc2_CycB_in_11"/>
        <qual:input qual:qualitativeSpecies="PTEN" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_Cdc2_CycB_in_22"/>
        <qual:input qual:qualitativeSpecies="Wee1" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_Cdc2_CycB_in_29"/>
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      <qual:listOfOutputs>
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          <qual:input qual:qualitativeSpecies="Cdc25" qual:transitionEffect="none" qual:sign="positive" qual:id="tr_E2F1_in_11"/>
          <qual:input qual:qualitativeSpecies="RB" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_E2F1_in_13"/>
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          </qual:listOfInputs>
          <qual:listOfOutputs>
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          </qual:listOfOutputs>
          <qual:listOfFunctionTerms>
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            <qual:functionTerm qual:resultLevel="1">
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                  <ci> E2F1 </ci>
                  <cn type="integer"> 1 </cn>
                </apply>
              </math>
                      </qual:functionTerm>
          </qual:listOfFunctionTerms>
        </qual:transition>
        <qual:transition qual:id="tr_PUMA">
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            <qual:input qual:qualitativeSpecies="p53_K" qual:transitionEffect="none" qual:sign="positive" qual:id="tr_PUMA_in_7"/>
            <qual:input qual:qualitativeSpecies="miR221" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_PUMA_in_21"/>
          </qual:listOfInputs>
          <qual:listOfOutputs>
            <qual:output qual:qualitativeSpecies="PUMA" qual:transitionEffect="assignmentLevel" qual:id="tr_PUMA_out"/>
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          <qual:listOfFunctionTerms>
            <qual:defaultTerm qual:resultLevel="0">
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            <qual:functionTerm qual:resultLevel="1">
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                  <apply>
                    <eq/>
                    <ci> p53_K </ci>
                    <cn type="integer"> 1 </cn>
                  </apply>
                  <apply>
                    <eq/>
                    <ci> miR221 </ci>
                    <cn type="integer"> 0 </cn>
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1192                  </apply>
1193                </apply>
1194              </math>
1195                      </qual:functionTerm>
1196          </qual:listOfFunctionTerms>
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                  positive" qual:id="tr_BCL2_in_14"/>
1202            <qual:input qual:qualitativeSpecies="PUMA" qual:transitionEffect="none" qual:sign="
                  negative" qual:id="tr_BCL2_in_16"/>
1203          </qual:listOfInputs>
1204          <qual:listOfOutputs>
1205            <qual:output qual:qualitativeSpecies="BCL2" qual:transitionEffect="assignmentLevel"
                  qual:id="tr_BCL2_out"/>
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1207          <qual:listOfFunctionTerms>
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1210            <qual:functionTerm qual:resultLevel="1">
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1213                  <and/>
1214                  <apply>
1215                    <eq/>
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1220                    <eq/>
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1223                  </apply>
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1227                    <cn type="integer"> 0 </cn>
1228                  </apply>
1229                </apply>
1230              </math>
1231                      </qual:functionTerm>
1232          </qual:listOfFunctionTerms>
1233        </qual:transition>
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1237            <qual:input qual:qualitativeSpecies="BCL2" qual:transitionEffect="none" qual:sign="
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1238          </qual:listOfInputs>
1239          <qual:listOfOutputs>
1240            <qual:output qual:qualitativeSpecies="BAX" qual:transitionEffect="assignmentLevel"
                  qual:id="tr_BAX_out"/>
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1242          <qual:listOfFunctionTerms>
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1250                    <eq/>
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1254                  <apply>
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1260              </math>
1261                    </qual:functionTerm>
1262          </qual:listOfFunctionTerms>
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1264        <qual:transition qual:id="tr_Caspase">
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1267            <qual:input qual:qualitativeSpecies="BCL2" qual:transitionEffect="none" qual:sign="
                  negative" qual:id="tr_Caspase_in_17"/>
1268            <qual:input qual:qualitativeSpecies="BAX" qual:transitionEffect="none" qual:sign="
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1270          <qual:listOfOutputs>
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1283                      <eq/>
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1291                    </apply>
1292                  </apply>
1293                  <apply>
1294                    <and/>
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1300                    <apply>
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1309                    </apply>
1310                  </apply>
1311                </apply>
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1314          </qual:listOfFunctionTerms>
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1316        <qual:transition qual:id="tr_TUG1">
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1320          <qual:listOfOutputs>
1321            <qual:output qual:qualitativeSpecies="TUG1" qual:transitionEffect="assignmentLevel"
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1323          <qual:listOfFunctionTerms>
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1333              </math>
1334                      </qual:functionTerm>
1335          </qual:listOfFunctionTerms>
1336        </qual:transition>
1337        <qual:transition qual:id="tr_miR221">
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1339            <qual:input qual:qualitativeSpecies="E2F1" qual:transitionEffect="none" qual:sign="
                  positive" qual:id="tr_miR221_in_14"/>
1340            <qual:input qual:qualitativeSpecies="TUG1" qual:transitionEffect="none" qual:sign="
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1341          </qual:listOfInputs>
1342          <qual:listOfOutputs>
1343            <qual:output qual:qualitativeSpecies="miR221" qual:transitionEffect="assignmentLevel
                  " qual:id="tr_miR221_out"/>
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1358                    </apply>
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1361                      <ci> TUG1 </ci>
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    </qual:transition>
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            qual:sign="positive" qual:id="tr_PTEN_in_1"/>
        <qual:input qual:qualitativeSpecies="p53_K" qual:transitionEffect="none" qual:sign="
            positive" qual:id="tr_PTEN_in_7"/>
        <qual:input qual:qualitativeSpecies="miR221" qual:transitionEffect="none" qual:sign=
            "negative" qual:id="tr_PTEN_in_21"/>
        <qual:input qual:qualitativeSpecies="WWP1" qual:transitionEffect="none" qual:sign="
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      <qual:listOfOutputs>
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            qual:id="tr_PTEN_out"/>
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      <qual:listOfFunctionTerms>
        <qual:defaultTerm qual:resultLevel="0">
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                <and/>
                <apply>
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              </apply>
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                <and/>
                <apply>
                  <eq/>
```

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                    <cn type="integer"> 1 </cn>
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                    <eq/>
                    <ci> miR221 </ci>
                    <cn type="integer"> 0 </cn>
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                    <cn type="integer"> 0 </cn>
                  </apply>
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                    </qual:functionTerm>
      </qual:listOfFunctionTerms>
    </qual:transition>
    <qual:transition qual:id="tr_AKT">
      <qual:listOfInputs>
        <qual:input qual:qualitativeSpecies="PTEN" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_AKT_in_22"/>
        <qual:input qual:qualitativeSpecies="mTOR2" qual:transitionEffect="none" qual:sign="positive" qual:id="tr_AKT_in_25"/>
      </qual:listOfInputs>
      <qual:listOfOutputs>
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        <qual:defaultTerm qual:resultLevel="0">
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              </apply>
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                <and/>
                <apply>
                  <eq/>
                  <ci> PTEN </ci>
                  <cn type="integer">1</cn>
                </apply>
                <apply>
                  <eq/>
                  <ci> mTOR2 </ci>
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              </apply>
            </apply>
          </math>
                    </qual:functionTerm>
      </qual:listOfFunctionTerms>
    </qual:transition>
    <qual:transition qual:id="tr_mTOR1">
      <qual:listOfInputs>
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                  qual:sign="negative" qual:id="tr_mTOR1_in_2"/>
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                  positive" qual:id="tr_mTOR1_in_23"/>
1480          <qual:input qual:qualitativeSpecies="ULK1_Beclin1" qual:transitionEffect="none"
                  qual:sign="negative" qual:id="tr_mTOR1_in_26"/>
1481        </qual:listOfInputs>
1482        <qual:listOfOutputs>
1483          <qual:output qual:qualitativeSpecies="mTOR1" qual:transitionEffect="assignmentLevel"
                   qual:id="tr_mTOR1_out"/>
1484        </qual:listOfOutputs>
1485        <qual:listOfFunctionTerms>
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1494                  <apply>
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1498                  </apply>
1499                  <apply>
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1502                    <cn type="integer"> 1 </cn>
1503                  </apply>
1504                </apply>
1505                <apply>
1506                  <and/>
1507                  <apply>
1508                    <eq/>
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1511                  </apply>
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1513                    <eq/>
1514                    <ci> AKT </ci>
1515                    <cn type="integer"> 1 </cn>
1516                  </apply>
1517                  <apply>
1518                    <eq/>
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1520                    <cn type="integer"> 0 </cn>
1521                  </apply>
1522                </apply>
1523              </apply>
1524            </math>
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1526        </qual:listOfFunctionTerms>
1527      </qual:transition>
1528      <qual:transition qual:id="tr_mTOR2">
1529        <qual:listOfInputs>
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                  qual:sign="negative" qual:id="tr_mTOR2_in_2"/>
1531          <qual:input qual:qualitativeSpecies="Sirt_1" qual:transitionEffect="none" qual:sign=
                  "negative" qual:id="tr_mTOR2_in_15"/>
1532          <qual:input qual:qualitativeSpecies="PTEN" qual:transitionEffect="none" qual:sign="
                  negative" qual:id="tr_mTOR2_in_22"/>
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                positive" qual:id="tr_mTOR2_in_23"/>
1534          <qual:input qual:qualitativeSpecies="mTOR1" qual:transitionEffect="none" qual:sign="
                negative" qual:id="tr_mTOR2_in_24"/>
1535          <qual:input qual:qualitativeSpecies="hTERT" qual:transitionEffect="none" qual:sign="
                negative" qual:id="tr_mTOR2_in_28"/>
1536        </qual:listOfInputs>
1537        <qual:listOfOutputs>
1538          <qual:output qual:qualitativeSpecies="mTOR2" qual:transitionEffect="assignmentLevel"
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1647            <apply>
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        <qual:input qual:qualitativeSpecies="mTOR1" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_ULK1_Beclin1_in_24"/>
        <qual:input qual:qualitativeSpecies="mTOR2" qual:transitionEffect="none" qual:sign="negative" qual:id="tr_ULK1_Beclin1_in_25"/>
      </qual:listOfInputs>
      <qual:listOfOutputs>
        <qual:output qual:qualitativeSpecies="ULK1_Beclin1" qual:transitionEffect="assignmentLevel" qual:id="tr_ULK1_Beclin1_out"/>
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                <eq/>
                <ci> mTOR1 </ci>
                <cn type="integer"> 0 </cn>
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                <ci> mTOR2 </ci>
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            </apply>
          </math>
                  </qual:functionTerm>
      </qual:listOfFunctionTerms>
    </qual:transition>
    <qual:transition qual:id="tr_WWP1">
      <qual:listOfInputs>
        <qual:input qual:qualitativeSpecies="Myc" qual:transitionEffect="none" qual:sign="positive" qual:id="tr_WWP1_in_10"/>
      </qual:listOfInputs>
      <qual:listOfOutputs>
```

```
1772          <qual:output qual:qualitativeSpecies="WWP1" qual:transitionEffect="assignmentLevel"
                  qual:id="tr_WWP1_out"/>
1773        </qual:listOfOutputs>
1774        <qual:listOfFunctionTerms>
1775          <qual:defaultTerm qual:resultLevel="0">
1776          </qual:defaultTerm>
1777          <qual:functionTerm qual:resultLevel="1">
1778            <math xmlns="http://www.w3.org/1998/Math/MathML">
1779              <apply>
1780                <eq/>
1781                <ci> Myc </ci>
1782                <cn type="integer"> 1 </cn>
1783              </apply>
1784            </math>
1785                    </qual:functionTerm>
1786        </qual:listOfFunctionTerms>
1787      </qual:transition>
1788      <qual:transition qual:id="tr_hTERT">
1789        <qual:listOfInputs>
1790          <qual:input qual:qualitativeSpecies="p53" qual:transitionEffect="none" qual:sign="
                  negative" qual:id="tr_hTERT_in_4"/>
1791          <qual:input qual:qualitativeSpecies="Myc" qual:transitionEffect="none" qual:sign="
                  positive" qual:id="tr_hTERT_in_10"/>
1792          <qual:input qual:qualitativeSpecies="PTEN" qual:transitionEffect="none" qual:sign="
                  negative" qual:id="tr_hTERT_in_22"/>
1793          <qual:input qual:qualitativeSpecies="AKT" qual:transitionEffect="none" qual:sign="
                  positive" qual:id="tr_hTERT_in_23"/>
1794        </qual:listOfInputs>
1795        <qual:listOfOutputs>
1796          <qual:output qual:qualitativeSpecies="hTERT" qual:transitionEffect="assignmentLevel"
                  qual:id="tr_hTERT_out"/>
1797        </qual:listOfOutputs>
1798        <qual:listOfFunctionTerms>
1799          <qual:defaultTerm qual:resultLevel="0">
1800          </qual:defaultTerm>
1801          <qual:functionTerm qual:resultLevel="1">
1802            <math xmlns="http://www.w3.org/1998/Math/MathML">
1803              <apply>
1804                <or/>
1805                <apply>
1806                  <and/>
1807                  <apply>
1808                    <eq/>
1809                    <ci> p53 </ci>
1810                    <cn type="integer"> 0 </cn>
1811                  </apply>
1812                  <apply>
1813                    <eq/>
1814                    <ci> Myc </ci>
1815                    <cn type="integer"> 0 </cn>
1816                  </apply>
1817                  <apply>
1818                    <eq/>
1819                    <ci> PTEN </ci>
1820                    <cn type="integer"> 0 </cn>
1821                  </apply>
1822                  <apply>
1823                    <eq/>
1824                    <ci> AKT </ci>
1825                    <cn type="integer"> 1 </cn>
1826                  </apply>
1827                </apply>
```

```
1828                <apply>
1829                  <and/>
1830                  <apply>
1831                    <eq/>
1832                    <ci> p53 </ci>
1833                    <cn type="integer"> 0 </cn>
1834                  </apply>
1835                  <apply>
1836                    <eq/>
1837                    <ci> Myc </ci>
1838                    <cn type="integer"> 1 </cn>
1839                  </apply>
1840                  <apply>
1841                    <eq/>
1842                    <ci> PTEN </ci>
1843                    <cn type="integer"> 0 </cn>
1844                  </apply>
1845                </apply>
1846              </apply>
1847            </math>
1848                    </qual:functionTerm>
1849        </qual:listOfFunctionTerms>
1850      </qual:transition>
1851      <qual:transition qual:id="tr_Wee1">
1852        <qual:listOfInputs>
1853          <qual:input qual:qualitativeSpecies="AKT" qual:transitionEffect="none" qual:sign="
                negative" qual:id="tr_Wee1_in_23"/>
1854        </qual:listOfInputs>
1855        <qual:listOfOutputs>
1856          <qual:output qual:qualitativeSpecies="Wee1" qual:transitionEffect="assignmentLevel"
                qual:id="tr_Wee1_out"/>
1857        </qual:listOfOutputs>
1858        <qual:listOfFunctionTerms>
1859          <qual:defaultTerm qual:resultLevel="0">
1860          </qual:defaultTerm>
1861          <qual:functionTerm qual:resultLevel="1">
1862            <math xmlns="http://www.w3.org/1998/Math/MathML">
1863              <apply>
1864                <eq/>
1865                <ci> AKT </ci>
1866                <cn type="integer">0 </cn>
1867              </apply>
1868            </math>
1869                    </qual:functionTerm>
1870        </qual:listOfFunctionTerms>
1871      </qual:transition>
1872    </qual:listOfTransitions>
1873    <listOfCompartments>
1874      <compartment constant="true" id="comp1"/>
1875    </listOfCompartments>
1876  </model>
1877 </sbml>
```