### S2_Table: Differential equations and species initial conditions

<table>
<thead>
<tr>
<th>Species</th>
<th>Differential Equations ( \frac{d[\text{Species}]}{dt} )</th>
<th>Species Initial Condition (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxygen Sensing Module</strong></td>
<td></td>
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</tr>
<tr>
<td>HIF1α</td>
<td>v1-v2-v3-v7</td>
<td>0.173</td>
</tr>
<tr>
<td>HIF1α-FIH complex</td>
<td>v3-v12</td>
<td>0.0183</td>
</tr>
<tr>
<td>HIF1α-PHD complex</td>
<td>v7-v13</td>
<td>0.0131</td>
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<tr>
<td>FIH-O(_2)-Fe-DG</td>
<td>v4+v12-v3</td>
<td>1.09</td>
</tr>
<tr>
<td>O(_2)</td>
<td>-v4-v8</td>
<td>Nx(21% O(_2)):209, Hx (2% O(_2)):19.9</td>
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<tr>
<td>FIH-DG-Fe</td>
<td>v5-v4</td>
<td>0.257</td>
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<tr>
<td>DG</td>
<td>-v5-v9</td>
<td>999</td>
</tr>
<tr>
<td>FIH-Fe</td>
<td>v6-v5</td>
<td>8.28e-3</td>
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<tr>
<td>Fe</td>
<td>-v6-v10</td>
<td>49.6</td>
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<tr>
<td>FIH</td>
<td>-v6</td>
<td>4.17e-4</td>
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<tr>
<td>CoCl(_2)</td>
<td>Constant</td>
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</tr>
<tr>
<td>HIF1α/OH</td>
<td>v11+v12-v13</td>
<td>5.39e-4</td>
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<tr>
<td>VHL</td>
<td>v14-v13</td>
<td>1.22</td>
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<tr>
<td>HIF1α/OH-VHL</td>
<td>v13-v14</td>
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<td>PHD2-O(_2)-Fe-DG</td>
<td>v12+v8-v7</td>
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<td>PHD2-Fe</td>
<td>v9-v8</td>
<td>0.947</td>
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<td>PHD2</td>
<td>v10-v9</td>
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<td>PHD2</td>
<td>-v10</td>
<td>2.29e-3</td>
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<td>HIF1α(_n)</td>
<td>v2-v15</td>
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<td>HIF1β(_n)</td>
<td>-v15</td>
<td>0.883</td>
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<td>TTP</td>
<td>v17-v16</td>
<td>0.0509</td>
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<tr>
<td><strong>HIF-dependent Transcription Module</strong></td>
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<tr>
<td>mTTP</td>
<td>v19-v18</td>
<td>9.35e-4</td>
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<tr>
<td>HIF1-dimer(_n)</td>
<td>v15</td>
<td>8.48e-3</td>
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<tr>
<td>mVEGFA</td>
<td>v20-v24-v31+v34</td>
<td>4.49e-6</td>
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<tr>
<td>VEGFA</td>
<td>v22-v23</td>
<td>2.09e-3</td>
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<tr>
<td>Pri-let-7(_n)</td>
<td>v21-v36</td>
<td>6.16e-5</td>
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<td><strong>VEGF Repression by MiR-15a Module</strong></td>
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<td>Pri-miR-15a(_n)</td>
<td>v25-v26</td>
<td>3.40e-3</td>
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<tr>
<td>Pre-miR-15a</td>
<td>v26-v27-v28</td>
<td>3.33e-3</td>
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<td>Dicer</td>
<td>v53-v54</td>
<td>1.04</td>
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<td>miR-15a</td>
<td>v28-v29-v30</td>
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<tr>
<td>AGO1</td>
<td>v41-v55-v42-v30</td>
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<tr>
<td>miR-15a RISC</td>
<td>v30-v31+v32</td>
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<td>v31-v32</td>
<td>1.06e-7</td>
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<td>mVEGFA/p-body</td>
<td>v32-v33-v34</td>
<td>1.25e-4</td>
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<tr>
<td><strong>Let-7 Biogenesis and Targeting Module</strong></td>
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<tr>
<td>Pre-let-7</td>
<td>v36-v35-v37</td>
<td>1.11e-5</td>
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<tr>
<td>Let-7</td>
<td>v37-v38-v42</td>
<td>4.79e-4</td>
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<tr>
<td>Let-7 RISC</td>
<td>v42-v49-v43+v44+v50</td>
<td>3.98e-3</td>
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<tr>
<td>mAGO1/p-body</td>
<td>v44-v45-v46</td>
<td>0.0192</td>
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<tr>
<td>Species</td>
<td>Differential Equations ( \frac{d[\text{Species}]}{dt} )</td>
<td>Species Initial Condition (( \mu \text{M} ))</td>
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<tr>
<td>---------------------</td>
<td>----------------------------------------------------------</td>
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<td>mAGO1</td>
<td>v40-v39-v43+v46</td>
<td>9.52e-4</td>
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<td>Let-7 RISC-mAGO1</td>
<td>v43-v44</td>
<td>6.74e-5</td>
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<td>mDicer</td>
<td>v47-v48-v49+v52</td>
<td>2.91e-3</td>
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<td>Let-7 RISC-mDicer</td>
<td>v49-v50</td>
<td>4.22e-5</td>
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<td>mDicer/p-body</td>
<td>v50-v51-v52</td>
<td>0.0376</td>
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<td>LNA, miR RISC</td>
<td>-v56</td>
<td>0</td>
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<td>miR RISC-LNA</td>
<td>v56</td>
<td>0</td>
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<tr>
<td>siRNA, mRNA</td>
<td>-v57</td>
<td>0</td>
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<tr>
<td>mRNA-siRNA</td>
<td>v57</td>
<td>0</td>
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</tbody>
</table>

S2_Table. Model differential equations and species initial conditions. Initial conditions here also refer to the steady-state (normoxia) concentration of each species. The different \( O_2 \) initial condition in the simulation corresponds to different \( O_2 \) abundance. PHD2, FIH, Fe, \( O_2 \), DG, HIF1\( \alpha \) initial conditions are estimated based on the measurements made by Tuckerman et al. \[1\]. \( \text{CoCl}_2 \) initial condition is changed to 200 \( \mu \text{M} \) to mimic hypoxia in a normoxic \( O_2 \) environment, and in all other simulations the level of \( \text{CoCl}_2 \) is zero \[2\]. To maintain a moderate complexity, the model assumes that transcription factors or enzymes in Hill-type (Michaelis-Menten) reactions are unconsumed, and mRNAs are unconsumed in translation.

References