Supplementary Material

Drug Target Optimization in Chronic Myeloid Leukemia Using Innovative Computational Platform

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List of Supplementary Figures and Tables

Supplementary Figure S1.

Supplementary Figure S2

All Supplementary tables are available at:
http://www.cs.le.ac.uk/people/np183/publications/2014/CML/

Supplementary Table S1. (Tab 1 in file SupplementaryTables1-3.xlsx)

Supplementary Table S2. (Tab 2 in file SupplementaryTables1-3.xlsx)

Supplementary Table S3. (Tab 3 in file SupplementaryTables1-3.xlsx)

Supplementary Table S4. (4 Tabs in file SupplementaryTable4.xlsx)

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Supplementary Figure and Table Legends

Figure S1. Illustration of model building through the BioModelAnalyzer Graphic User Interface (BMA GUI). (A) Membrane bound receptors are depicted in green, intracellular stand-alone proteins are depicted in red, constant proteins and cell factors are depicted in grey, and interactions are depicted as either pointed (positive) or bar (negative) arrows. Reciprocal interactions, or two-directional edges, are supported (not depicted). (B) Several input proteins (b-e) influencing the value of a single protein (a).

Figure S2. Stabilization analysis of the result found by Holtz et al. 2002 summarized in Table 1. (A) Base CP CML Model. (**B)** CP CML model after reducing the Bcr-Abl constant from 2 to 1. Note that in addition to the stable result of the proliferation phenotype shifting from 2 to 1, Apoptosis and Correct Differentiation shift from the stable values of 0 to oscillating between values 0 and 1, leading the entirety of the model to be labeled as a failure to reach stability.

Table S1. List of nodes in the network. Network ID refers to the internal label of the node. Proper name is Entrez name while Network Name is name given in construction of model. Cell fate is given for terminally-downstream gene nodes.

Table S2. List of edges in the network. BMA ID, Source ID, and Target ID refer to internal label of the node.

Table S3. List of edges in the network and corresponding sources.

Table S4.

1st Subtable:
KO1 and KO2 are the nodes knocked out identified by internal BMA ID as labeled in Supplementary Table 1 under the heading "Network ID." GA, SRC, A, P, CD are resulting phenotypes for the model - Growth Arrest, Self-Renewal Capacity, Apoptosis, Proliferation, and Correct Differentiation. A value of 0 corresponds to an extremely low or not present state of the phenotype and is labeled in red, a value of 1 is a moderate state and is labeled in yellow, and a value of 2 is a high state and is labeled in green.

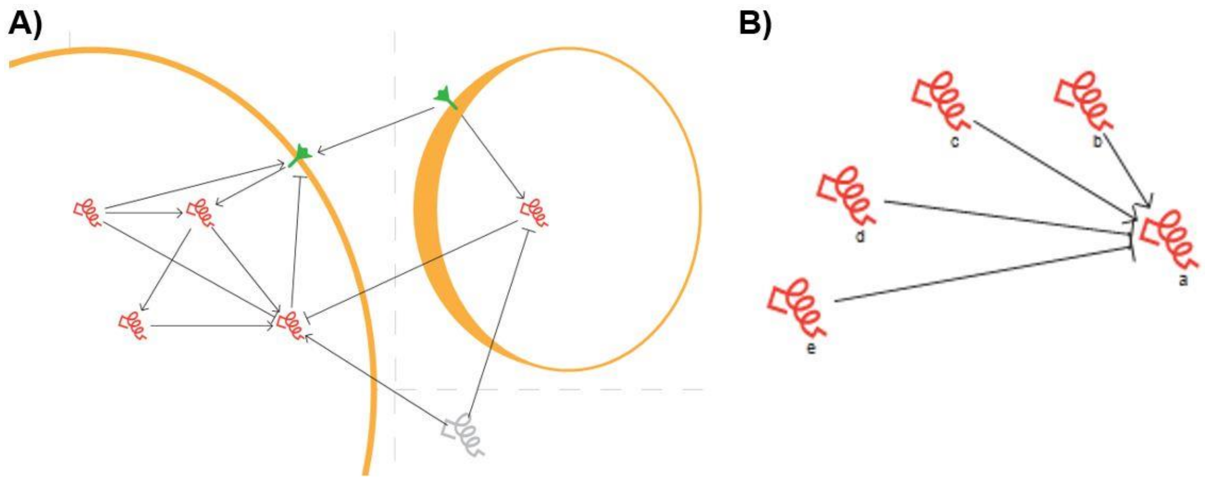
2nd Subtable:
Columns represent model results where double KOs in each of the three base models (Wild Type (WT), Chronic Phase (CP) and Blast Crisis (BC)) resulted in the same values for the six phenotype nodes. A value of 1 corresponds to the same values and is labeled in green. A value of 0 corresponds to dissimilar values and is labeled in red.

3rd Subtable:
Columns represent model results where double KOs in each of the three base models resulted in a normal phenotype (corresponding to values of 0 for growth arrest, and 1 for each of the other phenotype nodes.) A value of 1 corresponds to when this occurs and is labeled in green. A value of 0 corresponds to when this does not occur and is labeled in red.

4th Subtable:
Columns represent model results where double KOs in each of the three base models resulted in a normal phenotype (as described in the "Third Subtable") for the WT model, and where CP and BC models showed reduced survival and proliferation, defined as when SRC is below 2, Apoptosis is above 0, Proliferation is below 2, and Correct Differentiation is below 2. A value of 1 corresponds to when this occurs and is labeled in green. A value of 0 corresponds to when this does not occur and is labeled in red.

Table S5.
KO1 and KO2 are the nodes knocked out identified by internal BMA ID as labeled in Supplementary Table 2 under the heading "BMA ID." Please see the above legend for detailed description of each of the subtables.

Supplementary Figures



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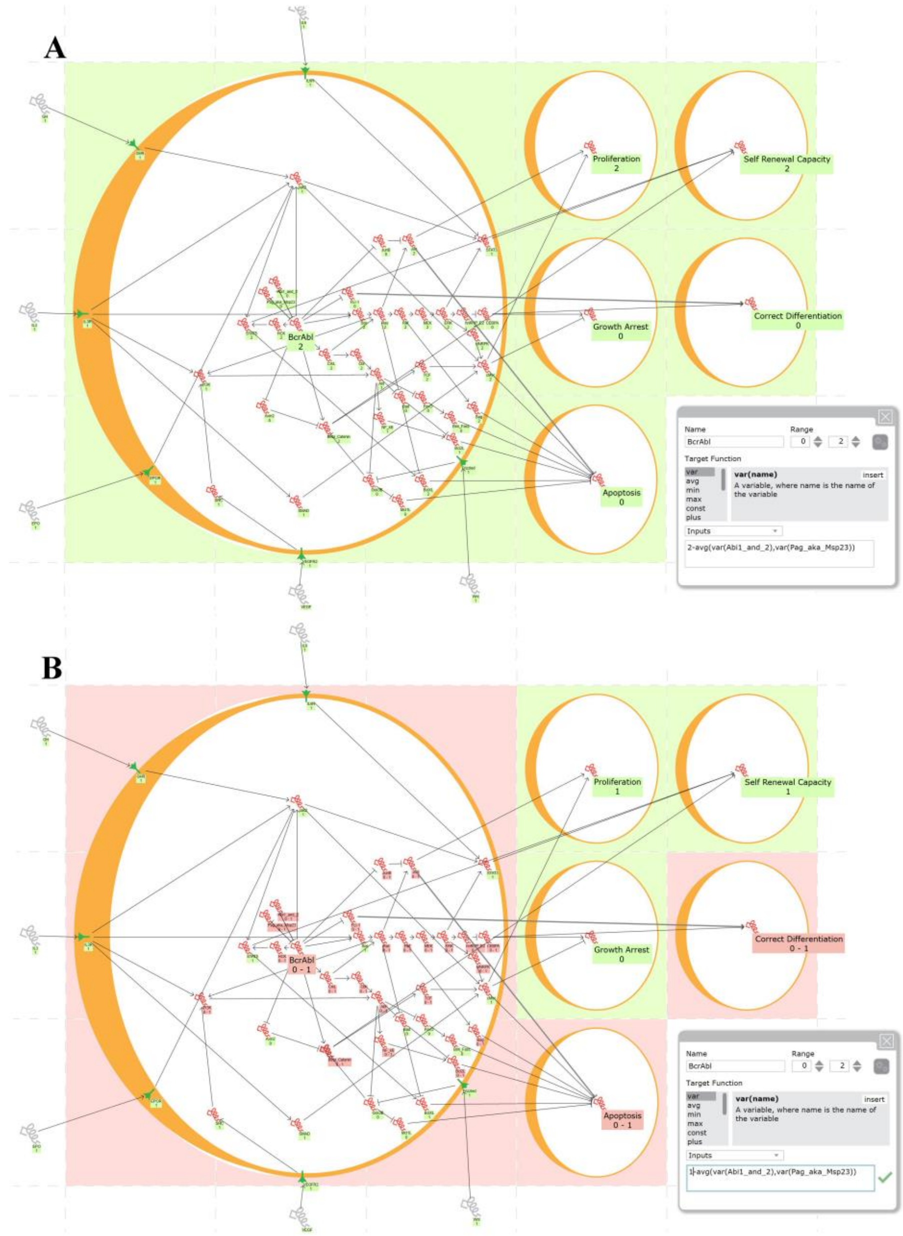

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