**Supplemental File SEE**

This document give additional detail related to the results of the applications of BLASTp and OptFill in the construction of the *i*Ede2091 model. These sections are a bit nuanced and repetitive and therefore where moved to this supplemental file.

***Bidirectional BLASTp to investigate OptFill solution viability***. For each OptFill solution incorporated into the draft models, a bidirectional BLASTp analysis was performed on enzymes linked to the reactions in each OptFill solution. For the first OptFill solution, containing reactions linked to enzymes common to three of four Aspergillus models, 20 enzymes were identified as linked to this set of reactions. Using the same bidirectional BLASTp procedure as previously described, 11 of these enzymes were identified in the *E. dermatitidis* genome, being matched to 21 genes. These genes were all annotated in the *E. dermatitidis* genome; therefore these enzymes may not have been identified by the BRENDA search of *E. dermatitidis* enzyme annotations due to sensitivity of the algorithm used for this search. These matches give a genetic basis for the inclusion of 11 of these reactions, in addition to the evidence that all these enzymes are supported in phylogenetically related organisms.

For the second OptFill solution, containing 3 reactions, 3 enzymes were identified as linked to the set of reactions in the solution, and two of these enzymes where identified in the *E. dermatitidis* genome. These two enzymes were linked to two genes. These genes were all annotated in the *E. dermatitidis* genome; therefore these enzymes may not have been identified by the BRENDA search of *E. dermatitidis* enzyme annotations due to sensitivity of the algorithm used for this search to the annotated string. These matches give a genetic basis for the inclusion of 2 of these reactions, in addition to the evidence that all these enzymes are supported in phylogenetically related organisms.

For the third OptFill solution, containing 21 reactions, 17 enzymes were identified as linked to the set of reactions in the solution, and 8 of these enzymes where identified in the *E. dermatitidis* genome. These 8 enzymes were linked to 18 genes. These genes were all annotated in the *E. dermatitidis* genome; therefore these enzymes may not have been identified by the BRENDA search of *E. dermatitidis* enzyme annotations due to sensitivity of the algorithm used for this search to the annotated string. These matches give a genetic basis for the inclusion of 13 of these reactions, in addition to the evidence that all these enzymes are supported in phylogenetically related organisms.

***Second use of OptFill to address metabolic gaps.*** To address the metabolic gaps in the third draft model, a tool developed by the authors, OptFill (Gudmundsson & Thiele, 2010), was used with a list of reactions derived from the list of enzymes common to two *Aspergillus* models. The database consisted of 88 reactions which were not already in the model. This database had 93 potential TICs with the model (largest size of 16 reactions) and a single connecting problem solution. This solution adds three reversible reactions to the model, which results in 632 metabolites being producible. Adding the CPs solution to the third draft model results in the fourth draft model consisting of 1610 reactions, of which 763 are capable of carrying flux (47.4%). The maximum rate of growth of this model was 0.0989 h-1 by allowing for 10 mmol·gDW-1·h-1 uptake of ethanol, sucrose, glucose, acetate, nitrate, sulfate, and phosphate. In this growth condition, carbon is the limiting nutrient.

***Third use of OptFill to address metabolic gaps.*** To address the metabolic gaps in the fourth draft model, a tool developed by the authors, OptFill (Gudmundsson & Thiele, 2010), was used, with a list of reactions derived from the list of enzymes unique to one *Aspergillus* model. The original database contained 320 reactions after removing any reactions already present in the third draft model. One round of database pruning was necessary to achieve a reasonable OptFill solution time, which reduced the database to 293 reactions. The database had 596 potential TICs with the model (largest sized of 16) and had over 200 connecting problem solutions. The first solution returned was accepted, which added 20 reactions from the database to the model, 10 of which were added reversibly. This resulted in 654 metabolites being producible by the model. Adding the CPs solution to the fourth draft model resulted in the final model, *i*Ede2091, consisting of 1630 reactions, of which 793 are capable of carrying flux (48.7%). The maximum rate of growth of this model was 0.0989 h-1 by allowing for 10 mmol·gDW-1·h-1 uptake of ethanol, sucrose, glucose, acetate, nitrate, sulfate, and phosphate. In this growth condition, carbon is the limiting nutrient. It should be noted that, on a minimal media where sucrose is provided as the primary carbon source, that is at a concentration two orders of magnitude higher than any other potential carbon source, the growth rate of *E. dermatitidis* is approximately 0.105 h-1 (Dadachova et al., 2007); however, since no rate measures were taken in the indicated study, it is difficult to interpret the accuracy of the modeled growth rate of *i*Ede2091.

REFERENCES

References used here also included in the main work.

Dadachova, E., Bryan, R. A., Huang, X., Moadel, T., Schweitzer, A. D., Aisen, P., … Casadevall, A. (2007). Ionizing radiation changes the electronic properties of melanin and enhances the growth of melanized fungi. *PLoS ONE*, *2*(5). https://doi.org/10.1371/journal.pone.0000457

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