Diversity of 2-oxoglutarate dependent dioxygenases dictates their synergistic association in modifying cell physiology.

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Introduction

The superfamily of 2OG-dependent dioxygenases, by definition, comprises members from all major taxa, and participates in neutralizing the effects of several forms of abiotic stress, viz., pesticides, hypoxia, and osmotic. The oxidative decarboxylation of 2-oxoglutarate to succinate is coupled with a concomitant substrate hydroxylation and, is in most cases, followed by an additional specialized conversion.

Methods

DB2OG, a generic-HMM based flat-file database (N > 3800) [1, 4]; H2OGpred, a server to predict the distribution of catalytic domains in a protein sequence using a library of pre-computed HMM profiles [2, 3]; Codes, PERL and R scripts coded in-house.

Results and Discussion

A generalized linear model (GLM) of system function (F), as a linear combination of participating 2OG-dependent enzymes was formulated as proof-of-concept.

The constants in the model represent a particular enzyme with its computed domain frequency and known kinetic data, whilst the coefficients were determined by a Monte Carlo approach .

Here, as an example, the roles of prolyl 4-hydroxlase (X1) and asparagine hydroxylase (X2) , as actuators of the hypoxia response were numerically investigated [1].

$F^\$$= (3.0266)X1 + (4.3943)X2 +0.9469

X1 : se = 0.4515, p = 1.3E-09, df = 99
X2 : se = 0.4954, p = 3.41E-14, df = 99

(\$) Data reproduced from Table 1 [1].

Conclusions

This novel, albeit abstract representation of alpha-ketoglutarate dependent enzymes clearly illustrates the major premise of this work, that, this superfamily can function as a systems-player, *in vivo*. The chemical diversity, shared metabolic intermediates, and hysteresis exhibited justify this notion.

References

1. Kundu S (2015) Unity in diversity, a systems approach to regulating plant cell physiology by 2-oxoglutarate-dependent dioxygenases. Front Plant Sci 6: 98.
2. Kundu S (2012) Distribution and prediction of catalytic domains in 2-oxoglutarate dependent dioxygenases. BMC Res Notes 5: 410.
3. H2OGpred, a HMM based server and library of empirically validated 2OG-dependent sequences: http://comp-biol.theacms.in/H2OGpred.html.
4. DB2OG, a flat-file database of predicted 2OG-dependent activity: http://comp-biol.theacms.in/DB2OG.html.