

Ontological Modeling of Two-Component Regulatory Systems

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Abstract

The two-component regulatory systems (TCSs), which comprise a sensor kinase and a response regulator, serve as a prevalent signal transduction system involving in multiple behaviors. To support systematic and interoperable representation of various types of TCS, we have initiated the development of a community-based Ontology of Two-Component Systems (OTCS). Bacterial PhoPQ TCS in *Escherichia coli* is used as an example TCS for OTCS modeling in the study.

Keywords:

OTCS, Two-component regulatory system, Ontology

Introduction

TCS is one of the well-known signal transduction system and exists among in nearly all prokaryotes, many Archaea, and eukaryotes such as plants, fungi, and yeasts (1). In general, the TCS consists of two proteins, a sensor kinase for sensing signals and a response regulator that affects the numerous cellular regulatory circuits. TCSs play a critical role in regulating virulence, antibiotic resistance, and adaptation (2). However, the signals and cellular response of the TCSs are complicated. To better understand TCSs, we initiated our development of the community-driven Ontology of Two-Component Systems (OTCS) to represent and integrate various relationships among TCSs, signals, TCSs regulon, and regulons' role.

Methods

The OTCS ontology design follows the Open Biomedical Ontologies (OBO) Foundry principle, and aligns with and reuses terms from the OBO ontology such as the Protein Ontology (PR) and the Ontology of Genes and Genomes (OGG). Protégé 4.3 OWL ontology editor (<http://protege.stanford.edu/>) was used for ontology establishment. Ontofox (<http://ontofox.hegroup.org/>) was used to obtain the related term from different ontologies.

Results

The OTCS key term 'two-component regulatory system' (OTCS_0000001) is defined as a subclass of RO:system, which is a subclass of 'material entity' in the Basic Formal Ontology

(BFO). The PhoPQ TCS is a common TCS as shown in many bacteria such as *E. coli*. PhoPQ TCS is essential for mediating the adaptation to magnesium limiting condition, stress resistance, and virulence (3). The PhoPQ includes a sensor protein PhoQ and a response regulator PhoP (Fig 1).



Figure 1. Example of bacterial TCS

More information are also added in OTCS. For example, the genes that encoded TCS proteins are also represented in OTCS. OTCS also defines different roles, such as 'bacterial sensor role' that inheres in TCS sensor proteins. As a widely used bacterial model, *E. coli* includes 30 TCSs. These TCSs, the TCS stimuli, and the TCS effector protein are first represented in OTCS. TCSs in other bacteria are also being added to OTCS. We will also evaluate how OTCS can be used to support TCS comparisons and knowledge discovery. The OTCS project website is located at GitHub:<https://github.com/biomedontology/otcs>.

Conclusions

We have initiated the development of the OTCS to support systematic and logic representation of TCS with the aim to not only integrate the knowledge of TCS but also systematically elucidate the TCSs regulatory network.

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