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Coupling retrosynthesis with automated in vitro and in vivo metabolic pathway engineering

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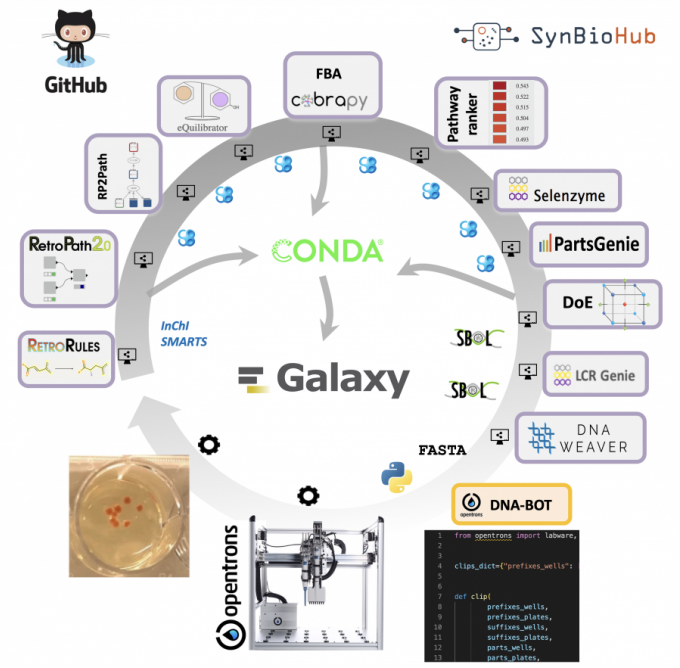
PURPOSE OF THE ABSTRACT
This presentation will introduce Galaxy-SynBioCAD [1], a Galaxy toolshed for synthetic biology, metabolic engineering, and industrial biotechnology. The tools and workflows currently shared on the toolshed enable one to build libraries of strains producing desired chemical targets covering an end-to-end metabolic pathway design and engineering process from the selection of strains and targets, the generation of pathways producing the targets, the design of DNA parts to be assembled, to the generation of scripts driving liquid handlers for plasmid assembly and strain transformations (cf. Fig. 1). Pathways are designed using retrosynthesis methods [2], and several template-based and template-free alternatives to perform that task will be compared. Data standards to enforce compatibility and to chain up tools into workflows will also be presented.

The link between pathway design and engineering will be illustrated with the build-up of a library of E. coli lycopene-producing strains in a study carried out at four different sites. The workflows were also benchmarked on literature and expert-validated pathways. Overall, 83% success rate was found in retrieving the validated pathways among the top 10 pathways generated by the workflows (cf. Fig 2).

Ongoing developments within the Galaxy-SynBioCAD toolshed will also be presented, these include integration of DoE and active learning modules for bioproduction in vivo and in cell-free [3,4].

FIGURES



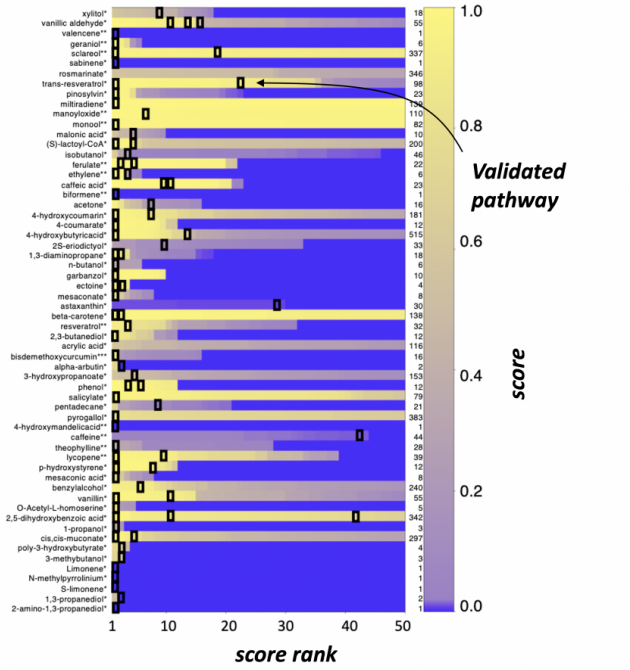


FIGURE 1

Galaxy-SynBioCAD nodes and worflows

Main nodes in the Galaxy toolshed

FIGURE 2

Ranking predicted pathways with machine learning global score.

Color code on the right side shows the machine learning global score (from 1 top to 0). Black boxes show the location of the literature or expert-selected pathways for a set 60 literature target engineered in E. coli (*), yeast (**) or P. putida (***)

KEYWORDS

Biochemical reaction networks | Computational platforms and environments | Metabolic engineering | Synthetic biology

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