



Cross-species metabolic pathways comparison - Focus on mouse, human and chicken lipid metabolism

Charles Bettembourg, Christian Diot, Olivier Dameron

► To cite this version:

Charles Bettembourg, Christian Diot, Olivier Dameron. Cross-species metabolic pathways comparison - Focus on mouse, human and chicken lipid metabolism. Journées Ouvertes Biologie, Informatique et Mathématiques (JOBIM 2011), Jun 2011, Paris, France. hal-02744649

HAL Id: hal-02744649

<https://hal.inrae.fr/hal-02744649>

Submitted on 3 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Cross-species metabolic pathways comparison

Focus on mouse, human and chicken lipid metabolism

Charles Bettembourg^(1,2), Olivier Dameron⁽²⁾, Christian Diot⁽¹⁾

(1) INRA, UMR598 Génétique animale, Rennes

(2) INSERM, UMR936 Modélisation conceptuelle des connaissances biomédicales, Rennes

Context

Lipid assimilation in animals is a major agronomic challenge. Furthermore, the human associated lipid diseases (e.g. obesity) is an important public health concern in industrialized countries. Lipid metabolism relies on some genetic factors which are mostly conserved among species. Thus, it is necessary to qualify and to quantify the differences and the similarities to compare the lipid metabolism between species.

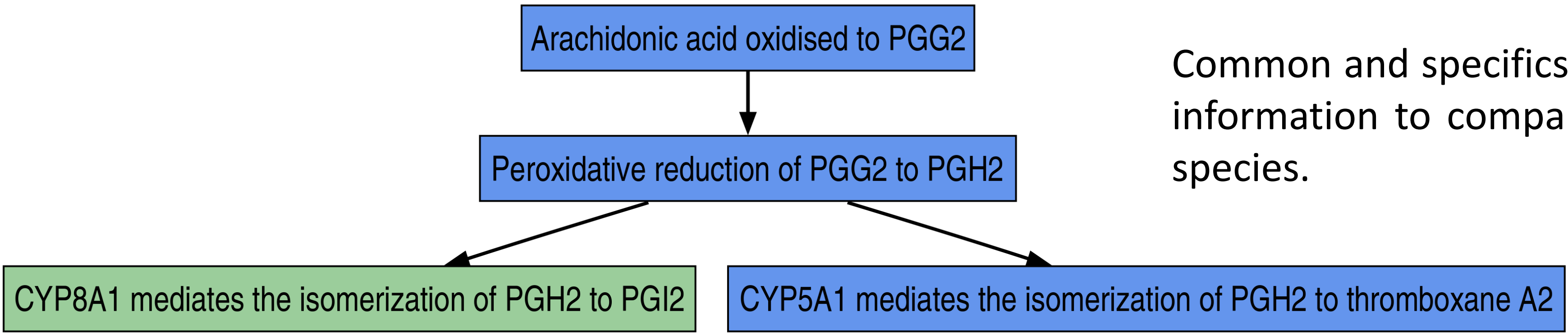
Objectives and strategy

A new knowledge-based method to compare metabolic pathways between species.

- Compare data from pathways databases like Reactome, KEGG and BioCyc. The low level of consistency, comprehensiveness and compatibility between these databases [1] forces us to use them all.
- Use the knowledge from Gene Ontology and its inference rules [2]. Measure the semantic similarities between the genes products by extending Wang's method [3].

1 - Identify automatically common and species specific steps

Extract of prostanoid metabolism: global comparison between mouse and chicken



2 - Quantify semantically the similarities and the differences

Common steps may not be fonctionnaly identical...
Let's zoom on the first step of prostanoid metabolism:

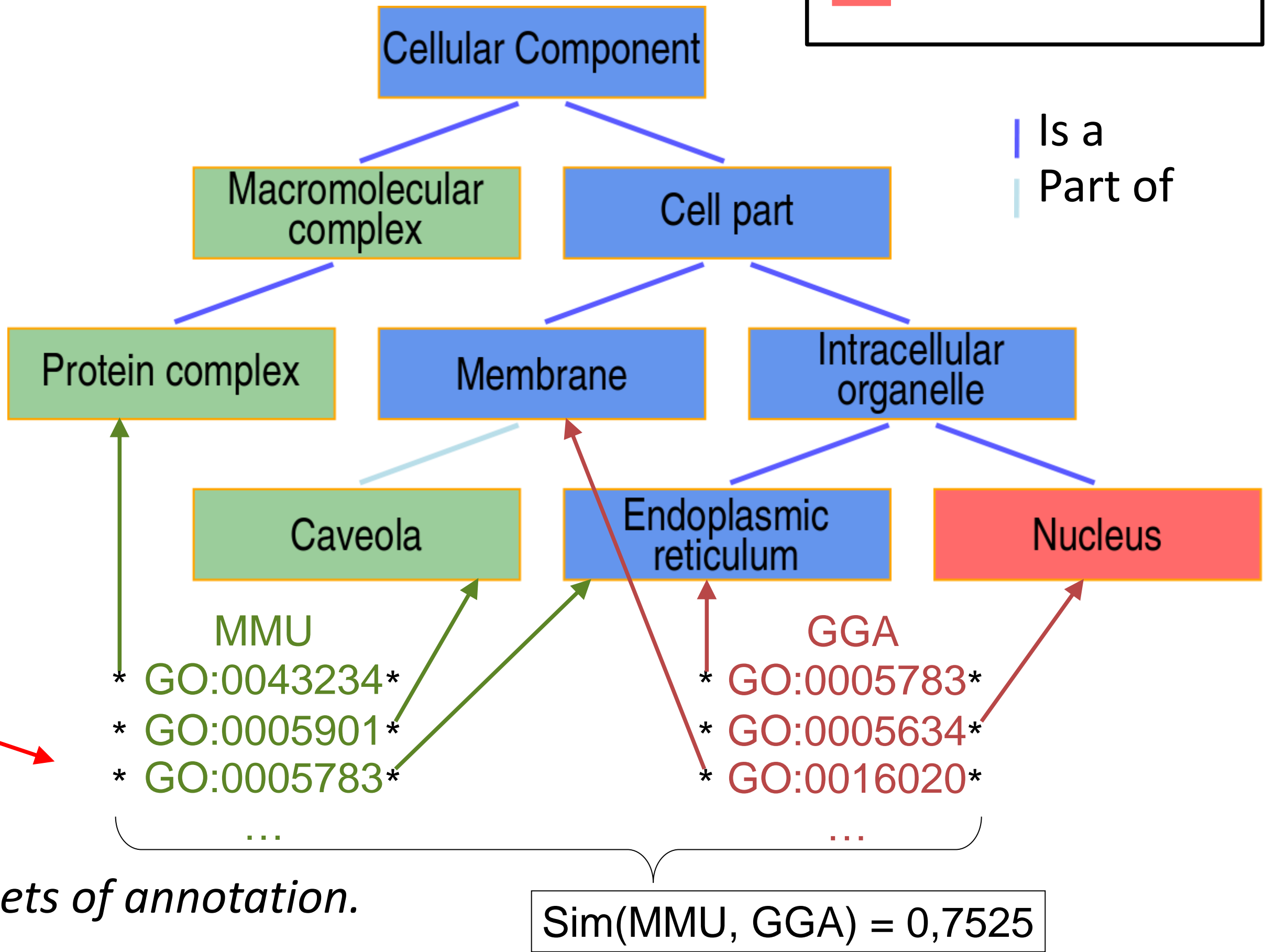
Reactants				Products			
#	Name	ChEBI	Localization	#	Name	ChEBI	Localization
2	Arachidonate	15843	ER Lumen	1	Prostaglandin G2	27647	ER Lumen
1	O2	15379	ER Lumen				

Enzyme: Prostaglandin G/H synthase (EC = 1.14.99.1)

The genes products of a common step between 2 species are described by different Gene Ontology terms.

Gene Ontology
annotation
of the enzyme

The *semantics* of GO has to be taken into account to compare the sets of annotation.



3 - Validate the method using simulated and bibliographic data

- Final result of the comparison between 2 species for a metabolic pathway provides estimations of similarity and specificity.
- The first validation step uses a simulated pathway with fictive gene products annotations to compare obtained and expected results. This step allows us to adjust the weight of the different parameters of our method.
- In order to find well documented pathway that are necessary to evaluate the method, we develop and use a search tool called GO2PUB (<http://go2pub.genouest.org>) that enable retrieving bibliography on PubMed using the Gene Ontology terms.
- Final validation will be provided by comparing the results of our automatic method and human expectations. This step will be performed for several well known pathways.

[1] D. Soh, D. Dong, Y. Guo and L. Wong, Consistency, comprehensiveness, and compatibility of pathway databases. BMC Bioinformatics, 11:449, 2010.

[2] S.Y. Rhee, V. Wood, K. Dolinski and S.F. Draghici, Use and misuse of the gene ontology annotations. Nat Rev Genet., 9(7):509-15, 2008.

[3] J.Z. Wang, Z. Du, R. Payattakool, P.S. Yu and C.-F. Chen, A new method to measure the semantic similarity of GO terms. Bioinformatics, 23:1274-1281, 2007.