

SQL Database Task

Chemosensation in Mammals

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1 Aim

This project aims to compare chemosensation within the olfactory systems of four mammalian species. This will be achieved by using the SQL language to query the gene ontology database [Consortium, 2015].

2 Introduction

2.1 The Main and Accessory Olfactory Systems

The nasal cavity of mammals contains receptors for the sensation of chemicals from the environment. The systems for detection are physically split into the olfactory system and the accessory olfactory system (containing the vomeronasal organ) [Tirindelli et al., 2009]. Historically, it was believed that the main olfactory system detected odorants and the vomeronasal system detected pheromones. However, it is now thought that the distinction between them is not as clear as once thought [Xu et al., 2005].

Odorants are any chemical which are deemed have a 'scent'. On the other hand, pheromones are chemicals used as a method of communication between members of the same species and initiate, what seems to be, an innate behavioural response [Wyatt, 2014]. Odorants and pheromones are just two types of chemicals which can be detected by mammals; we shall not consider any others here.

The process of chemosensation has several steps [Quignon et al., 2012]. Firstly, receptors in the nasal cavity capture molecules. For the olfactory system these are usually volatile molecules, and in the vomeronasal organ the molecules tend to be captured in fluid-phase. Secondly, the chemical signal is converted to an electric signal, which is then transmitted to the brain. Olfactory and pheromonal signals are often sent to very different parts of the brain, consequently having very distinct effects.

Both the main and accessory olfactory systems have been very well studied in mammals, but from here the focus will be on the study of dogs, mice, rats and humans. Rodents, and particularly mice, have been especially well studied because of the ease of working with them in a laboratory setting, and the fact that their olfactory systems are extremely well-developed [Tirindelli et al., 2009].

The vomeronasal organ specifically will now be considered. In rodents, two families of G-protein coupled receptors have been discovered, V1R and V2R (vomeronasal receptor, types 1 and 2.) There has been found to be wide variation in the number of V1R genes detected in mammals. Rodents have more than 100 whereas dogs and humans have fewer than 10 [Quignon et al., 2012].

Dogs, highly social animals, are known to use scent as a method of communication, and this communication could involve the use of pheromones. However, it is now thought that the main olfactory system, which is overdeveloped in dogs, is used in the place of pheromone communication. This is supported by the fact that dogs do not exhibit a flehmen response [Adams and Wiekamp, 1984]. The flehmen response is a lip-curl type gesture which is thought to encourage the transport of pheromones into the vomeronasal organ, and is exhibited by many mammals, most notably by horses.

Primates seem to rely on chemical communication relatively little in comparison with other mammals [Tirindelli et al., 2009]. There is still much controversy as to whether human pheromones exist, and if so, to what extent they are utilised.

2.2 The Gene Ontology Database

The gene ontology database (GO) [Consortium, 2015] describes the framework for the model of biology. As stated on the website:

The GO defines concepts/classes used to describe gene function, and relationships between these concepts. It classifies functions along three aspects

- *molecular function, molecular activities of gene products,*
- *cellular component, where gene products are active, and*
- *biological process, pathways and larger processes made up of the activities of multiple gene products.*

In addition, the GO includes annotations which are statements describing the functions of specific genes, using concepts in the gene ontology.

3 Method

3.1 Counting Receptors

In order to compare the numbers of main olfactory and vomeronasal receptors in various mammalian species, the code listing 1 was constructed. The query was run multiple times, with changes to the type of receptor and species searched for.

The query selects from the results of two sub-queries, the sub-queries here being labelled table1 and table2. The first sub-query selects all the gene products associated with the terms 'olfactory' and 'receptor', and the second sub-query finds the identification number for the species 'canis lupus familiaris'. The overall query selects results from the sub-query results and combines them.

```
SELECT
    table1.id,
    table1.symbol,
    table1.dbxref_id,
    table1.full_name,
    table2.id,
    table2.genus,
    table2.species
FROM
    (SELECT *
     FROM gene_product
     WHERE full_name LIKE "%olfactory%"
        AND full_name LIKE "%receptor%")
AS table1,
    (SELECT *
     FROM species
     WHERE genus="canis"
        AND species="lupus familiaris")
AS table2
WHERE table1.species_id=table2.id
GROUP BY table1.symbol;
```

Listing 1: SQL code for finding the number of olfactory receptor genes for the species 'canis lupus familiaris'.

In order to get an idea of what proportion of the gene products for each species are made up of olfactory and vomeronasal receptors, a simple query (listing 3) was run on the total_gps_by_species table (where 'gps' here stands for gene products).

3.2 Studying a Gene Product

One of the main functions of the gene ontology database is to create a formal list of terms used within the scientific community when discussing genes and gene products.

The next task undertaken was to relate the information found in the first part of our experiment to the gene ontology terms. Therefore, code listing 2 was constructed.

A specific gene product was chosen at random from the results of query 1. The SQL code was used to search for gene ontology terms linked to this chosen gene product. In order to inform this search further code listing 4 was constructed which provided useful information such as the number of terms to expect from the search.

```
SELECT
    association.id,
    association.term_id,
    term.name,
    term.term_type
FROM
    association
    INNER JOIN term ON (association.term_id=term.id)
WHERE gene_product_id="281015"
GROUP BY term_id;
```

Listing 2: SQL code for finding gene ontological terms associated with a specific gene product.

4 Results and Analysis

4.1 Counting Receptors

The number of rows generated from running listing 1 was counted and the results are tabulated in table 1.

Common Name	Genus and Species	Olfactory Receptors	Vomeronasal Receptors	Total Gene Products
Dog	Canis Lupus Familiaris	749	0	25133
Mouse	Mus Musculus	1116	317	24212
Rat	Rattus Norvegicus	1504	178	38948
Human	Homo Sapiens	529	6	166025

Table 1: A table showing the number of gene products labelled as either an olfactory or a vomeronasal receptor within the gene ontology database. The results are listed for four mammalian species, and the numbers can be compared against the total number of gene products for each species.

Table 1 shows that, of the mammals studied here, each species has many fewer vomeronasal receptors than olfactory receptors. This could be explained by the fact that, in general, there are many more distinct odorants than pheromones for each species. The table also shows that there is a wide variety in the number of both olfactory and vomeronasal receptors between species.

Particularly significant seems to be the fact that humans and dogs have very few or no vomeronasal receptors, which clearly contrasts with the numbers found in mice and rats. This is consistent with the findings of Quignon et al. [2012], and may point to pheromones being a relatively insignificant means of communication for these species.

Table 1 also shows that, while in absolute terms, the number of chemosensory receptors in humans is relatively similar to that in dogs, in comparative terms with the total number of gene products in the database, humans appear to have fewer receptors. This is consistent with the fact that dogs seem to have a much more acute sense of smell than humans. Likewise, it could be surmised that mice and rats also have an acute sense of smell, much more so than humans.

4.2 Studying a Gene Product

The gene product with `gene_product_id="281015"` (a canine olfactory receptor gene) was selected at random from the results of query 1. The results from running code listing 2 are presented in table 2.

Name	Term Type
Plasma membrane	Cellular component
Integral component of membrane	Cellular component
Membrane	Cellular component
Signal transducer activity	Molecular function
G-protein coupled receptor activity	Molecular function
Olfactory receptor activity	Molecular function
Signal transduction	Biological process
G-protein coupled receptor signaling pathway	Biological process
Sensory perception of smell	Biological process
Response to stimulus	Biological process
Detection of chemical stimulus involved in sensory perception of smell	Biological process

Table 2: Listing the gene ontological terms associated with a specific canine olfactory receptor gene product, and their respective term types.

Table 2 shows that there are relatively few gene ontological terms connected with a specific gene product. Given that the gene product in question is a canine olfactory receptor, the terms found appear confirm what we know about how chemosensation takes place, as described in section 2.1 and by Quignon et al. [2012].

5 Conclusion

The differing numbers of chemosensory receptors found in four species of mammal, have successfully been studied. Conclusions have therefore been made about innate differences between these species. Examples of gene ontological terms associated with such gene products have also been listed, and confirm current thought about the process of chemosensation. These achievements have fulfilled the stated aim of this project.

It should be noted that using SQL to query the gene ontology database is a highly efficient method of interacting with the data therein. However, the sheer number of tables within the database, and the many varied functions they can provide makes constructing an appropriate query a daunting task.

It should also be noted that comparing numbers of gene products within the gene ontology database poses a lot of problems, for several reasons. Firstly, different species have been studied to varying degrees. It might be this which accounts for the differences in numbers between species, rather than innate differences. Secondly, whilst the database is closely controlled, it is still added to by different research bodies all over the world. Different laboratories work in different ways and use different terms, and this is reflected in the additions made to the database. For example, when querying the number of gene products for vomeronasal receptors in mice, it was found that the database had 317 entries for the species 'mus musculus', but an additional 33 entries labelled with the sub-species 'mus musculus musculus'. Genetically speaking, there is likely to be very little differences between sub-species of 'mus musculus', but the difference in labelling mean it is difficult for the querier to make categorical inferences from their results.

As a consequence, the results of section 4.1 should not be taken as conclusive. Equally, whilst the terms listed in table 2 do seem to confirm our current understanding, they can only be seen as instructive when used in conjunction with other information.

A possible extension of this task would be to compare ontology terms for all gene products found from query 1, rather than just one. It could be asked whether there is a lot of variation in the terms and number of terms found. This might tell us about the variation within the function of receptors. It might be particularly interesting to compare difference in the ontological terms for olfactory and vomeronasal receptors.

A Additional Code

```
SELECT *
FROM
    total_gps_by_species
WHERE
    species_id="1332221"
    OR species_id="336870"
    OR species_id="1469474"
    OR species_id="448500";
```

Listing 3: SQL code to find the total number of gene products by species listed within the gene ontology database.

```
SELECT
    total_terms_per_gp.gene_product_id,
    gene_product.symbol,
    gene_product.species_id,
    gene_product.full_name,
    total_terms_per_gp.total_terms,
    total_transitive_terms_per_gp.total_transitive_terms
FROM
    gene_product
    INNER JOIN total_terms_per_gp
        ON (gene_product.id=total_terms_per_gp.gene_product_id)
    INNER JOIN total_transitive_terms_per_gp
        ON (gene_product.id=total_transitive_terms_per_gp.gene_product_id)
WHERE id="281015";
```

Listing 4: SQL code giving a summary of the information provided by the gene ontology database about gene product "281015".

References

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